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Dr. R.R. Varma
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Giridhar Eye Institute
Kochi - 682 020
Ph: 0484-2312303 (H)
Mob: 98470 40840

Joint Secretary
Dr. Arup Chakrabarti
Chakrabarti Eye Care Centre
Kochulloor, Trivandrum 695 011
Ph: 0471-2555530
Mob: 9946410540

Immediate Past President
Dr. P. Rajagopalan Nair
Raj Bhavan
Palakkad - 676 013
Ph: 0491-2535676 (R)
Mob: 94476 45676

Immediate Past Secretary
Dr. Sahasranamam
No. 30, Vinayaka Nagar
Trivandrum 695 018
Ph: 0484-2490421 (R)
Mob: 9846020421

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How Effective Is Your Front Office?

The next time you get a chance, stand in an unobtrusive corner of your reception area and watch what happens when patients enter or call. Do your staff members call long-time patients by name? Do they smile when they talk to patients? Do they at least look up from their work when a patient approaches? When the phone rings do they pick it up? Do they answer questions fully and patiently?

If the answer to any of these is ‘no’, you may be losing revenue and referrals.

Your front line staff, whether in the office or on the phone are the public face of your practice. If that face is not welcoming or worse still….is unresponsive or outright hostile…..it will drive patients away. If you let your staff give you a reputation for ignoring patients, referrals from other physicians could suffer too.

If your staff has problems in treating patients right your first move should be to train them. By meeting your employee’s human need for money, recognition and training them in skills they need to do their work, you encourage them to work as a professional thereby establishing a positive practice culture.

But not every employee responds to training, respectful treatment or even monetary incentives. Those who don’t, should be replaced, quickly to avoid conflict that will drag down the staff morale and interfere with the teamwork.

Traditionally ophthalmic practices mostly hire candidates with training as nurses or medical assistants to staff their office. But people with clinical backgrounds do not always have strong customer service orientation that practices need to compete for patients. It is easier to train some one who has good people skills to be a good clinical assistant than to try to teach some one with years of experience to be friendlier. If you hire some one who has worked for 20 years in Government hospitals, she will not be willing to move from her seat, and is less likely to be patient oriented and friendly. In a way it is better to hire fresh hands and train them the way you want them to get things done. Choose people with sound people skills who are likely to gel as a team. Newly hired employees without a medical background will require extensive training on how to talk to patients, how to educate them, knowledge on fundamentals of eye anatomy and physiology and all other technical details to impart correct information to the patient. Patient co:ordinators are often the face of the practice, answering patient questions and advising them on available procedures, lenses and the logistics. People who have worked in the hotels and hospitality industry or in call centres have excellent people skills and are service oriented - it may be a good idea to employ a few personnel from this sector.
Your employees should be trained to greet your patients by name. It is also worth while to note personal information in the chart, like your patients children's ages, upcoming events like weddings or trips. This helps establish continuity in the relationship. Looking patients in the eye while talking helps build confidence and trust. Make it a rule to have all your employees wear name tags as everyone wants to know to whom they are talking to. Patients will be able to tell you by name who is treating them well and who is not. Give patients brochures to share with family and friends. Every patient leaving your clinic should have something in their hand that they can pass on for a potential referral.

By consistently connecting with your patients you not only build bonds with them, you make them ambassadors of your practice and more referrals will come through patient word-of –mouth.

Your staff has to familiar with all these ‘common sense’ strategies to provide your patients with a warm human experience that they are likely to remember and tell other. Enhancing patient experience pays..........treat them right and they will refer their family and friends to you.

Reference:

Dr. Meena Chakrabarti MS DO DNB
Editor, KJO
Orbital Pseudotumor

Dr Renuka Srinivasan MS ¹, Dr Datta Gulnar MS ²

Introduction

Ophthalmologists in the early 1800s made an interesting observation that several patients with presumed orbital tumors showed spontaneous improvement without any treatment. Until then proptosis was considered as prima facie of orbital neoplasm. Panas coined the term “pseudoplasm” for these puzzling cases. Birchfield in 1930 used the term orbital pseudotumor for such cases ¹,². Improvements in diagnostic techniques as also better understanding of the pathology of orbital pseudotumor helped us to define orbital pseudotumor as a nonspecific idiopathic, benign inflammatory process characterized by polymorphous lymphoid infiltrate with varying degrees of fibrosis. It is also known as idiopathic orbital inflammatory syndrome (IOIS). Pseudotumor orbit accounts for 10% of orbital tumors ³. The peak incidence of the condition is in fourth and fifth decade but it can also occur in children. There is no sex predilection. It is usually unilateral though bilateral involvement is possible in children. Orbital pseudotumor is usually a monophasic illness but it can be recurrent, especially in children. It remains a diagnosis of exclusion, as it is diagnosed after excluding orbital tumors, thyroid eye disease and systemic inflammatory disease. IOIS is characterized by its chronicity, and classified based on anatomic location, or histologic subtype ³,⁴.

Classification/Types

Based on the onset

- Acute
- Subacute
- Chronic

Depending on the target tissues involved

- Diffuse
- Localised
- Anterior orbit
- Posterior orbit
- Extraocular muscles
- Optic nerve
- Lacrimal gland

Histopathological classification

- Classical or Cellular
- Granulomatous
- Eosinophilic
- Vasculitic
- Desmoplastic/Fibrous

Pathogenesis

The cause and pathogenesis still remains to be elucidated. Infections, post infections, autoimmune, genetic, environmental factors have been proposed as causes ¹,⁵,⁶. Successful treatment of the condition with corticosteroids and other immunosuppressive agents suggests an autoimmune mechanism ⁷. It is mediated by both B and T lymphocytes ⁵. The acute form of the disease consists of polymorphous infiltrate while the subacute and chronic forms have increasing fibrovascular stroma ¹.

¹ Prof. of Ophthalmology, Dept of Ophthalmology, JIPMER Puducherry, ² Sr. Resident
**Clinical features**

IOIS can present with varying range of clinical features depending on the orbital structures involved, the degree of inflammation and fibrosis. The presentation is usually acute with proptosis, diplopia, orbital pain, eyelid swelling, ptosis, chemosis and visual loss. Relapses and remissions with or without treatment are not uncommon.

Pseudotumour with significant desmoplastic change typically present with slowly progressive visual loss, diplopia or proptosis. Commonly involved structures include orbital fat, lacrimal gland, extraocular muscles, others being, optic nerve, sclera and tenon. Orbital involvement may be focal resulting in pseudotumor variants, myositis, dacryoadenitis, optic perineuritis, periscleritis and sclerotenonitis. A posterior pattern of pseudotumor presents with symptoms of orbital apex syndrome. Patient has signs of optic nerve dysfunction and ophthalmoplegia. These include diplopia, decreased vision, dyschromatopsia, visual field defects, relative afferent pupillary defect and disc edema.

The diverse forms of orbital pseudotumour have varying clinical picture.

**Dacryoadenitis** - Pseudotumour of lacrimal gland has typical presentation of dacryoadenitis. The characteristic sign is “S” shaped ptosis with associated superotemporal conjunctival chemosis and congestion. The lateral rectus muscle being in close proximity is commonly involved resulting in painful ophthalmoparesis and diplopia.

**Orbital myositis** – This condition is a common variant of IOIS presenting with diplopia and pain typically exacerbated on ocular movement. There is restriction of ocular movement in the field of action of the affected muscles. Localized conjunctival injection and chemosis are seen at the tendinous insertion of involved muscle. Medial and superior recti are commonly involved. The entire muscle including the belly and tendon is enlarged.

**Idiopathic sclerosing orbital inflammation**

Idiopathic sclerosing orbital inflammation (ISOI) (Fig. 1) is a rare pathological subgroup of pseudotumor accounting for 5% to 7.8% of cases. The onset is insidious presenting with diplopia, decreased vision and proptosis. ISOI is diagnosed based on the characteristic histological picture of marked fibrosis with sparse mixed chronic inflammatory infiltrate. It has a predilection for the posterior superior or lateral orbit especially the lacrimal gland, rich in lymphocytes which play a critical role in causing fibrosis. The sclerosing variant is associated with systemic multifocal fibrosclerosis like retroperitoneal fibrosis, mediastinal fibrosis, sclerosing cholangitis, Riedel’s sclerosing thyroiditis and pachymeningitis. This form of pseudotumor typically does not respond to steroid therapy.

**Paediatric pseudotumor**

The clinical features of IOIS are peculiar in children. 6-16% of cases occur in the first two decades of life. Bilateral involvement is common and is associated with iritis, and optic disc edema. The associated constitutional symptoms in children lead to erroneous diagnosis. Recurrences are common and morbidity is high. Eosinophilia of peripheral blood and in tissue biopsy is a feature seen in one third of cases. In children it is important to exclude orbital cellulitis, dacryoadenitis, rhabdomyosarcoma, retinoblastoma, neuroblastoma, dermoid cyst and hemangioma before diagnosing pseudotumor.

**Diagnosis**

The diagnosis of pseudotumour orbit is usually clinical and confirmed by prompt response to steroids. In order to rule out the systemic conditions mimicking pseudotumor complete physical examination is essential followed by complete hemogram, erythrocyte...
sedimentation rate, C-reactive protein level, antinuclear antibody and antineutrophil cytoplasmic antibodies. Histopathological testing is required when the clinical presentation is atypical recurrent or persistent. Imaging is indicated when there is threat to vision or loss of function and in lesions involving the lacrimal gland or the orbital apex.

**Histopathology**

The classical form of orbital pseudotumor is the cellular variety which presents acutely and mimics lymphoid tumors. The cellular infiltrate of orbital pseudotumor tends to be diffuse and multifocal in contrast to lymphoid neoplasm. It consists of hypocellular polymorphous infiltrate composed of mature lymphocytes, plasma cells, macrophages and polymorphonuclear leukocytes. Atypical findings are tissue eosinophilia, granulomatous inflammation, vasculitis and desmoplasia.

Eosinophils are present in pediatric pseudotumor in particular. Eosinophil degranulation contributes to tissue fibrosis. Granulomatous inflammation with multinucleated giant cells and non-caseating granuloma can mimic sarcoidosis. Histological features of true vasculitis limited to the orbit are rarely found and primarily affects small arteries and arterioles. Chronic forms of the disease are characterized by increasing fibrous component. Lymphoid follicles with germinal centers are also observed in the chronic phase. Extraocular muscle, fat and lacrimal gland are replaced with fibrous tissue. The desmoplastic response can ultimately result in dense fibrosis and entrapment of orbital structures and mass effect. Some cases are primarily sclerotic in nature presenting insidiously with no prior acute phase. They have scant cellular infiltrate with dense desmoplastic stroma.

Histopathological diagnosis can be arrived at by fine needle aspiration and cytology (FNAC) or incisional biopsy. FNAC is an useful diagnostic tool in a presumed case of orbital pseudotumor as the condition mimics tumor both clinically and radiologically. Being a simple procedure done under topical anesthesia it saves the patient from the inconvenience of orbital exploration.

**Imaging**

Ultrasoundography (USG), computed tomography and magnetic resonance imaging (Fig. 2) are useful diagnostic imaging modalities in pseudotumor orbit. The appearance of pseudotumour in imaging varies depending on whether the involvement is diffuse or localized. Typically there is diffuse enlargement of extraocular muscles inclusive of the tendon in pseudotumour. In USG the lesion has low internal reflectivity (10% to 40%) due to absence of interfaces and sound attenuation is minimal. The borders are well defined when the lesion is localized and poorly defined in diffuse lesions. A “T” sign is seen in associated posterior scleritis due to effusion in Tenon's space. CT demonstrates similar findings which enhances with contrast. Pseudotumour appears hypointense to fat on T1 weighted images and isointense or hypointense to fat on T2 weighted images with marked gadolinium enhancement. MR imaging now provides prognostic significance as well. Lesions that appear hyper intense compared with cerebral cortex on short inversion time inversion-recovery (STIR) images reportedly respond well to corticosteroid therapy whereas lesions that are hypointense or isointense compared with extraocular muscle respond poorly.

**Differential Diagnosis**

The differential diagnosis includes thyroid eye disease, orbital cellulitis, Wegener’s granulomatous, lymphoma, leukemia, sarcoidosis, amyloidosis, dermoid cyst. It is of paramount importance to distinguish pseudo-
tumors from true neoplasm of orbit. The therapeutic response to corticosteroids is misleading and provides wrong assurance as some improvement can occur in other diseases. Presence of thyroid lid signs and tendon sparing extraocular muscle enlargement helps in differentiating it from IOIS. Orbital cellulitis is accompanied by signs of systemic toxicity including fever, and leucocytosis with shift to left. A thorough systemic work up will help in differentiating pseudotumor from systemic affections like sarcoidosis, lymphoma, leukemia's. Rarely orbital affection may be the only sign of the systemic disease. In the absence of systemic disease, histopathology aids in differentiating IOIS from other conditions. Fine needle aspiration biopsy or open biopsy may be performed for this.

**Treatment**

The spectrum of adjuvant treatment in IOI is broad and evolving. Options include corticosteroids, radiation therapy, non steroidal anti-inflammatory drugs, cytotoxic agents (chlorambucil, cyclophosphamide), corticosteroid sparing immunosuppressants (for example, methotrexate, cyclosporine, azathioprine); intravenous immunoglobulin, plasmapheresis, and the newest class, biologic treatments, which includes anti-tumor necrosis factor alpha (TNFα).

**Oral steroids:** The mainstay of therapy is corticosteroid which has diagnostic sensitivity of 78 % due to the prompt response of the condition to steroids. Recurrence rate of 50-60 % has been reported by previous studies with corticosteroids. Dose ranging from 60-100 mg/day is initiated. High dose oral steroid for 2-3 weeks followed by slow tapering is recommended. Effective immunosuppression needs to be in sufficient dose and maintained for the duration of active disease. Intravenous pulse steroids are reserved for patients with rapid progression of symptoms. Failures in corticosteroid treatment may be termed primary, if there is no improvement despite adequate steroid dosage; recalcitrant, if there is breakthrough inflammation during tapering steroid dosage; recurrent, if the pseudotumor recurs after a period of remission. The systemic side effects due to prolonged steroid therapy includes cushingoid symptoms and signs, growth retardation, weight gain, risk of development of gastrointestinal bleeding, and inability to obtain follow-up on steroid therapy.

**Intraorbital injection of triamcinolone acetonide:** 20-40 mg has also been shown to be effective in the treatment of IOIS. with reduced systemic side effects of oral steroids.

**Immunosuppressants:** Cyclophosphamide 200mg/day is used to treat patients with recurrence on steroid therapy. Cyclosporine 2.5mg/kg and methotrexate 7.5-12.5mg/kg are the steroid sparing drugs used.

**Immune modulators:** Biological immunomodulators have revolutionized the treatment of autoimmune diseases. Infliximab (chimeric monoclonal antibody), TNF-α blocker at 6 weekly dosage schedule of 3-5 mg/kg has been recently introduced in the treatment armamentarium of IOIS. TNF inhibition is associated with increase in antinuclear antibodies and systemic lupus erythematosus, hence concomitant methotrexate therapy is recommended.

**Radiation –** Radiotherapy is used to treat patients intolerant or resistant to steroids. Dose ranging form 1500 – 2500 cGy over 10-15 days is appropriate in steroid resistant cases. Average time taken for response to radiotherapy is 3-8 months. Localized mass, presence of lymphoid follicles, absence of eosinophils and initial response to steroids are good prognostic factors for response to radiotherapy.

**Complications**

Desmoplastic component of pseudotumour results in fibrous entrapment of extraocular muscles resulting in restriction of ocular movements and diplopia. Mass effect caused by both inflammation and desmoplasia causes compressive optic neuropathy and dysfunction of ocular motor nerves. Obstruction of venous drainage results in orbital congestion. IOIS has the tendency to spread intracranially, paranasal sinuses, into infratemporal and pterygopalatine fossa through the major openings in the posterior orbit; optic canal, superior and inferior orbital fissure. Hence in cases with persistent or recurrent or progressive clinical symptoms contrast enhanced computed tomography and magnetic resonance imaging is indicated. In the presence of extraorbital extension, biopsy should be performed to exclude other conditions mimicking ISOI. IOIS causes
open angle glaucoma secondary to raised episcleral pressure. Engorged ciliary processes/ posterior scleritis with choroidal effusions/ relative obstruction of vortex veins with swelling of uvea pushing iris-lens diaphragm are the mechanism put forward for secondary angle closure glaucoma caused by pseudotumor.

Conclusion
Orbital pseudotumor comprises a significant proportion of cases of orbital lesions. It should be considered in the differential diagnosis of acute proptosis in adults. Orbital pseudotumor is typically characterized by the rapid development of pain, proptosis, and swelling around the eye and orbit. Ultrasound and computed tomographic (CT) scanning typically shows a diffuse infiltration of the orbit, an inflammation of the eye wall (sclera), and/or T-sign (with the optic nerve). Orbital pseudotumor related orbital masses typically have poorly defined margins. Patients with classic findings of orbital pseudotumor may be treated without a biopsy. These cases typically respond rapidly to steroid therapy (which helps confirm the diagnosis). Atypical cases of orbital pseudotumor usually undergo biopsy which helps establish the diagnosis.

References
Efficacy of Combining Pneumatic Displacement of Submacular Haemorrhage With Intravitreal Bevacizumab Injection (IVB) for Choroidal Neovascular Membranes (CNVM) Associated With Submacular Haemorrhage

Dr Sonia Rani John DNB, Dr Arup Chakrabarti MS DO, Dr Meena Chakrabarti MS DO DNB

Abstract:

**Purpose:** Analysis of the efficacy of combining pneumatic displacement of sub macular hemorrhage with intravitreal Bevacizumab injections in the management of sub macular hemorrhage of varying etiologies, of less than 30 days duration.

**Method:** Prospective, consecutive noncomparative interventional case series of 30 eyes with CNVM and submacular hemorrhage who underwent pneumatic displacement with IVB, followed by prone positioning for 5-7 days. Efficacy of procedure was assessed by fluorescein leakage and OCT evidence of regression.

**Results:** BCVA improvement in 50% (15 patients) was associated with displacement of submacular blood within 7 days. Fluorescein leakage decreased in 92% (28 patients) of eyes. Reduction in central retinal thickness by 25% of baseline observed in 80% (p<0.01) and visual recovery at 3 months (p<0.01) were associated with smaller lesions and non AMD lesions.

**Conclusion:** Combining pneumatic displacement with IVB was effective for CNVM associated with submacular hemorrhage. Smaller GLD, younger age, non AMD choroidal neovascular membranes and treatment within 72 hours of onset of submacular hemorrhage predicted a favorable prognosis.

Introduction

Submacular hemorrhage is an important cause for acute visual loss. The visual outcome in patients with submacular hemorrhage is especially poor if the hemorrhage is thick, involves the fovea, or covers a large area of the macula and is associated with an underlying CNVM especially in age related macular degeneration.

The evolution of surgical techniques for the management of submacular hemorrhage has passed through the following stages.
2. 1989: Mechanical removal of clot with CNVM.
3. 1991: Sub retinal t-PA with removal of liquefied blood without removal of CNVM.
4. 1996: Intravitreal t-PA with gas \(^3\) (Herriots technique).
5. 1998: Intravitreal gas only \(^4\).
6. 2001: Sub retinal t-PA and pneumatic displacement \(^5\).
7. 2007: Pneumatic displacement and Intravitreal Bevacizumab \(^6\).
8. 2008: Intravitreal t-PA, expansile gas and Intravitreal bevacizumab \(^7\).

The Herriots technique of intravitreal t-PA and gas injection can be performed in the out-patient clinic being a fast and safe procedure. Some studies have not reported good visual outcomes and it is also unclear whether intravitreal t-PA can penetrate into the retina. Animal studies on rabbits by Motohiro Kamel et al \(^8\) have demonstrated the ability of t-PA to diffuse into the sub retinal space after intravitreal injection. Ohiji and colleagues \(^9\) reported a series of 5 patients treated with pure perfluoropropane gas and face down positioning in the management of submacular hemorrhage. Displacement occurred completely or partially in all 5 eyes. The visual outcome following displacement depends on the macular status and hence it is important to treat the macular pathology at the earliest. The last two years heralded the use of intravitreal anti-VEGF injections especially the use of intravitreal Bevacizumab (Avastin) injection in the management of ocular neovascularisation arising from diverse etiologies. Excellent results of regression of choroidal neovascular membranes associated with AMD following intravitreal Bevacizumab \(^9,^{10}\) has been reported by various authors.

The aim of our study was to assess the efficacy of pneumatic displacement of submacular hemorrhage using intravitreal perfluoropropane gas (without adjunctive t-PA) in combination with intravitreal Bevacizumab (Avastin) injection in a consecutive series of 30 patients as a pilot study to determine its safety and efficacy in displacing blood from under the fovea and causing regression of the underlying choroidal neovascular membrane.

**Methods:** 30 consecutive patients with submacular hemorrhage of 1-30 days duration between March 2006 and March 2008 underwent intravitreal injection of 0.3 ml of pure perfluoropropane gas and 0.05 ml of 1.25 mg Bevacizumab (Avastin). Postoperatively all patients maintained prone positioning for 5 days. All procedures were performed by a single retinal specialist (MC). Inclusion criteria included submacular hemorrhage < 30 days duration with blood under the fovea and a small to medium sized hemorrhage ≥ 5 DD in size.

All patients underwent a complete ocular evaluation before the intervention. A detailed cardiology evaluation was also performed to rule out thromboembolic risk factors. The best corrected visual acuity, applanation tonometry, detailed fundus evaluation, fundus photography and optical coherence tomographic scans of the macula were performed in all patients.

After obtaining an informed consent, the procedure was performed in the OT under strict aseptic precautions. All procedures were performed under topical anesthesia using Xylocaine jelly 2% (ASTRA-IDL). 0.3 ml of pure perfluoropropane gas was injected first through the pars plana 3.5 mm from the limbus using a 30 G needle. Paracentesis was performed using a paracentesis knife and the eye was kept patched after indirect ophthalmoscopy to visualise the disc. All patients were advised to use topical antibiotic drops, non steroidal anti inflammatory drops and topical dorzolamide drops (once at bedtime) for 5 days. Strict maintenance of prone positioning was advocated for a period of 5 days.

Patients were reviewed at day 1, 7 and 30 days after the procedure. Repeat fundus photography, fluorescein angiography and OCT were performed on the 7\(^{th}\) and 30\(^{th}\) postoperative days.

The efficacy of the procedure was assessed by

1) Degree of subfoveal blood displacement by comparing the pretreatment fundus photographs with the 7\(^{th}\) POD photographs. Degree of displacement of blood from under fovea was graded as complete, partial or no displacement.
<table>
<thead>
<tr>
<th>No.</th>
<th>Age/ Sex</th>
<th>Duration (Days)</th>
<th>Size DD</th>
<th>Pre Rx</th>
<th>OCT (μm)</th>
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<td>250</td>
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<td>6/18</td>
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<td>CF 2m</td>
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<td>3/60</td>
<td>CNVM</td>
<td>1500</td>
<td>260</td>
<td>VH</td>
</tr>
</tbody>
</table>

DD: Disc Diameter, m : months, R.; Treatment, BCVA: Best corrected visual acuity; GLD: Greatest lesion diameter, F: Female, M: male, CF: Counting figures, HM: Handmotion, CF CF: Counting fingus close to face, CNVM: Choroidal Neovascular Membrane; VH: Vitreous hemorrhage, RPE: Retinal Pigment Epithelium
2) Best corrected visual acuities at 1 month and 3 rd postoperative months.

3) Degree of fluorescein leakage was assessed by comparing the pretreatment and post treatment angiograms.

4) OCT evidence of regression by measuring the central retinal thickness, and resolution of sub retinal blood/ fluid.

The results obtained were compared with already published results on pneumatic displacement.

Results: Thirty eyes of 30 patients (9 females and 21 males) with submacular hemorrhage ≤ 30 days underwent a combination of intravitreal gas and Bevacizumab injections. The pre and postoperative data of all 30 patients with sub macular hemorrhage is given in Table 1.

The mean duration of follow up was 6 months. The age of the patients ranged from 34 years to 75 years. (Mean 62.3 +/-10.3 years) and the duration of symptoms ranged from 1 to 30 days (Mean 12.3 +/-6.8 days). The size of the hemorrhage ranged from 5 DD to 28 DD in size. (Mean 12.5+/-4.3 DD) (Tables 2, 3, 4). The preoperative fluorescein angiogram was not contributory in any of the cases. Pre intervention OCT measure of central retinal thickness ranged from 259 μm-660 μm (Mean = 459.5 μm).

The procedure resulted in complete displacement of blood in 15 (50 %) of the 30 patients at 1 week follow up (Fig 1). Partial displacement occurred in 13 eyes (49.9 %) and no displacement in 2 eyes.

Prior to treatment, the best corrected visual acuities ranged from 5/60- HM with 8 patients having a vision of only hand movements. The duration of follow up ranged from 3 months to 24 months (Median 6 months)

At the end of one month, 50 % out of the 30 patients had a significant improvement in visual acuity which was associated with displacement of sub macular blood. The improvement of vision ranged from 6/60 - 6/9 from the pre intervention visual acuity, (HM - 5/60). In 2 eyes with no displacement of sub retinal blood there was no visual improvement. Vision also did not improve in 2 eyes with retinal pigment epithelial rips.

The improvement of visual acuity compared to the pretreatment level (Table 5) was statistically significant in the first and third month. (p<0.01 and p<0.05) The final visual acuity was better than 6/60 in 24 of the 30 eyes.

The central retinal thickness measured by OCT decreased from a pre – treatment value of 432+/-SD 100.1μm to a post – treatment mean thickness of 282.7 +/-sd 55.7μm.(Table 6) The mean difference in central retinal thickness was statistically significant by the paired t test (p < 0.01) showing that the treatment was efficacious in reducing the macular thickness.

We tried to correlate age of patient, duration of submacular hemorrhage before surgical intervention, etiology, and the greatest lesion diameter with the post operative results of visual acuity, degree of reduction of fluorescein leakage and reduction of central retinal thickness.

The visual scores at 1 month and 3 months were analyzed to asses if there was a relationship to variables such as age of the patient, duration of the lesion, and the size of the lesion (Table 7 and Table 8 ).It was seen that there was no statistically significant difference between the variables assessed and improvement in
visual acuity. The change in OCT values of the central retinal thickness was analyzed to assess if there was a relationship to variables such as age of the patient, duration of the lesion, and the size of the lesion (Table 9). It was seen that there was no statistically significant difference between the variables such as age of the patient and duration of lesion and reduction in central retinal thickness. However, a statistically significant correlation between pre-treatment lesion size and reduction in central retinal thickness (p<0.05) could be made out.

Complications associated with the procedure included 1) mild vitreous hemorrhage which cleared spontaneously in 7 eyes. 2) Retinal pigment epithelial tears in 2 eyes. 3) Non resolving vitreous hemorrhage necessitating a subsequent pars plana vitrectomy in 3 eyes.

Considering the effect of duration of submacular hemorrhage before surgical intervention on the final visual result it was seen that 12/16 eyes with a duration ≤ 10 days had a final visual acuity of ≥ 6/60.

Fluorescein angiographic leakage decreased significantly (when the 1st post intervention angiogram was compared with the 30 days post operative angiogram) in 92 % of eyes. Redirection in CRT by 25 % of baseline nature occurred in 80 % of the patients.

Based on the etiology of the lesion responsible for the sub retinal hemorrhage, the patients were grouped into
1. CNVM due to AMD - 10 eyes
2. Idiopathic CNVM - 6 eyes
3. PCV - 3 eyes
4. Ruptured macro aneurysm - 5 eyes
5. Unknown cause - 5 eyes

We also tried to correlate the etiology of the CNVM with the response to therapy with respect to visual recovery and reduction in central retinal thickness (Table 10)

The best response to therapy was seen in eyes with idiopathic CNVM and myopic CNVM while the worst response was seen in patients with CNVM due to age-related macular degeneration.

**Discussion**

Our pilot studies assessed the efficacy of combining pneumatic displacement with intravitreal bevacizumab in the management of submacular hemorrhage of < 30 days duration due to various etiologies. Previous studies 4 have demonstrated the efficacy of intravitreal injection of 0.3 ml pure expansile gas in causing displacement of submacular hemorrhage. However, mechanical displacement alone was not sufficient to treat the underlying pathology responsible for the submacular hemorrhage. Small case series have reported the safety and efficacy of combining pneumatic displacement with intravitreal t-PA and Bevacizumab 7. Since t-PA is expensive and there are well-documented reports on retinal toxicity to t-PA as well as doubts regarding its ability to penetrate into the sub retinal space on intravitreal injection, we decided to conduct our study without using t-PA as an adjunct.

Displacement of the submacular blood was achieved in 28/30 eyes in our series with 50 % achieving complete displacement by 7th post operative day.

Significant improvement in visual acuity in 50 % of eyes, reduction in fluorescein angiographic leakage in 82 % and 25 % reduction in baseline OCT thickness was achieved at 3 months follow up.

The best visual results were associated with younger age, shorter duration of hemorrhage, smaller GLD and non AMD lesions. Comparing our results with other studies show (Table 11) that the efficacy of combining pneumatic displacement with IVB was more and resulted in better visual results.

Combining pneumatic displacement with IVB resulted in the dual actions of displacing the submacular blood as well as providing IVB monotherapy to the underlying pathology. Larger series with longer follow up is necessary before validating the efficacy of this procedure.
Table 5. Effectiveness of treatment on vision (based on score)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Mean</th>
<th>SD</th>
<th>N</th>
<th>Group</th>
<th>mean difference</th>
<th>paired ‘t’</th>
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<td>2.8</td>
<td>30</td>
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<td>6.4</td>
<td>10.55**</td>
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<td>2.9</td>
<td>30</td>
<td>1 M Vs 3 M</td>
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*: Significant at 0.05 level  **: Significant at 0.01 level

Table 6. Effectiveness of treatment on OCT

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<th>SD</th>
<th>N</th>
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**: Significant at 0.01 level

Table 7. Comparison of difference in score regarding vision at 1 month (based on pre treatment) based on selected background variables

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Table 8. Comparison of difference in score regarding vision at 3 month (pretreatment) based on selected background variables

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Table 9. Comparison of percentage decrease in OCT score (pretreatment) based on selected background variables

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<td>10</td>
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<tr>
<td>70-79</td>
<td>37.8</td>
<td>12.9</td>
<td>10</td>
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<tr>
<td>Duration</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upto 10</td>
<td>31.6</td>
<td>15.6</td>
<td>13</td>
<td>t</td>
<td>0.09</td>
</tr>
<tr>
<td>Above 10</td>
<td>31.2</td>
<td>11.8</td>
<td>17</td>
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<td></td>
</tr>
<tr>
<td>Size of lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upto 10</td>
<td>27.9</td>
<td>12.9</td>
<td>11</td>
<td>F</td>
<td>3.35*</td>
</tr>
<tr>
<td>11-14</td>
<td>27.2</td>
<td>14.9</td>
<td>10</td>
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<tr>
<td>15+</td>
<td>40.3</td>
<td>7.5</td>
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</table>

*: Significant at 0.05 level

Table 10. Correlation of the visual acuity with etiology

<table>
<thead>
<tr>
<th>Etiology</th>
<th>No: of eyes</th>
<th>Displacement</th>
<th>Pre R, V_A</th>
<th>Mean post R, V_A</th>
<th>P value</th>
</tr>
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<tr>
<td>CNVM in AMD</td>
<td>10</td>
<td>+</td>
<td>CF 1m</td>
<td>5/60</td>
<td>0.005</td>
</tr>
<tr>
<td>Idiopathic CNVM</td>
<td>6</td>
<td>+</td>
<td>5/60</td>
<td>6/12</td>
<td>0.004</td>
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<td>PCV</td>
<td>3</td>
<td>+</td>
<td>CFCF</td>
<td>6/60</td>
<td>0.01</td>
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<tr>
<td>Myopic CNVM</td>
<td>5</td>
<td>+</td>
<td>5/60</td>
<td>6/36</td>
<td>0.005</td>
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<tr>
<td>Ruptured macroaneurysm</td>
<td>3</td>
<td>Not displaced in 2/3 eyes</td>
<td>HM</td>
<td>HM</td>
<td>0.02</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>+</td>
<td>CF 1m</td>
<td>6/18</td>
<td>0.001</td>
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</table>
References


Table 11. Comparison with other studies.

<table>
<thead>
<tr>
<th>Authors / years</th>
<th>Procedure</th>
<th>No: of eyes</th>
<th>Displacement</th>
<th>Vision</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blodi et al; 2001</td>
<td>t-PA + Intra vitreal Gas</td>
<td>14</td>
<td>10/14</td>
<td>-</td>
<td>AMD</td>
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<tr>
<td>Hassan et al;1999</td>
<td>t-PA + Gas</td>
<td>15</td>
<td>15/15</td>
<td>14/15 eyes 2 line improvement</td>
<td>AMD</td>
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<td>Herriot ; 1999</td>
<td>Gas alone</td>
<td>5</td>
<td>5/5</td>
<td>3/18 AMD eyes</td>
<td>AMD</td>
</tr>
<tr>
<td>Ohiji et al ;1998</td>
<td>Gas alone</td>
<td>20</td>
<td>16/20</td>
<td>-</td>
<td>AMD</td>
</tr>
<tr>
<td>Mahesh G;2003</td>
<td>Gas alone</td>
<td>20</td>
<td>16/20</td>
<td>13/20 eyes V ≥ 20/20</td>
<td>AMD &amp; non AMD</td>
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<tr>
<td>Chakrabarti 2008</td>
<td>Gas + IVB</td>
<td>30</td>
<td>18/30</td>
<td>15/30 eyes V ≥ 6/60</td>
<td>AMD &amp; others</td>
</tr>
</tbody>
</table>
Intravitreal Monotherapy With Bevacizumab (IVB) and Triamcinolone Acetonide (IVTA) Versus Combination Therapy (IVB and IVTA) for Recalcitrant Diabetic Macular Edema

Dr Meena Chakrabarti MS DO DNB, Dr Sonia Rani John DNB, Dr Arup Chakrabarti MS DO

Abstract

Purpose: To ascertain whether addition of Triamcinolone acetonide to intravitreal Bevacizumab injection increased the efficacy in management of Diabetic Macular Edema (DME) and assess the pattern of DME that correlated with a favorable response.

Method: In a prospective randomized interventional study, 60 eyes received one of the three interventions. Group B (IVB): 20 eyes; Group T (IVTA): 20 eyes and Group BT (combined IVB and IVTA): 20 eyes.

Results: Visual improvement was similar in all three groups. Reduction in central retinal thickness (64 % BT Vs 59 % B Vs 45 % T); recurrence of clinically significant macular edema (15 % B and BT Vs 70 % T); elevated intraocular pressure ( 17 % T Vs 22 % BT Vs 5 % B) were observed. Greater edema and sub retinal fluid predicted a favorable response to both IVB and IVTA.

Conclusion: TA did not add to therapeutic efficacy of IVB, but increased the incidence of elevated intraocular pressure.

Introduction

Recalcitrant diabetic macular edema is characterized by the accumulation of plaques of hard exudates in a grossly edematous retina, not amenable to the standard modalities of therapy and showing a very poor visual potential. These patients usually have a poorly controlled glycaemic status of long duration with associated co-morbid condition such as systemic hypertension, dyslipidemia and chronic renal failure. Majority of these eyes would have had several sittings of laser photocoagulation and hence it is necessary to employ alternative treatment modalities.

Initial reports on uncontrolled interventional case series reported an unprecedented efficacy of intravitreal steroids in reducing diabetic macular edema often accompanied by significant improvement in visual acuity. These uncontrolled series were followed by randomized placebo-controlled trials demonstrating the efficacy of IVTA compared with standard of care, both short term and long term. The beneficial effect of intravitreal injection of triamcinolone acetonide in most...
cases lasted for 6-9 months. In the Intravitreal Triamcinolone acetonide for clinically significant Diabetic Macular Edema that persists after laser treatment study (TDMO), the mean number of injections was only 2.4 over 2 years with a total potential for five injections. It has also been reported that repeated intravitreal injection may not be as effective as the initial treatment. The high incidence of adverse effects which include cataract (54 %), glaucoma (20-40 %) and need for trabeculectomy (6 %) demands caution in its use.

The introduction of IVTA has been a major advance in the treatment of refractory diabetic macular edema. The high risk of steroid related adverse effects however leaves room for improvement and innovation in treatment strategies. Focal/Grid laser photocoagulation after IVTA has been shown to maintain improved vision and may reduce recurrent macular edema.

Patients with diabetic macular edema have been found to have increased levels of VEGF in the vitreous. Hence intravitreal injection of anti VEGF may have a role in reducing diabetic macular edema. Their efficacy is similar to IVTA, but they do not cause adverse events associated with corticosteroids. On the other hand, frequent injection (every 4-6 weeks) for an extended period may be required, making injection related complications such as infectious endophthalmitis a major draw back.

There are very few studies on the efficacy of combining triamcinolone acetonide and bevacizumab (an anti VEGF antibody). We undertook a pilot study to compare the efficacy of intravitreal monotherapy with Triamcinolone and Bevacizumab versus combination of Bevacizumab and triamcinolone in the management of recalcitrant DME not amenable to laser treatment. We also assessed the OCT patterns in recalcitrant DME which showed a favorable response to intravitreal injection of Triamcinolone and Bevacizumab.

### Methods

The study was designed as a prospective randomized interventional study which recruited 60 patients who fulfilled all the inclusion criteria from March 2006 – March 2008. The inclusion criteria for enrolment into the study were:

1. Diabetic age ≥ 10 years
2. Good Glycaemic Control (Hb A₁C ≤ 7 gm %)
3. Stable Renal Status
4. Controlled serum lipid level
5. H/o prior Focal/ Grid laser PHC (≥ 3 sittings) ≥ 6 months to time of enrolment into the study.
6. Presence of DME clinically and angiographically
7. OCT showing CRT ≥ 300 μm
8. Absence of significant lens opacity
9. Absence of macular ischemia
10. Absence of VMT or a taut posterior hyaloid phase in OCT.

Exclusion criteria were poorly controlled diabetes with associated nephropathy and dyslipidemia, significant cataract precluding fundus evaluation or presence of macular ischemia. The patients were randomized to receive one of the three modes of interventions tested in this study.

- **Group B**: Received 0.05 ml / 1.25 mg Intravitreal injection of Bevacizumab.
- **Group T**: Received 4 mg / 0.1 ml Triamcinolone acetonide injection intravitreally.
- **Group BT**: Received both Bevacizumab and Triamcinolone acetonide injections administered intravitreally.

All patients underwent a thorough preoperative evaluation. The best corrected visual acuity was determined after dilated refraction. Slit lamp biomicroscopy of the macula, applanation tonometry and indirect ophthalmoscopic evaluation of the fundus were performed and the findings noted. The degree of cataract was assessed prior to intervention. All patients underwent a fluorescein angiographic evaluation and OCT assessment of central retinal thickness and pattern of edema as part of the baseline evaluation. An informed consent was obtained in all the patients. The intervention was performed under strict aseptic precautions in the operation theatre under topical anesthesia in all the patients. Paracentesis was performed to bring the IOP under control and the eye was kept patched for an hour after the procedure. Postoperatively 3 hours after the procedure applanation tonometry was performed in all patients using the Keeler Pulsair non contact tonometer. The patients were
instructed to use topical antibiotic drops qid, topical non steroidal anti inflammatory drops qid and topical dorzolamide drops once at bed time for a period of 7 days postoperatively. Counseling on the appearance of floaters and slight visual blurring were discussed with the patients.

The patients were followed up on day 7, 30 days and 90 days after the procedure. At each visit an assessment of the glycaemic status, control of BP, renal status and serum lipid profile was assessed. FFA and OCT were performed at 30 days and 90 days after the procedure. Refraction, tonometry, slit lamp evaluation for cataract and biomicroscopic macular evaluation for degree of macular edema was performed at all visits. Response to therapy was assessed by 1) Improvement in the best corrected visual acuity 2) Slit lamp biomicroscopy and OCT showing reduction in retinal thickness 3) FFA showing decrease in fluorescein leakage 4) Progression of lenticular changes 5) Presence or absence of post treatment IOP spike and 6) Recurrence

Follow up data in the IVTA group (Fig 1), IVB group (Fig 2) and combined group (Fig 3) showing regression of macular edema.

**Results**

This study was designed as a prospective randomized comparative interventional case series which recruited 60 patients enrolling 20 patients for each mode of intervention. The patients were of the age group ranging from 45-70 years (Mean age 58 years). There were 46 males and 14 females in our study giving a M: F ratio of 2:1. The mean duration of diabetes was 13.5 years (Range 7 years -20 years) and the mean value of glycosylated hemoglobin at baseline was 6.7 (Range 5.9 - 7.5). Associated co-morbid conditions were:

1. Hypertension : 25 (41.67 %)
2. Hyperlipidemias : 40 (66.67 %)
3. Chronic Renal failure : 3 (5 %)
4. Both HT and HL : 30 (50 %)
5. No associated disease : 15 (25 %)

50 % of the patients had proliferative diabetic retinopathy associated with maculopathy and 50 % had background diabetic retinopathy with clinically significant macular edema. In group T (IVTA Group) an improvement in visual acuity was observed in 9/20 eyes (45 %) who showed a mean reduction of central retinal thickness in the OCT scans from a baseline mean CRT value of 550 μm ± 26 μm to 285 μm ± 20 μm. This 45 % reduction in central retinal thickness persisted up to 6-9 months after which the recurrence of CSME was observed in 15 of the 20 eyes (75 %). These eyes underwent focal/grid laser photocoagulation / or repeat IVTA in 4 eyes (20 %).
In the remaining 11 patients the mean reduction in central retinal thickness was by 20% of baseline value (from a mean CRT at baseline of 550 μm ± 26 μm to 350 μm ± 20μm) at 6 months follow up. Although there was no improvement in visual acuity, the vision stabilized at the baseline level. Recurrence of edema was noticed in 9/11 patients (81.81%).

Progression of cataract was noticed in 6 eyes (30%) and 2 patients with significant cataract underwent phacoemulsification with foldable IOL implantation under topical anesthesia.

Intraocular pressures increased to mid twenties in 3 eyes (15%) but could be controlled medically with single antiglaucoma medication (Dorzolamide).

There were no cases of endophthalmitis, vitreous hemorrhage or retinal detachment in this group.

Group B (Intravitreal Bevacizumab injection): An improvement in visual acuity was observed in 11/20 eyes (55%) in this group. All 20 eyes showed some reduction in central retinal thickness, however a 25% reduction from baseline value was obtained in 59% of our patients in this group. Maximum beneficial effect was observed within 30 days of the injection and with additional laser therapy the effect persisted up to 9 months. Repeat injection was not necessary up to 12 months. However some increase in CRT was noticed in 15% of patients after 9 months for which additional laser was given. Further follow up alone will give an idea of the course of disease and the necessity for reinjections. Elevation in intraocular pressure was noticed in one patient (5%) which was amenable to medical therapy.

Group BT (Combined IVTA & IVB): An improvement in visual acuity was observed in 60% (12/20) eyes. The reduction in the central retinal thickness was maximum in this group and was observed in 64% of eyes. The reduction in retinal thickness peaked at one month post injection and persisted up to 9 months. Recurrences in 15% of eyes were similar to group B showing than an additional injection of TA did not have any effect in preventing recurrences. A higher incidence of elevated intraocular pressure in 22% of cases questioned the efficacy of adding TA, when IVB alone would have sufficed.

Table 1. Effectiveness of treatment on Vision

<table>
<thead>
<tr>
<th></th>
<th>MEAN</th>
<th>SD</th>
<th>N</th>
<th>MEAN DIFF</th>
<th>PAIRED ‘t’ TEST</th>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>BT</td>
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<tr>
<td>AT</td>
<td>11.8</td>
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<td>1.6</td>
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<td>2.1</td>
<td>20</td>
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</table>

Fig. 4. Efficacy of intervention with respect to vision gain
There was no statistically significant difference between the increase in visual scores in the 3 groups by ANOVA test and hence all three modalities are equally effective with respect to visual gain.

**Effectiveness of Treatment on Central Retinal Thickness**

- There was a mean decrease in CRT of 167 μm, 201μm and 208μm in the IVTA, IVB and the combined group which was statistically significant by the paired “t” test (p=0.000) (Table 2).
- There was no statistically significant difference in the decrease of central retinal thickness in the 3 groups by the ANOVA test (p=0.110) & hence all 3 interventions were equally effective.

Analysis of the complications showed that the incidence of cataract formation was highest in the IVTA & Combined Groups (30%). Elevated intraocular pressures were observed in 15% of patients in the IVTA Group and in 25% in the combination group while only one patient (5%) had elevated intraocular pressure in the IVB group. The correlation was not statistically significant by the chi squared test (Chi$^2$ = 3.17; p = 0.208). The highest rate of recurrence of CSME was observed in the IVTA group (70%) and occurred within 6 months of the intravitreal pharmacotherapy. Clinically significant macular edema recurred in 15 % of the patients randomised to receive IVB & combined pharmacotherapy. This correlation was statistically significant by chi squared test p=0.000 (Table 3).

- There was no added benefit in adding IVTA to IVB.

All 3 groups are similar with respect to age, sex, diabetic age, HbA1C, pre treatment vision, and baseline central retinal thickness on OCT and hence they are comparable.

Table 2. Effectiveness of treatment on OCT

<table>
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<tr>
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<th>SD</th>
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<th>MEAN DIFFERENCE</th>
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<th>P</th>
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<td>BT</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>BT</td>
<td>538.1</td>
<td>73.8</td>
<td>20</td>
<td>208 μm</td>
<td>17.02**</td>
<td>0.000</td>
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<td></td>
</tr>
<tr>
<td>BT</td>
<td>539.5</td>
<td>65.6</td>
<td>20</td>
<td>20 μm</td>
<td>17.06**</td>
<td>0.000</td>
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<tr>
<td>AT</td>
<td>338.8</td>
<td>67.2</td>
<td>20</td>
<td></td>
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</tbody>
</table>

Table 3. Comparison of Complications

- **CATARACT:** 30% in IVTA group alone developed cataract
- **GLAUCOMA:** Increase in IOP in 15% IVTA GP, 5% IVB GP, & 25% Combined GP was not statistically significant by chi squared test (Chi$^2$ = 3.17, p=0.208)
- **RECURRENT:** In 70% IVTA, 15% IVB, 15% Combined group was statistically significant by chi squared test (Chi$^2$ = 18.15, p=0.000)

- There was a mean increase of 1.6,1.6 &1.7 in the pre treatment and post treatment visual scores in the IVTA,IVB and the combined group which was statistically significant by the paired “t” test(p=0.005 in IVTA group, p=0.001 in the IVB group ,& p=0.000 in the combined group) (Table 1, Fig. 4).

Table 4.

<table>
<thead>
<tr>
<th>OCT GRADING</th>
<th>Pre injection CRT (Mean)</th>
<th>Post-injection CRT (Mean)</th>
<th>Pre-injection vision (Mean)</th>
<th>Post-injection vision (Mean)</th>
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<tbody>
<tr>
<td>Diffuse edema</td>
<td>500 μm</td>
<td>309 μm</td>
<td>5/60</td>
<td>6/18</td>
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<tr>
<td>Cystoid edema</td>
<td>422 μm</td>
<td>315 μm</td>
<td>3/60</td>
<td>5/60</td>
</tr>
<tr>
<td>Subfoveal serous RD</td>
<td>418 μm</td>
<td>256 μm</td>
<td>CF 2m</td>
<td>6/36</td>
</tr>
<tr>
<td>Plaques of H/E</td>
<td>325 μm</td>
<td>250 μm</td>
<td>CF1m</td>
<td>CF1m</td>
</tr>
<tr>
<td>Combination</td>
<td>550 μm</td>
<td>350 μm</td>
<td>CF 2m</td>
<td>4/60</td>
</tr>
</tbody>
</table>
We divided the patients into 4 groups based on the preinjection OCT findings 1) Diffuse edema 2) Cystoid edema 3) Subfoveal serous retinal detachment 4) Plaques of hard exudates under fovea. 5) Combination and tried to correlate with the response to therapy as measured by CRT and improvement in vision.

Our results showed that maximum reduction of central retinal thickness and maximum visual gain were observed in eyes with greater degree of diffuse macular edema and presence of subfoveal serous RD (Table 4).

Discussion

The role of steroids is mediated through 1) Suppression of VEGF 2) Stabilizing the leakage from retinal vessels 3) Suppression of the release of endothelial cell activators and 4) Possibly its anti-inflammatory action.

Initially uncontrolled interventional case series reported an unprecedented efficacy of intravitreal steroids (usually triamcinolone acetonide) in reducing diabetic macular edema accompanied by significant improvement in visual acuity. These uncontrolled series were followed by randomized placebo controlled trials demonstrating the efficacy of IVTA compared with standards care both short and long term.

Several studies in eyes with persistent DME despite focal and/or grid laser photocoagulation have demonstrated the efficacy of IVTA over laser. However the NEI (National Eye Institute) sponsored trial have conclusively shown that a focal/grid laser photocoagulation gave longer lasting beneficial effects when compared to the transient effect of intravitreal triamcinolone acetonide injection.

Although most studies have shown a beneficial effect the optional dosage of IVTA is still somewhat confusing. Audren F et al conducted a randomized prospective trial comparing the efficacy of 2 mg Vs 4 mg of Triamcinolone acetonide in the management of diffuse diabetic macular edema. This results showed that there was no dose dependent difference in the response to intervention. However Lam DS et al and Spandau UH et al demonstrated close dependency in the response to intravitreal injection of triamcinolone acetonide. The beneficial effect of an intravitreal injection of triamcinolone acetonide in most cases lasts for 6 months – 9 months and repeated injection may not be as efficacious as the initial treatment.

The high incidence of steroid related adverse effects such as (1) necessity for cataract extraction in 54% of phakic treated eyes (2) steroid related evaluation of IOP in 44% of treated eyes necessitates the use of caution. In order to avoid the adverse effect associated with intravitreal therapy, particularly infectious endophthalmitis, the use of periocular steroids in the management of diabetic macular edema has been studied. The results of these trials have been contradictory to each other showing either a beneficial effect or no appreciable effect of the intervention on DME.

Investigators continue to report their experience with intravitreal injections of Bevacizumab, a humanized monoclonal IgG antibody directed against all five VEGF isoforms, in the setting of primary therapy. In a study of 51 patients, Haritoglou et al. observed that at 6 weeks after a single Bevacizumab injection, patients with DME resistant to other therapies had increased visual acuity as well as decreased central retinal thickness by OCT relative to pre-injection baseline, though the effect on visual acuity was not sustained at 12 weeks. The Pan – American Collaborative Retina Study Group studied intravitreal Bevacizumab as a primary treatment for DME in 78 eyes of 64 patients and found, at six months, over 96% of eyes had either stable or improved visual acuity or reduction in the mean central retinal thickness by OCT. A phase II DCRC.net study of 109 patients compared two doses of Bevacizumab to focal laser photocoagulation and demonstrated its efficacy in decreasing DME in some eyes. To date, no phase III trials have been reported that demonstrate a clear benefit for Bevacizumab in the treatment of DME.

While Ranizumab, an affinity-matured humanized monoclonal antibody fragment directed against all VEGF isoforms, is currently in clinical trials for DME, its off label use in DME patients is limited likely as a result of its increased cost and less widespread availability world wide, as compared to Bevacizumab. Clinical trials in DME patients are limited as a result of its increased cost and less widespread availability
worldwide, as compared to Bevacizumab. Clinical trials in DME patients are ongoing. Two pilot studies of 10 patients each, suggested that it was well tolerated and may have some efficacy in promoting improvement in visual acuity and reduction in central retinal thickness by OCT. The READ – 2 (Ranibizumab for edema of the macula in diabetics) studies, a phase II trial comparing the relative efficacy of Intravitreal Ranibizumab, macular laser photocoagulation, and the combination of both treatments among patients with DME, who have not received prior laser is currently ongoing. Six months outcomes suggests a greater improvement in visual acuity for patients undergoing intravitreal Ranibizumab alone as compared to laser or combination treatments.

A report on 101 consecutive eyes with DDME treated with intravitreal Bevacizumab, resulted in both anatomic and functional improvement. Interestingly, the reduction of retinal thickness and improvement of BVCA were detected within the first 4 weeks after the injection in most of the patients. In addition, both doses (1.25 mg and 2.5 mg) were associated with improvement of BVCA and a greater reduction in central macular thickness, and no difference in between were found. Ocular tolerance of the 2 different doses of IVB was demonstrated, and no serious systemic adverse events were noticed during the study.

There are several studies in the literature on the intravitreal administration of antibodies against VEGF for DDME. However, none of them deal with anti-VEGF as a primary treatment. Haritoglou et al reported that intravitreal Ranibizumab has the potential to maintain or improve BVCA and reduce retinal thickness in patients with DDME not responding to previous treatments such as photocoagulation, intravitreal injection of triamcinolone, or vitrectomy. Their follow-up period was too short (6 weeks) to provide specific treatment recommendations. Kumar and Sinha reported results of 20 eyes with DDME treated with IVB dose of 1.25 mg that had not responded to previous photocoagulation. Their follow-up period was 6 months. They concluded that IVB resulted in a significant decrease in macular thickness and improvement in visual acuity at 3 months, but the effect was somewhat blunted, though till statically significant at the end of 6 months. The current study compares favorably with these reports, and confirms their findings with longer follow-up and a larger no of patients. Further more, at the 6 month follow-up time point we noticed a small worsening of vision as described by Kumar and Sinha. When we analyzed our data comparing eyes that had 1 or 2 injections against those eyes that had 3 or more injections, there was a significant drop in BVCA at 6 months in the “1 or 2 injections” group, and not in the “3 or more injections” group. This suggests the need for repeat injection. (63.4 %) needed at least a second injection at a mean of 15.7 ± 11.9 weeks (range: 4 to 64 weeks).

The results of this retrospective study demonstrated the efficacy of 1.25 mg or 2.5 mg of IVB as primary treatment of DDDME, as 49.5 % of eyes showed anatomical and functional improvement. In addition, our results suggest a reduced risk of visual acuity loss in eyes with DDME treated with IBV (82.2 % of eyes). We found that the anatomical and visual benefit of the intravitreal Bevacizumab appears and reaches its maximum value during the first month and maintains itself over 12 months. Nevertheless, we did not find statistically significant differences between the 2 doses of Bevacizumab evaluated.

A phase 1 study (the READ-1 Study, Ranibizumab for Edema of the macula in Diabetes, sponsored by the Juvenile Diabetes Research Foundation) of 20 patients with DME treated with repeated intravitreal injections 0.5 mg of ranibizumab, showed evidence of biological activity of ranibizumab in DME as well as safety and tolerability (Nguyen, et al. 2006). In the Phase 1 study, patients were given intravitreal ranibizumab at baseline and at months 1, 2, 4, and 6. Results showed that at month7, one month after the final administration of ranibizumab and the primary endpoint of the study, the median reduction of the excess foveal thickness was 97%, and there was a median improvement of 10 letters.

There have been no adverse events that were believed to be related to the study drug; in particular, intraocular inflammation was not observed.

The READ-2 Study is a Phase 2 randomized, multicenter clinical trial sponsored by the Juvenile Diabetes Research Foundation. The study enrolled 126 patients from 14 clinical centers throughout the United States.
Each study subject in the trial was randomized 1:1:1: to 1 of 3 treatment groups.

Group 1 (ranibizumab only)

Group 2 (Laser)

Group 3 (ranibizumab and laser)

The patients were followed every 12 weeks until month 24 (secondary time endpoint). At any study visit, if there is an increase of a specified amount of retinal thickness on OCT that meets re-treatment criteria, the patients will have the opportunity to receive a ranibizumab injection of ranibizumab injection plus laser 7 days later.

The re-treatment criteria for patients in all 3 randomized groups are an absolute retinal thickness in OCT central subfield of ≤ 250 mm (at time of study visit).

Combination Therapy

As diverse mechanism and patterns of DME are recognized, clinicians are using multi-model therapies to approach DME. In theory, targeting various pathologic mechanisms of DME with combination therapies may have a more lasting effect on reversing and maintaining a clinical benefit to patients. Commonly Focal Laser Photocoagulation is being combined primarily with Ocular Steroid therapy (either IVTA or PSTTA) or anti VEGF agents. This strategy seeks to take advantage of the more immediate effects of pharmacologic agents while employing laser therapy for long term stabilization. Anti VEGF agents have been used to salvage eyes refractory to steroid therapy, in eyes experiencing steroid related side effects, and more recently in combination with IVTA therapy with positive results. Pharmacological agents also used at the time of vitrectomy surgery help to prevent recurrent DME.

The present study also has tried to compare the efficacy of monotherapy with combined modalities of treatment. A comparative analysis of the response to all three modalities of treatment is given in TABLE 5

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>Group T</th>
<th>Group B</th>
<th>Group BT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vision</td>
<td>45 %</td>
<td>55 %</td>
<td>60 %</td>
</tr>
<tr>
<td>Resolution</td>
<td>45 %</td>
<td>59 %</td>
<td>69 %</td>
</tr>
<tr>
<td>IOP</td>
<td>17 %</td>
<td>5 %</td>
<td>22 %</td>
</tr>
<tr>
<td>Cataract</td>
<td>30 %</td>
<td>-</td>
<td>30 %</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>RD</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Recurrence</td>
<td>75 %</td>
<td>15 %</td>
<td>15 %</td>
</tr>
</tbody>
</table>

Thus the result of this study show that:

1. IVTA has an excellent transient effect of causing resolution. Recurrences in 75 %, elevated IOP in 17 % of cases point to the fact that IVTA should be advised with caution and the patients monitored regularly after intervention.

2. IVB is as efficacious or more so with respect to visual gain (45 % Vs 55 %) and resolution of CSME ( 45 % Vs 59 %). The incidence of elevated IOP in only 5 % and recurrence in 15 % point to the fact that IVB may be a better option to IVTA

3. Combining IVB with IVTA, did not have the expected effect of doubling the resolution and visual recovery. A higher incidence of glaucoma in 22 % makes this combination unsafe. The incidence of recurrence was same as in IVB group.

These results comprehensively prove that there is no added benefit of combining IVB and IVTA.

4. Greater degree of diffuse edema and presence of sub foveal serous RD are indicators of a favorable response to IVTA and IVB.
5. The prediction of poor visual prognosis included poor preoperative vision, HbA1C > 7 during the study period, plaques of hard exudates under fovea and presence of large cystoid spaces under fovea.

Our results compared favourably with those of Soheilian et al and Ahmadieh et al. who also demonstrated that there was no added beneficial effect of combining IVTA & antiVEGF therapy (Table 5).

Maximum reduction of central retinal thickness and maximum visual gain were obtained in eyes with greater degree of diffuse DME and in the presence of subfoveal serous RD. These eyes responded best to IVTA/ or IVB

<table>
<thead>
<tr>
<th>Author</th>
<th>Publication</th>
<th>Procedure</th>
<th>CRT</th>
<th>Vision</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pacola et al</td>
<td>BJO 2008</td>
<td>IVTA vs. IVB</td>
<td>decrease with IVTA</td>
<td>Increase with IVTA</td>
<td>IVTA SUPERIOR TO IVB on short term</td>
</tr>
<tr>
<td>Shimura .M et al</td>
<td>AJO 2008</td>
<td>IVTA vs. IVB</td>
<td>decrease with IVTA</td>
<td>Increase with IVTA</td>
<td>IVTA SUPERIOR TO IVB on short term</td>
</tr>
<tr>
<td>Soheilian et al</td>
<td>Retina 2008</td>
<td>IVB vs. IVB +IVTA vs. LASER</td>
<td>DECREASED</td>
<td>INCREASED</td>
<td>IVB superior to laser/ No benefit for adding TA</td>
</tr>
<tr>
<td>Ahmadieh .H</td>
<td>Graefes Arch 2008</td>
<td>IVB vs. IVB + IVTA</td>
<td>DECREASED</td>
<td>INCREASED</td>
<td>No benefit for adding TA / ↑ IOP IN 8.1%</td>
</tr>
<tr>
<td>Chakrabarti M et al</td>
<td>Retina 2008</td>
<td>IVB IV vs. TA vs. IVB + IVTA</td>
<td>DECREASED</td>
<td>INCREASED</td>
<td>No benefit for adding TA / ↑IOP IN 22%</td>
</tr>
</tbody>
</table>


12. Avitabile T, Longo A et al. Intravitreal Triamcinolone compared with macular laser grid photocoagulation for


Central Corneal Thickness and Relating Factors - A Prospective Observational Study

Dr. Anna Elias DNB, Dr. A. Giridhar MS DO, Dr. Mahesh G. MS DO DNB FRCS(Ed), Dr. Savita Bhat MS DO DNB MNAMS, Dr. Ramkumar DO MS

Abstract

Aim: To investigate the association between central corneal thickness and degree of myopia, corneal curvature, axial length and age.

Methods: It was a prospective observational study. 53 emmetropic subjects and 53 myopes were studied. Central corneal thickness was measured in all patients with an ultrasonic pachymeter. Axial length was measured using an A-scan and corneal curvature was measured using a Keratometer. CCT was correlated with degree of myopia, axial length, corneal curvature and age using the Karl Pearson's Correlation Coefficient.

Results: 106 patients (203 eyes) were recruited for the study. The age of patients ranged from 18 to 45 years, with a mean of 32 years. Myopia ranged from −0.5D to −17.5D with a mean of −2.8D. The mean CCT was 543.11 microns. The mean axial length was 23.69 mm and the mean corneal curvature was 43.68D.

Karl Person's Correlation Coefficient was as follows:
- CCT & degree of myopia : r = 0.11 p = 0.122
- CCT & corneal curvature : r = −0.23 p = 0.001
- CCT & axial length : r = 0.038 p = 0.944
- CCT & age : r = 0.0048 p = 0.696

Conclusion: There was no correlation between CCT & degree of myopia. There was a significant negative correlation between CCT & corneal curvature. There was no correlation between CCT & age or axial length.

Key Words: Myopia, CCT

Introduction

Although the true etiology of myopia is still unknown, the cornea is responsible for approximately two-thirds of optical refraction and its role in myopia has consequently been studied intensely over the years. Most of the changes in the myopic eye are located in the posterior segment namely, thinning of the retina and sclera, posterior staphyloma, choroidal atrophy and
a higher incidence of retinal detachment. Changes in the anterior segment associated with myopia are still under debate. The myopic eye is known to be longer than the normal emmetropic eye. If this is the result of general growth, one might expect the cornea to have grown thicker than normal. If instead, the myopic eye is larger due to a mechanism similar to that of a balloon being inflated, one would expect the cornea to be thinner than normal according to a simple stretching theory. An emmetropic eye could then be compared to a sphere and a myopic eye to a prolate spheroid.

Myopia is increasing in prevalence among the populations of East Asian origin. Estimates of the proportion of myopia in the young population of South East Asian countries range from 30% to 60%. With increasing rates of myopia, refractive surgery such as laser in situ Keratomileusis (LASIK) has become popular in Asia. When undertaking such surgery to correct myopia, central corneal thickness (CCT) is an important consideration to prevent the cornea from becoming too thin after treatment.

Studies that have attempted to investigate the effect of refractive errors on CCT have reported conflicting results. Some studies have reported no correlation between corneal thickness and level of myopia, whereas some studies have found the cornea to be thinner in more myopic eyes.

Central corneal thickness (CCT) indicates corneal physiologic health and affects the measurement of intraocular pressure (IOP). A thin central cornea is a risk factor for development of glaucoma in patients with ocular hypertension. A thin scleral bed in deeply excavated optic nerves has been the quintessential finding in advanced glaucomatous eyes. This has further led to a hypothesis that thinness of the corneas may be an indication of generalized weakness of the ocular integument associated with longer eyes with a thin scleral bed of lamina cribrosa. Studies have tried to determine if thin corneas are associated with longer globes.

**Aim**

The purpose of the study was to determine the correlation between CCT and 4 variables, namely, degree of myopia, corneal curvature, axial length and age of the patient.

**Materials & Methods**

A prospective observational study was done. 106 consecutive patients were enrolled in the study; 53 patients were myopes and 53 patients were emmetropes. Patients were in the age group 18 years to 45 years. Subjects with previous ocular surgery, glaucoma or any disease affecting the corneal thickness were excluded.

All patients underwent a complete ophthalmic evaluation. Central corneal thickness was measured with an ultrasonic pachymeter (Pacscan 300p, digital biometric ruler, Sonomed). Axial length was measured using an A Scan (Echorule2, Biomedix). Corneal curvature was measured using a Keratometer.

Statistical Analysis was done using SPSS V.11 and Microsoft Excel. Correlation between CCT and four factors namely, degree of myopia, axial length, corneal curvature and age of patient was studied using Karl Pearson’s correlation co-efficient. A probability of 0.05 was considered statistically significant.

**Results**

106 patients (203 eyes) were recruited for the study. 53 patients were myopes and 53 patients were emmetropes.

<table>
<thead>
<tr>
<th>Table 1 Demographic Features of Study Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
</tr>
<tr>
<td>No. of Eyes</td>
</tr>
<tr>
<td>No. of Myopes</td>
</tr>
<tr>
<td>No. of Emmetropes</td>
</tr>
<tr>
<td>Age: Range (years)</td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Sex: Females</td>
</tr>
<tr>
<td>Males</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Demographic Features of Myopia &amp; central corneal thickness – split in groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myopes (Diopeters)</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>0 – 3</td>
</tr>
<tr>
<td>3 – 6</td>
</tr>
<tr>
<td>More than 6.0</td>
</tr>
<tr>
<td>CCT (Microns)</td>
</tr>
<tr>
<td>&lt; 500</td>
</tr>
<tr>
<td>500 – 550</td>
</tr>
<tr>
<td>550 – 600</td>
</tr>
<tr>
<td>&gt; 600</td>
</tr>
</tbody>
</table>
Table 3. Characteristics of central corneal thickness & Myopia in patients central corneal thickness (Microns)

<table>
<thead>
<tr>
<th>Range</th>
<th>Mean (SD)</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>453-620</td>
<td>543.11 (30.61)</td>
<td>541</td>
</tr>
</tbody>
</table>

Myopia (Diopters)

<table>
<thead>
<tr>
<th>Range</th>
<th>Mean (SD)</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>-2.8 (2.65)</td>
<td>-2</td>
</tr>
</tbody>
</table>

Table 4. Characteristics of Corneal Curvature & Axial Length of patients.

<table>
<thead>
<tr>
<th>Corneal Curvature: (Diopters)</th>
<th>Range</th>
<th>Mean (SD)</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>39.37 – 47.50</td>
<td>43.68 (1.41)</td>
<td>43.62</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Axial Length (MM)</th>
<th>Range</th>
<th>Mean (SD)</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.03 – 30.88</td>
<td>23.69 (1.31)</td>
<td>23.48</td>
<td></td>
</tr>
</tbody>
</table>

Table 5. Correlation between central corneal thickness & relating Factors.

<table>
<thead>
<tr>
<th>Karl Pearson’s Correlation Analysis</th>
<th>Correlation Co-efficient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCT &amp; degree of myopia</td>
<td>0.11</td>
<td>0.122</td>
</tr>
<tr>
<td>CCT &amp; corneal curvature</td>
<td>-0.23</td>
<td>0.001</td>
</tr>
<tr>
<td>CCT &amp; axial length</td>
<td>0.0048</td>
<td>0.944</td>
</tr>
<tr>
<td>CCT &amp; age</td>
<td>0.038</td>
<td>0.696</td>
</tr>
</tbody>
</table>

Discussion

The study attempted to determine the correlation between CCT and four variables, namely degree of myopia, corneal curvature, axial length and age of the patient.

The mean (SD) CCT was 543.11 (30.61) microns. This is comparable with similar studies. Fam et al\(^2\) in a study on 714 Chinese patients had a mean of 534.5 microns. Chang’s \(^8\) series had a mean of 533 microns, whereas Vijaya et al. \(^9\) reported the mean (SD) CCT in a normal rural South Indian population to be 505.9 (31.10) microns.

This study showed no statistically significant difference between CCT in myopes and emmetropes. There was no correlation between degree of myopia and CCT (Pearson r = 0.11, P=0.122). This result is in agreement with previous studies.
agreement with majority of previous studies (1). Von Bahr\(^4\) first generated interest in the correlation between myopia and CCT in 1956, when he reported thinner corneas in myopia less than \(-4\)D. Similar findings were also reported by Tokoro et al\(^{10}\), Chang et al\(^8\), Touzeau et al, Srivannaboon and Alsbirk from Greenland. However other studies by Liu Z and Pflugfelder\(^{11}\), Price et al\(^{12}\) and Pedersen et al\(^1\) could find no correlation between CCT and degree of myopia. Table 6 gives an overview of published papers with information on myopia and central corneal thickness.

There was a negative correlation (Pearson \(r = -0.23\)) \((P = 0.001)\) between CCT and corneal curvature. The correlation was significant at the 0.01 level (2-tailed). Similar results were reported by Atsuo Tomidokoro et al in the Tajimi Study from Japan\(^{13}\). A study done on Singaporean children\(^{14}\) showed that the radius
of corneal curvature correlated with CCT (Pearson \( r = 0.19, P < 0.001 \)) significantly.

There was no correlation between CCT and axial length. Mitsugu Shimmyo et al in their study, corneal thickness and axial length, studied ocular parameters of 1084 eyes. They found no statistically significant association between CCT and axial length. Subgroup analysis by age, gender and race failed to show an association.

There was no statistically significant association between CCT and age. (Pearson \( r = 0.038, P = 0.696 \)). Other studies have shown CCT to be inversely related to age. In the study by Eun Suk Lee et al, CCT of Korean patients with glaucoma showed an inverse relationship between age and CCT (Pearson \( r = -0.12; P < 0.0001 \)). CCT decreased by 2.8 microns per decade. This relation was also significant in the multivariate model (\( P=0.01 \)).

Myopia is increasing in prevalence and may be a growing problem in the future. Investigations in Denmark, Iceland, Japan and North American aboriginal populations have indicated the increasing prevalence of myopia. Consequently there is a higher rate of refractive surgeries to correct myopia. With Lasik there is a general concern that one should not thin the cornea further than a given amount. It is therefore prudent to measure central corneal thickness prior to surgery.

A thin central cornea is a risk factor for the development of glaucoma in patients with ocular hypertension. In the Ocular Hypertension Treatment Study (OHTS), a multivariate model that included IOP, CCT was the most powerful component of the predictive model. CCT is the most heritable aspect of ocular structure (more than refraction, axial length or optic disc size), suggesting it is under exquisite genetic control.

**Conclusions**

This study has shown that CCT has no correlation with degree of myopia. CCT was significantly associated with corneal curvature. There was no association between CCT and axial length or age.

**References**

Anatomical and Visual Acuity Results of Macular Surgery

Dr. Gopal S Pillai MS, Dr. Natasha Radhakrishnan MS, Dr. Tufela Shafi MS

Aims: To evaluate the anatomical and visual acuity results of macular surgery

Methods: Vitrectomy performed for macular pathologies between January 2006 and March 2008 were retrospectively analyzed. OCT patterns, central macular thickness and visual acuity were evaluated preoperatively, at 1st week, 1st month and 3 months respectively. Pre and post operative macular thickness and visual acuity were statistically compared.

Results: 40 eyes of 40 patients underwent 25 Gauge vitrectomy for macular holes (n=22), ERM (n=10) and vitreomacular traction (n=8). Visual acuity improved in all the cases. In 80% of cases, visual acuity improved by 1 line and in 50% of cases, visual acuity improved by 2 lines or more. In 40% of cases, visual acuity improved by more than 3 lines. OCT showed significant reduction of macular thickness in the ERM and VMT group (p<0.05). Macular holes showed significant closure rates (81.81%).

Conclusions: Optimally performed macular surgery had good visual and anatomical results. OCT helped significantly in patient selection and surgical decision making. Preoperative visual acuity better than 6/60 was a good prognostic indicator.

Introduction

Macular surgery has become a common treatment for idiopathic macular holes, epiretinal membranes, vitreomacular traction and clinically significant macular edemas. The refinement of techniques has improved the success rate of surgery with fewer complications. The procedure typically consists of a pars plana vitrectomy, removal of the posterior hyaloid, membrane dissection or epiretinal membrane peeling and fluid-air or fluid-gas exchange with some period of prone positioning following surgery. A number of surgical technique by variations have been used in an attempt to improve anatomic success (closure of the macular hole) and functional success (improved visual acuity).

Some studies have suggested that removal of the internal limiting membrane (ILM) is helpful in improving the percentage of eyes that achieve closure of the macular hole. In contrast, one study found no improvement in macular hole surgery when the ILM was peeled. There is controversy about whether the ILM should be stained with indocyanine green (ICG) or other agents, such as trypan blue. Staining the ILM improves the ability to completely remove the ILM and usually decreases the operative time needed to remove the ILM during vitrectomy. Some studies have found that ICG-assisted removal of the ILM improves results, whereas other have found that ICG makes no difference. Some studies have found that ICG has a negative effect on the results of macular hole surgery. A recent randomized study found no
significant differences in visual acuity comparing ICG with trypan blue.20

After the advent of OCT, more and more cases of vitreomacular traction and epiretinal membranes are diagnosed as well as managed. The anatomical difficulty of the cleavage planes are easily made out by the OCT.

In this study, we looked at the anatomical and visual results of the macular surgeries

Methods

The anatomical and visual acuity results of macular surgery were evaluated in a retrospective, consecutive case series of 40 eyes that underwent surgery between 2006-2008. The study was performed in the author’s practice and was in conformity with the Declaration of Helsinki. The diagnosis of a macular hole, epiretinal membrane or VMT was made by the surgeon and confirmed by OCT. All patients were treated by a single surgeon (GSP) using an Alcon Accurus 25 gauge surgical system.

Patients were eligible if they had a primary idiopathic or traumatic macular hole, epiretinal membrane or vitreomacular traction with symptoms of blurred vision of 1 year or less. Eyes with other significant macular diseases such as diabetic retinopathy or prior vitrectomy were excluded. The preoperative data collected included patient age, macular hole stage (confirmed intraoperatively), central macular thickness by OCT, visual acuity measured on a Snellen chart with current correction, and intraocular pressures. Patients were examined postoperatively at 1 day, 1 week, 4 weeks and 3 months. Additional postoperative visits were performed as necessary. Results of a standard ophthalmologic examination including current corrected Snellen visual acuity, status of the macular hole, intraocular pressures, and any postoperative complications were also recorded.

The primary outcome variables were central macular thickness and visual acuity at 3 months. Categorical variables were compared using chi-square tests, and numerical variables were compared using t tests or analysis of variance with post hoc testing for multiple comparisons, when appropriate.

The basic surgical technique included a pars plana vitrectomy using a 25-gauge vitrectomy system in all eyes with removal of the posterior hyaloid. Active aspiration with the vitrectomy probe or a vacuum cleaner needle was used to create the posterior vitreous detachment in all eyes. The vitreous was removed in the periphery as far as could be safely reached to allow a large gas bubble fill. This was followed by epimacular dissection techniques.

ERM removal was performed with microforceps to pinch and lift the ERM. Some cases were stained with triamcinolone and some cases were not.

The goal was to remove the ERM completely around the macula. Confirmation of ERM removal was primarily determined by the presence of a pale edema in the perimacular retina where the ERM had been successfully removed. This allowed the “edge” of the removed ERM to be identified in some eyes so further removal could be performed.

ILM was stained by triamcinolone only because ICG was used to stain the ILM and remove all of the perimacular ILM in many studies and was found to be toxic. After performing the core vitrectomy, triamcinolone was injected into the vitreous and posterior hyaloid was stained. After inducing a PVD, the ILM was stained again in selected cases. In cases where ILM was visible with the stain, it was not restained.

Removal of the ILM was started usually by grasping the ILM with flat-tipped vitreoretinal forceps and lifting the ILM until a break in the ILM developed. The edge of the ILM was grasped with the forceps and peeled circumferentially around the macular hole for a distance of at least 3 disc diameters. Occasionally, a sharp microvitreoretinal blade was used to create a small nick in the ILM to lift an edge to grasp with the forceps. Rarely would ILM removal extend beyond the temporal vascular arcades. A fluid-air exchange was then performed, and residual intravitreal fluid was again aspirated about 5 minutes after the initial fluid-air exchange to try to obtain a complete gas fill.

Results

Mean age, preoperative visual acuity, duration of symptoms and intraocular pressure were identical in all the three groups. However central macular thickness was significantly higher in the vitromacular traction
group when compared to the ERM group. Central macular thickness was not measured in the macular hole group, but the closure rates were studied.

Among the 22 macular holes, there were 5 at stage 3 and 17 cases at stage 4. The differentiation between stage 3 or 4 was made by OCT preoperatively and also confirmed during surgery.

The macular hole was closed at 3 months in 18 of 22 eyes (81.8%) in the MH group. In 4 cases the hole became smaller in size, but remained open. Visual acuity was improved in all cases by at least 1 line. In 14 cases (63.63%) acuity improved by more than 2 lines and in 8 cases (36.36%) acuity improved more than 3 lines. All the 4 holes which remained open were in stage 4 and were over 700 microns in diameter.

The average central macular thickness in the epimacular membranes was 342.4 microns. The mean visual acuity of these cases were 6/36. The average postoperative visual acuity improved to 6/18. The average central macular thickness decreased to 208.4 microns after 3 months of surgery. (p<0.05)

In cases with vitreomacular traction, the average central macular thickness was 459.3 microns and the mean visual acuity was 6/60. Mean postoperative central retinal thickness decreased to 203.4 microns and the mean visual acuity improved to 6/18. (p<0.05)

Visual acuity improved in all the cases. In 80% of cases, visual acuity improved by 1 line and in 50% of cases, visual acuity improved by 2 lines or more. In 40% of cases, visual acuity improved by more than 3 lines.

**Discussion**

The success of macular surgery has improved over the past 20 years with refinements in surgical techniques with a higher likelihood of achieving macular hole closure and improving visual acuity compared to early studies. Some of the early innovators of macular hole surgery, such as Kelly and Wendel, advocated removal of what they described as cortical vitreous strands from the perimacular retina before the fluid-air exchange to help release any traction from residual cortical vitreous. Their technique resulted in limited dissection around the edges of the macular hole, usually with forceps. The success rate for closing macular hole was 73% in their early series, so they and other surgeons attempted to refine their surgical technique to achieve macular hole closure and visual acuity improvement in a larger percentage of eyes.

Adjuvants such as transforming growth factor β2, plasma, serum, and platelet lysate were used extensively in the 1990s to try to improve the results of macular hole surgery, but the use of adjuvants have largely been abandoned. It was seen that ILM peeling seemed most beneficial in eyes with larger macular holes. Most recent studies have confirmed that ILM removal improves the results of macular hole surgery.1–6, and one study that found no improvement had a sample size of only 22 eyes.7

The role of ICG staining of the ILM is more controversial where some studies found a benefit (or at least no harm) while others found evidence of toxic effects, resulting in poorer visual acuity or increased central scotomas. This suggests that the concentration of ICG, the way it is used to stain the ILM around the macular hole, and how completely the ICG is removed may have a role in potentiating or avoiding the harmful effects of ICG. ICG can cause macular toxicity, as was noted with early ILM staining techniques for macular holes that used unfiltered ICG. The technique by which ICG is used may influence whether ICG toxicity occurs in an individual eye, although some eyes may be more susceptible to ICG toxicity. The present study attempted to minimize the amount of ICG in the vitreous cavity by staining with triamcinolone only. Further this study used 25 gauge vitrectomy which has made the postoperative recovery of the patient very smooth and fast.

The current study has several limitations inherent in a retrospective, nonrandomized study. One limitation was a smaller sample size in eyes with macular membranes and VMT compared to the macular holes. Because the series was a consecutive series, little selection bias would be expected, since the same technique was used...
in all eyes with macular problems. All other features of the macular surgery were identical, such as the surgeon, gauge of the vitrectomy system (25 gauge), intraocular gas tamponade and prone positioning (1 week). Another limitation is that visual acuities were taken using snellen acuities. A third limitation is that cataracts were not removed in all phakic eyes by the last follow-up visit. The author believes that the study limitations would not likely change the primary findings of the study.

Macular surgery with 25 gauge vitrectomy has become a day care surgery and no admission is needed for its purpose. We have understood that the eyes with better visual acuities tended to do better.

Conclusions
Macular surgery when performed optimally had good visual and anatomical results. A judicious case selection was possible with OCT screening prior to surgery. Macular holes had good closure rates and OCT clearly demonstrates the same. OCT further demonstrates the reduction of thickness and normalisation of OCT after removal of ERM and VMT. Preoperative visual acuity better than 6/60 was a good prognostic indicator.

References
Central Retinal Venous Occlusion - A Clinical Study

Dr. Raju K V MS, Dr. Anju Abdulkhader MS

Abstract

Aim: To study the clinical profile, visual outcome and sequelae of central retinal vein occlusion.

Materials and Methods: The study was conducted on thirty patients attending the Ophthalmology OP of Calicut Medical College during a period of one year. Screening for risk factors like hypertension, diabetes, hyperlipidemia and collagen vascular diseases was done. All patients were tested for best corrected visual acuity, Slit lamp, Intraocular pressure, Gonioscopy and Fundus. Laboratory examination for hematological parameters was done in all cases and electrocardiography and echocardiography were taken whenever relevant. Systemic risk factors were treated in consultation with the concerned specialties.

Results and Conclusions: Central retinal vein occlusions are a disease of the elderly population. Non ischemic CRVO is more common than ischemic type. Most important risk factors identified were hypertension, diabetes and hyperlipidemia. Initial visual acuity is a good predictor of final visual outcome. Neovascular glaucoma developed 4-6 months after occlusion. Early detection of rubeosis and timely intervention with PRP can prevent onset of complications.

Keywords: CRVO, visual outcome, sequelae

Introduction

Central retinal venous occlusion is among one of the most devastating ocular conditions leading to permanent visual loss in elderly population. The visual outcome of central retinal venous occlusion is variable, ranging from stable but reduced vision to profound visual loss. This is a case series study of central retinal venous occlusion in a tertiary referral hospital community. In this study, an attempt has been made to correlate the clinical profile, various risk factors, visual outcome and ocular sequelae of central retinal venous occlusion.

Materials and Methods

The present study was conducted in Calicut Medical College on thirty patients diagnosed to have central retinal venous occlusion over a period of 1 year. Patients with prior episodes of central retinal venous occlusion were also included in the study.

A detailed history with regard to visual loss, past history with relevance to systemic diseases like diabetes, hypertension, bleeding disorders, collagen vascular diseases were recorded in detail. Ocular risk factors like POAG and ocular hypertension were also noted.

Ocular examination included recording of best corrected visual acuity, examination of eyes under torch light, measurement of intra-ocular pressure, slit lamp...
examination for neovascular glaucoma and dilated fundus examination using direct and indirect ophthalmoscopes. Whenever possible fundus photographs and fluorescein angiography were taken.

Laboratory examination including complete hemogram, fasting blood sugar and serum lipid profile were done as basic investigations. Whenever indicated, special tests like X-ray chest, ECG, Echo were taken. Other tests like Mantoux, ANA, sickling test, antiphospholipid antibody, protein C were done whenever relevant.

Patients were followed up at 1 month, 3 months and at 6 months. During each visit, the visual acuity, slit lamp examination, IOP measurement and fundus examination were recorded and sequelae like fundus neovascularization, rubeosis iridis and neovascular glaucoma were noted.

**Observations**

Majority of cases of CRVO were nonischemic and constituted 63.3 % of the total number of cases. Rest 36.7 % of the cases were of ischemic variety. Patients presenting with CRVO ranged from 32 to 80 yrs. Mean age of patients presenting with nonischemic CRVO was 51.7 ± 7.8 yrs and that of ischemic CRVO was 61.5 ± 9.7 yrs (Table 1). Patients with papillophlebitis were also included in the study, which may account for higher incidence of nonischemic CRVO among the younger population. Maximum incidence of ischemic and nonischemic CRVO was between 50-59 yrs.

Both ischemic and non ischemic CRVO were more common in males. In ischemic CRVO, 81 % were males and this was found to be statistically significant (p< 0.05). In nonischemic 63 % were males (p>0.05). Maximum incidence of CRVO among males and females was in 50 – 59 age group. The left eye was involved more commonly (57 %). In one patient there was evidence of old venous occlusion in the other eye. Among the patients with CRVO, 90 % presented with sudden painless visual loss, whereas 7 % complained of headache and blurring of vision. In 3 % it was incidentally detected. Patients presenting with sudden painless visual loss usually had ischemic CRVO or macular hemorrhage.

CRVO occurs predominantly in elderly patients. CRVO is said to be associated with various systemic disorders. In our study, hypertension was the commonest. It was seen in 56.6 % of patients (Table 2). Thirty six percent were diabetic. Both DM & HT were seen in 13 %. The hypertensives in the study were on regular treatment. Diabetic patients had irregular blood sugar levels even though they were on antidiabetic drugs. Other systemic diseases observed were hyperlipidemia and coronary artery disease. One patient had mitral valve prolapse. The most important positive investigation was serum lipid profile. Twenty seven percent had elevated serum cholesterol level with no systemic evidence of hyperlipidemia. Three patients had raised ESR but no systemic illness. One patient had increased PCV. Local risk factors were also noted. This included POAG (6 %) in ischemic CRVO and NTG (3.3 %) in nonischemic CRVO.

The visual outcome was closely monitored. Patients with ischemic CRVO had a uniformly decreased vision at presentation with majority of cases having visual acuity < 4/60. At 3 months, 72% remained with vision < 2/60. At 6 months, 63% had vision < 2/60 with 2 patients developing NVG. (Table 3) Patients with

<table>
<thead>
<tr>
<th>Table 1: Age distribution of CRVO</th>
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<tr>
<td>Age group</td>
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<tr>
<td>-----------</td>
</tr>
<tr>
<td>30-39</td>
</tr>
<tr>
<td>40 – 49</td>
</tr>
<tr>
<td>50-59</td>
</tr>
<tr>
<td>60-69</td>
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<tr>
<td>70-79</td>
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<tr>
<td>80 &amp; above</td>
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<th>Table 2: Systemic factors</th>
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<tr>
<td>Systemic diseases</td>
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<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>DM</td>
</tr>
<tr>
<td>DM &amp; HT</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Coronary artery disease</td>
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<td>Mitral valve prolapse</td>
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<tr>
<th>Table 3: Visual outcome in ICRVO over 6m</th>
</tr>
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<tbody>
<tr>
<td>Visual acuity</td>
</tr>
<tr>
<td>--------------</td>
</tr>
<tr>
<td>PL-CFCF</td>
</tr>
<tr>
<td>1/60-2/60</td>
</tr>
<tr>
<td>3/60-4/60</td>
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<td>5/60-6/60</td>
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ischemic CRVO presented with a very poor visual acuity which persisted even at 6 months of follow up. Visual acuity worsened with onset of neovascular glaucoma.

In nonischemic CRVO, at presentation, 57.8% had vision <6/60 and 31.5% had vision between 6/18 – 6/36. 10.5% had good vision ≥ 6/12. At three months, 68.4% had moderate vision between 6/18 – 6/36 while 15.7% had vision < 6/60. At six months, 57.8% had vision between 6/18 – 6/36 and 26.3% had vision ≥ 6/12. (Table 4) Eighty percent had improved to moderate to good visual acuity at 6 months. 15.7% had persistently poor vision. Poor visual acuity at 6 months was noted to be due to persistent macular oedema, macular haemorrhage or ischemic maculopathy.

Table 4: Visual outcome in NICRVO over 6m

<table>
<thead>
<tr>
<th>Visual acuity</th>
<th>At initial presentation</th>
<th>3months</th>
<th>6months</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td>&lt;6/60</td>
<td>11</td>
<td>57.8</td>
<td>3</td>
</tr>
<tr>
<td>6/18 – 6/36</td>
<td>6</td>
<td>31.5</td>
<td>13</td>
</tr>
<tr>
<td>≥ 6/12</td>
<td>2</td>
<td>10.5</td>
<td>3</td>
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</table>

**Sequelae of CRVO**

Rubeosis iridis was noted in 18% of patients with ischemic CRVO within four to seven months and they went on to develop neovascular glaucoma one to two months later. Optic atrophy was noted in one patient with co-existing POAG. Nine percent of patients developed NVE. Macular edema persisted in 27% of patients and vision remained poor in these patients.

In patients with nonischemic CRVO who regained good vision at six months, sequelae noted were formation of microaneurysms (21%) and collaterals (16%). Persistence of macular edema and pigment mottling led to reduced visual acuity. No cases of nonischemic CRVO in the study developed neovascularization of the anterior or posterior segment.

**Discussion**

CRVO is predominantly a disease of the elderly with more than 90% of CRVO patients being older than 50 years, but it has been reported in all age groups. In our study the mean age of presentation of nonischemic CRVO was 51.7 years and that of ischemic CRVO was 61.5 years. The mean age of onset of vein occlusion was 63 years in one large case series study by Hayreh et al. He also noted that patients with nonischemic CRVO are about 5 years younger than those with an ischemic occlusion.

Males predominate over females in most of the published series of CRVO. In our series the male-female ratio in nonischemic CRVO was 63:37, in ischemic CRVO 81:19.

Most patients presented with sudden painless visual loss. Patients with nonischemic CRVO usually presented with milder symptoms. Left eye was more commonly affected than right, this difference was more in ischemic CRVO. In a large study of 544 eyes with nonischemic CRVO and 191 eyes with ischemic CRVO by Hayreh et al, ischemic CRVO showed a trend toward more left eye involvement, with no difference in the nonischemic CRVO.

Various risk factors and associations have been described for CRVO. They may be local (in the eye or central retinal vein), systemic, or hematologic. It is well established that CRVO is significantly more common in patients with raised intraocular pressure (IOP) and glaucoma. Two of our patients (6%) with CRVO had POAG and one patient (3%) had NTG. According to Dreyden et al, 40% or more of patients with CRVO had POAG and one patient (3%) had NTG. According to Dreyden et al, 40% or more of patients with CRVO had preexisting OAG or this condition developed during follow up. In a study by Hayreh et al, 22% of patients with CRVO had IOP of more than 22 mm Hg.

Many systemic conditions have been associated with CRVO. Important systemic risk factors observed in our study were hypertension, DM, hyperlipidemia and coronary artery diseases. In the Eye Disease Case-Control Study Group they found a significant association of diabetes mellitus, cardiovascular disease, and arterial hypertension in ischemic CRVO and arterial hypertension in nonischemic CRVO.

Hematologic abnormalities have been documented in various types of venous occlusions. Lupus anticoagulant factor, antiphospholipid antibody syndrome, protein C deficiency and activated protein C resistance have been cited as risk factors for CRVO in young. No specific etiology could be found in our patients in younger age groups <40 who presented with CRVO. Most of them had nonischemic type of occlusion. CRVO in young individuals is often considered a distinct entity and...
many of these patients have no identifiable underlying cause despite extensive investigations. A presumed inflammatory cause is proposed.¹⁰

Patients with ischemic CRVO (Fig: 1) presented with very poor visual acuity, which persisted even at 6 months of follow up. In six percent of patients with CRVO who developed neovascular glaucoma, visual acuity worsened after the onset of glaucoma. According to Hayreh, vision in ischemic CRVO was < 6/60 in majority of cases with a central scotoma. In nonischemic CRVO 84% had moderate to good visual acuity (> 6/36) while the rest 16% had visual acuity < 6/60. Reduced visual acuity at initial presentation was due to macular oedema or macular haemorrhage. Some patients had associated conditions like ARMD. According to study by Hayreh, in nonischemic CRVO, final visual acuity was 6/18 or better in 65 %, 6/36 to 6/60 in 20 %, and <6/60 in 15%.³ CVOS study has reported that visual acuity outcome in CRVO was largely dependent on initial acuity ¹¹. Eyes with good initial vision have a good chance of maintaining excellent vision while a poor visual outcome is seen in those who had poor initial acuity.

18 % of patients with ischemic CRVO developed NVI within 4 months and they all developed NVG within 1 to 2 months of appearance of new vessels. NVE (Fig: 2) and sheathing were noted in 9 %. Persistent poor visual acuity in ischemic CRVO was due to development of NVG and persistent macular oedema. Commonest sequelae in nonischemic CRVO were development of microaneurysms (21 %) and collaterals (16 %) (Fig: 3) in those whom vision improved. Persistence of macular oedema led to non improvement of vision.

Rubeosis iridis or NVG was not noted in any of the patients with nonischemic CRVO. According to literature, incidence of rubeosis is 20 % among CRVO.¹²,¹³,¹⁴ Among ischemic eyes, rubeosis with or without NVG occur in 45 to 80 % and this usually develop by 4-7 months of the occlusion. In nonischemic eyes the rate of iris neovascularisation has been reported to be less than 5 %. Neovascularisation of optic disc or retina is a rare complication but has been reported in 24 % of ischemic CRVO ¹⁵.

**Conclusion**

CRVO is a multifactorial disease, common among elderly population. Nonischemic variety accounts for most cases of CRVO. Preponderance of hypertension, diabetes mellitus, and hyperlipidemia were seen in patients with CRVO. No specific etiology could be elucidated for CRVO in younger patients. Eyes with good initial vision have a better chance of maintaining excellent vision while a poor visual outcome is seen in those who had poor initial acuity.
References


Management of Subluxated Lenses

Dr. Sonia Rani John DNB, Dr. Meena Chakrabarti MS DO DNB, Dr. Arup Chakrabarti MS

Introduction

Subluxation of lens signifies partial displacement of crystalline lens or cataractous lens from its central position in the pupillary area.

![A subluxated clear lens](image1)

Fig. 1. A subluxated clear lens

Etiology

Subluxation of lens may be congenital or acquired. Congenital subluxation of lens can occur as an isolated anomaly or associated with heritable disorders. The acquired subluxation of lens may occur due to hypermaturity of cataract, trauma, stretching, pull and degeneration of the zonule.\(^1,2,3,4\)

Signs of Zonular damage should be sought in every patient especially if there is history of ocular trauma or pseudo-exfoliation (PXF).

- Systemic abnormalities associated with zonular weakness (Marfan’s, Weil Marchesani, Homocysteinuria) may not always be present. Hence a loose cataract may be overlooked with severe surgical consequences. Waneela MV Margress et al\(^5\) describe 5 subtle signs of zonular damage that should be looked for as a warning sign. These includes
  1. Visibility of the lens equator during eccentric gaze.
  2. Decentered nucleus in primary position
  3. Iridolenticular gap.
  5. Focal iridodonesis.

Obvious signs of subluxation are less easy to miss and includes phacodonesis, vitreous prolapse, iridodonesis, and lens subluxation.

![Anterior segment images demonstrating various degrees of subluxation of the crystalline lens](image2)

Fig. 2. Anterior segment images demonstrating various degrees of subluxation of the crystalline lens

Even without development of cataract, subluxation of the crystalline lenses can induce significant visual symptoms such as large refractive errors, anisometropia, or amlyopia in a child undergoing visual development. Historically surgical treatment for subluxated lens was undertaken with great caution.
because of attendant complications and poor visual outcome.

Surgical management was limited to Surgical iridectomies, Laser iridectomy, discission, or ICCE.

Patients who underwent ICCE were either left aphakic or prescribed aphakic correction, or CL or were advised Epikeratophakia. An ACIOL in an older patient was another option that was considered. These patients ended up with graft rejection, retinal detachment, glaucoma and gross visual loss.

Advances that have been made in the surgical management of patients with weak/missing zonules are SICS, Pars plana lensectomy and aphakic CL wear or 2nd ACIOL implantation, suturing PCIOL to ciliary sulcus/posterior aspect of iris, introduction of CTR (capsular tension rings), MCTRs (modified capsular tension rings), CTSs (capsular tension segments) and the possibility of small incision phacoemulsification with in the bag IOL implantation.

Management

Timing of surgery is critical and is governed by the amount of subluxation. Children who are in their visually formative years, need early surgery if they have a large amount of subluxation. Early surgery and visual rehabilitation prevents development of amblyopia or permits early initiation of amblyopia therapy. In children with minimal amounts of subluxation that is compatible with normal visual development can be followed up without surgical intervention.

An initial assessment of the BCVA for distance and near should be performed. Several attempts at refracting the child is necessary before deciding whether he is seeing best with the phakic or aphakic correction. If the subluxation is not large and there is no eminent danger of the lens dislocating posteriorly or anteriorly observation with institution of amlyopia therapy is all that is necessary.

If amlyopia cannot be effectively treated by conventional means such as glasses, contact lens, or patching, surgical treatment is advisable.

Surgical treatment is also advisable if there is
1. Progressive subluxation.
2. Lens bisects pupil
3. Threatened posterior or anterior dislocation
4. Any case of poor visual acuity in an older child or adult. attributable to subluxated lens.

Preoperative evaluation

Comprehensive preoperative examination is necessary to increase the chances of surgical success.

a) The surgeon should make a note of the “area of zonular weakness” by drawing it. He should also
   i. Characterize the areas of zonular weakness in terms of degree of involvement.
   ii. Location of the defect.
   iii. Presence / absence of vitreous prolapse.
   iv. Presence / absence of phacodonesis: Phacodonesis is most dramatic prior to pupillary dilation, as dilation often stabilizes the CB and iris, dampening any iris - lens movement.

A surgeon should be wary of inferiorly subluxated lens as such subluxation is often indicative of 360° of very significant zonular damage combined with the effect of gravity. When the patient is made to lie down the lens will fall back posteriorly. In this situation it is unlikely that the surgeon will be able to remove the lens while preserving the capsular bag for PC IOL support. PPL should be considered in these cases.

b) Gonioscopy should be performed in older children to access for angle recession, synchiae etc if ACIOL implant is considered.

Patients should be counseled with regards to a sutured PCIOL / or a CTR.

c) The presence of comorbid conditions affecting visual outcome should be assessed.

d) Evaluation by internists to rule out systemic associations is also necessary.

e) Discontinuing oral anticoagulants as most if these patients have also cardiovascular diseases and may be on anticoagulant therapy.

A thorough ocular examination including a cycloplegic refraction, slit-lamp examination and detailed fundus evaluation should be done to assess the extent of subluxation and to plan the treatment approach. The
presence of iridodonesis, phacodonesis, lens edge and visible zonules, and relatively deep or an irregularly deep anterior chamber should be noted. If the lens is clear, look for irregular red reflex, displacement of “Y” sutures, and high refractive error. Intraocular pressure recording (IOP) and gonioscopy must be carried out.

Systemic examination is important. A thorough family history, complete cardiovascular and musculoskeletal evaluation may be needed in Marfan’s syndrome. In doubtful cases sodium nitroprusside test for homocystinuria must be done before subjecting the patient for general anesthesia.

Management of Clear Subluxated Lens
Conservative Approach

A minimally subluxated crystalline lens requires only observation and periodic follow-up. If the subluxation causes visual disturbances due to induced astigmatism or myopia, the management includes a cycloplegic refraction and subjective verification with prescription of full correction. Examination of undilated, aphakic and phakic portions of the pupil should be done to ascertain whether the patient has got unilateral diplopia or confusion. Appropriate spectacle correction with aphakic glasses, contact lenses or prisms is provided which gives better visual improvement than phakic correction. Argon or Nd:YAG laser iridoplasty can be tried to enlarge the aphakic portion of pupil.

Management of Subluxated Cataract

Lens extraction via a small incision PE and PCIOL implantation should be attempted in every case and the basic surgical principles are described below.

Surgical principles to be understood include

1. Incision should be placed away from area of zonular weakness to help reduce stress on the existing zonules during PE. Unfortunately majority of the patients have generalized zonular weakness. In this situation the surgeon should place the incision in the gradient opposite to the zone of maximum zonular weakness. However, the surgeon should not jeopardize his surgical ability by operating in a meridian he is uncomfortable with.

2. Surgeon should work through the smallest incision possible without compromising the ability to perform necessary maneuvers. This will minimize fluid egress through the incision and prevent anterior chamber collapse. The initial AC entry should be just large enough to introduce a visco cannula.

3. A generous amount of highly retentive viscoelastic is placed over the area of zonular dialysis to help tamponade the vitreous and to maintain a deep non collapsing AC.

4. The capsulorhexis is started in an area remote from the dialysis to help utilize the counter acting forces of the remaining healthy zonules.

5. A second instrument is used for counter traction or to push the lens into view if it is significantly decentered under the iris.

6. When there is extensive zonular loss or weakness it may be a good strategy to start the rhesis by cutting the anterior capsule with a sharp tipped blade.

7. A rhesis of 5.5 mm – 6mm will facilitate all manipulations of the nucleus.

8. Hydrodissection: should be performed carefully yet thoroughly to maximally free the nucleus thereby decreasing zonular stress while manipulating the nucleus.

9. A soft nucleus can be completely prolapsed into the anterior chamber to simplify removal and virtually eliminate all zonular stress.

10. Phacoemulsification should be performed using low vacuum and aspiration settings in order to keep the bottle height at a minimum, a technique known as ‘slow-motion Phaco developed by Robert Osher.

11. Bottle height: it is important to keep the bottle at an optimum height, neither too high nor too low.

   a. Very high bottle height can in turn force fluid through weak areas of the zonules hydrating the vitreous resulting in positive pressure, anterior chamber shallowing and vitreous prolapse.

   b. Too low bottle height can result in an out flow, which is greater than inflow again resulting in
shallowing of anterior chamber, a negative pressure in AC and further vitreous prolapse as the anterior segment is less pressurised than the posterior segment.

12. Divide and or chop technique are preferred in eyes with zonular weakness. This technique minimises zonular stress during phacoemulsification if surgeon is careful to apply equal forces in opposing directions to avoid displacing the nucleus.

13. “Visco dissect” nuclear halves / quadrants in areas of zonular weakness. The viscoelastic should be injected below the nuclear fragment and the capsular bag- lifting the nuclear fragment as well as expanding and stabilizing the capsular bag. Additional cortical removal by visco dissection will limit stress on the remaining zonules during aspiration of cortex.

14. Automated Irrigation and Aspiration device is not preferred for cortex removal as it can hydrate vitreous and increase vit prolapse. Manually aspirate with a 24/27 G canula striping cortex in a tangential manner instead of radially to limit stress on zonules. A J’ cannula can be used for sub incisional cortex. Ensure removal of all vitreous from the anterior chamber if it is present. Use ‘Dry vitrectomy’ with automated vitrector after filling anterior chamber with viscoelastics. For significant vitreous loss a bimanual vitrectomy should be performed.

IOL placement options

1. The surgeon should decide if it is safe to use an ACIOL or PCIOL.

2. If an ACIOL is used the remnants of the capsular bag should be removed to prevent contraction and opacification.

3. If the surgeon uses a PCIOL it should be either
   a. Sutured to the scleral wall or
   b. Placed in the capsular bag

Ciliary sulcus placement of PCIOL without suture fixation in an eye with significant zonular compromise is not recommended.

Placement of PCIOL into the capsular bag

1. Placement of PCIOL into the capsular bag is challenging when there is significant zonular weakness as one must achieve IOL centration, and maximize long term stability.

2. Use of 6 mm optic diametre IOL decreases the chances of undesirable edge-glare symptoms should lens decentration occur post operatively. Haptic configuration designed for broad contact with equatorial capsular bag increases the chances of long term centration. Use of silicone plate haptic IOL should be avoided in the presence of zonular dialysis as there is greater chance of capsular contraction and decentration.

3. Insertion of CTR to provide 360° capsular bag expansion and greater stabilization.

4. If the ZD is located at the incision site, lens placement is more difficult.
   a. One Option is to first place the entire lens into the AC. Then using a two handed technique, the superior haptic is inserted into the capsular bag followed by a similar maneuvre for the inferior haptic.

5. Orientation of the IOL: There are 2 schools of thought.
   a. Orienting the IOL in a plane parallel to the zonular dialysis (ZD) in order to take advantage of the remaining intact zonules. This orientation will provide optimum support but may induce ovaling of the capsular bag and an increased risk of postoperative decentration.
   b. Placing one haptic in area of ZD will ensure stretching of the bag and decrease ovaling. However it should be borne in mind that only one haptic is adequately supported.

It is recommended to orient the haptics in whichever axis that provides the best centration intraoperatively. This is accomplished by careful rotation of PCIOL.

Capsular Tension Ring (CTRs)

- Drs Witschel and Legler (1993) from Germany demonstrated that CTRs could provide both intraoperative and postoperative stabilization of
the capsular bag. Produced by Morcher GmbH, in Stuttgart, Germany and made of polymethyl methacrylate (PMMA), this ring can be inserted into capsular bag at any point after a continuous curvilinear capsulorhexis has been completed.

- Use of CTR is contra indicated if a CCC is not attained or if a posterior capsular rent occurs.
- In eyes with profound zonular compromise or lens subluxation may not achieve adequate stabilization or centraction despite CTR placement.

Long term stability even in presence of CTR is doubtful in eyes with progressive zonular weakness such as Marfans, PXF etc. Phacoemulsification with the proper use of endocapsular device can give excellent results in patients with subluxated cataracts at the main incision during PE and cortical aspiration. This guiding suture is used to retrieve the CTR from the eye should a posterior capsular rent occur during phacoemulsification or cortex removal. If the procedure is uneventful the suture is cut and removed.

**Standard capsular tension ring**

Credit goes to Hara and Yamada for introducing endocapsular ring in the year 1991 for maintenance of the circular diameter of capsular bag. Later the device was further refined and modified for managing severe degree of subluxated lenses.

The standard CTR is made of polymethyl methacrylate (PMMA) material and has an oval shaped cross section with eyelets at both free ends (Fig.5). It is a compressible circular ring with two smooth edged end terminals.

CTR is manufactured by Morcher GmbH (Struttgarf, Germany) and Ophtek (Groningen, The Netherlands).
Type 14, MR – 1400,
For Normal Eyes
Expanded 12.3mm,
Compressibility 10.0mm,
Axial Length < 24mm

Type 14A, MR – 1410,
For Highly Myopic Eyes
Expanded 14.5mm,
Compressibility 12.0mm,
Axial Length < 28mm

Type 14C, MR – 1420,
For Normal or Myopic Eyes
Expanded 13.0mm,
Compressibility 11.0mm,
Axial Length 24 - 28mm

Fig. 6. Morcher CTRs

and is US-FDA approved. The Morcher ring, also known as Reform ring, comes in three different sizes based on the uncompressed diameter (Fig.6).

**Capsular ring size**

Selection of CTR size is based on capsular bag dimensions. A large capsular bag usually requires a larger ring; 13mm ring is being most commonly used. White to white corneal measurement and axial length can be used as a rough guide in the selection of CTR. It would be appropriate to use a larger CTR in adults with highly myopic eyes.

Step 4: Placement of IOL in the bag and has the CTR is no different than routine cases, infact it may be even easier as the bag is better supported.

Step 5: Suturing the CTR to Scleral wall for support.

a) Robert Osher has desired a technique of suturing the CTR to the scleral wall by straddling the CTR with 10⁰ prolene double suture. This technique although it works well involves risk of rupturing the capsular bag since it is under stretch due to presence of CTR.

Vladimic Pfizer’s technique involves needle passage thro a small peripheral capsulorhexis. However the integrity of the capsular bag is violated and the risk of rupture is present.

In more severe subluxation, modified CTR, like Cionni’s M-CTR with one or two eyelets attached to the central ring is used and a posterior chamber IOL (PCIOL) placed in-the-bag.

Robert Cionni:s Modified CTR (MCTR)⁸,⁹,¹⁰ has an unique fixation hooklet designed for scleral fixation without violating the integrity of capsular bag. The fixation hook courses anteriorly and centrally in a second plane, wraps around the capsulorhexis edge and rests on the residual anterior capsular rim.

**Modified capsular tension ring (M-CTR)**

The standard CTR is unable to provide adequate intraoperative support and centration of the bag in

![Ring with single eyelet](image1)
![Ring with double eyelets](image2)

Fig. 7. Cionni’s modified capsular tension ring

![Modified capsular tension segments](image3)

Fig. 8. Cionni’s modified Capsular Tension Segments
grossly subluxated cataracts or lenses. Cionni developed the modified CTR (M-CTR) (Morcher – GmbH) called Cionni ring in the year 1998. This ring provides a solution to extensive zonular deficiency or damage or progressive zonular damage by allowing the surgeon to anchor the capsular bag to the sclera.

3 modules are currently available.

Model 1 L: Single fixation hook distant from insertion end of the ring.

Model 2 C: Single fixation hook near insertion end of the ring.

Model 2 L: has 2 fixation hooks which is very useful in patients with significant zonular weakness and may be the ring of choice in patients with progressive zonular weakness as in Marfan’s Syndrome.

The Cionni’s modified ring has an open ring design with one (model I-L or I-R) or two (model 2-L) fixation eyelets attached to the central ring (Fig 7). The eyelet allows the ring to be sutured to the sclera. It protrudes 0.25mm forward from the body of the ring and then sits anterior to the anterior capsular rim and allows maintenance of capsular bag integrity on suturing to the sclera. A 9.0 prolene is preferred over 10.0 prolene as the incidence of breakage is less with the former. An adequately sized rhexis is essential to prevent iris chaffing, pigment dispersion and chronic uveitis.

An eccentric rhexis has to be performed in order to be certain that after the bag is recentred, the capsulorhexis opening is recentered as well.

**Capsular tension segment**

Capsular tension segment (CTS) is a partial ring of 90-120 circumference, and is made of PMMA (Fig. 8 & 9). It has a radius of 5mm and an anteriorly positioned fixation eyelet like M-CTR. This was designed by Ahmed and was manufactured by Morcher GmbH. CTS is useful for cases with profound zonular insufficiency. The CTS provides support in the transverse plane, when sutured to the scleral wall. When circumferential support is needed, a CTR may be implanted in conjunction with an already positioned CTS. The CTS in available in 3 sizes having radius of curvature of 4.5 mm, 5 mm and 5.5 mm.

The choice of endocapsular support device depends mainly on the nature of zonular weakness, degree of zonular loss, and the extent of zonular instability. CTRs are indicated in cases of mild, generalized zonular weakness or in small localized zonular dialysis of less than 3-4 clock hours. In more advanced or progressive...
cases of zonular instability, the Cionni M-CTR or the CTS is indicated. Indications of CTR, M-CTR and CTS are given in Table 1.

Closed chamber endocapsular phacoemulsification combined with ECR, in patients with mild to moderate subluxation of lens not associated with complications such as secondary glaucoma and retinal detachment, often gives encouraging visual results. The implantation of ECR has provided safety and efficiency during phacoemulsification and IOL implantation, significantly reduced the rate of complications and overall improved visual results.

References


Orbicularis Plication for Ptosis

Dr. Mathew Joseph MS

Abstract

The orbicularis oculi muscle is carefully dissected from the skin and is exposed up to almost the lid margin. The distal fibres then are joined to the proximal orbicularis fibres. The skin flap is sutured back in place.

Introduction

The technique of orbicularis plication for ptosis was developed by Dr. Daljit Singh of Amritsar. In effect this means the revolutionary idea of making the same muscle do exactly opposite actions, in the same position. It was first presented at the conference of the American College of Eye Surgeons, at Miami, Florida, USA in February 2001. The results shown were very impressive. He has done over 265 cases. The paper was published in the Annals of Ophthalmology in 2006.

The most common cause of ptosis is poor levator action, which is usually congenital. Up till now, the only two available surgical techniques were the levator resection and the frontalis sling. Even though levator ‘strengthening’ is the logical thing to do, very often its action is so poor, and the muscle is even so fibrotic that, little is gained by way of dynamic function. The same applies to the frontalis sling of strips of fascia lata or even sutures, both of which are totally inelastic, making them both functionally and, even cosmetically unacceptable. Both the surgical techniques have unpredictable results and often lead to lid lag and, or, lagophthalmos.

Discussion

As mentioned earlier, the ingenuity of the technique lies in making the same muscle do seemingly exactly opposite actions while still in its original attachments. When the eyes are open, the orbicularis is in a relaxed state. In this state, by shortening the muscle, the lid is made to be kept open. The lid will close when the orbicularis contracts, as in its normal action. I prefer to only dissect up to about 0.5 cm above the lid margin. The distal muscle fibres near the lid margin are then joined to the proximal fibres by means of three 6 zero Vikryl mattress sutures, thus pulling up the lid. The skin is sutured back with interrupted 6 zero silk. A firm dressing is given to prevent bleeding and is left in place for 48 hours. The dressing is repeated for 24 hours more, and then the wound is left open to heal, with thrice daily application of ung. Neosporin. The skin sutures are removed after about 10 days to 2 weeks.

Method

The skin is incised near the upper orbital margin, just below and parallel to the eye brow. The skin is carefully separated from the underlying orbicularis muscle fibres, up to about 0.5 cm above the lid margin. The distal fibres then are joined to the proximal orbicularis fibres. The skin flap is sutured back in place.

The patient in the illustration (Fig. 1) is a 30 year-old male, a driver by profession, had ptosis of left eye...
from birth. From Fig. 2 it is clear that levator action was negligible. Two weeks post-op (Fig. 3) the result is quite satisfactory. Frontalis action is nearly totally absent. Fig. 4 shows good closure without any lid lag at all. There is no redundant skin which was apparent at the end of the surgery.

I have found this technique much easier to perform, more satisfying and predictable than either of the two current methods in use.

References

180 Years of Evolution in Tonometry

Dr. Meena Chakrabarti MS DO DNB, Dr. Sonia Rani John DNB, Dr. Arup Chakrabarti MS DO

The technology used to estimate intraocular pressure has evolved tremendously since Sir William Bowman emphasized the importance of ocular tension measurements. In an address delivered at the 1826 meeting of the British Medical Association, Sir William underscored the critical role that digital estimation of ocular tension played in his practice. (In this case the term “digital” refers to palpation of the eyes using the fingers – the digits.)

Soon afterwards, digital palpation tonometry became an essential clinical skill to be mastered by all ophthalmologists. When mechanical tonometry was first introduced in the late 1800s, many ophthalmologists felt so confident with their ability to estimate IOP by palpation that they viewed the new technology as inferior. Schnabel, in a 1908 address to the Vienna Ophthalmological Society, stated that although he did not object in principle to mechanical tonometry, he expected “…very little from this test since digital tonometry by an expert is a much more accurate test.”

Impression tonometry

Although Albrecht von Graefe is credited with the first attempts to create instruments that mechanically measured IOP in the early 1860s, his proposed instruments were neither designed nor built. Rather, it was Donders who designed the first instrument capable of estimating IOP – albeit not accurately – in the mid 1860s. The principle behind Donders instrument was to displace intraocular fluid by contact with the sclera. Ophthalmologists first measured the curvature of the sclera at the site of contact and then used the measurement as a reference plane to measure the depth of indentation produced by the tonometer. Smith and Lazerat refined this technology in the 1880s, and the discovery of cocaine by Carl Koller in 1884 led the way to corneal impression tonometry. Using corneal anesthesia, corneal tonometry became the definitive choice for IOP measurement because it offered a well-defined and uniform site of impression.

The major shortcoming of impression tonometry was that it displaced so much fluid upon contact with the eye that the measured readings were highly variable and mostly inaccurate. What was needed was a way to displace a minimal amount of fluid to record IOP.

Indentation (Schiotz) tonometry

This type of tonometry uses a plunger to indent the cornea. IOP is determined by measuring how much the cornea is indented by a given weight. The test is less accurate than applanation tonometry and is not commonly used today by ophthalmologists and optometrists. However, some family medicine or urgent care doctors still use the Schiotz tonometer. The first commonly used mechanical tonometer was designed and introduced by Hjalmar Schiotz in the early 1900s. The instrument was simple, easy to use, and relatively precise. It was quickly accepted and became the new gold standard beginning the 1910s. (Fig 1)

Innovations in calibration led to its increased use, and a tremendous amount of knowledge about the normal and glaucomatous eye was quickly acquired.

Chakrabarti Eye Care Centre, Kochuullloor, Trivandrum 695 011
E-mail: tvm_meenarup@sancharnet.in

Ophthalmic Instrumentation
Applanation Tonometry

This breakthrough came in 1867 when Adolf Weber designed the first applanation tonometer that gave a highly defined applanation point without indentation. After two decades of skepticism, the value of applanation tonometry was re-discovered when Alexei Maklakoff and others introduced new versions of applanation tonometers. (Fig 2)

In the early 20th century, there were about 15 tonometer models in use. (Fig 3) However, digital palpation tonometry remained the “gold standard” among most ophthalmologists during the early 1900s.

Goldmann introduced an adjustment for ocular rigidity in the 1950s, which led to the development of the Goldmann applanation tonometer. (Fig 4) The Goldmann tonometer displaces so little fluid that variations in ocular rigidity were then thought to be mostly negligible.

Goldmann applanation tonometry

The Goldmann applanation tonometer (GAT) is a variable force tonometer, which makes a static measurement of the force required to flatten a fixed area of the cornea. For the past fifty years, it has been considered to be the clinical gold standard in IOP measurement. When Hans Goldmann designed the tonometer, he recognized that certain corneal effects (e.g., resistance to deformation) would influence pressure measurements. (Fig 5) Therefore he based his calculations on the resistance to deformation of an average corneal thickness (520 microns) and estimated that the resistance to deformation would be cancelled by the surface tension generated by the pre-corneal tear film when the area applanated had a diameter of 3.06 mm.

Facts on Applanation Tonometers

- Assumptions (Imbert-Fick Law)
  - CCT = 520um and consistent
  - Surface tension
  - Corneal / Scleral rigidity
- Measurement variability: +/- 3mmHg
- Based on Imbert-Fick principle
  - Pressure = force/area
- 0.1g force to applanation head 3.06mm = 1mmHg
- Surface tension and ocular rigidity
  - Negate each other
- BUT, assumption of CCT 520um….
- Other factors: corneal curvature, elasticity

Non-contact Tonometry (NCT)

Non-contact (also called air-puff) tonometers do not touch the eye because they use a puff of air to flatten (applanate) the cornea. Once initiated, the puff force increases until the cornea is applanated by a predetermined amount. The tonometer then translates this force into a measure of IOP.

Because the air puff tonometer relies on corneal applanation, (Fig 6) it is subject to the same potential measurement errors induced by variations in corneal properties, as is the Goldmann tonometer.

Principle of NCT

The NCT was the brainchild of Grolman and was introduced in 1972. A puff of air creates a constant force, which momentarily deforms the cornea. It is difficult to determine the exact nature of corneal deformation, although it is postulated that the central cornea is flattened at the moment the pressure measurement is made.

Types of NCT

1. Table mounted – Xpert NCT
2. Hand held - Pulsair tonometer from Keeler

Pneumatic System

Generates a puff of room air which is directed against the cornea.

At the moment the central cornea is flattened, the greatest numbers of reflected rays are received, which is recorded as the peak intensity of light detected. The time from an internal reference point to the moment of maximum light detection is converted to IOP based
on prior comparison with readings by Goldmann tonometry. In the newer version the force of air required to achieve peak light detection is the measured variable when air puff is automatically triggered on meeting the alignment criteria.

**Fallacies with NCT**

The time interval for an average measurement is 1 to 3 ms (1/500th of the cardiac cycle) and is random with respect to the phase of the cardiac cycle, so that the ocular pulse becomes a significant variable and it cannot be averaged as with other tonometers. Glaucomatous eyes have significantly greater range of momentary fluctuations in IOP. It is recommended that more than 3 readings within 3 mm Hg range be taken and averaged as IOP.

This phenomenon can be directly observed by viewing pulsation of mires during Goldmann tonometry. (Fig. 7) (To some degree, Goldmann takes this pressure variation into account because measurements are made when the inner aspects of the pulsating mires just touch.) In some individuals, IOP can vary as much as 5 or 6 mm Hg within one second while the choroid fills and empties. The NCT has no ability to determine at what point in an individual’s intraocular pressure cycle the IOP was measured.

**Accuracy**

Comparisons against Goldman applanation tonometers indicate that NCT is reliable within normal IOP range. The reliability is reduced in the higher pressure ranges and is limited by abnormal corneas and poor fixation. One study indicated that central corneal thickness has a greater influence on NCT than on Goldmann tonometry.

**Advantages**

- comfort
- no contamination
- no chance of corneal abrasion
- no reactions to topical anesthetics
- of value in mass screening and in studies of newer antiglaucoma drugs

**Caution**

There have been reports of sub epithelial air bubbles after repeated use of NCT.

NCT is a safe and reliable method of measuring IOP. Caution to be used when measuring glaucomatous eyes as lower pressure may be recorded at IOPs above the normal range as in abnormal corneas.

**Problems with the applanation standard**

Until the late 1990’s, the Goldmann applanation tonometer enjoyed an unchallenged 45-year reign as the “gold standard.” However, two thought provoking events caused many to begin questioning whether GAT was measuring true IOP in a variety of situations: the acceptance and use of refractive surgery, and publication of the Ocular Hypertensive Treatment Study (OHTS) results.

- Thin cornea = risk for progression
  - Ocular Hypertensives (OHTS)
  - POAG
  - Normal Pressure Glaucoma (NPG)
- GAT underestimates IOP in these eyes (and overestimate in thick cornea)
  - Mounting evidence regarding GAT inaccuracies

**Refractive Surgery and Applanation Error**

As soon as radial keratotomy (RK) became commonplace, Ophthalmologists observed differences in pre- and post-operative Goldmann IOPs. Commonly, IOP was found to decrease by 3 to 5 mm Hg after surgery. Similar observations were made with newer refractive technologies such as Photorefractive Keratectomy (PRK) and Laser Assisted In-Situ Keratomeilusis (LASIK).

Some observers accounted for this apparent pressure decrease exclusively in terms of the decrease in central corneal thickness caused by the PRK and LASIK surgery. However, with the case of radial keratotomy (RK), a decrease in CCT could not explain the IOP changes because RK causes no decrease in CCT. Indeed, one could argue that post-RK corneas often show increased CCT resulting from varying degrees of corneal edema.
OHTS, CCT, AND GAT

Although the central theme of the well-known Ocular Hypertensive Treatment Study was an analysis of the tendency for ocular hypertensives to convert to primary open angle glaucoma (POAG) over time (with or without treatment), it was also an opportunity to observe the effect of variables other than IOP in this tendency. CCT was one variable measured in OHTS subjects. Among the results of this portion of the study, the investigators reported that they had observed an increased propensity to convert from ocular hypertension to POAG in those individuals who had comparative low CCT (under 545 microns). They suggested that an error in GAT imposed by variability in CCT might cause an under- or overestimation of IOP when measured with Goldmann.

Applanation Tonometry and Central Corneal Thickness

Given the compelling results of the OHTS, it seems quite natural that investigators would start to look closely at the true impact of CCT on the Goldmann measurement. Ironically, in the early 1950’s, Hans Goldmann revealed in his renowned (but seldom read) publications that IOP measurements with his tonometer could be seriously flawed if the subject’s corneal biomechanics did not fulfill certain stringent criteria. CCT was one of the significant criteria that Goldmann discussed.

A commonly used CCT correction formula was published by Ehlers. The fundamental supporting concept for this correction formula is that as corneas get thinner, GAT reads too low. If CCT is “average,” GAT is essentially correct. And, if the cornea is thicker than average, GAT overvalues true manometric IOP.

Other IOP correction formulae beyond Ehlers’ formula have also been developed. Below, is a simplified version of the Orssengo-Pye Formula that has been advocated by James Tsai and Stephen Trokel at Columbia University.

\[
\text{Corrected IOP} = \frac{(CCT-545)}{50} \times 2.5 \text{ mm Hg}
\]

This simplified formula instructs the clinician to correct IOP by 1.0 mm Hg for every 20 microns of CCT variation from the 545 standard. For example, a patient with a 645-micron cornea has a 5 mm Hg Goldmann overestimation and a patient with a 445-micron cornea has a 5 mm Hg underestimation.

However, as is usually the case with most biological functions or processes, things are not so simple as these formulae and correction tables suggest. Newer investigations have shown that the formulae represented an incorrect and sometimes dangerous oversimplification of the complex relationship between corneal biomechanics and IOP.

A Problem with CCT-based Corrections – Corneal Elasticity

An easy way to think of corneal elasticity is in terms of relative corneal rigidity or softness. Reliable GAT measurements rely on average corneal rigidity. When the cornea is more rigid than average, GAT reads too high, and, when the cornea is softer than average, GAT reads too low.

Some corneal scars, high CCT (without edema or refractive surgery), and microcornea can cause a cornea to be unusually rigid. The circumstances that can cause a cornea to be unusually soft seem to be more common.
Low CCT
Edematous corneas – regardless of CCT
Children under age 7 – regardless of CCT
High corneal diameter
History of any corneal refractive surgery – regardless of CCT
Endothelial dystrophies
Epithelial dystrophies

Can we do better than the 50 year old “Gold Standard?”

In view of recent investigations, interest in tonometry has increased and research engineers were charged with the mission of developing a better understanding of various corneal properties and their respective influences on GAT measurements, as well as developing new techniques to more accurately determine true IOP.

With these goals in mind, the technology has taken two different directions: the Reichert Ocular Response Analyzer and The PASCAL Dynamic Contour Tonometer (Ziemer Ophthalmic Systems, AG, Switzerland) have been developed.

The Reichert Ocular Response Analyzer (ORA)

The Reichert Ocular Response Analyzer utilizes a “dynamic bi-directional applanation process” to measure both the biomechanical properties of the cornea and the IOP. The basic output is a Goldmann-correlated applanation pressure measurement (IOPG) and a measure of corneal tissue properties called corneal hysteresis (CH), which is related to viscous damping in the corneal tissue. The CH measurement also provides a basis for two additional parameters measured by the ORA: the corneal-compensated intraocular pressure (IOPCC) and the corneal resistance factor (CRF).

IOPCC is an IOP measurement designed to be less affected by corneal properties than is IOP measured by Goldmann or NCT. IOPCC has essentially a zero correlation with CCT in normal eyes and stays relatively constant pre- versus post-LASIK.

CRF appears to be an indicator of the overall “resistance” of the cornea to applanation and is significantly correlated with CCT and GAT, but not with IOPCC.

Understanding hysteresis: elastic, viscous, and visco-elastic materials

In order to understand the Ocular Response Analyzer, a brief discussion of properties of visco-elastic materials will be presented. Elastic materials are those for which strain (deformation) is directly proportional to stress (applied force) independent of the length of time or the rate at which the force is applied. Therefore, if the elastic modulus of a structure (e.g., a steel beam) is known, one can easily predict the amount of force required to bend it a specific amount.

Viscous materials are those for which the relationship between strain and stress depends on time or rate of force application.

The human cornea is a complex visco-elastic structure.

The corneal hysteresis measurement is an indication of viscous damping in the cornea. In other words, it is related to the ability of the cornea to absorb and dissipate energy. Subjects whose corneas exhibit low CH can be thought of in simple terms as having a “soft” cornea.

Operation of the Ocular Response Analyzer

The ORA utilizes an air pulse to apply force to the cornea and an advanced electro-optical system to monitor the resultant corneal deformation. Alignment to the patient’s eye is fully automated.

A precisely metered, collimated air pulse causes the cornea to move inwards, past applanation, and into a slightly concave shape. Milliseconds after applanation, the air pump shuts off and the pressure declines in a smooth fashion. As the pressure decreases, the cornea begins to return to its normal configuration and once again passes through the applanated state. An applanation detection system monitors the cornea throughout the entire process and pressure values are recorded for the inward and outward applanation events.
Fig 1. Schiotz Tonometer.

Fig 2. Maklakoff’s original tonometer, circa 1885.

Fig 3. Maurice applanation apparatus, circa 1951.

Fig 4. Dr. Hans Goldmann and the Goldmann applanation tonometer.

Fig 5. An older prototype model of the Goldmann Applanation tonometer

Fig 5 An applanated cornea showing a reading of 20

Fig 6. The original AO (Reichert) non-contact tonometer.

Fig 7. Intraocular pressure pulsation.

Fig 8. Reichert Ocular Response Analyzer

Fig 9. The difference between “inward” applanation pressure and “outward” applanation pressures defines corneal hysteresis.
One might initially expect these two pressure values to be the same. However, viscous damping in the cornea causes delays in the inward and outward applanation events, resulting in two different pressure values. The average of these two pressure values provides a repeatable, Goldmann-correlated IOP value (IOPG). The difference between these two pressure values is corneal hysteresis (CH). The ability to measure this effect is the key to understanding the biomechanical properties of the cornea and their influence on the IOP measurement process.

**CH, CRF, and IOPCC: New Ocular Parameters**

Ongoing clinical studies over the past three years have shown that CH is a function of corneal properties and not an artifact of any other variable. Corneal hysteresis is a phenomenon that results from the dynamic nature of the air pulse and the viscous damping inherent in the cornea.

The corneal resistance factor is also derived from this response. CRF is a measurement of the cumulative effects of both the viscous and elastic resistance encountered by the air pulse while deforming the cornea. CRF exhibits the expected property of increasing at significantly elevated pressures.

Although CH and CRF are related, in some instances they are significantly different, and each provides distinct information about the cornea. Corneal-compensated IOP is a pressure measurement that utilizes information provided by the corneal hysteresis measurement to provide an IOP value that is less affected by corneal properties.

Although the manufacturer of the ORA cannot yet claim to be measuring “true intraocular pressure,” early investigations have demonstrated that IOPCC is a better indicator of the real IOP than traditional NCT or GAT can provide.\(^7\)

**The Pascal – Dynamic Contour Tonometer (DCT)**

Dynamic contour tonometry (DCT) is a novel measuring technique using the principle of contour matching instead of applanation to eliminate the systematic errors...
inherent in previous tonometers. These factors include the influence of corneal thickness, rigidity, curvature, and elastic properties.

The PASCAL is a relatively new device that uses DCT to measure IOP. Although this device is similar in appearance to a Goldmann, the PASCAL® it is unlike Goldmann applanation in that it is not a variable force tonometer.

PASCAL uses a miniature pressure sensor embedded within a tonometer tip contour-matched to the shape of the cornea. The tonometer tip rests on the cornea with a constant appositional force of one gram. This is an important difference from all forms of applanation tonometry in which the probe force is variable.

When the sensor is subjected to a change in pressure, the electrical resistance is altered and the PASCAL’s computer calculates a change in pressure in concordance with the change in resistance.

The contour matched tip has a concave surface of radius 10.5 mm, which approximates the cornea’s shape when the pressures on both sides of it are equal. This is the key to the PASCAL’s ability to neutralize the effect of intra-individual variation in corneal properties. 18-21

Once a portion of the central cornea has taken up the shape of the tip, the integrated pressure sensor begins to acquire data, measuring IOP 100 times per second. A complete measurement cycle requires about 8 seconds of contact time. During the measurement cycle, audio feedback is generated, which helps the clinician ensure proper contact with the cornea.

**Conclusion**

Today, digital palpation tonometry has largely been replaced by more sophisticated technologies used to estimate IOP. Today’s instruments are far more accurate and easier to use. Yet, sometimes, there is no good substitute for palpation tonometry. For example, some optometrists and ophthalmologists may still have to rely on digital palpation to estimate IOP in patients who are uncooperative.

**References**

2. Schnabel I., Klin Montasbl Augenh 1908; 48:318
14. Carolyn Y. Shih, MD; Joshua S. Graff Zivin, PhD; Stephen L. Trokel, MD; James C. Tsai, MD - Clinical Significance of Central Corneal Thickness in the Management of Glaucoma Arch Ophthalmol. 2004;122:1270-1275
15. Liu and Roberts, JCRS, JCRS 31, Issue 1, p 146-155 (January 2005)


22. Pacific Optometry Continuing Education Programme : Intraocular Pressure And Glaucoma , Kirstein 28.08.2006 08:32 Uhr

Drops for AMD

Dr. Sonia Rani John DNB, Dr. Meena Chakrabarti MS DO DNB, Dr. Arup Chakrabarti MS DO

Introduction

AMD is the most important cause of visual loss among the elderly, affecting over 10 million individuals in the United States of America and, many more worldwide. AMD is the leading cause of irreversible vision loss in the developed world affecting an estimated 25% of individuals over the age of 75. In the past 10 years, significant research has enhanced our understanding about the epidemiology, biochemical composition and pathogenesis of age related macular degeneration. Recognition that unexpected inflammatory mechanisms, especially complement, macrophages and oxidants are major contributors to drusen formation has become a paradigm shift in our understanding.

AMD manifests itself by loss of central vision loss and is generally classified into 2 types. The disease initially manifests itself as dry or atrophic AMD and is associated with retinal cell death without neovascularization. Dry AMD can progress in minority of cases (10% - 15%) to wet or neovascular AMD, which is associated with blood vessel formation and leakage involving the macula. While vision loss is slower in dry than in wet AMD, patients with atrophic AMD can eventually lose significant vision. In addition, they are at constant risk of developing the neovascular form of AMD.

While the treatment for the more rapidly progressive stage of AMD - neovascular or wet AMD had evolved rapidly in recent years, currently there is no medical therapy or surgical intervention available to slow the development or prevent progression from the more insidious, non exudative, stage of the disease. Failure to develop effective treatments for the non exudative form of the disease means that the macula will continue to deteriorate ultimately suffering permanent, irreversible, damage.

Treatment for wet AMD is expensive as well as invasive, but have been highly successful because they do not merely limit or arrest further disease progression, but they frequently lead to improvement in visual function.


Problems with existing therapies are visual loss with subfoveal lesion and high rate of recurrence in those subjected to thermal laser. PDT is unable to improve visual acuity and is associated with recurrence. Anti-VEGF agents require frequent intravitreal injections and there is possibility of tachyphylaxis.

Topical installation of drops is the most common method used to administer treatments for ocular disease. Productive absorption via topical delivery has been described as occurring by 2 routes; trans-corneal and trans conjunctival / trans scleral. Trans scleral absorption is limited by drainage, lacrimation and tear – dilution, tear turnover and the corneal epithelial barrier. These are certain pathways by which drugs can penetrate and disperse into the posterior ocular tissues after topical administration. For e.g, through the pars plana directly or by lateral diffusion across the sclera followed by penetration of Bruch’s membrane and the retinal pigment epithelium.
The most significant challenge for effective topical therapy is finding molecules that are small, potent and have charge characteristics suitable for enhanced ocular penetrance. Additionally, because topical therapy results in significant gut exposure through lacrimal drainage, systemic exposure can be significant.

The advantages of topical therapy include decreased risk of complications (endophthalmitis, decreased cost and increased convenience). The disadvantages of topical therapy include decreased bioavailability at the retina (lacrimal washout), decreased compliance, more frequent administration (compared to depot injections) and increased latency before therapeutic effect seen (compared to intravitreal injections).

VEGF-triggered fluid leakage can be prevented by a drug applied topically in eye drop form. The availability of a topically applied inhibitor of vascular permeability would represent a therapeutic advance with potential widespread application (diabetic macular oedema, CNV, retinal vein occlusion). The ability to provide effective topical therapies for intraocular neovascularization could revolutionize the current care of many diseases that lead to these conditions.

**Combretastatin A4 Phosphate (Zybrestat, Oxigene)**

**Mechanism of action:** Zybrestat is a vascular disrupting agent (VDA) which targets endothelial cells of the already established neovascular tissue leaving other blood vessels relatively unscathed.

Vascular disrupting agents can be divided into 2 types.

1. Small molecule directed VDAs.
   a. Tubulin- binding agents.
   b. Flavonoids.
2. Ligand directed VDAs

Zybrestat is a tubulin binding agent which disrupts the endothelial cytoskeleton. It acts on endothelial tubulin causing depolymerisation of microtubules that results in confirmational changes and loss of blood flow. It also disrupts the VE-cadherin- catenin complex that binds cells together and leads to loss of cell-cell contact. This increases vascular permeability and decreases blood flow.

Animal studies have proved that when zybrestat is applied topically to the surface of the eye, the drug is absorbed and result in concentrations of the drug in the retina and choroid that are within the expected therapeutic range. Human studies with intravenous zybrestat in patients with subfoveal CNVM in pathological myopia showed that all subjects maintained (i.e, a decrease of < 3 or more lines) VA at 3 months follow up and decreased size and leakage of CNV. Systemic side effects included headache, hypoesthesia, nausea, tachycardia.

**ATGOOZ (Mecamylamine, CoMentis)**

ATG-3 is an antagonist of the nACh (nicotinic Acetyl Choline) receptor pathway in the vasculature and is being studied as an anti-angiogenic therapy for neovascular AMD.

Nicotine is an agent of angiogenesis. It acts via nicotinic acetylcholine receptors that mediate fast synaptic transmission. Nicotine acetyl choline receptor (nACHR) has been recently demonstrated on vascular endothelial cells. Nicotine increases endothelial cell proliferation, reduces apoptosis and increases capillary network formation in vitro. It enhances the angiogenic response to inflammation, ischemia, atherosclerosis and neoplasia. Nicotine is associated with increased blood flow and tissue growth.

The proangiogenic effects of nicotine are mediated by non neuronal nAChR and might involve the elaboration of nitric oxide, prostacyclin and VEGF. nACHRs are involved in the native angiogenic response and that this pathway is distinct from those triggered by VEGF. Nicotine induces morphological changes in endothelial cells identical to those induced by VEGF.

Thus ATG-3 inhibits endogenous as well as VEGF induced angiogenesis in human retinal endothelial cells. Following topical administration as ATG-3 drops, the compound has excellent penetration to the back of the eye in multiple animal species with no systemic side effects consistent with very low levels of the compound found in the blood following eye drop application.

CoMentis successfully completed a Phase I study in healthy volunteers in 2006. The ongoing phase II study plans to randomize 333 patients receiving maintenance therapy with an Anti-VEGF agent to 1 of 3 treatment
groups: 2 different doses of ATG 003 administered twice daily. All patients will be treated for up to 48 weeks, during which time they will be monitored to assess the drug’s safety.

**OT 551 (Othera)**

OT – 551 is a small patented molecule that acts on oxidative stress and disease induced inflammation. A number of scientific publications from leading researchers in ophthalmology have linked both oxidative stress and inflammation to the progression of geographic atrophy and the ensuing vision loss. OT-551 has demonstrated a dose dependent protective effect on photoceptor activity in an animal model of AMD and has been shown to reach the back of the eye after topical dosing in multiple species. This profile supports the rationale for studying the drug in patients with degenerative retinal conditions such as geographic atrophy. OT – 551 is the first eye drop ever to be tested in a clinical trial as treatment for dry AMD.

OT 551 down-regulates over expression of nuclear factor Kappa B (NF-KB). NF-KB is involved in regulation of approximately 2000 genes which fall into 4 broad functional categories including immuno regulatory and inflammatory genes, anti-apoptotic genes, genes which regulate cell proliferation and genes that encode negative regulators of NF-KB. Thus NF-KB inhibition leads to anti-oxidative, anti-angiogenic and anti-inflammatory effects. Animal studies have proved that OT-551 protects retina from oxidative damage and blocks angiogenesis.

The OMEGA (OT-551 Multi-center Evaluation of Geographic Atrophy) study is a randomized, double – masked, dose – ranging multi-center, phase 2 study of topical OT-551 in patients with geographic atrophy associated with AMD. The experimental drug used was OT-551 0.3 % or 0.45 % ophthalmic solution, 2 drops 4 times daily.

**TargeGen (TG 100801/ TG 101095)**

TargeGen is a small molecule, topically applied (eye drop), multi-target kinase inhibitor developed for the treatment of macular degeneration and other debilitating diseases of the eye. They inhibit multiple targets simultaneously and tends to result in a robust therapeutic effect.

TG 100801 is actually a prodrug. The active form is TG 100572. The prodrug allows even better penetration and greater VEGF inhibition than the actual drug itself.

TargeGen belongs to the class of tyrosine kinase inhibitors, working on kinases that are involved in the VEGF signaling pathway. It inhibits downstream VEGF activation of endothelial cells and block the effect of VEGF on receptors. TG 101095 was designed to inhibit both VEGFR and JAK 2; which is a key signaling kinase downstream of erythropoietin (EPO). EPO is linked to the pathogenesis of diabetic retinopathy.

Topical administration results in very high levels at the choroid. The recommended regimen is twice daily dosage of 1 % TargeGen for 30 days. The drug appears to enter the eye via a trans –scleral route.

A phase 2 open-label randomized pilot study of safety and preliminary efficacy of TG 100801 in patients with choroidal neovascularization due to AMD is ongoing.

**Pazopanib (GW 786034, GSK)**

Pazopanib is a multitargeted tyrosine kinase inhibitor. Receptor kinases are involved in transmitting a signal from cell membrane receptors (such as the receptors for VEGF) to centres within the cell. Kinase inhibitors block this signal from reaching the intended targets within the cell, thereby preventing the cell from responding to the stimulus. In the case of VEGF, a kinase inhibitor can prevent blood vessels from growing and leaking even though VEGF is present and binding to endothelial cells.

Pazopanib is an investigational, oral angiogenesis inhibitor used to treat renal cell carcinoma. Pazopanib is currently in Phase III development for the treatment of advanced or metastatic RCC.

A multitargeted kinase inhibitor such as pazopanib targets multiple VEGF family members. It blocks VEGF R₁, VEGF R₂ and VEGF R₃ with 50 % inhibitory concentration. Pazopanib also has substantial activity directed against platelet derived growth factor (alpha), PDGF beta, C- kit (stem cell factor receptor), fibroblast growth factor receptor 1(FGFR1), FGFR 3 and C-fms. By blocking all these different receptors, it is hoped that the pericytes and endothelial cells that make up the CNV membrane can be destroyed.
Vascular endothelial growth factor (VEGF), platelet derived growth factor (PDGF), fibroblast growth factor (FGF), angioproteins etc. act by binding to tyrosine kinase receptors on endothelial and other stromal cells.

Researchers state that either systemic or local administration of pazopanib causes regression of already established CNV, making it a good candidate for clinical trials in patients with neovascular AMD. Such clinical trials are already under way.

**OcuCure: (OC-1O X)**

OcuCure is a selective tubulin inhibitor which prevents new blood vessels from sprouting (anti-angiogenic activity) as well as directly target the elimination of newly formed blood vessels (angiolytic activity). This dual mechanism more completely addresses the uncontrolled blood vessel growth associated with AMD. Therefore, the OcuCure approach could lead to better long-term visual outcomes.

OC-1OX is lipid soluble and crosses the human cornea, it achieves therapeutic concentrations at the retina-choroid. The drug achieved a corneal level of 100 %, a lens / vitreous level of 11 % and a retina – choroid – sclera level of 83 % in rats when given once every hour for 4 hours.

**Conclusion**

A number of other topical therapies are also being investigated. Some that have shown positive results in initial studies include AdGVPEDF (Phase – I), feuretinide (phase 2), glatiramer acetate (phase 2 and 3), REDD 14 NP (phase I), JSM 6427 (phase I), POT-4 (phase 1), AGN 211745 (phase 2) and E10030 (phase 1).

Eye drops offer significant benefits over other treatment methods, in terms of cost, convenience and patient adherence, the fact that this approach is being explored by multiple companies is encouraging and bodes well for the future of dry AMD treatment as it has now became conceivable that patients diagnosed with the condition will not be forced to accept developing wet AMD as an inevitable consequence.

**References**

3. Rick Trevino, OD VA Progress toward topical therapy of AMD. Outpatient clinic Evansville, IN http://richardtrevino.net
10. Clinical Trials. gov. The OMEGA Study. Use of eye drops to treat geographic atrophy associated with age-related macular degeneration (Dry AMD).
12. A study to evaluate the pharmacodynamics, safety and pharmacokinetics of pazopanib drops in adult subjects with neovascular AMD.
Brown Syndrome

Dr. Ramesh Murthy  MD FRCS

Introduction
Brown syndrome was first described by Harold W Brown in 1949 as the superior oblique tendon sheath syndrome. Brown believed that the syndrome was due to the congenital paralysis of the inferior oblique muscle leading to a short anterior tendon sheath of the superior oblique. The incidence of this condition is 1 in 450 cases of strabismus; approximately one in 20,000 live births. The actual incidence may be higher as many cases are asymptomatic. There is equal predilection for both sexes in congenital Brown syndrome. Wright noted that 5% cases are bilateral and idiopathic Brown syndrome has a higher preponderance in females (63%) and traumatic acquired Brown in males (82%).

Etiology
Congenital Brown syndrome was initially believed by Brown to be due to a short anterior tendon sheath. Another possible cause was a congenital or acquired anomaly of the superior oblique tendon limiting passage of the tendon through the trochlea. The concept of a short or inelastic tendon is a well accepted theory based on the fact that a tenotomy can relieve the limitation to elevation in adduction. Wright demonstrated by his computer model in 1999, that a tight or inelastic muscle-tendon complex was the best fit for Brown syndrome pattern of deviation. Spontaneous resolution of Brown syndrome can be explained by the possible cause of the problem being in the trochlea or tendon trochlea complex. Persistent embryonic trabeculae between the tendon and the trochlea can inhibit the passage of the tendon through the trochlea. Helveston proposed the theory of abnormal telescoping where he showed that the tendon-slackening distal to the trochlea comes from a telescopic elongation of the central tendon. Some patients with idiopathic click can be explained by the presence of a trochlear problem. Chronic movement of the superior oblique tendon through the trochlea can result in a traumatic tenosynovitis with tendon swelling and stenosis of the surrounding sheath – this has been named as the trigger-thumb analogy theory.

Acquired Brown syndrome can be a result of surgeries on the superior oblique like a tuck, scleral buckling procedures and external valves like Molteno or Ahmed valve. These can create adhesions and prevent full relaxation of the tendon. Sinus operations near the trochlea can also cause Brown syndrome. Dog bites in this region can also cause Brown syndrome with superior oblique palsy, the “canine tooth syndrome”. The click syndrome is caused by inflammation leading to dilatation of the tendon limiting movement through the trochlea. This can occur commonly following rheumatoid arthritis, systemic lupus erythematosus or Sjogren syndrome.

Genetic transmission has been reported though in most cases it is sporadic. Occurrence in monozygotic twins has been reported. Autosomal dominant inheritance with incomplete penetrance and variable expression has been proposed.

Clinical features

Classification

- The most common classification is congenital and acquired. Congenital cases are less likely
to improve spontaneously and more likely to need surgery. Acquired cases especially inflammatory can improve spontaneously.

Brown syndrome has also been classified as

a) mild – no hypotropia in primary or adducted position
b) moderate – hypotropia in adducted position
c) severe – hypotropia in primary position

A third classification was proposed by Jampolsky^5

a) True Brown syndrome – no hypotropia in primary position or down gaze
b) Brown syndrome plus – vertical deviation in primary position or adduction ± head posture.

Clinical features

The diagnostic features in Brown syndrome include deficient elevation in adduction, less deficiency in the midline, minimal or no elevation deficiency in the abducted position, minimal or no superior oblique overaction, V pattern with divergence in upgaze and restricted forced ductions. Anomalous head posture with hypotropia in the primary position or a downshoot in adduction may be present. Audible click and tenderness in the trochlear region may be present in inflammatory cases. V pattern exotropia may be present in bilateral involvement.

Spontaneous resolution of congenital Brown syndrome over years has been noted. The click syndrome represents a stage towards resolution. Inflammatory conditions may show waxing and waning especially cases of rheumatoid arthritis. Improvement is unlikely after scleral buckling or glaucoma surgery.

Differential diagnosis

1. Isolated inferior oblique palsy: This is characterized by overaction of the superior oblique muscle and positive Parks’ three step test. Forcedduction test is free in inferior oblique palsy.

2. Double elevator palsy: Limitation of elevation is present in both adduction and abduction. In addition the patients have ptosis or pseudoptosis.

3. Congenital fibrosis syndrome: The differences include restricted elevation in abduction and esotropia on attempted upgaze.

Fig. 1. A 14 year old male presented with Right Brown syndrome. Note the limitation of elevation of the right eye in left upgaze in the nine gaze photograph.

Fig. 2. Superior oblique expander surgery: (a) The superior oblique tendon is located and 2 double armed non absorbable suture (5-0 ethibond) are passed a few millimeters apart. The tendon is cut between the sutures. (b) The silicon band (5-7 mm in size) is cut and secured between the cut ends of the superior oblique tendon, thus lengthening the tendon.

Fig. 3. A ‘chicken suture’ may be passed in place of the silicon band and the tendon ends can be secured with sufficient laxity in this manner.
4. Blow out fracture of the inferior orbital wall: The elevation deficiency is more marked in abduction. Imaging reveals a fracture and there may be associated enophthalmos.

5. Thyroid ophthalmopathy: The elevation deficiency is worse in abduction than adduction.

6. Adherence syndrome: During inferior oblique surgery adhesions may form due to fat prolapse and limit elevation in abduction.

Management

Evaluation

The vision needs to be checked to rule out amblyopia. Abnormal head posture if present is indicative of the presence of fusion. Forced duction testing needs to be performed to confirm the diagnosis.

Non surgical management

Spontaneous improvement is known to occur. Hence it may be prudent to observe cases where there is no threat to binocularity. Elevation in adduction exercises can improve the condition in congenital cases or in cases where there is intermittent Brown syndrome. Injection of corticosteroids has been reported to improve the Brown syndrome in patients with inflammatory disease. Systemic treatment of the underlying disease may improve cases of acquired Brown syndrome.

| Table 1. Differentiating features of Brown syndrome, primary superior oblique overaction and inferior oblique paresis. |
|-------------------|-------------------------------------------------|-------------------------------------------------|---------------------------------|
| Criteria          | Brown syndrome (inelastic superior oblique muscle-tendon complex) | Primary superior oblique overaction | Inferior oblique paresis |
| Limitation of elevation in adduction | Usually severe (-3to-4); common | Usually mild; not common | Usually severe (-3to -4); not common |
| Bilateral involvement | Rare (5-10%) | Common | Unusual |
| Vertical deviation | None or small (<10 PD) | Bilateral small(<10 PD) | Usually large (>10 PD) |
| Superior oblique overaction pattern | None or minimal | Yes, marked | Yes, marked |
|                     | None or V pattern Y- subtype with divergence in upgaze | A-pattern Lambda subtype with divergence in downward gaze | A-pattern often convergence in upgaze |
| Fundus torsion       | None in primary or primary, increasing in upgaze | Intorsion in primary, downgaze, intorsion in | Intorsion in upgaze increasing in downgaze |
| Head tilt test       | Negative | Negative | Positive |
| Forced duction       | Positive | Positive | Positive |

Surgical management

Indications

When there is a loss of binocularity, with the chance of development of amblyopia and the child does not develop an abnormal head posture, surgery is indicated. Mild Brown syndrome needs to be observed. If there is presence of primary position hypotropia and unacceptable downshoot on adduction, surgery can be considered. Acquired cases due to the presence of a scleral explant or a glaucoma filtering valve need to be operated.

Surgical techniques

Sheathectomy was proposed by Brown initially, but the surgery did not yield satisfactory results. Superior oblique and trochlear luxation consists of removing the tendon from the trochlea by luxating the trochlea. This procedure is no longer practiced. Technically easier procedures include superior oblique tenectomy or tenotomy. Though elevation can improve with this surgery, a significant proportion (50-80%) of patients develop superior oblique palsy as Brown syndrome is generally not associated with superior oblique overaction. A Z-tenotomy of the superior oblique was also tried, though this was also unsatisfactory and associated with superior oblique palsy. Simultaneous inferior oblique recession was advised by Parks and Eustis when performing a
tenotomy or tenectomy. While this technique reduced the risk of postoperative superior oblique palsy, about 20% of the patients still had superior oblique underaction. Superior oblique tendon expander surgery was proposed by Wright in 1991. In this technique a retinal silicone band about 5 to 7 mm is cut and sewn to cut ends of the superior oblique tendon with non absorbable sutures. High success rate was reported with a low incidence of superior oblique palsy. A chicken suture can be passed in lieu of an expander to retain the cut ends of the superior oblique together. Superior oblique recession produces a graded slackening of the tendon. Undercorrections are common and the problem with recessing the tendon is that it changes the characteristics of the superior oblique tendon insertions and results in postoperative complication of limited depression.

Complications of surgery include superior oblique palsy which is the most common complication. Palsy usually develops slowly and may be difficult to correct. Undercorrection can occur following surgery, but the effect may improve gradually over time. Silicone expander surgery if performed incorrectly can lead to adhesions and rarely may extrude. Care must be taken not to damage the sheath of the superior oblique. Inadequate care during surgery can lead to damage to the superior rectus muscle.

It is important to remember that Brown syndrome cannot be cured but one can only attempt to improve the field of binocular single vision, improve the elevation in adduction and eliminate head posture. Hence prudence is advised before attempting any surgery for Brown syndrome.

**References**

Culture Negative (Sterile) Postoperative Endophthalmitis

Dr. Meena Chakrabarti MS DO DNB, Dr. Sonia Rani John DNB, Dr. Arup Chakrabarti MS DO

Given its high visual morbidity, postoperative endophthalmitis represents one of the most feared complications of intraocular surgery. This condition is most often encountered after cataract extraction, the most commonly performed operations. The incidence of postoperative endophthalmitis is approximately 0.1% after cataract surgery.

Patients with acute postoperative endophthalmitis present with pain, photophobia, floaters, reduced vision, an inflamed anterior segment including a variable hypopyon, and vitritis. In the EVS, the median time to presentation to a study center was on postoperative day 6, and typical organisms included coagulase-negative staphylococci (46.9 %), other gram-positive organisms (15.5 %), and, much less commonly, gram-negative organisms (4.1 %). Culture-negative or culture-equivocal cases were also common in the EVS (17.9 % and 12.9 %, respectively) and may be due in part to the strict criteria for laboratory-confirmed growth in this multicenter study.

The culture-negative group had a significantly lower frequency of hypopyon on presentation (55 % vs. 85 %) and final outcome of no light perception (2 % vs. 18 %) (p < 0.01) than the culture-proven group.

We present a case of culture negative endophthalmitis managed surgically.

49 years old male patient, a known but well controlled diabetic and hypertensive, underwent an eventful phacoemulsification with foldable intraocular lens implantation under topical anesthesia in his right eye. The first post operative review on the evening of the surgery showed a clear cornea, and a well centered IOL securely within the capsular bag. The post operative regimen was discussed with him and he was advised review after 5 days.

On the 2nd post operative review, the patient complained of gross diminution of vision after a period of a good visual recovery lasting for 2 days. He was otherwise asymptomatic and did not have pain, lid edema, discharge or watering. Ocular examination revealed a vision of hand movements right eye and 6/6P in the left eye. Intra ocular pressure by noncontact applanation tonometry was 7 mm (OD) and 14 mm (OS). Slit lamp examination showed a clear cornea, and, moderately severe anterior chamber reaction with flare, cells and a 2 mm hypopyon. The IOL was not visible as it was covered with yellowish, dirty looking cocoon membrane (Fig. 1).

Fig. 1. Showing the IOL covered with Cocoon membrane
injection. It was also advised to continue systemic orally administered ciprofloxacin and tapering doses of oral steroids.

The patient tolerated the procedure well and had significant visual improvement to 6/9 (Fig. 5). Repeat smear and cultures were also sterile.

**Discussion**

On comparing factors associated with a positive culture isolate, presence of corneal infiltrates and hypopyon were significantly correlated to positive culture. Systemic diabetes, presence of surgical predisposing factors such as exposed knots, loose sutures, section gape or iris prolapse and secondary surgical procedures following cataract surgery, earlier onset of symptoms, poorer presenting vision, presence of corneal oedema, intraocular lens implantation and media haze at presentation were not significantly associated with culture positivity. Eyes with a positive culture were more likely to have an unfavourable visual outcome compared to culture-negative eyes (P=0.013).

Factors associated with an ‘unfavourable’ outcome included presenting visual acuity of light perception or worse, presence of corneal infiltrates, presence of fibrinous anterior chamber reaction, surgical section involvement, aphakia, hypopyon, media clarity at presentation grade IV or worse, vitreous tap smear positivity and systemic diabetes

Cultures have demonstrated a couple of weaknesses against endophthalmitis. When you look at any study of endophthalmitis, you’ll get 25 to 30 percent rate of culture-negative endophthalmitis. These patients have endophthalmitis, but the cultures of their aqueous and vitreous are negative. There are several possible reasons for this. It may be that culture techniques aren’t sensitive enough or the sample that’s taken isn’t big enough to grow the bacteria. Hence in a fourth to a third of
endophthalmitis cases you don’t know what you’re treating. Another issue is that cultures aren’t immediate and there’s a period of time where you’re not sure what you’re treating. Culture negativity could also be due to an erroneous diagnosis as in post uveitic cataract, TASS, dropped lens fragments, Masquerade etc. Sample may be inadequate, the site of sampling may be inappropriate, there may have been an inordinate delay in transport and processing or the fault may lie with the poor sensitivity of tests.

Polymerase chain reaction offers several advantages over conventional cultures which are listed below

**Advantages of PCR over conventional microbiological tests**

<table>
<thead>
<tr>
<th>Conventional tests</th>
<th>PCR tests</th>
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<tbody>
<tr>
<td>Require larger clinical sample size</td>
<td>Does not require larger clinical sample size</td>
</tr>
<tr>
<td>Require longer time for completion of the tests. Isolation and identification of an infectious agent needs more than 48 hours.</td>
<td>Require less than 24 hours for completion of the tests to identify the required infectious agent</td>
</tr>
<tr>
<td>Prior antibiotic therapy interferes with the tests for detection of bacterial agents</td>
<td>Prior antibiotic therapy does not interfere with the tests for detection of bacterial DNA</td>
</tr>
<tr>
<td>Viruses are liable and often their infectivity to tissue cultures is reduced in the clinical specimens during transport to the laboratory and storage of the same</td>
<td>Since DNA is stable its detection is not affected</td>
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**Fast Real-time PCR**

To overcome the disadvantages of cultures, Pablo Goldschmidt, and co-workers devised a new version of the PCR test that retains PCR’s high sensitivity but speeds up the already quick process. They recently published a study of their fast real-time PCR, or f-real-t PCR, in which they compared it to both culturing and direct exam by a microscope. In their study, the researchers equipped their PCR test with DNA of the usual suspects when it comes to endophthalmitis: *Staphylococci; Streptococci; Haemophilus; Pseudomonas; Enterobacteria; Acinetobacter; Propionibacteriaceae and Corynebacteria*. To put the PCR to the test, they then took 100-μl samples of vitreous fluid and 50 μl of aqueous humor from endophthalmitis cases, as well as vitreous fluid and aqueous from non-infective disorders after adding an internal control.

The f-real-t PCR was highly sensitive, detecting 0.01 colony forming units of bacteria per microliter with no confounding cross-reactivity with fungi. It correlated 100 percent with the culture-positive results. The samples from non-infective cases tested negative. It even caught organisms that culture missed; 60 percent of the endophthalmitis samples tested culture-positive, but 90 percent were positive on f-real-t PCR. What’s more, while it took several hours to a couple of days for the cultures to return identification, the f-real-t PCR was complete in 90 minutes.

Advances in investigational modalities may make identification of infective organism possible in all cases of infection.

**References:**


Multiple Myeloma Presenting As Primary Orbital Tumour – A Case Report

Dr. Bindu N Das MS ¹, Dr. Sandhya Ram MS ², Dr. Jalal MS ²

Introduction

Multiple myeloma and its related plasma cell dyscrasias are characterized by an abnormal proliferation of a single clone of highly specialized lymphocytes engaged in the production of a specific immunoglobulin. Mean age at presentation is between 40-70 yrs with peak in the 7th decade.

It accounts for about 10% of all haematological malignancies with an incidence of about 5.5 cases per 100,000 population.

Orbital involvement as a manifestation of multiple myeloma is very rare. It accounts for 0.1 – 0.5 % of all orbital tumours. Less than 50 cases of such involvement has been described in literature.

Recently we came across a case of multiple myeloma with orbital involvement.

Case Report

A 50 yrs old female presented in our OP with a history of painless, progressive drooping of her (R) upper lid of 2 ½ months duration and a swelling in the superolateral part of (R) orbit of 2 months duration (Fig.1). The swelling was painless, gradually progressive and no relation with posture or coughing. There was no history of diplopia, fever, weight loss, or trauma. She had chronic low back ache since 15 yrs and has been on treatment with analgesics. She also had a thyroid nodule excision at the age of 13 yrs, the details of which were not available.

Ocular Examination

Examination of the right eye showed an eccentric proptosis with a forward, downward and inward displacement of the eye ball. The proptosis was due to a swelling of about 8x5 cm over the superolateral part of (R) orbit (Fig.2). The skin over the swelling was normal. The swelling was firm, non tender, non pulsatile and non compressible. The posterior border could not be palpated and the overlying bone was eroded.

Elevation of the (R) eye ball was restricted minimally. Visual acuity and tension was normal and the pupil reacted briskly to light. Fundus examination showed choroidal folds. Left eye was within normal limits.

System examination revealed no abnormalities except for a scar over the front of neck (thyroid nodule excision) and a tenderness over L4-L5 region of spine.

Based on the clinical findings, a diagnostic possibility of a malignant tumour of the lacrimal gland or a metastasis from a primary (possible thyroid) was made.

A CT scan of the head and orbit was ordered, which revealed an enlarged (R) lacrimal gland, destruction of the orbital plate of frontal bone with intracranial and scalp extension and compression upon the globe. Multiple lytic lesions in the skull were also seen suggesting the possibility of a malignant tumour of the lacrimal gland or metastasis (Fig. 3 & 4).
Fig. 1. Swelling in the superolateral part of the orbit displacing the globe

Fig. 2. Lacrimal gland pushed downwards

Fig. 3 & 4. CT showing swelling with overlying bone erosion

Fig. 5 & 6. Digital X-ray skull showing multiple punched out lytic lesions

Fig. 7. FNAC from the swelling showing plasma cells

Fig. 8. Bone marrow trephine biopsy showing plasma cells
Plain X-ray skull was taken which showed multiple, punched out, lytic lesions (Fig.5 & 6). Thus a differential diagnosis of multiple myeloma was also made.

FNAC from the swelling was performed using a 23 G needle. The aspirate was haemorrhagic. Microscopic examination revealed polygonal cells with moderate cytoplasm and a single, large eccentric nucleus (Fig.7).

A cytologic diagnosis of plasmacytoma was thus given and a detailed work up was advised to rule out systemic involvement.

Thus haematological investigations like ESR was repeated which showed 90 mm/ 1st hr. (Initially – 49 mm/hr).

Hb was 12.4 g%

LFT, RFT, S.Calcium, S. Phosphorous were within normal limits. Urine Bence Jones Proteins was absent on repeated examination and serum electrophoresis was negative for myeloma proteins.

Plain X-ray pelvis showed sclerosis of L4-L5 area. The patient was then transferred to the haematology department where she underwent a bone marrow trephine biopsy. It revealed infiltration by group of plasma cells comprising about 20% of the cell group (Fig.8).

A final diagnosis of multiple myeloma manifesting as orbital involvement at presentation was thus made.

The patient was put on CDT (Cyclophosphamide, Dexamethasone and Thalidomide) regime. She responded fairly well to the treatment.

Discussion

Orbital involvement in multiple myeloma is a very rare finding. Less than 50 cases of such involvement is described in the literature. Orbital involvement can occur in one of the following ways.

a. As a part of systemic multiple myeloma with local bone destruction from an isolated plasmacytoma.
b. Extramedullary plasmacytoma from orbital soft tissue.
c. Secondary extension to the orbit of a sinus.

In most cases, the onset is insidious with slowly progressing proptosis accompanied by pain, diplopia and visual impairment. Intracranial extension can lead to papilloedema and cranial nerve palsies. Other ocular manifestations include conjunctival and corneal crystalline deposits, scleritis, episcleritis, secondary glaucoma, uveal plasmacytoma, hyperviscosity retinopathy, retinal vasculitis etc.

Non specific symptoms like low grade fever, malaise, anorexia etc are common. Careful examination and performing the relevant investigations help in reaching the diagnosis earlier.

Imaging features of orbital multiple myeloma have been described in few cases. CT shows thinning of the overlying bone or causing marked bony expansion and destruction. MRI shows low signals on T1 weighted images and high signals in T2 images.

Since the clinical outcome is significantly worse in patients with systemic involvement as compared to those with solitary plasmacytoma an early cytologic diagnosis of extramedullary involvement in multiple myeloma helps in timely institution of appropriate treatment.

References

Bilateral Optic Nerve Glioma in a Case of Neurofibromatosis

Dr. K.V. Raju  MS, Dr. Jesheena  DO

Introduction

Neurofibromatosis Type 1 (NF-1) is a relatively common autosomal dominant disorder. In addition to multiple peripheral neurofibromas, NF-1 predisposes to central nervous system (CNS) tumors like optic nerve glioma, neurofibroma, ependymoma and meningioma. Bilateral optic nerve gliomas is relatively uncommon in NF-1 and optic nerve glioma usually presents as slowly progressive visual loss. Here we report a case of NF-1 with bilateral optic nerve glioma, presenting as sudden onset of defective vision in one eye.

Case report

22 year old female presented to our department with history of sudden onset of defective vision in right eye of 3 days duration, not associated with redness, pain, or photophobia.

There was no history of trauma to the eye. There is history of multiple swellings and hyperpigmented lesions all over the body since 10 years of age, progressively increasing in numbers. There is no history of similar illness in the family.

General examination showed multiple cafe au lait spots, cutaneous neurofibromas [fig. 1], molluscum fibrosum and axillary freckles. Neurological examination of motor, sensory, and cerebellar systems were normal.

Ocular examination showed 0.5 x 0.5mm sized firm swelling on right upper lid, decreased corneal sensation and grade 2 relative afferent pupillary defect in right eye. Vision in right eye was 6/60, with defective colour vision. Left eye vision was 6/6. Slit lamp examination showed prominent corneal nerves in both eyes and Lisch nodules at 5 O’clock in right eye, 2 and 4 O’clock in left eye. Fundus examination of right eye showed pale optic disc with well defined margin and normal vessels. Indirect ophthalmoscopy showed normal retinal periphery. Ophthalmoscopic examination of left eye was normal.

Investigation

MRI brain and orbit showed diffusely thickened non enhancing right optic nerve suggestive of optic nerve glioma [fig. 2]. Thickening was noted in the intra orbital portion of left optic nerve also. Non-enhancing patchy hyperintensities on T2 weighted images noted in globus pallidus, thalamus, brainstem, middle cerebellar peduncle [fig. 3] and supra tentorial white matter – likely to represent hamartomas in white matter and deep gray matter.
Patient was diagnosed as a case of Neurofibromatosis type 1 from the clinical picture. As the patient presented with sudden onset of significant defective vision on right eye with RAPD and there was a delay in getting MRI, we started on systemic steroids in view of possible retrobulbar optic neuritis. Even though MRI showed optic nerve glioma, we continued on steroid as the patient’s vision was improving. As the patient was not willing for any intervention for glioma, she was discharged and advised follow up with tapering dose of steroids. On follow up at 2 weeks, patient’s vision was 6/9 which improved to 6/6 with -0.25 Dsph.

**Discussion**

Neurofibromatosis type 1 is a neurocutaneous syndrome characteristically associated with freckles in non-exposed areas, café au lait spots, Lisch nodules and cutaneous neurofibromas. Patients are at an increased risk of developing neoplasms of nervous system like optic nerve glioma, neurofibroma, ependymoma and meningioma. Optic nerve glioma develops in 15% of patients with NF-1, may be unilateral or bilateral and usually presents as slowly progressive painless loss of vision. Rarely it can present as sudden loss of vision due to hemorrhage into the glioma.

Our patient has got axillary freckles, café au lait spots, lisch nodules and cutaneous neurofibromas – fulfilling the criteria for diagnosing neurofibromatosis type 1. MRI showed bilateral optic nerve glioma. The patient presented with sudden loss of vision in right eye, which is unusual in optic nerve glioma - where the present action is as slowly progressive loss of vision. MRI did not show any evidence of haemorrhage into glioma to produce a sudden loss of vision. As the patient improved to normal vision, possible etiologies for loss of vision in our patient are unrelated optic neuritis or nonspecific inflammatory changes in the glioma, which might have improved with steroids.

So in conclusion, we present a case of bilateral optic nerve glioma in NF-1, which is relatively uncommon and sudden loss of vision in our case could be due to nonspecific inflammatory changes in the glioma or due to unrelated retrobulbar optic neuritis.

**References**

3. Theos A Korf. BR. Pathophysiology of NF-1 Ann. Internal Med.2006;144:842-849

![Fig. 2. Shows bilateral optic nerve glioma on T2 weighted MRI](image1)

![Fig. 3. Shows hamartoma in cerebellum](image2)
Siderotic Cataract

Dr. Sonia Rani John DNB, Dr. Arup Chakrabarti MS DO, Dr. Meena Chakrabarti MS DO DNB

Siderosis bulbi is a sight threatening complication of a retained intraocular iron containing foreign body and may occur 8 years to 18 years after ocular injury. The clinical findings include iris heterochromia, pupillary mydriasis, cataract formation, and retinal pigmentary degeneration. Progression is likely to occur more when the intraocular iron containing foreign body is localized in the posterior segment of the eye. Delay in foreign body removal may cause disintegration of the foreign body with oxidized ferrous particles deposited throughout the eye. Hence even after a thorough parsplana vitrectomy and foreign body removal, siderotic changes can still progress.

In this case report we present a young man who had progression of siderotic changes following intraocular foreign body removal and presented after a year with a siderotic cataract.

A 30 year old Gulf employee sustained injury to his right eye 8 months prior to presentation. Injury was sustained while heating ball bearings of iron, which burst and struck the white of his right eye. He was given first aid and topical antibiotic drops for the injured eye. This conservative approach was continued till he returned home after 8 months. He had noticed progressive diminution of vision in the right eye. At presentation he had a vision of counting fingers at 2 meters improving to 6 / 36 with pin hole in his right eye.

Applanation tonometry was 13 and 15 mm in his right and left eyes respectively. The right eye showed features of ocular inflammation in the form of 2 + flare and cells as well as plenty of vitreous cells. The pupil was mid dilated and reacting sluggishly. Fundus examination showed a grade III media haze and a whitish encapsulated foreign body was observed in the inferior periphery. A Scan USG was performed which confirmed the presence of a retained intraocular foreign body located on the retinal surface inferiorly. Plain X-ray orbit showed a radio opaque shadow suggestive of a retained intraocular foreign body in right eye.

The patient underwent pars plana vitrectomy with REM magnetic foreign body removal under local anesthesia. He had an uneventful post operative period and was discharged with a quiet eye, clear lens and good fundus view. There was also significant visual improvement to 6 / 12 (R) on the 15th postoperative day.

The patient next reported for review after a year. He complained of blurring of vision in the right eye which occurred 6 months after a satisfactory visual gain post operatively. Ocular examination revealed a visual acuity of 6/36 NIG and NIP, N24 (RE), good mydriasis, Grade II nuclear sclerosis, pigment on corneal endothelium and anterior vitreous face as well as anterior sub capsular rust staining. Specular microscopy showed an adequate endothelial cell count with normal morphology (right eye: 2552 / mm² and 2565/ mm² in the left eye).

The patient underwent a temporal clear corneal phacoemulsification by the phaco- chop technique with good visual recovery of 6/ 6 on the first post operative visit.
Discussion

Siderosis bulbi is defined as a coloration of the eye by fine rust particles in suspension or in solution in the fluids of the eye. The condition is associated with a mild but progressive ocular inflammation of the uveal tract with degeneration resulting in a gradual destruction of sight. Iron is deposited in the epithelial tissues of iris, ciliary body, lens, retina and RPE. Deposition of ferric ions causes production of oxidants, resulting primarily in damage to the photoreceptors and RPE.

A variety of ocular manifestations may be associated with siderosis bulbi such as Adies pupil, pupillary...
mydriasis, constricted visual fields, night blindness, corneal staining, iris heterochromia, sub epithelial rust deposits on anterior lens capsule, cataract, retinal pigmentation, optic atrophy and secondary open angle glaucoma.

In patients with retained intraocular foreign body in whom the foreign body removal is delayed, siderosis bulbi can manifest after surgery. Hence it is necessary to follow up all patients with delayed intraocular foreign body removal with serial ERG.

ERG monitoring will help record various stages in the development of siderosis. There is an initial stage in which both positive and negative components of ERG can increase and this stage is too early to be recognized clinically. Later the ERG becomes negative and, finally extinct even though the retina may function reasonably well. These two changes are irreversible.

Electroretinography can be used to follow-up the course of developing siderosis and provides useful information as to when a decision has to be made as to the advisability of undertaking a foreign body removal.

References
Worm Wobble - Subconjunctival Dirofilaria

Dr. Arup Chakrabarti MS DO, Dr. Sonia Rani John DNB, Dr. Meena Chakrabarti MS DO DNB

**Introduction:** Ocular zoonotic infections by filarial worms are not uncommon. Most of them are caused by the genus Dirofilaria. Human dirofilariasis caused by Dirofilaria Repens have been reported to occur widely throughout Asia, Europe and Africa. Reports of this infection from India are however limited. The involvement of the eye may be periorbital, subconjunctival or intra ocular. In this report we describe a case of Dirofilaria Tenuis presenting as a subcutaneous swelling of the bulbar conjunctiva.

**Case Report:**
A 60 year old lady reported to our out-patient department with foreign body sensation in the right eye of 2 days duration. On examination, there was a nodular swelling in the inferomedial quadrant of the right eye. Slit lamp examination showed a motile worm in the subconjunctival space. (Fig 1 & 2) There was no other skin nodule anywhere on the body. There was no lymphadenopathy. The patient was not suffering from any other systemic or local manifestation. Routine laboratory tests were within normal limits. Blood smear was negative for microfilaria. There was no eosinophilia.

Using topical anaesthesia, the live parasite was surgically removed by excising the conjunctiva, under the slit lamp microscope. The extracted worm was milky white resembling white thread (Fig 3 & 4). The worm was thin and cylindrical wearing 12 cm in length with a maximum diameter of 45 mm. Microscopic examination of the worm revealed that the anterior end of the worm was slightly tapering and had a rounded head. The parasite had a thick unsegmented cuticle with characteristic longitudinal ridges and cross striations. The oral end showed a conspicuous mouth cavity. The posterior end was bulbous. Based on the morphologic features, the worm was identified as *Dirofilaria Tenuis*.

**Discussion**
Human dirofilariasis is a cosmopolitan zoonosis. The dirofilaria are natural parasites of mammals and are transmitted to man by zooanthrophilic mosquitoes. Though nearly forty species of dirofilaria have been identified, only a few have been reported to cause human infection; the most common being Dirofilaria...
Immitis, a parasite of dogs, D.Tenius, a parasite of raccoons, D.Repens, a parasite of dogs and cats and D.Ursi a parasite of bears. Formally D. Repens and D. Immitis which are dominantly parasites of dogs, were of epidemiological bearing in man. However during the last 20 years, a few other species of Dirofilaria infections were notified, especially by A. Joseph. Ophthalmic dirofilariasis is transmitted to humans by common insect vectors like Anopheles, Culex and Aedes mosquitoes. The first case of human ocular dirofilaria was reported by Addario in 1885 from Milan, Italy. Since Aedes index has risen upto 20 times over the years in Kerala, it is imperative to focus on the epidemiology of these infections.

Cases of human subcutaneous and ocular infection with D.Repens have been reported sporadically from France, Italy, Turkey, Africa , Thailand , USA and South East Asia. The species vary according to the geographical area with D.Tenuis being common in United States and D.Repens in Europe, Middle East and South East Asia. D. Repens is most frequently responsible for human dirofilariasis.

Symptoms vary in severity. In most cases the infections are asymptomatic or mild and uncomplicated, especially until the worm dies. Only after their death insitu painful inflammatory reactions occur around the worms causing subcutaneous nodular lesions, necessitating excision. During the migration of the worm through subcutaneous tissue inflammatory reactions may develop like mild fugitive swelling or subcutaneous nodule which can be painful and tender. These nodules occur preferably in areas not covered by clothes especially head.

The most common symptoms in ocular dirofilariasis are localized pruritus, pain, swelling, oedema, hyperemia of the conjunctiva, sensation of movement under the skin of the conjunctiva. Other ocular findings include:

1. Small subconjunctival granulomas containing D. Repens or D.Tenuis.
2. Corneal oedema caused by the organism in anterior chamber.
3. Scleral nodules caused by dirofilaria.
4. Lid oedema, signs of orbital inflammation, tenonitis or orbital pseudotumor.
5. Intense intraocular reaction, keratitis, vitreous opacities and secondary glaucoma caused by living intraocular filariae.
6. Retinal haemorrhages from vitreous parasites.
7. Unilateral RPE disturbances simulating retinitis pigmentosa from intraocular Dirofilaria etc.

However allergic reaction with fever, urticaria and facial oedema may occur. In majority of instances, parasites are found in excised nodule and tissue biopsy specimens. Less frequently they are removed from the tissues intact. Female worms are found more frequently than male.

Diagnosis is usually established with the surgical removal of the adult worm. Microfilaria have never been reported in humans. Eosinophilia occurs in less than 15 % cases with D. Immitis and rarely with D.Repens. In this case also reported blood smears were negative for microfilaria and there was no eosinophilia.

There is wide variation in the reported size of male and female worms in different part of the world. All dirofilaria have fine transverse striations on the cuticle and abundant somatic musculature. D.Repens is a nematode with a long thin filiform appearance All except D.Immitis and few others have prominent external longitudinal ridges. Longitudinal ridges of D.Repens are broader and less distinct. They have rounded anterior end with buccal cavity. In contrast to the rounded short tail of female worm the male worms have a coiled tail.

Surgical removal of the worm not only establishes the diagnosis in most cases but presents a definitive cure. Oral therapy with DEC 2 mg / kg destroys other not yet visible worms despite the fact that human dirofilariasis is usually regarded as an infection by a single worm.

References:
In a lighter vein

Ad-va-nces & Ad-ver-sities

RRV

Commercialisation of the medical profession has resulted in something called marketing creeping into our lives. We used to call it advertising in the past. Anywhere from internet to the backside of auto-rickshaws might carry ads for products and procedures; doctors and departments ad hoc omne.

Once upon a time, advertisements were taboo in the medical world. Those of us older than forty might remember the times when there were no huge hoardings proclaiming the merits of one hospital or larger than life size photographs of doctors holding ophthalmoscopes in their hand on the way-side. Nor got handed out bit notices advising you where one could get ones piles and anal fistulae treated. But the clever ones among us had ways and means to circumvent the word of old Hippocrates.

One veteran had boards put up by the roadside. They were innocent looking directional boards before junctions near his house showing which way to go to reach the railway station/ bus stand/ court. But the other fork of the road was marked with the name of the doctor. Another belonging to an earlier generation had another trick. During the first show in the major theatres, immediately after the intermission a hand-written slide would be projected. It said ‘If Dr. So-and-so M.B.B.S, M.R.C.P, F.A.M.O.U.S. is in the theatre, please contact Such-and-such Hospital. There is an emergency case waiting’. But he got too smart for his own good and overplayed his hand. He did it once too often. And got found out.

Touting or canvassing was and is considered the lowest form of advertisement. Some hospitals do pay the referring doctor/ G.P., euphemistically calling it the referral fees. Some time back one among our community (let us call him Dr. X) raised it to the level of a fine art by recruiting auto-rickshaw drivers as touts. Passengers with red eyes or poor vision or talking about eye doctors were the targets. One morning, the wife of Dr. Y, a colleague hired an auto-rickshaw from the railway station and asked him to go to the house of Dr. Y. “Why do you want to go to an inferior doctor when we have got some one like Dr. X in our town?”, the driver swung into action. “But I am Dr. Y’s wife” she said. “May be”, he was insistent, “but if you go to Dr. X once you will never go to any other doctor”.

Eye Banking in India

Dr. Rachel Jose MS¹, Dr. Sandeep

Need for eye banking
Relatively greater attention has been given to cataract surgeries considering the fact cataract blindness is the major cause of blindness in India. Though, corneal blindness is much less in frequency, the gravity of the problem is serious considering the fact, firstly, over 50% of corneal blindness occur in children in contrast to cataract blindness which is the disease of old age. Secondly, the economic loss due to corneal blindness is much more than cataract blindness.

This again is due to two factors. The corneal grafting being a super-specialized branch requires trained corneal surgeons, dependent on donor cornea, more tedious surgery and demands meticulous, close and longer follow up. Also being the childhood disease, man-year loss is 5 times more than cataract patients which leads to less production and in turn indirectly adds economical burden on the society. According to estimate, there is a need of 1,00,000 corneas in the country however we are able to procure approx. 38,000 only on 2008. We are striving to fill this gap by having good eye banking services including proper tissue procurement, processing, and improved storage media with enhanced publicity for eye donation.

History
Ever since the first “successful” human to human corneal transplant was done in 1903 at Czechoslovakia by Zirm to visually rehabilitate a patient with alkali burn, the technique of corneal transplantation underwent various changes and transformed into a clinically acceptable procedure for the corneal blind. However, no corneal grafting was performed till Filatov, a Russian Ophthalmologist, considered to be father of keratoplasty, performed the surgery in 1935 by utilizing human donor cornea from the eyeball stored in moist chamber at 4°C.

In response to demand of human corneal tissue by increasing number of ophthalmologist, first Eye Bank for sight restoration was started in the state of New York in 1944 by Palton. Since then eye banking movement has spread worldwide. In India, the first eye bank was established in 1945 at Madras [Chennai] and the first successful corneal transplantation was carried by Dr. Dhanda of Indore in 1960.

Concept
Eye Bank is an organization which deals with the collection, storage and distribution of the donor cornea for the purpose of corneal grafting, research and supply of eye tissue to other eye banks for ophthalmic purpose. Comprehensive and detailed standards of eye banking have been formulated to assure consistency, quality, proficiency, and ethics in dealing with eye tissue for harvesting, transportation, transplantation and research. It also deals with activities related to community awareness and motivation for eye donation. According to available information, there are 238 functional Eye-banks in the country [Table 1].

Organization and setup of an ideal Eye Bank
An eye bank should be registered with competent authority in the state under “Transplantation of Human

¹Additional Director General, Ministry of Health and Family Welfare
Organs, Act 1994” and strictly adhere to related stipulation, notification and guidelines on health institutions issued by regulatory and civic agencies. It should ideally be located within or near a hospital complex and for long term sustainability should be attached to 4-5 eye donation centres.

**Manpower:** Health personnel are critical workforce for running any institution effectively and efficiently and same is true with eye bank. They should be trained in all measures related to quality control activities. Eye bank should be manned by an executive director/administrator [1] who could be a trained ophthalmologist, eye bank manager [1], technician [2], counselors [atleast 2], secretary/ data entry operator/ and telephone operator, sweeper, driver.

**Infrastructure and equipments:** Each eye bank should have space for office reception, waiting area, preparation area, processing area with laminar flow hood, sterile area, evaluation zone, store room, toilets etc. Basics units comprise of refrigerator, slit lamp biomicroscope, specular microscope, hot air oven, autoclave, vehicle, and telephone connection. Each eye bank laboratory must possess a minimum of six sets of cornea rim excision and enucleation sets, four thermocol boxes and 20 collection bottles with eye ball stands. Instruments are mainly used either for donor eye ball enucleation procedure or corneo-scleral tissue removal/preparation for donor tissue preservation.

**Documentation:** Clinical and administrative documents are very important for smooth functioning of eye banks. Various recording and reporting forms could include donor information; consent forms; death certificates form; harvested donor eye data; cornea evaluation format; haemo-dilution; eye donor medical particulars; tissue utility data/discarded data; distribution information; outcome forms; accounting/ financial reports; waste disposal; accreditation, quality control measures forms and general correspondence.

**Challenges, Issues and Concerns**

There are various challenges, issues and concern that impede harvesting requisite number of cornea in the country. Some of these are poor integration of existing eye banks, lack of motivation amongst general public regarding eye donation; myth, misconception and taboo’s associated with eye donation; inadequate infrastructure, facilities and services for removal of eyeballs/cornea at the time of death; shortage of trained manpower, lack of transport and poor means of communication.

National Programme for Control of Blindness [NPCB], Government of India initiatives in upscaling Eye Banking in India:

- Support for setting/strengthening Eye Banks in Government/voluntary sectors as per approved XIth five-year [2007-12] plan.
- Non-recurring assistance upto Rs 15 [fifteen] lakh for equipments, instruments, medicine, and furnishing and fixtures.
- Recurring assistance of Rs 1500 [one thousand and five hundred] per pair of eyes towards honorarium of eye bank staff, consumables including preservative material and media, transportation, POL [petrol-oil-lubrication] and contingencies.
- Recurring assistance of Rs 10,000 [ten thousand] only per month towards salary of eye donation counselor on contract basis.
- Support to Eye Donation Centres
- Non recurring assistance upto Rs 1 [one] lakh for strengthening/developing Eye donation centres

### Table 1: Number of Functional Eye Banks in India

<table>
<thead>
<tr>
<th>States/UTs</th>
<th>Functional eye banks</th>
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<tbody>
<tr>
<td>1. Maharashtra</td>
<td>52</td>
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<tr>
<td>2. Tamilnadu</td>
<td>24</td>
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<tr>
<td>3. Andhra Pradesh</td>
<td>24</td>
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<tr>
<td>4. West Bengal</td>
<td>16</td>
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<td>5. Gujarat</td>
<td>15</td>
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<td>6. Kerala</td>
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<td>7. Karnataka</td>
<td>14</td>
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<td>8. Uttar Pradesh</td>
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<tr>
<td>9. Punjab</td>
<td>10</td>
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<tr>
<td>10. Rajasthan</td>
<td>10</td>
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<tr>
<td>11. Madhya Pradesh</td>
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<tr>
<td>12. Delhi</td>
<td>09</td>
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<tr>
<td>13. Haryana</td>
<td>07</td>
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<tr>
<td>14. Chandigarh</td>
<td>06</td>
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<tr>
<td>15. Bihar</td>
<td>06</td>
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<tr>
<td>16. Puducherry</td>
<td>03</td>
</tr>
<tr>
<td>17. Assam</td>
<td>02</td>
</tr>
<tr>
<td>18. Orissa</td>
<td>02</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>238</strong></td>
</tr>
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</table>

Source: Eye Bank Association of India [EBAI], 2008
Recurring assistance of Rs 1,000 [one thousand] per pair of eyes collected

Financial support to voluntary organization to the tune of Rs. 1000/- for corneal transplantation.

Training of eye surgeon on corneal surgery and enucleation

NPCB has been working with various stakeholders including voluntary organizations like Eye Bank Association of India [EBAI], an umbrella body of all eye banks/eye donation centres in the country to strengthen eye donation movement in the country.

ORBIS International, an NGO assisted government in Eye Banking and Eye donation activities by appointing ‘Grief Counselors’ on contract basis in few hospitals.

NPCB has organized various workshops and consultative processes to formulate road map for eye banking in India including adoption of international standards to optimize resources.

NPCB has been organizing various awareness generation activities with regard to Eye donation in the country. The programme along with stakeholders observes “Eye Donation Awareness Fortnight” from 25th Aug to 8th Sep every year through out the country. In this regard, spiritual/religious leaders are being contacted to sensitize them on this issue and seek their involvement.

Health personnel will be exposed in a phased manner on the procedures of eye removal through a documentary movie under integrated Training of National Rural Health Mission [NRHM].

NPCB has launched Hospital Cornea Retrieval Programme [HCRP] a strategy for increasing eye donation by informing, counseling and motivating relatives of terminally ill patients, accident victims and patients suffering from other grave diseases admitted in the hospitals.

States have been issued instructions to display contact details of functional Eye Banks in all wards/casualty departments of government health institutions.

Currently, eye balls can be enucleated by a Registered Medical Practitioner as stipulated under Transplantation of Human Organ Act, 1994.

A suggestion has been mooted for a trained technician to remove eyes/cornea after death. It has gone to Law Ministry for consideration so as to study its wider ramification.

**Facts about Eye Donation**

1. Almost anyone of any age and sex can pledge to donate eyes after death. This can be done even if donor wears glasses, has cataract or has undergone eye surgery successfully. All that is needed is a clear, healthy cornea.

2. The eyes of the deceased can be donated whether he/she has pledged the eye during life or not. At the same time, eyes cannot be removed without the consent of the next of kin, even if the deceased has already pledge his eyes.

3. The eyes have to be removed within 6 hours of death. So the nearest eye bank or eye collection centre must be informed immediately irrespective of the initial pledging centre/eye bank.

4. Eye lids of the dead should be closed immediately after death. Head end should be elevated, fans should be switched off and a wet piece of cloth could be placed over the covered eyes. Antibiotic drops, if available may be applied to keep the eye moist.

5. In case of death being reported from other than hospital, eye bank team with a doctor/technician will reach the donor site including home. No fee is charged to the family for eye donation.

6. Eye removal takes only 15-20 [fifteen to twenty] minutes and leaves no scar or disfigurement of the face.

7. Eye donation gives sight to two blind persons. One blind person is given one eye.

8. On reaching eye bank, eyes are examined, processed and used for corneal transplant operation as early as possible.

9. The recipient of cornea will always remain anonymous but the family should be satisfied knowing that the eyes have been used to restore vision of blind person[s].

10. The donated eyes are never bought or sold. Eye donation is never refused.
Capsulo-cortical Adhesions (CCA) and Phacoemulsification (PE)

Dr. Arup Chakrabarti MS DO, Dr. Sonia Rani John DpNB, Dr. Meena Chakrabarti MS DpNB

One of the basic requirements of modern techniques of phacoemulsification is free rotation of the nucleus. Sometimes it may be difficult or impossible to rotate the nucleus despite meticulous cortical cleaving hydrodissection. This is usually due to the presence of capsulocortical adhesion (CCA). CCAs are characterized by adhesions between the capsule and cortex. They may be anterior, posterior, equatorial or a combination. They are characterized by a definite area of translucence between the capsule and underlying opaque cortex.

Discussion

- Detection of CCA is important before hydrodissection
- Meticulous dilated slitlamp evaluation preoperatively is mandatory
- CCA may be missed in non dilating pupil or dense cataract
- Can be diagnosed intraoperatively even if missed initially
- Meticulous cortical cleaving hydrodissection is necessary in presence of CCA
  - Fluid injection after tenting of anterior capsule, close to capsular fornix
  - Mechanical lysis with cannula or cyclodialysis spatula
  - Signs of successful hydrodissection
  - Fluid wave across the posterior capsule
  - Shallowing of anterior chamber
  - Prominent capsulorhexis edge
  - Release of tapped fluid from the rhexis margin when nucleus is tapped back.
- In presence of equatorial adhesions, further multi-quadrant hydrodissection to be done before attempting nucleus rotation.
- Milky fluid emanating from area of adhesions could be result of lysis of adhesions
- Time to perform rhexis and hydrodissection more patients with CCA.

Guidelines in Patients with CCA

- CCA is a frequent phenomenon and is often underdiagnosed
- Establish diagnosis preoperatively
- Cautious in Total Cataract/Small Pupils
- TB Staining of the Anterior Capsule
- Meticulous cortical cleaving hydrodissection.
- Hydrofreedissection may be beneficial
- No Forcible Nucleus Rotation
- CTR/Injector to be Kept Handy

Conclusion

- Thorough preoperative dilated slitlamp evaluation mandatory
- Intraoperative evaluation to detect missed cases.
- Increased suspicion when lens milk visualized in preoperatively undiagnosed cases.
Different types of CCAs seen on diffuse illumination

CCA seen on retroillumination

Diffuse CCAs

CCAs seen under slit beam-There is no definite area of translucence between the capsule and underlying opaque cortex. They may be focal or diffuse

Focal CCAs

Lens milk is seen in all Furry epinuclear surface seen cataracts regardless of its type in CCA

- A 3 point cortical cleaving hydrodissection and hydrofree dissection to be performed before attempting nucleus rotation.

Reference

Management of Branch Retinal Vein Occlusion

Dr. Mahesh P. Shanmugham MD 1, Dr. Gopal S. Pillai MS 2, Dr. Rajesh MS 3, Dr. Shane Mathew MS 4, Dr. Thomas Cherian MS 5, Dr. Meena Chakrabarti MS 6

65 year Old Doctor, with no systems riskfactors. First presented in Nov 2007 with defective vision in lower field of the left eye

Visual Acuity RE 6/9, LE 6/6, NV with present glass N 6, N 8 and intraocular tension of 19 Right Eye and 21 Left Eye.

Fig. 1. (a) Fundus appearance at presentation showing a non-ischemic BRVO in the left eye. (b) FFA showing a well perfused non ischemic BRVO left eye

Fig. 2. Fundus photograph taken after 2 months showing increase in retinal hemorrhages with macular hemorrhages and edema.

Fig. 3. (a) OCT 4 months after presentation showing macular edema with a central retinal thickness of 550 mm and subfoveal serous retinal detachment (b) Fundus picture and FFA taken 4 months after presentation showing ischemic conversion with neovascularisation of optic disc and large areas of capillary non perfusion.

Fig 4. Fundus picture at 8 weeks post sectoral laser photocoagulation showing some amount of resolution of macular edema

1 Sankara Eye Hospital, Bangalore, 2 AIMS, Kochi, 3 Al-Salama Eye Hospital, Perinthalmanna, 4 Vasan Eye Care Centre, Trivandrum, 5 Little Flower Hospital, Angamaly, 6 Chakrabarti Eye Care Centre, Trivandrum
Fundus Picture (Fig. 1a) and fluorescein angiography suggestive of non-ischemic (BRVO) branch retinal vein (Fig. 1b) occlusion.

The patient was managed conservatively for 6 months with resolution of hemorrhage. On review after 2 months the patient complained of defective vision in his left eye. Ocular examination revealed a visual acuity of 6/18 N\textsuperscript{18} N\textsuperscript{18} and N\textsuperscript{18} N\textsuperscript{18} in the left eye. Fundus examination (Fig. 2) showed and increase in retinal hemorrhages with macular hemorrhages and edema. Conservative treatment was continued and the patient reviewed again after 3 months. Review on 4/2008 showed central retinal thickness of 550 microns with subfoveal serous RD (Fig. 3a)

In view of the large areas of capillary non perfusion (Fig. 3b) and worsening of the macular edema sector laser photocoagulation was performed along with focal laser treatment. The patient reported for review on 6/2008.

Vision had deteriorated 6/24 N\textsuperscript{24} in the left eye.
Fundus examination showed worsening of oedema at the macula (Fig. 4)

Your opinion pertaining to the following issues is solicited.

**Dr. P. Mahesh Shanmugam**

1. **What will be your line of management?**

This is a 55 year old gentleman who presented with early, partial, superotemporal branch retinal vein occlusion in his left eye that has progressed to a more severe occlusion with loss of vision and neovascularization and ischemic maculopathy ultimately. No pertaining systemic history is available.

Fundus picture at initial presentation shows superotemporal branch retinal vein occlusion with macular edema. Though the patient’s distant vision is 6/6, near vision is N8 and an OCT would have been preferable and would allow one to quantify the macular edema – subtle worsening of the macular edema on follow-up will prompt one to intervene.

It is important at this stage to look for the causative disease – based on the fundus pictures and clinical history provided there are two possible causes. There are definite arteriosclerotic changes in both eyes hinting at the possibility of systemic hypertension. The intraocular pressure is at the upper level of normal.

I would have evaluated the patient for systemic hypertension and glaucoma and also for diabetes mellitus. I would not have suggested any active intervention other than control of systemic disease if any and to treat him with anti-glaucoma medication if proved to have glaucoma. I would have reviewed him in 3-4 weeks.

As indicated in the case report, I would have also treated the patient with sectorial scatter laser once the neovascularization is documented, along with macular laser photocoagulation.

The patient continues to have persistent macular edema 2 months after laser photocoagulation with some resolution of the hard exudates. I would suggest a fluorescein angiogram at this stage to look for areas of focal leakage and treat them with focal laser or with grid laser if there is leakage of indeterminate origin. Macular edema may persist because of peripheral ischemia (as seen by the persistent NVD in the fundus photograph) and further fill-in laser photocoagulation of peripheral avascular retina is necessary.

If the macular edema persists 3-4 months after a good grid and focal laser photocoagulation, I would consider anti-VEGF injection.

2. **Your schedule for follow up of a patient with vein occlusion.**

As this patient has good vision and early, partial branch retinal vein occlusion, I would have reviewed him in 3-4 weeks time to look for subtle progression of the disease such as increased edema on OCT, loss of vision, increasing retinal hemorrhages etc.,. The signs of progression will prompt me to treat the patient at the earliest. I would also advice the patient to self-evaluate his vision using the news paper and an Amsler chart and to report earlier than the scheduled appointment if he notices loss of vision.

3. **Investigations**

Ocular investigations: Other than color fundus photograph, an OCT is necessary. In this patient relevant investigation to rule out glaucoma is also necessary. Fundus fluorescein angiography after resolution of the hemorrhages to look for...
macular ischemia, source of macular edema and neovascularization is advisable.

Systemic investigations should include evaluation of blood pressure and diabetes mellitus. If either of these is positive, further investigation is usually not necessary in an elderly patient. A basic work-up that includes complete blood count, erythrocyte sedimentation rate, hemoglobin and peripheral smear is necessary. If the systemic diseases are under good control and the patient experiences repeated attacks of branch retinal vein occlusion,

a. serum homocysteine levels
b. cardiac evaluation (includes examination by a physician, electrocardiogram, echocardiogram and carotid doppler examination)
c. protein C, S, anti-thrombin, ANA and other investigations are necessary to rule out rare causes in young patients with vein occlusion. These are most often not necessary in the elderly.

4. When do you initiate laser treatment?

I would initiate sectorial scatter photocoagulation with onset of proliferative disease as in this patient or grid / focal laser treatment of macular edema, in persisting macular edema after clearance of hemorrhages (usually 4-6 months after the occurrence of the vein occlusion).

5. Role of intravitreal Pharmacotherapy

I do prefer intravitreal pharmacotherapy in the acute stage of the vein occlusion in an attempt to restore the edematous macula to its original anatomy at the earliest to decrease the chances of irreversible intrinsic damage. My choice of pharmacotherapy is with anti-VEGF agents after ensuring that the patient is not at an increased risk for thromboembolic disease. A cut-off vision such as less than 6/18 Snellen vision or documented progression of the disease can be used to initiate treatment. An OCT provides necessary evidence of progression of the disease by documenting worsening macular edema.

6. Role of combination therapy

After keeping the macula dry with the aid of anti-VEGF agents, I would consider macular photocoagulation once the macular hemorrhages clear, as combination treatment is likely to reduce the need for repeated anti-VEGF injections. A peripheral sectorial laser photocoagulation may be considered in patients with persistent or recurrent macular edema – in these patients the peripheral ischemia may be stimulus responsible for persistent macular edema.

Dr. Gopal S Pillai

1. What will be your line of management?

The clinical pictures and fluorescein angiographic pictures as of November 2007 clearly depicts a typical nonischemic suproteimal branch retinal vein occlusion. There are also changes of arteriosclerosis (Shie’s classification stage III) in both eyes. We can also see the artery cross over the vein and compressing the vein in one location. However with vision of 6/6, N6, our management would be conservative, as was done in this case. We would also get an OCT through the macula to look for evidence of CME. Even with 6/6 vision, there may be CME on OCT, even though that would not have made a difference in our management as the vision was unaffected. Anyway, that would have allowed us to document the presence or absence of CME. BRVO study has been the only randomized clinical trial in the management of BRVO and it has clearly defined the management aspects of BRVO. The final end result in observed and favorable cases were better than 6/12 in a majority of patients. I personally do not hesitate to deviate from the BRVO study recommendations in cases where I feel that the end result can be better than 6/12 with modern management modalities.

2. Your schedule for follow up of a patient with vein occlusion

BRVO patients are followed up monthly for the initial 3 months and there after if there is improvement, then, I would follow up 2 monthly for the next 6 months. After that we may maintain a 6 monthly follow up. Each visit, we would look for vision, IOP, anterior segment and iris examination, resolution of hemorrhages, increase or decrease of edema or appearance of neovascularisation. If the patient is improving, we may consider laxing of the follow up schedule. If there is a worsening from one visit to the next, we may consider FFA and OCT and then treatment depending on the same.

3. Investigations

This patient is 65 years and has arteriosclerotic retinopathy also. He is in a typical risk group of
developing BRVO. Hence, we would get a general medical consult with blood pressure, lipid profile and other basic investigations and if anything is found positive, we will emphasize the need for its treatment for the resolution of the eye condition. If we are dealing with a young patient with BRVO, then we may consider other investigations also like peripheral blood smear and blood picture, coagulation studies, protein s and protein c, homocystine levels and anti cardiolipin factor. Some patients with long standing hypertension may have to be investigated for end organ damages due to hypertension as advised by the physician. We should actively discuss with the patient that the retinal vessel block is just an indication that many vessels in the body may be defective because of the underlying systemic disease.

4. When do you initiate laser treatment?

Scatter laser treatment is planned when there is neovascularisation or extensive areas of ischemia. In cases with CME we may consider focal laser if it is associated with areas of ischemia. We would also ablate the areas of ischemia along with the focal laser if they are large areas.

5. Role of intravitreal Pharmacotherapy.

When there is significant CME, our initial management was focal macular laser up till 5 years back, but as of now, in significant CME, in cases with good perfusion, we treat the patient with an anti VEGF injection and wait for the edema to come down. In most such cases, there is a significant increase in vision and reduction of macular edema and if there is recurrence of CME we may consider re injection for the patient. We have found in personal experience that a single re injection is needed in about 40 % of patients and more than 1 re injection in 15 % of cases. We have also seen that ranibizumab has a stronger ability to flatten the retina and improve vision than bevacizumab (nonrandomized study). We feel that if the edema is high, then there is no need to wait as waiting will cause anatomical changes in the fovea and thereby reduce the visual prognosis in such cases.

Triamcinolone acetonide also has good results in the management of BRVO. However the chances of glaucoma is more in cases with vascular block as many patients may be predisposed and so steroid responders.

In cases where anit VEGF is contraindicated, we may consider IVTA or a posterior subtenons kenacort.

But in cases with ischemia, we would be very conservative with anti VEGF injections and may follow the BRVO study recommendations on laser. This is because there are some reports of anti VEGF agents increasing the ischemia.

The basic idea is that in cases with good prognosis, defended by BRVO study as an end result better than 6/12, we want to raise the bar from 6/12 to near about 6/6 as the end result with the newer pharmacotherpies available to us.

6. Role of combination therapy.

In recurrent macular edemas in well perfused retinas, which require more than 1 reinjection, we would plan a focal macular laser after anti VEGF injections. If large areas of ischemia are present, then we would be more comfortable ablating the large areas of ischemia with scatter laser. In neovascularisations, which are very large, I use combination therapy with anti VEGF followed by scatter laser.

Additional comments on this case

In this case, worsening of vision was probably due to increasing ischemia due to progressive block of the vessel. This could be due to compression of the vein by the artery in the common adventitious sheath as seen in the picture and the FFA. Retrospectively this case may have been a candidate for sheathotomy. (I do not have any personal experience on sheathotomy.)

Dr. Rajesh P

1 When the BRVO is perfused with no macular edema as when the patient presented the first time I would have suggested observation and would have called the patient for follow up after 3 months or asked the patient to report if there was any decrease in vision. Investigations to find out the cause of BRVO also would have been done.

When he presented with worsening of occlusion and drop in vision in Jan 2008, considering that there was not much retinal hemorrhage I would have done a ffa to asses the macular perfusion first. I would also have given an intravitreal agent like triamcinolone or avastin in the first instance even if
FFA had not been possible. In case of minimal edema PST 80 mg would have been another option.

The FFA picture in 4/2008 shows extensive foveal ischemia. Oct shows sub retinal and intraretinal fluid which warrants the use of intravitreal agent like triamcinolone. In the presence of capillary drop out involving almost 2/3 of the perifoveal capillary network I would not have done macular laser. Since there is already accumulation of hard exudates, to prevent further exudate deposition during resolution of edema, lipid lowering drugs could have been prescribed if the lipid levels were above the borderline.

When there is a worsening of edema as in 6/2008 I would have thought about switching to avastin or if there had been an initial resolution with IVTA, repeated the injection. Combined ivta and avastin is also worth a try according to some reports.

2. Follow up often depends on the initial treatment given to the patient. If ivta or pst is given the patients are followed up at 2 weeks intervals for the first month to check the iop. Patients who have received PST may also require repeat injection at 2 -3 weeks. Those who have received intravitreal injections are also advised to report if there is any worsening of vision, increase in pain, photophobia etc to rule out endophthalmitis. If FFA was not possible due to extensive hemorrhage it is done when the hemorrhage has cleared. After one month the patients are followed up at 1 month interval for the next two months. In the mean time decision regarding further treatment –either further injections or LASER is made. These patients are subsequently followed up at 3 monthly intervals or if there is a decrease in vision.

In patients with extensive area of capillary non perfusion chances of neovascularisation of the retina is there and they are followed up at 3-4 month intervals for 1 year and at 6 month intervals for the next 3 years.

3. Glaucoma has to be ruled out. HT.DM AND DYSLIPIDEMIA have to be investigated for. A complete hematological work up including hb, tc, dc, esr, peripheral smear, platelet count, ct, pt, apt t, may also be done if vascular occlusion cannot be explained by common associations. If clinical features are suggestive, myeloma or other hyper viscosity syndromes also has to be ruled out. In young individuals vasculitis and causes of vasculitis also have to be considered. Serum homocysteine levels and protein cs levels also have to be assessed in young patients. fluorescein angiography helps to assess foveal perfusion and also the extent of retinal ischemia. Oct can be of help to quantify the macular edema, presence of CME and any subfoveal fluid and to asses the response to treatment.

4. LASER for macular edema is done only after FFA when retinal hemorrhages have cleared sufficiently and only for perfused macular edema. Laser is the only treatment supported by evidence to be beneficial to these patients. In practice Laser is done for perfused macular edema in patients who have not received any treatment and also for persisting or recurring perfused edema after treatment with intravitreal agents. Some patients can have a natural resolution of the edema in the first three months which may be facilitated by intravitreal agents and hence laser is done only after 3 months. It is done in a grid fashion in the area of capillary leakage with special attention to ablate the leaking micro aneurysms. Collaterals should be avoided at the time of LASER.

Neovascularisation occurs in only 22% of patients with capillary nonperfusion more than 5DD by 4 years (BVOS data). Scatter laser may cause constriction of the visual field. Also approximately 12% of patients who have received prophylactic scatter laser still develop neovascularisation. Hence Laser for neovascularisation is done only after the patient has developed nve or nvd. An exception is where the patient is likely to be noncompliant or has difficulty to maintain the follow up.

5. Intravitreal pharmacotherapy for macular edema is initiated as early as possible. this is given even before FFA is possible; to limit the edema induced damage. There are few concerns about anti vegf agents preventing development of collaterals and thus the natural resolution of edema. Hence Ivta is often preferred as the first line of management. In patients with glaucoma, known steroid responders’ avastin is given. Patients receiving intravitreal
therapy can often have recurrence of edema and may require laser or additional injections. It has to be stressed that visual recovery after the treatment is decided by the extent of foveal ischemia.

In neovascularisation with vitreous hemorrhage avastin may help to clear the media and facilitates further laser treatment. The chance for worsening of the tractional component and the need for a subsequent surgery also has to be highlighted. In non resolving vitreous hemorrhage and threatening macula avastin can be given intravitreally 1 week before surgery to reduce the bleeding during surgery.

6. Combined treatment for macular edema can be tried when the edema is not severe and when there is not much retinal hemorrhage. Combined laser and ivta has been found to yield better visual outcomes than laser alone. Combined treatment but was found not to have as good visual outcome as ivta alone in another study. No strong evidence is available to support combination treatment and further studies are required. Combination of ivta and avastin is an option available when edema is not responding to other treatment modalities.

Dr. Shane Mathew

Here we are dealing with an elderly gentleman with branch retinal vein occlusion in left eye evolving to an ischemic one which is non responsive to laser photocoagulation showing worsening of edema and visual acuity, with borderline intraocular pressure.

First of all it is important to ask for risk factors in the form of hypertension, diabetes mellitus, ischemic heart diseases, history of stroke/thromboembolic events etc and get a systemic evaluation done. In the mean while I would like to check for presence of neovascularisation of iris or and neovascularisation of angle; presence of which may warrant aggressive laser photocoagulation.

I feel he is extremely lucky to have 6/24 N24 with this much macular non perfusion. Angiogram done in April 2004 shows evidence suggestive of neovascularisation. During fundus evaluation I would look for skipped areas of photocoagulation, assessing the need for fill in photocoagulation, pressure of epiretinal membranes and type of macular edema. Coming to macular edema an Optical Coherence Tomography at this stage would be ideal to decide on the cause for worsening. If vitreo macular traction is responsible for it, then vitrectomy would be the ideal choice. But for pure edema; at this stage I would prefer to inject Anti VEGF instead of steroids as pressures are in borderline; after explaining to the patient the goal, risks and benefits of treatment, and augment with fill in photoagulation in the form of sectorial photoagulation and focal to area of edema may be after a week of injection. (My rationale being that Anti VEGF takes care of VEGF up regulation and thus help in regression of neovascularisation, reducing edema (if not controlled can lead to secondary changes at macula reducing the vision even further.) and photocoagulation taking care of hypoxia which is the primary pathology.) Here I would like to avoid treating over collaterals.

I would like to review the patient after 4 weeks to asses the response. If edema is decreasing one could wait for 2-3 months. If edema is not showing any response I would like to try intra vitreal steroids this time taking into consideration its potential risks.

Combination Therapy could also be called as “Laser plus Therapy”. Laser plus something else! Adjunctive intra vitreal therapy provides several benefits including rapid onset of action especially with Anti VEGF agents and dramatic visual improvements. Patients are visually quiet satisfied. Adding Intravitreal therapy also eliminates initial worsening of vision that might be caused by initiation of laser therapy. It is effective in case involving media opacities, it controls neovascularisation and as a pre treatment; may potentially make macular laser safer. At the same time disadvantage of intravitreal therapy may be considered; it is invasive, potentially blinding, effects may be short lived. Further more long-term treatment may impair neuro protection and recurrent cost of treatment may also be an issue.

I would not prefer combination therapy in the form of steroids with Anti VEGF initially in this case, as we all know these agents give only short term benefit and steroids may cause rise in intraocular pressure, and cataract. Failing not to mention that anti VEGF can rarely worsen ischemia.

Dr. Thomas Cherian

1. In view of the worsening of oedema, I would consider injecting a VEGF inhibitor at this point.
Following injection, the OCT will be repeated after 2 weeks, we expect the macular oedema to come down. This will be followed by a repeat FFA, and further Laser, if necessary (either microaneurysms or capillary non perfusion areas).

2. On presentation, I would do an OCT. This is a baseline. I would get the blood sugar, BP and lipid profiles checked and call the patient back with reports. Any variation has to be taken care of. I would call back the patient once in 6 weeks and repeat the OCT. Interference (FFA, injection and / or Laser) will be only after 3 months, unless the patient is hard pressed for time.

3. OCT on presentation. Blood sugar, BP, Lipid profiles. In younger individuals, especially with CRVO, ask for a Serum protein C and Protein S. Carefully, look for signs of vasculitis, do a vasculitis workup, if necessary. OCT is repeated every 6 weeks. If there is no improvement in 3 months, I would consider an FFA. In CRVO, I would get an ERG also done, since this will pick up ischaemia, quite early.

4. I would laser almost all BRVOs, for preventing a possible vitreous hemorrhage in future. For CRVOs, I would laser only if there is NVD OR NVE, since a panretinal photocoagulation might cut off the peripheral vision, which the patient may have. Still, I might not wait for a neovascular glaucoma to develop, as recommended by learned experts (SS Hayreh).

5. In macular oedemas, not resolving in 3 months, I would consider intravitreal injections, preferably Bevacizumab (Avastin). Triamcinolone, if at all, has to be used with caution in vein occlusions, a careful follow up of the IOP should be made in such cases.

Combination therapy for BRVO with macular oedema would be my choice. Any VEGF inhibitor injection, I would follow up with a Laser (Sector photocoagulation). Again, in CRVOs, I would follow up an injection with laser, only if there is NVD / NVE.

Compilation

This 65 year old male patient with no obvious risk factors was under follow up and treatment for a branch retinal vein occlusion is in his left eye. He underwent a baseline systemic work up which included fasting and post prandial blood sugars, serum lipid profile and blood pressure. He also underwent a baseline glaucoma work up which was non contributory. During the course of follow up he developed worsening of visual acuity, ischemic conversion and aggravation of macular edema for which sector laser photocoagulation was initiated. 2 months post laser there was recurrence of macular edema for which he underwent additional fill in sectoral photocoagulation along with intravitreal Bevacizumab 0.05 ml/1.25 mg injection. There was good resolution of the macular edema and stabilization of visual acuity at 6/18 N8.

A thorough comprehension of the natural history of retinal venous occlusive disease is required in order to initiate treatment strategies at the earliest. All ocular and systemic risk factors for developing retinal vein occlusion should be addressed. While medical therapies have primarily addressed the sequelae of vein occlusion, surgical therapies have generally focused on anatomically circumventing or resolving the vein occlusion. Current management strategies for Branch retinal vein occlusion is given in table 1

**Current Management Strategies for Vein Occlusion**

| Observation | Grid pattern laser photocoagulation |
| Intravitreal Pharmacotherapy | (Triamcinolone Acetonide / Anti VEGF) |
| Sustained Steroid release devices | Vitrectomy with arterio-venous sheathotomy |

To date Grid Laser photocoagulation is the only advocated treatment modality for non ischemic macular edema in eyes with BRVO. It is prudent to wait until neovascularization is present before initiating scatter laser photocoagulation in eyes with BRVO, although treatment may be initiated in eyes with extensive ischemic disease if following up is questionable.

Intravitreal steroid or anti-VEGF therapy is currently employed for reducing macular edema in BRVO. The potential ocular side effects of steroids and potential systemic effects of anti–VEGF agents should be discussed with the patient and an informed consent obtained before the procedure. Despite wide spread use of intravitreal triamcinolone, long–term
data are still awaited. The results of the SCORE study will determine the true efficacy and safety of intravitreal triamcinolone.

In the management of BRVO, medical therapies should be considered before pursuing surgical options. Currently surgical therapy has very few indications. Pars plana vitrectomy with endolaser may be appropriate in eyes with non clearing vitreous hemorrhage. Non randomized studies have shown some benefit of Arteriovenous sheathotomy in re-establishing retinal perfusion, reducing intravitreal hemorrhage, and macular edema and in improving visual acuity. It is thought that decompression of the vein in this manner will allow venous recanalisation and displacement of the thrombus from blockage site with the return of distal circulation.

Combined medical and surgical therapies require more study before inclusion as a standard of care.

The visual outcome of BRVO id generally favorable with 30% having 6/18 or both vision. As shown by the BVOS, grid laser photocoagulation can be used in cases of perfused BRVO with persistent vision loss to treat any macular edema with only moderate visual expectations. Scatter laser PHC is recommended for neovascular sequelae. After the initial visual acuity assessment, IOP measurement, anterior segment examination, undilated gonioscopy, dilated fundus evaluation and subsequent FFA and OCT can be obtained. Affected patients should be followed monthly for 6 months. And at each visit undilated gonioscopy, IOP measurement and dilated fundus examination is necessary to detect neovascularization. NVG occurs in 40-60% of eyes with non perfusion ³ 10 DD often by 3 months post occlusion.
After medical school, he served an internship at the University of Iowa, then his residency at the Wilmer Institute at Johns Hopkins Hospital and a fellowship at the Armed Forces Institute of Pathology. In 1963 he joined the faculty of the newly established Bascom Palmer Eye Institute at the University of Miami Medical School, where he stayed for 32 years. When he and his wife, Margy Ann, moved back to Nashville in 1995 to be near their daughter and her family, he joined the faculty at Vanderbilt.

Dr. Gass began his career practicing general ophthalmology, and during this time became actively involved in ocular surgery for cataract, glaucoma, orbital and retinal diseases. He became interested in the new technique of fluorescein angiography that for the first time permitted the detailed photographic study of physiological as well as anatomical changes in the retina and choroid. This new technique and his skills in ocular pathology led to his future clinical and research interests in degenerative inflammatory and neoplastic diseases of the inner eye. He is also the author of “Stereoscopic Atlas of Macular Diseases: Diagnosis and Treatment,” the premier medical textbook on macular diseases. One of his main efforts has been simply sorting the many inflammatory disorders of the eye that appear similar in nature, but have very different causes and outcomes. Previously they were either unrecognized or lumped together under less specific names.

He is also well known for his work in finding the link between acute zonal occult outer retinopathy (AZOOR) and other retinal syndromes and in the treatment of diffuse unilateral subacute neuroretinitis. The disease, common in tropical areas, is caused by a worm that
gains entrance into the bloodstream, invading the area between the retina and choroid and causing severe vision loss in one eye.

Not just literally but figuratively, Don Gass wrote the book on blinding macular diseases, and in tackling this subject he took on an unusually difficult task,” O’Day said. When he began his work in the early 1960s, the tools he had to work with were primitive or non-existent, yet he opened up the field so effectively with his discoveries that it became attractive to a whole new cohort of other bright minds, many of whom he trained and who now continue his work.

In the two academic institutions where Donald Gass spent his professional career he was much loved by faculty, residents, fellows and staff, and above all by his patients, for whom he did so much. The image that will forever endure with many is the one they saw every week. It is of a man sitting, surrounded by colleagues, residents, students and fellows. All are peering at photographs of the retina and the conversation is animated — all are engaged.

In addition to the “influential ophthalmologist” honor, Dr. Gass received numerous awards throughout his career, including the 1987 establishment of the Gass Medal in his honor by the Macula Society, given for outstanding contribution in Macular Disease. He also received the Distinguished Faculty Scholar Award at the University of Miami in 1989; the Mildred Weisenfeld Award for Excellence in Ophthalmology in 1999 from the American Association for Research and Vision in Ophthalmology; the Helen Keller Prize for Vision Research in 2001; the Laureate Recognition Award of the American Academy of Ophthalmology in 2004; and the Vanderbilt University School of Medicine Distinguished Alumnus Award in 2004. He also served as director of the American Board of Ophthalmology from 1976 through 1983.

“Don Gass was the premier retina specialist in the world,” said Paul Sternberg Jr., M.D., George W. Hale Professor of Ophthalmology and Visual Sciences and chair of the department. “He had a remarkable ability to unravel the complexities of numerous retinal conditions, paving the way for innovative treatments. As a teacher he was unparalleled, captivating both the young resident and the seasoned specialist with his encyclopedic grasp of the field, as well as his charming recollections of the patients from whom he made his observations,” he said.

“As an academician, his textbook, nicknamed ‘the Gass Atlas,’ has become a must read for every ophthalmologist in training and a well-worn standard on all of our bookshelves. As a person, he was humble, soft spoken and delightfully absent minded. His decision to spend his retirement working at the Vanderbilt Eye Institute was an incredibly generous gift to all of us who worked with him and learned from him, as well as to the many patients of Middle Tennessee who benefited from his care.”

Anderson Spickard Jr., M.D., who was a classmate of Dr. Gass’s in medical school, said he and Dr. Gass were paired as anatomy partners the first day of medical school. “He couldn’t write in cursive, but could print faster than any of us. We used his notes to study for exams,” he said.

“He was extremely bright. He could listen to obscure lectures that many of us couldn’t even understand, and interpret them for the rest of us. He was a quiet man, but was always thinking about something extraordinary.”

Dr. Gass is survived by his wife of 54 years, Margy Ann, and children, John Donald Gass of Danville, Calif., Carlton Simpson Gass, M.D., of Miami, Dean Simpson Gass of Charlotte, N.C., and Media Lee Yawn, of Nashville.
Fibrin glue versus sutures for attaching the conjunctival autograft in pterygium surgery: a prospective observer masked clinical trial

S Srinivasan, M Dollin, P McAllum, Y Berger, D S, BJO 2009; 93:215-218

Pterygium recurrence is the most common complication of pterygium surgery and is a frequent source of frustration for the patients and surgeons. Pterygium excision and leaving behind a bare sclera has a high recurrence rate (40-75%). Pterygium excision with conjunctival autograft has a lower recurrence rate (3-5%). The autograft can be attached using sutures or fibrin glue. Fibrin glue (eg. Tisseel) is a two component fibrin sealant which mimics natural fibrin. The aim of the study was to compare the degree of conjunctival autograft inflammation, subconjunctival hemorrhage (SCH) and graft stability following the use of sutures and fibrin glue during surgery.

The study was a prospective observer masked clinical trial. 40 eyes of 40 patients undergoing primary pterygium surgery with conjunctival autograft were allocated into two groups-Group I (n=20) had fibrin glue and Group II (n=20) had sutures to attach the autograft. Free conjunctival limbal based autograft from the supero-temporal quadrant with tenons removed was used. Limbus to limbus and stromal side down orientation were maintained in the procedure. Post operatively antibiotics, steroid eye drops and standardized digital slit lamp photograph were taken at 1 week, 1 month and 3 months. Sutures were masked using photo editing software. Two masked observers objectively graded the digital photographs for degree of inflammation, SCH and graft stability.

34 of the patients completed the study. In the fibrin glue group the degree of inflammation was much less at one month (p=0.019) and 3 months (p=0.001) with no difference at 1 week. The fibrin group showed more stability at week (p=0.258), 1 month (p=0.076) and 3 months (p=0.624). No difference in SCH was noted between the groups.

This is the first prospective clinical trial confirming that conjunctival autografts secured with fibrin glue in pterygium surgery are more stable and produce less inflammation than those secured with sutures.
Effect of Phacoemulsification on Intraocular Pressure in Eyes with Pseudoexfoliation- A Retrospective Study


Pseudoexfoliation syndrome is characterized by the accumulation of fibrillar extracellular material on the surface of various ocular tissues. It is the most common identifiable cause of open angle glaucoma, associated with cataract and high rates of complication in cataract surgery. The aim of this study was to assess the short term and long term effects of uneventful phacoemulsification with PCIOL implantation for visually significant cataract in large series of Pseudoexfoliation eyes with or without glaucoma in terms of BCVA, IOP and glaucoma medication requirements. They retrospectively analyzed 1122 eyes with PXF with uneventful surgery of which 882 eyes didn’t have glaucoma (PXF) group, and 240 had glaucoma (PXG) group.

On a comparative analysis of the outcome they found that the mean IOP was statistically significantly reduced through 7 yrs postoperatively compared with preoperatively in PXF group. The PXG group had reduced the mean IOP for 1 year and reduced glaucoma medication requirement at almost all postoperative time intervals. Higher the mean preoperative IOP, greater the reduction of mean postoperative IOP. IOP spikes (>30 mm of HG) I day postoperatively occurred in 4 % in PFX group and 17 % in PXG group. Postoperatively, 2.7 % of PXF eyes progressed to a need for lasers and/or glaucoma surgery.

In conclusion long term reduction in mean IOP occurred in PXF eyes with and without glaucoma. Glaucoma progression in both groups was low, suggesting a protective effect of phacoemulsification on IOP in these eyes.

Short Term Safety and Efficacy of Intravitreal Bevacizumab for Pseudophakic Cystoid Macular Edema- A Retrospective Case Series.

Antonio Barone, Vincenzo Russo, Francesco Prascina, Retina 29:33-37, 2009

Cystoid Macular Edema also known as Irvine–Gass syndrome, is still recognized as one of the most common causes of poor visual outcome following cataract surgery. Spontaneous resolution of the edema is the most likely natural course in this pathology. However, up to 2 % of patients will not have spontaneous resolution of the edema and must be treated. Prompt treatment on recognition of the disorder is warranted, because if macular edema has been present for several months there is likely irreversible change in the macula. In some cases the CME is refractory to medical treatment including topical corticosteroids, topical non-steroidals and periocular steroid treatment.

In this study the authors from Foggia, Italy, sought to determine the feasibility, safety and clinical effect of
intravitreal Bevacizumab (Avastin) in patients with refractory cystoid macular edema after uncomplicated cataract surgery. 10 eyes of ten patients affected by pseudophakic cystoid macular edema refractory to medical treatment treated with at least one intravitreal injection of 1.25 mg of Bevacizumab were enrolled in the study. Follow up visits included Early Treatment Diabetic Retinopathy Study visual acuity testing, Optical Coherence Tomography imaging and ophthalmosopic examination. The follow up was six months. All eyes had improved best corrected visual acuity and no eyes had worse visual acuity. The mean baseline best corrected visual acuity was 20/80 and the mean final best corrected visual acuity 20/32, the difference was statistically significant (p<0.0001). The mean central macular thickness at baseline (546.8mm; range, 359-720mm) decreased significantly (228.7, 190-280mm). No ocular or systemic adverse events were observed.

The authors conclude that intravitreal Bevacizumab is safe and well tolerated in patients with pseudophakic cystoid macular edema.

Compiled by Dr. Reesha MBBS, Dr. Ann DO
Clinical Diagnosis and Management Of AIDS (HIV) in Eye

Edited by Ashok Garg, Scott WCousins, Kirit Mody, David Meyer
Published by Jaypee Brothers, New Delhi
First Edition -2008
Price Rs 895/-

With a current prevalence of 100 million infected the world over and a projected prevalence of 200 million by year 2010 HIV/AIDS undoubtedly is one of most devastating disease pandemic of this century faced by mankind. The disease – AIDS was first detected in 1981 in Los Angels, USA. Since then it has progressed rapidly in last 2 decades with 100 percent fatality and world wide distribution. It is necessary to diagnose this disease in early stages to prevent multi-systemic disease to fulminant especially AIDS related infections in ophthalmology which can be devastating in terms of ocular morbidity and visual acuity. Extensive research is going on worldwide for the effective anti-HIV drugs/injection therapy but with moderate success.

This multi-authored textbook has been written to impart knowledge to ophthalmologist about this dreaded disease which is spreading worldwide at the alarming rate. At present no other International ophthalmology book is available on this complex subject.

In this International book there are 21 comprehensive chapters written by international masters of this field covering all aspects from anatomy, pathophysiology of AIDS, investigations, various treatment modalities and recent advances, all treatment options including the latest drugs and injection therapy with complete pharmacotherapeutics have been included in this book for better clinical management of ophthalmic HIV infections. A CD ROM is being given with this book showing various clinical ophthalmic conditions in AIDS in a beautiful way along with surgical options.

This book has been written in a true team spirit and will be useful companion to ophthalmologist dealing with HIV ophthalmic infections in their clinical practice.

Ashok Garg and co-editors deserve credit for putting together a remarkable overview of what is known to date concerning this virus not just from a fundamental point of view but in particular its repercussions on the eye, diagnosis of the numerous infections and their treatment.

Through the combined efforts of immunology, chemotherapy and surgery, patients now have chance to recover a normal life and decent functional vision. The reader will appreciate the contribution from the very well-known international panel that took part in bringing out this book.
Optical Coherence Tomography in Retinal Diseases

Edited by Sandeep Saxena, Travis A Meridith
Published by Jaypee brothers, New Delhi
First Edition-2008
Price –Rs: 2465/-

Optical coherence tomography achieves cross-sectional imaging of tissue by measuring the echo delay and intensity of back-reflected infra light from internal tissue structures. Using a classic optical measurement technique known as low-coherence interferometry in combination with special broad band width light, optical coherence tomography achieves high-resolution cross-sectional visualization of tissue morphologic characteristics.

In less than a decade, Optical Coherence Tomography (OCT) has revolutionized the diagnosis of retinal and macular diseases. This technology is indispensable in providing quality patient care by expanding the clinical observations with a view of retina with higher resolution than is appreciated by the human eye. Saxena and Meredith have edited a book that demonstrates both the qualitative and quantitative advantages of OCT as applied to the patterns of various retinal disorders. These disorders range from vitreoretinal interface disorders, such as epiretinal membranes and macular holes, to intrinsic disorders within the retina (macular edema), and choroidal processes. The authors are selected respected international authorities from both medical and surgical subdivisions of the retinal domain.

Optical coherence tomography has shown us the role of the vitreous in the evolution of macular holes and the masquerading processes that can sometimes be difficult to differentiate clinically. In cystoid macular edema resulting from retinal vascular diseases, OCT is the best method for quantitatively assessing the outcome of any medical or intervention.

Optical coherence tomography is the best way of determining the anatomic effect of a treatment. It can be used to identify and quantify macular edema, and to measure retinal thickness changes in response to therapy. It helps in making clinical decisions and also in patient education and medical record documentation.

This book summarizes the present knowledge of optical coherence tomography in various medical and surgical management of diseases of retina. The value of this book lies in the clinical experiences and expertise of the contributing authors.

Salient features of this book are

- Summarizes the present knowledge of optical coherence tomography in various medical and surgical diseases of retina.
- Twenty- three chapters.
- Over 1100 colored and black and white figures.
- Contributions from respected international authorities from both medical and surgical subdivisions of the retinal domain.
- Sixty –two global contributors.
- Valuable text for ophthalmologists in vitreoretinal practice.

It is encouraging that improvements in OCT technology continue to develop. Currently the axial resolution of 10 microns and lateral resolutions of 20 microns still make it difficult to separate layers within the retina. Higher resolutions shown by Dr. Drexler in this book, promise axial resolutions of 3 microns that demonstrate the different cellular layers within the retina. This will be a useful tool of studying in vivo the effects of vitreoretinal interface changes on the layers of cells within the retina, the final outcomes of surgical intervention on the retinal structure.

It is apparent that OCT has become the most useful non-invasive diagnostic modality. Expansion of this technology to glaucoma and the anterior segment is undoubtedly not far behind. Thos book summarizes the state of the art in practical and clinical aspects of OCT for retinal disorders.
The emergence of Optical Coherence Tomography (OCT) in the recent years has changed forever, the way we 'look at' or shall we say 'look thorough' the retina. The OCT provides, in real time, high resolution cross-sectional images of the macula very similar to obtaining in vivo histopathological sections. It represents a major advance in the diagnosis of the retinal disease and has found rapid acceptances among the retina specialists.

The authors have attempted to share their experience of Stratus OCT (Tm) in various macular disorders. They found it helpful in diagnosing and monitoring the response to various therapies and interventions and above all identifying the correct therapeutic approach in a given patient. It finds extensive application in diagnosis, management and follow-up of diabetic macular edema, macular hole, taut posterior hyaloid membrane, vitreofoveal traction, idiopathic central serous chorioretinopathy, sub macular pathology and many more areas that are divided into 22 chapters. For ease of comprehension, they provide with brief case summaries, fundus photograph, fluorescein angiography and the OCT images and the follow-up images for most of the patients that they share with the readers.

OCT is not a substitute for a thorough clinical examination, fundus imaging or various angiographic techniques but is a great adjunctive tool to probe the mysteries of retinal disease. It has major limitations in obtaining images through a cloudy media or trying to look at the choroidal pathology. The authors strongly recommend that to obtain optimum information from the OCT, it be best performed by the clinician himself or herself.

It is indeed very encouraging to note the OCT has, at present, become one of the most important adjunct tools for the diagnosis, assessment and management of macular diseases. In recent years, OCT has also emerged as a valid tool for assessment of retinal nerve fiber layer and optic disc evolution in pre-perimetric glaucoma. The role of OCT in various neuroophthalmological disorders is still emerging. Based on the clinical experiences, Dr.Sushmita Kaushik and Dr.Ramandeep Singh have contributed a new section on 'Glaucoma.'
CME Programmes

STATE CONFERENCES
CME 2009
5th July 2009
Chakrabarti Eye Care Centre, Trivandrum
Hotel Residency Towers, Trivandrum
Dr. Arup Chakrabarti
9946410540

INTERNATIONAL SYMPOSIUM
Medical Retina: Looking into the future
18-19th July 2009
Giridhar Eye Institute, Kochi
Dr. S.J. Saikumar
98470 40480

NATIONAL CONFERENCES
Indian Intraocular implant and Refractive Surgery Convention
July 11-12, 2009
Hotel Taj Coromandel, Chennai, India
Organizing Secretary: Dr. Amar Agarwal
91-44-28 115871

DARSHAN 2009
57th TNOA Annual Conference
7-9th August 2009
Codissia Trade Fair Complex
Dr. V. Narendran
0422-4360400
www.tnoa2009.com

Kalpavriksha 2009
National PG CME Programme
October 1-4, 2009
Dr. Agarwal’s Eye Hospital, Chennai

INTERNATIONAL CONFERENCES
World Glaucoma Congress
July 8-11, 2009
Boston, Massachusetts, USA
www.worldglaucoma.org

XXVII Congress of the European Society of Cataract and Refractive Surgeons
12-16th September 2009
Barcelona, Spain
www.escrs.org

AAO-PAAO 2009
24-27th October, 2009
San Francisco
www.aao.org/2009

ASCRS.ASOA
Boston 2010
9-14th April 2010
www.ascrs.org / www.asoa.org

WOC 2010
World Ophthalmological Congress
5-9 June 2010
Berlin, Germany
www.woc2010.de

APAO Sydney 2011
21-24 March 2011
Sydney Convention and Exhibition Centre,
Sydney, Australia
+6129254 5000
Posterior Segment Imaging: Tips and Tricks

**POSTERIOR SEGMENT IMAGING**
- SLIT LAMP
- FUNDUS CAMERA
- VIDEO INDIRECT OPHTALMOSCOPE
- OCT
- B SCAN USG
- OPERATING MICROSCOPE

**SLIT LAMP IMAGING: TYPES**
- Dual Diffuse Illumination
- Thin Slit Illumination (Background Illumination)
- Broad Tangential Beam
- Retro Illumination
- Sclerotic Scatter Illumination

**DUAL DIFFUSE ILLUMINATION**
- Low Magnification Survey Photographs
- Demonstrates General Status Of Eye and Surrounding Tissue
- Maximum Slit Lamp Beam Width
- Diffusion Cap Over Slit Prism
- Illuminator at 45° to Microscope
- Background Illuminator

**THIN SLIT ILLUMINATION**
- Topographic Structural Changes
- 3 Layered Corneal Structure
- EPITHELIUM: Fine Bright Line
- STROMA: Thick Band Of Medium Reflectivity
- ENDOTHELIUM: Thin Bright Line Furthest From Incident Light
- Assessment of Anterior Chamber Depth

**BROAD TANGENTIAL BEAM**
- Assess Corneal Transparency over a Larger area

**RETROILLUMINATION**
- Study SILHOUTTE of the Lesion of Interest
- Bounce Lighting Effect
- Reflective Structures: Iris and Retina
- Semicircular Illumination
- Iris Retroillumination: Soon after Instilling Dilating Drops, Slit Beam Shortened and Configured to a Small Square or a Circle
- Lens Retroillumination: Maximum Pupillary Dilatation

**DUAL DIFFUSE ILLUMINATION**
SCLEROTIC SCATTER ILLUMINATION
- Widespread Pathology
- Moderately Wide Slit beam
- Angled to Strike Limbus

GONIOPHOTOGRAPHS

IMAGES FROM FUNDUS CAMERA
- OBJECTIVE LENS: Freedom From Dust and Impression Of Nose
- FOCUSING EYE PIECE
  Focus “CROSS-HAIR” RETICLE
  Crucial Reference Point for Focusing Fundus Image
- CAMERA ALIGNMENT
  150 mm Separation Between Objective Lens and Cornea
  Ring Shaped Reflection of Light Source on Cornea

RELAXING ACCOMODATION
- Focus On Far Away Object
- Photograph With Both Eyes Open
- Turn Eye Piece Counterclockwise & Blur Cross Hair

COMPOSING
20°,30°,50°,
PHOTOGRAPHIC MONTAGE
FINE FOCUSING

ARTIFACTS - ORANGE CRESCENT
- CAMERA IS MALALIGNED
- MOVE CAMERA TO OPPOSITE DIRECTION

ARTIFACTS - BLUE PERIPHERAL HAZE
- Camera Too Far from the Eye
- Move Camera Forward

ARTIFACTS - Bright Blue White Centre Reflex
- Camera Too Close to the Eye
- Move Camera Backward

ARTIFACTS PERIPHERAL VERTICAL TAN / WHITE STreaks
- Lashes are responsible
- Retract Before Photography

ARTIFACTS
- Spots/ Streaks Persisting In Field
- Tears and Dust are responsible

ARTIFACTS
- ORANGE and RED IMAGE WITH NO DETAIL
  Patient has blinked during capture

Dr. Meena Chakrabarti, Editor, KJO
**GENERAL INSTRUCTIONS TO AUTHORS**

The Kerala Journal of Ophthalmology (KJO) is a quarterly; peer reviewed one, devoted to dissemination of the latest in ophthalmology to the general ophthalmologists as well as to specialists in the various subspecialties of this discipline. It invites submission of original work dealing with clinical and laboratory materials.

Authors submitting materials to this journal are requested to adhere STRICTLY to the norms laid down below. The matter must be typed on one side of the paper. A margin of 1” must be left all around and the material must be double-spaced. A page should contain not more than 25 lines. Two copies of the text in paper and one copy in a CD must be submitted to the Editor and the corresponding author is advised to keep another copy with him. The corresponding author must give it in writing in his covering letter that the same matter will not be submitted elsewhere if accepted. He must also enclose the copyright transfer of his work to this journal. The papers sent will be subjected to peer review. The accepted manuscripts become the permanent property of this Journal. The author is informed that, if his work is returned to him for correction / clarification after peer review, he should effect the same and send the manuscript back to the Editor within one month. Each manuscript component mentioned here under must begin with a new page and the pages are to be numbered at the right tip corner starting from the Title page.

1. **TITLE:** The title of the work must be brief and precise. It should not exceed two lines and 40 characters (including comma, period) Author(s) full name(s) must be given along with his (their) degree and the affiliations. Corresponding author's name, correct address (including e-mail and Fax, if available) and phone number must be mentioned at the bottom left hand corner of the first page.

2. **ABSTRACT:** The abstract is to be given in the beginning itself. It should not exceed 200 words. It must contain the aim, methodology, results and conclusion. For case report, summary / conclusion alone is to be given.

**KEY WORDS** (maximum five) in capitals are to be included at the end of Abstract.

3. **INTRODUCTION:** Describe the aim of the study, along with the hypotheses that were tested. Only necessary references are to be given.

4. **METHOD:** Give in detail the materials used and the methods employed. Describe the type of study. Pharmacological names only must be mentioned for the drugs used and, if proprietary name is used, then the manufacturers name must be given in parentheses. Except for standard, well-accepted abbreviations (Including SI Units), all others must be introduced in parentheses when the full term is used for the first time in the article.

5. **RESULTS:** Give only the results obtained by the study under discussion. State the statistics in the correct scientific form (P value, mean etc). Results based on assumptions must not be given. Indicate in the text the place where the tables have to be inserted.

6. **DISCUSSION:** The discussion should be to the point and relevant to the subject under discussion. This section can be combined with the previous one if the author desires. Avoid speculations. Use only standard abbreviations or the abbreviations already introduced.

7. **ACKNOWLEDGEMENT:** This is to be made only to those who were directly and scientifically involved with the preparation of the paper. Permitting authorities, technicians, photographers who assisted in the work need not be mentioned.
8. REFERENCES: The references should be given in numerical order in which they first appear in text and not in alphabetical order (Citation Order System). It should be numbered consecutively in the text. The references will not be checked by the Editor or by the Peer reviewer and hence the author is solely responsible for its completeness and the accuracy. Period should not be employed anywhere in the references. Personal communication, unpublished data and poster references, if mentioned, should be in the text itself and the source mentioned in parentheses. References should be in the following form:-

*Journal reference:* Author(s) full title, Journal name (as abbreviated in Index Medicus), volume number, pages and year. If there are more than three authors, then mention the first three authors and then ‘et al’.

*Book reference:* Authors(s) (& Editor, if any), title of book (and chapter), publisher, place of publication, page number (s) of the cited portion and year.

9. THE LEGEND: The legend for the illustrations (and tables, if necessary) must be given in a separate sheet of paper and should be typed double-spaced.

*Illustrations:* The photos and figures should be prepared in glossy prints with good contrast and of the size 6” x 4”. Only salient details should be included. On the back of the illustration, the figure number in text, title of the paper, the first author’s name and the top side (marked with an arrow) must be specified. Except for arrows, no text is to be on the photos. It is the duty of the author(s) to get the patient’s written permission when the subject is identifiable in the photo. Submit two sets of illustrations. Illustrations from other Journals and books are usually not accepted. If used, it rests with the author(s) to get the copyright permission from the original author / publisher and this permission letter must be sent to the Editor at the time of submitting the manuscript. For Histological figures the stain and magnification used should be noted e.g.: - H & E Stain x 70.

10. TABLE: It should be in double space. Each table must have an Arabic numeral (except for single table) and a title both in a single line. Each column in the table must have a short heading. If a table is large, then it must be continued in a second page, which also must have the table number and the title. Avoid vertical lines in the tables. Two sets must be submitted.

The manuscripts are to be sent to The Editor by Courier Mail or by Registered post. The corresponding author will receive communication from the Editor within two weeks of receiving the manuscript.

11. All manuscripts are subjected to editorial board review.

12. Other Categories of Manuscript

a) Original Articles should generally not exceed 3,000 words or 12 double – spaced pages.

b) Review Articles: can be on topics of relevance to clinical practice, research methodology, community ophthalmology or investigative work, of relevance to visual science. These articles should include up to date review of existing literature, and summarize the current status / preferred practice for that particular topic.

Brief reports are short communication of new instruments, new laboratory techniques or surgical techniques as well as interesting case reports with unique findings. These should not exceed 1000 words with a maximum of 2 illustrations. They should follow the format - introduction, case, and discussion. No more than 8 references should be cited. Each brief report must begin with a 75-100 word summary that highlights the significance of the articles.
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