ABSTRACT

Raised intraocular pressure is a frequently encountered complication of uveitis. Intraocular homeostasis, maintained by the impermeable blood-ocular barrier, is important to guarantee optimal visual function. During uveitis breakdown of the blood-ocular barrier occurs, allowing the influx of proteins as well as inflammatory and immunocompetent cells. The combination of action of inflammatory cells and the mediators they release; and the chronic corticosteroid therapy used to treat the uveitis can participate in the pathogenesis of uveitic glaucoma. These factors alter the normal anatomic structure of the anterior chamber and angle. Management of uveitic glaucoma may be difficult because of the numerous mechanisms involved in its pathogenesis and is guided by careful delineation of the pathophysiology involved in each individual case. This article reviews, in detail, the pathogenesis of uveitic glaucoma and its therapies, with emphasis on the recent developments in the subject.

Keywords: Uveitis, Glaucoma, Ocular hypertension, Uveitic glaucoma.

INTRODUCTION

Glaucoma is a relatively common but serious complication of uveitis that may result from a mixture of mechanisms. Historically, the association between uveitis and glaucoma was first reported by Beer in the early nineteenth century. Since then the understanding of the pathophysiology and mechanisms of uveitic glaucoma has advanced significantly but managing glaucoma associated with uveitis remains a challenge.

DEFINITION

An important difference between patients with secondary uveitic glaucoma and those having primary glaucoma is that in former the damaging mechanism is nearly always raised IOP. Increased IOP may be seen with any type of intraocular inflammation (Table 1).

When IOP is elevated for only a short period and does not induce either optic nerve or visual field damage, the term ‘uveitis-related ocular hypertension’ may be used. The term ‘uveitic glaucoma’ may be used only when uveitis is associated with elevated IOP, glaucomatous optic nerve damage and/or glaucomatous visual field defects.

First international SUN workshop reached a consensus that the term glaucoma should not be considered synonymous with elevated intraocular pressure in a patient with uveitis, but that it should be reserved for those situations where there is either observed glaucomatous disk damage or demonstrated visual field loss. The term elevated intraocular pressure should be used for those situations where there is an intraocular pressure above a defined normal range or when there is an increase in intraocular pressure from baseline during a study with longitudinal data. However, different definitions of uveitic glaucoma have been used by different authors in literature, mostly pertaining to raised IOP keeping it in perspective of root pathology in damage.

EPIDEMIOLOGY

The overall prevalence of secondary glaucoma in uveitis clinic-based studies has varied from 5.2 to 41.8%, although historically, the diagnosis has often been made on the basis of intraocular pressure (IOP) elevation alone.

Panek et al found 23 patients (31 eyes) out of 100 patients (161 eyes) to have SG by criteria of IOP alone yielding prevalence rate of 23% (19.3% of eyes). They also reported that SG developed in both eyes of patients with bilateral inflammatory disease. Merayo-Lloves et al in their study included the presence of either pathological cupping of the optic

<table>
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<th>Table 1: Uveitic conditions associated with secondary glaucoma</th>
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<tr>
<td><strong>Anterior</strong></td>
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<tr>
<td>Idiopathic uveitis</td>
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<tr>
<td>Infectious uveitis</td>
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<td>Arthritis-associated uveitis</td>
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<td>Fuchs’ heterochromic iridocyclitis</td>
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<td>Posner-Schlossman syndrome</td>
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<td>Traumatic uveitis</td>
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<td>Lens-induced uveitis</td>
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disk or a glaucomatous field defect with elevated IOP above 21 mm Hg in definition of glaucoma. Sustained IOP elevation above 21 mm Hg but without optic disk or visual field changes were defined as ocular hypertension. From a total population of 1,254 cases of uveitis, SG was found in 153 eyes of 120 patients (12% of eyes; 10% of patients) and OHT was detected in additional 86 patients (7%). In a retrospective study of 374 cases, Saouli et al determined prevalence of OHT to be 12% (45 cases) with evidence of glaucomatous optic neuropathy seen in three patients only. Takahashi et al reported SG in 293 eyes (18.3%) of 217 patients (19.6%) in a retrospective study of 1,099 patients (1,604 eyes) from Japan. Among the 293 eyes with SG, 114 eyes (38.9%) had an abnormal visual field-related to high IOP. In a recent study, Herbert et al found the prevalence of raised IOP in the studied eyes as 41.8% (143 of 342). The prevalence of raised IOP requiring treatment was 29.8% (102 of 342) which referred to eyes with IOP greater than 30 mm Hg with or without optic disk and field changes or IOP greater than 21 mm Hg with glaucomatous optic disks and/ or visual fields. There were 33 eyes with a diagnosis of glaucoma (9.6% of all eyes). All these eyes had glaucomatous visual field defects and optic disk cupping.

Although several retrospective reports have described the prevalence of glaucoma in patients with uveitis, there have been few studies reporting the incidence of this complication. In a retrospective review of 391 patients, the incidence of glaucoma at 3 and 12 months after acute uveitis was 7.6%. In patients with chronic uveitis, the incidence of glaucoma at 1, 5 and 10 years was 6.6, 11.2 and 22.7 respectively.

Authors recently presented their data of 200 eyes of 200 patients of uveitis at World Glaucoma Congress 2009 at Boston, and reported a prevalence of raised IOP above 21 mm Hg to be 21% (42 patients) and prevalence of glaucomatous disk damage to be 6% (12 patients). The prevalence of secondary glaucoma seems to be related to a number of factors. These include the age at presentation, the type of uveitis and chronicity and severity of uveitis. Prevalence of UG and risk factors for same have been summarized in Table 2. Patients with these risk factors should be monitored closely and raised IOP should be treated promptly.

### Age at Presentation

Although uveitis is generally a condition of the third and fourth decades, in a series of 71 patients presenting with their first episode over the age of 60 years, one-third of the 30 patients with anterior uveitis were observed by the authors to have elevated IOP at presentation. Increasing age was correlated with raised IOP in another study.

Similar to these studies, authors found out increasing age to be a significant risk factor associated with raised IOP in uveitis in their data on 200 uveitic patients. The odds ratio of developing raised IOP in the age groups of 21 to 40 years, 41 to 60 years and 61 to 80 years compared with age group of 0 to 20 years was found to be 9.4, 8.75 and 30 respectively (p < 0.05).

The effects of age reflect an imbalance between trabecular meshwork (TM) function and the inflammatory load. With age, any inflammatory insult may unmask declining TM function, whereas in the young severe inflammation is required.

The overall prevalence of glaucoma in children with uveitis is low, ranging from 5 to 13.5%. The visual prognosis for these children, however, is poor. Kanski reported that 50% of children with uveitic glaucoma in his series lost light perception within an 8.5 year follow-up period. Sijssens et al reported elevated IOP in 35% of 147 cases (256 eyes) of uveitis in children less than 16 years of age during a follow-up of 5 years with bilateral disease seen in 92% of patients. The incidence of uveitic glaucoma in adults varies enormously but when all forms of uveitis are considered, the prevalence of secondary glaucoma in adults varies from 5.2 to 19%, similar to that found in children.

### Classification of Uveitis

Anterior uveitis accounts for 70% of all uveitis cases and most cases of uveitic glaucoma, although only 5% of anterior uveitis patients are affected. Merayo-Lloves et al reported predominant clinical type associated with secondary glaucoma

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patients (eyes)</th>
<th>Prevalence</th>
<th>Conclusions</th>
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<tr>
<td>Herbert HM et al</td>
<td>257 (402)</td>
<td>41.8%</td>
<td>Risk factors include increasing age and duration, steroid use, chronic and active uveitis</td>
</tr>
<tr>
<td>Takahashi T et al</td>
<td>1,099 (1,604)</td>
<td>18.3%</td>
<td>Active anterior uveitis was seen in 72%</td>
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<td>Saouli N et al</td>
<td>374</td>
<td>12%</td>
<td>PAS greater than 180 degree in only 7.5%</td>
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<tr>
<td>Saouli N et al</td>
<td>374</td>
<td>12%</td>
<td>Steroid-induced glaucoma seen in 8.9%</td>
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<tr>
<td>Merayo-Lloves J et al</td>
<td>1254</td>
<td>16.6%</td>
<td>Most common etiology was herpetic</td>
</tr>
<tr>
<td>Panek WC et al</td>
<td>100 (161)</td>
<td>19.3%</td>
<td>Risk factors include active, granulomatous and anterior uveitis</td>
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<tr>
<td>Sijssens KM et al</td>
<td>147 (256) (&lt; 16 years)</td>
<td>35%</td>
<td>SG more common with anterior uveitis</td>
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<td>SG more common with JIA-associated uveitis and with ANA-positive cases</td>
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was anterior uveitis seen with 67% of patients while intermediate, posterior and panuveitis were found in 14%, 14% and 14% of patients respectively. Similarly in another study, it was found that 72.4% eyes with elevated IOP secondary to uveitis had significant symptoms of active inflammation in the anterior segment of the eye. Further, the study compared the IOP level before the therapy among the anatomical diagnosis of uveitis which was significantly highest in anterior uveitis followed by intermediate and posterior uveitis. It may be that the aqueous outflow pathway is less influenced by inflammation predominantly affecting the posterior segment and hence the prevalence of IOP elevation is probably lower in intermediate and posterior uveitis. In pars planitis, for instance, secondary glaucoma was not reported as a significant problem in two sizeable studies. It may be that secondary glaucoma causes less visual morbidity in such conditions as Behcet’s syndrome and congenital toxoplasmosis than retinal complications.

All these studies identified anterior uveitis as the most common entity associated with secondary glaucoma but many did not find this to be a significant factor. Herbert et al did not find any significant association of raised IOP with anatomic distribution of uveitis. Similarly, Sijssens et al reported that in their study although intermediate uveitis had the highest percentage of elevated IOP during follow-up, there were no significant differences observed between the different localizations of uveitis. Neri et al performed a retrospective review of medical records of 391 consecutive patients with uveitis attending a subspecialty clinic of an academic institution during a 3-year period. They did not find a statistically significant difference in the incidence of glaucoma among the different parts of the eye affected (iridocyclitis, posterior uveitis or panuveitis). In their data, authors found out anterior uveitis to be the most common clinical type associated with raised IOP (52.4%) which they attributed to anterior uveitis being the most common entity in the study. Intermediate uveitis had the highest percentage of elevated IOP (27.8%). All the patients with IOP greater than 35 mm Hg were identified to have significant anterior segment inflammation. Overall, the analysis did not reveal a significant association between anatomical location of inflammation and raised IOP. It may be that the propensity to increased use of steroids with intermediate and posterior uveitis will act to mask any such association per se.

Uveitis can be classified based on clinicohistopathological features into granulomatous and nongranulomatous types. Granulomatous uveitis is said to be associated with greater propensity to formation of posterior and anterior peripheral synechiae and hence greater risk of secondary glaucoma. Merayo-Lloves et al reported granulomatous uveitis to be the predominant clinical type associated with SG with prevalence rate of 76%. A study of 374 cases of uveitis from France again found this association to be significant (45.4% OHT in granulomatous vs 8.9% in nongranulomatous). The authors did not find presence of granulomatous uveitis to be a significant factor associated with secondary glaucoma.

Course of Uveitis

The prevalence of secondary glaucoma also increases with chronicity of uveitis as reported by Herbert et al. In their retrospective study of 402 eyes of 257 patients, the prevalence of raised IOP was 26.0% in acute uveitis and 46.1% in chronic uveitis. Similarly, the prevalence of raised IOP requiring treatment in acute uveitis was 15.1% and for chronic uveitis was 33.8%. Both these results were statistically significant. Another study reported chronic and recurrent course of uveitis as to be predominantly associated with secondary glaucoma. In the author’s data of 200 patients, the course of disease in anterior uveitis revealed significant difference between glaucomatous and nonglaucomatous uveitic populations (p < 0.05). Patients with recurrent uveitis had an odds ratio of 4.90 and patients with chronic uveitis had an odds ratio of 3.61 when compared with patients with acute uveitis in favor of developing secondary glaucoma.

Neri et al found the incidence of glaucoma at 3 and 12 months to be 7.6% after acute uveitis and 6.5 and 11.1% at 1 and 5 years respectively in chronic uveitis. Panek et al in a retrospective study of 161 eyes in 100 patients found SG in 26% of eyes with chronic uveitis and 12% with acute disease although a statistically significant difference was lacking between these two groups. They, however, stated that increased IOP associated with acute disease was not a significant management problem, generally responding well to brief periods of medical therapy. On the contrary, glaucoma associated with chronic uveitis usually required prolonged medical therapy for control of pressures. They also reported visual field loss to be a problem in chronic uveitis only. Similarly, no significant differences were seen for developing elevated IOP and SG between those with chronic or acute uveitis in a retrospective study of 256 eyes of 147 children with uveitis under the age of 16 years.

Duration of Disease

Herbert et al have correlated number of years since diagnosis with raised IOP and found the relation to be significant. The incidence of glaucoma in chronic uveitis was reported to increase with time from 6.6 to 22.7% at the end of first year and after 10 years of follow-up respectively. Authors also reported higher mean duration of disease process in patients with secondary glaucoma compared with uveitic patients without glaucoma in their study. This was however, not found to be significant. A number of recurrences in patients with and without glaucoma were also not found to be significant.

Increasing prevalence of glaucoma with chronicity and duration of disease probably reflects the cumulative detrimental effect of inflammation and probably the consequence of chronic corticosteroid therapy on an initially normal TM.

Activity of Uveitis

As already stated above, a study from Japan found that 72.4% of eyes with raised IOP had significant anterior segment
inflammation. Saouli et al similarly found that the OHT was most often in phase with intraocular inflammation. Another retrospective review of case notes of 257 patients (402 eyes) attending a specialist uveitis clinic over a 3-month period revealed that 47.4% (83 of 175) of eyes with active uveitis had raised IOP, whereas 35.9% (60 of 167) of eyes that were quiescent at review had raised IOP. The authors noticed a marginally significant association between uveitis activity and raised IOP but did not find any significant association between disease activity and raised IOP requiring treatment and hence advised for these results to be interpreted with caution.

In their study of 200 uveitic eyes from India, authors reported healed uveitis to be significant factor related to raised IOP. However, no such association was seen on multivariate analysis. They reasoned that the association probably reflects the cumulative effect of restoration of the secretory function of ciliary body, the longer duration of disease and use of steroids as therapy.

**Angle of Anterior Chamber in Uveitis**

Takahashi et al reported that at the time of high IOP, out of 293 eyes, there were only 7.5% with peripheral anterior synechiae (PAS) wider than 180° of the TM, 37.2% with PAS smaller than 180° and the other 55.3% had no PAS. Merayo-Lloves et al also reported open angles in majority of eyes in their study (80%).

Gonioscopic findings have been evaluated by only few studies in literature. Authors found angle to be open in 70.0 and 47.6%; partly closed (PAS less than 180°) in 18.0 and 26.2%; and closed (PAS greater than 180°) in 12.0 and 26.2% patients with uveitis and uveitic glaucoma respectively. This difference was found to be significant (p < 0.001). All the patients with uveitic glaucoma having closed angle had significant anterior chamber inflammation; however, the anatomical location of inflammation and level of IOP rise did not show any association with anatomy of angle. The odds ratio of developing glaucoma in patients with closed and partly closed was 5.08 and 2.64 respectively. Relationship of the former was also confirmed on multivariate analysis.

**Severity of Uveitis**

The presence of posterior synechiae has been used as an index of severity. Fifty-one patients with JRA-associated uveitis were divided by Wolf et al into two groups according to the presence or absence of PS as an indicator of severity. A remarkable difference in the frequency of secondary glaucoma was noted between the two groups (45% in the former and 17% in the latter). Similarly, Neri et al found posterior synechiae to be present more frequently in patients with secondary glaucoma. In the same study, 14.5% patients with chronic uveitis without glaucoma had a deterioration of the best corrected visual acuity (BCVA). The same was seen in 31.7% patients with chronic uveitis with glaucoma and this difference was found to be significant. Authors stated that it is unknown that whether the presence of posterior synechiae or the deterioration in visual acuity has a causal relationship with glaucoma or simply is a reflection of more severe inflammation.

In the work from India, median BCVA, extent of posterior synechiae, presence of cataract and gross macular abnormalities were evaluated as indicators of severity of uveitis. Patients with uveitic glaucoma were found to have poorer median BCVA and higher prevalence of gross macular abnormalities including healed cystoid edema in uveitic patients with secondarily raised IOP (p < 0.05). The extent of posterior synechiae and presence of cataract were not found to be significant factors for same.

**Use of Steroids**

Based on diagnosis made on clinical observation, Takahashi et al found the proportion of steroid-induced glaucoma to be 8.9%. Saouli and Brézin noted corticosteroid-induced IOP rise in only two cases out of 45 cases of OHT. Panek et al in their record of 161 eyes of 100 patients did not report any case of raised IOP secondary to steroid response although all but one patient were off steroid therapy. Herbert et al reported a positive correlation between the requirements for corticosteroid treatment (topical, oral or both) and raised IOP but it was not confirmed on multivariate analysis but stated that patients on corticosteroids may be at a greater risk for developing raised IOP.

Sijssens et al in their study on pediatric uveitis reported SG to be significantly more frequent following periocular steroid injection although the number of injections or the presence of juvenile idiopathic arthritis did not bear any significance. Systemic steroid use was not found to be of any influence.

Similarly, authors reported prevalence of steroid-related IOP rise to be 28.6% in 42 patients with uveitic glaucoma. They found a significant association between prevalence of raised IOP and topical, periocular and systemic steroid use. Relationship of raised IOP with steroid was also confirmed on multivariate analysis.

It is generally accepted that steroids need to be used at the onset of uveitis, with the possibility of coupling them with immunosuppressant drugs. Steroid dose should be tapered as soon as possible according to clinical criteria to avoid serious side effects. It is postulated that a treatment of more than 6 months represent an additional risk to develop glaucoma.

**Specific Uveitic Syndromes**

Neri et al did not find any statistically significant difference in the incidence of glaucoma between idiopathic vs nonidiopathic glaucoma. In contrast to this report, the majority of studies in the literature have observed that the prevalence of secondary glaucoma associated with uveitis varies depending on the particular cause of the disease.

In Fuchs’ heterochromic cyclitis, reported prevalence ranges from 15 to 27%, a proportion of patients, however, may remain asymptomatic for a longer period than in inflammatory
uveitis which may result in a relative under diagnosis of the syndrome and perhaps an overestimate of the true frequency of secondary glaucoma.6

The Posner-Schlossman syndrome and herpetic keratouveitis, on the contrary, are rarely asymptomatic. In the former, IOP elevation is a sine qua non and in the latter, IOP elevation is common at presentation.7 In one published series 28% of herpetic keratouveitis eyes developed IOP elevation with 12% requiring long-term glaucoma therapy.37 Misirocchi et al reported the prevalence of SG in herpes simplex keratouveitis and zoster uveitis to be as high as 54 and 38% respectively.38

Westfall et al reported the prevalence of elevated IOP (>21) in patients with active retinochoroiditis secondary to toxoplasmosis to be as high as 38%. This prevalence was much higher than in the control group (10%) of age- and gender-matched patients with active unilateral anterior uveitis and the difference was statistically significant.39

Elgin et al reported the prevalence of secondary glaucoma in patients with Behcet’s disease in a retrospective study. Out of 230 eyes of 129 patients with ocular involvement of Behcet’s disease, 47% had chronic posterior uveitis. A total of 10.9% of patients developed secondary glaucoma, including steroid- or inflammation-induced open-angle glaucoma, angle closure glaucoma or neovascular glaucoma.40

Uveitis related to juvenile idiopathic arthritis (JIA) is the most common form of childhood uveitis and has a high rate of complications of particular note is 10 to 30% prevalence of secondary glaucoma in patients with chronic anterior uveitis associated with it because of the poor visual prognosis.41-43 Kanski and Shunshi observed secondary glaucoma in 17% of 277 patients but more significantly 35% of affected eyes were reported as losing all light perception.21 De Boer et al observed secondary glaucoma in 44% of children with JIA-associated uveitis.44 Foster et al found that uveitic glaucoma or elevated IOP occurred in 42% of patients with JIA-associated uveitis at intervals ranging from 0.6 to 58 years after the onset of ocular disease with a mean time of onset of 9.2 years.45 In a prospective study conducted in Finland, 426 children diagnosed with JRA were followed for a mean of 4.5 years. A total of 104 children (24.4%) developed uveitis during the follow-up period. Glaucomatous optic nerve damage occurred in 8% of those with uveitis.46 The difference in reported prevalence of glaucoma between these two studies may be due to a variety of factors including differences in the patient population, improved treatment methods and different methods of defining or detecting the presence of optic nerve damage.6,47 Late presentation48 and very high corticosteroid response rate in children7 have been identified as reasons for poor prognosis of secondary glaucoma in JIA.

The most common cause for SG in uveitis, however, remains idiopathic acute anterior uveitis, even though the reported prevalence is lower.14,16,17 A study of relative frequency of SG per disease showed that herpes virus-associated uveitis was most likely to cause SG (23%) followed by Fuchs’ heterochromic iridocyclitis (19%), Vogt-Koyanagi-Harada (18%), JRA (16%), syphilis (14%) and sarcoidosis (12%) though most of SG cases were secondary to idiopathic uveitis, sarcoid and JIA-associated uveitis. Herpes virus-associated iridocyclitis was the leading cause of posterior uveitis, associated with SG, while sarcoidosis accounted for the majority of posterior intermediate and panuveitis cases.14

Large hospital-based study from Japan reported the proportion of patients with secondary glaucoma in each clinical entity of uveitis as 100% in Posner-Schlossman syndrome, 34.1% in sarcoidosis, 30.4% in herpetic anterior uveitis, 20.8% in Behcet’s disease, 20.0% in human leukocyte antigen (HLA)-B27-related acute anterior uveitis, 16.4% in Vogt-Koyanagi-Harada’s disease, 16.2% in human T-lymphotropic virus type 1 (HTLV-1) uveitis, 11.6% in ocular toxoplasmosis, 16.1% in other entities of defined etiology and 15.1% in idiopathic uveitis. The unique epidemiological feature to the location of hospital in the study was high prevalence of HTLV-1 uveitis and ocular toxoplasmosis.16

Specialist uveitis clinic-based study from tertiary eye care center in India established etiology in 76 out of 200 cases (38%) of uveitis and in 12 out of 42 cases (28.7%) of uveitic glaucoma. The highest prevalence was seen in Posner-Schlossman syndrome (100%) followed by herpetic keratouveitis and Fuchs’ heterochromic uveitis (33% each).44

A four times higher prevalence has been observed in HLA-B27-positive patients compared with HLA-B27-negative individuals in anterior uveitis.13 A systemic disease was observed in 30% patients in a study of 147 patients of uveitis under the age of 16 years. SG was significantly more often observed in children with JIA-associated chronic anterior uveitis and ANA (Antinuclear antibody)-positive children.18

PATHOGENESIS

Uveitic glaucoma is a complex entity which arises from a combination of several biochemical and cellular mechanisms inherent in the inflammatory process. Uveitic glaucoma represents something of a paradox because of the natural tendency for the IOP to reduce in acute inflammation. Table 3 summarizes the pathogenesis of uveitic glaucoma.

Cellular and Biochemical Changes in Aqueous Composition in Uveitis

Inflammatory Cells

Experimental evidence shows that T cells play a major role in the pathogenesis of uveitis. T-cells have been demonstrated to be the most abundant cell type in uveal tissue, retina, aqueous and vitreous of patients with uveitis.49 In experimental autoimmune uveitis (EAU), T cells appear to play a pivotal role in the genesis and propagation of inflammation,50 however, anterior chamber infiltrates seem to be composed largely of polymorphs and macrophages.
Prostaglandins (PGs) can produce many of the signs of ocular inflammation, including vasodilatation, miosis and increased protein content in the aqueous humor.5,6 The elevated protein content of the aqueous humor may be due to increased vascular permeability.5,5 PGs released in early phases of the inflammatory process have complex interactions on IOP. They can disrupt the blood-aqueous barrier and either increase or decrease IOP.5,6,5,7 Even though aqueous dynamics studies showed that PGs increase aqueous outflow and significantly lower conventional outflow, the precise effect of PGs on IOP during the complex course of uveitis remains difficult to determine.5

### Inflammatory Mediators (Cytokines) and Toxic Agents (Oxygen Free Radicals)

Cytokines are soluble polypeptides that are secreted principally by monocytes/macrophages and lymphocytes, although any cell that participates in the immune response may secrete them. Cytokines may influence the IOP in uveitic eyes by increasing the inflammation, by stimulating neovascularization and by having a direct effect on aqueous humor dynamics.5,8

Tissue growth factor β-2 (TGFβ-2), a potent immunosuppressive that is normally present in the eye, is decreased or absent in the aqueous and vitreous of eyes with various inflammatory disorders.5,9 Neovascularization, an occasional feature of the inflamed uvea, may develop in response to IL-1, tumor necrosis factor alpha (TNF-α), fibroblast growth factor (FGF), epidermal growth factor (EGF), transforming growth factor beta (TGF-β), granulocyte macrophage-colony stimulating factor (GM-CSF) and platelet-derived growth factor.5,8 Wakefield and Lloyd hypothesized that cytokines such as IL-1, TNF, interferon-gamma (INF-γ) and GM-CSF can promote ocular hypertension by increasing aqueous production or decreasing aqueous drainage.5,8 Park and Latina showed that INF-γ is a potent inhibitor of human TM cell phagocytosis in vitro by disturbing the cytoskeletal organization necessary for phagocytosis. Chronic inhibition of the trabecular meshwork cells may reduce aqueous outflow and increase IOP.5,11

Oxygen free radicals are liberated by macrophages and PMNs. The damage to the outflow pathway caused by these cells may lead to secondary glaucoma. There are no reports on the direct effects of oxygen free radicals on IOP.5

Finally, other biochemical substances released during the inflammation process could increase or decrease IOP. For example, antagonists of angiotensin converting enzyme (ACE) are known to lower IOP, so the high levels of ACE present in the aqueous humor and serum of patients with sarcoid uveitis could explain, at least in part, the elevation of IOP that is seen in these patients.6,2

### Morphologic Changes in the Anterior Chamber Angle

All these cellular and biochemical changes in the aqueous can result in morphologic changes in the anterior chamber angle that may or may not be detected gonioscopically. The angle may be closed, partly closed or open. The level of IOP will depend upon the rate of aqueous humor production by the ciliary body.
Closed-angle Glaucoma

1. **Posterior synchiae and pupillary block**: In patients with uveitis, inflammatory cells, protein, fibrin and debris in the aqueous can stimulate posterior synchiae (PS) formation between the posterior iris surface and anterior lens capsule, the vitreous face in aphakic patients or posterior chamber intraocular lens (IOL) or residual capsule in pseudophakic patients. The rapidity and severity with which posterior synchiae form is related to the type, duration, severity of the uveitis and delay in treatment of uveitis, for example, posterior synchiae occur more commonly in granulomatous than in nongranulomatous uveitis. The greater the extent of the posterior synchiae, the lesser the pupil is able to dilate and the greater the risk for further synchiae formation in subsequent recurrences. When synchiae involve all 360 degree, they totally block the flow of aqueous from the posterior to the anterior chamber, resulting in iris bombe and acute angle-closure glaucoma. The risk for synchiae formation can be better evaluated using laser flare photometry. Under the value of 30 photons/ms, the risk for synchiae formation is very low and there is no need for prophylactic mydriasis, except when a strong granulomatous reaction is present.

2. **Peripheral anterior synchiae**: Peripheral anterior synchiae (PAS) are a common complication of anterior uveitis, particularly when granulomatous can result in progressive angle closure. PAS may be secondary to inflammation, neovascularization or iris bombe. PAS develop more frequently in eyes with preexisting narrow angles or those narrowed by iris bombe secondary to posterior synchiae or by forward rotation of the ciliary body. In eyes with PAS that involve less than 360 degree, the remaining open angle may be compromised by the presence of pigment, which may contribute to trabecular obstruction. Even when anterior portions of the trabecular meshwork remain visible on gonioscopy, the angle can be functionally closed. Continued PAS formation can result in total closure of the angle.

3. **Forward rotation of the ciliary body**: Hyperacute inflammation, edema, supraciliary or suprachoroidal effusion may result in forward rotation of the ciliary body leading to nonpupillary block angle-closure glaucoma. Similar pathogenic mechanism has been reported in patients with AIDS, Vogt-Koyanagi-Harada syndrome, hemorrhagic fever with renal syndrome, Pars planitis and uveal effusion syndrome.

4. **Primary angle-closure glaucoma**: Any eye predisposed to angle closure that develops anterior uveitis can subsequently develop acute-closure glaucoma secondary to stress, mydriatic treatment or changes associated with uveitis. It may occasionally be difficult to establish in inflamed eyes with acute angle-closure glaucoma whether inflammation or primary acute angle-closure was the primary event.

Open-angle Glaucoma

Open-angle mechanisms are probably the most common causes of elevated IOP in uveitis.

1. **Aqueous hypersecretion**: Aqueous hypersecretion may result from blood-aqueous barrier breakdown. This may result in IOP elevation in uveitis even if aqueous outflow remains normal. This mechanism however remains controversial.

2. **Mechanical blockage and cellular depletion**: The trabeculum may be mechanically blocked by serum components, TM precipitates or inflammatory cells and debris. Inflammation, neovascularization or iris bombe may cause a reduction in the diameter of the trabecular pores, resulting in resistance to aqueous outflow. This mechanism is thought to be cause of raised IOP in acute herpetic uveitis and Posner Schlossman syndrome.

Resistance to outflow is also believed to vary with the rate of TM perfusion. Laboratory data suggest that a TM perfusion rate of less than 1 ml/min may have a deleterious influence on TM function. It is possible that reduced aqueous production by the inflamed ciliary body as observed in uveitis may contribute to elevated outflow resistance because of suboptimal aqueous perfusion of the outflow pathway.

4. **Damage to trabeculum and endothelium secondary to chronic inflammation**: With severe, chronic or repeated episodes of uveitis, permanent changes in TM may result in loss or dysfunction of trabecular endothelial cells, scarring of the meshwork or Schlemm’s canal and obstruction of the trabeculum by a hyaline membrane, ultimately impeding outflow.

5. **Corticosteroid-induced glaucoma**: Administration of steroids by any route can occasionally increase IOP in both normal eyes and uveitic eyes in susceptible individuals. Clinically, IOP rise occurs 2 or more weeks after initiating therapy, but it may occur anytime and usually returns to normal after discontinuation of the drug. Corticosteroids increase IOP by decreasing aqueous outflow. Corticosteroids are the first line of drugs used to treat uveitis. It is often impossible to know whether the IOP rise subsequent to steroid therapy is due to restoration of aqueous production, the use of the steroid or both. In patients with unilateral uveitis, a provocative test with topical steroid may
be performed on the opposite eye; however, in patients with bilateral uveitis, a fall in IOP as steroids are tapered may be the only evidence of steroid-induced ocular hypertension, but the IOP drop could also be secondary to the recovery of TM function or recurrence of inflammation.5

If steroid-induced glaucoma is suspected, corticosteroids may be tapered, although this can lead to a recrudescence of the uveitis. An alternative approach is to use a lower concentration of the drug or a drug with lesser tendency to elevate IOP, such as fluorometholone.73 In some cases of mild uveitis, corticosteroids can be successfully replaced by nonsteroidal anti-inflammatory drugs while in severe cases, it may be best to replace the corticosteroids with an immunosuppressive agent to control inflammation.

In some patients, IOP can remain elevated for 18 months or longer after repository corticosteroid injection despite glaucoma therapy requiring surgical removal of the depot-steroid or filtration surgery.2

6. Primary open-angle glaucoma: In some cases, preexisting primary open-angle glaucoma (POAG) may also contribute to the uveitic component in OHT. If the POAG was not diagnosed prior to the uveitic episode, the differential diagnosis between POAG and uveitic glaucoma may become difficult.

**Combined-mechanism Glaucoma**

Combinations of all of the aforementioned mechanisms may conspire to elevate IOP and cause damage to the optic nerve head in uveitis. A combination of partial angle closure, partial open angle with damaged trabecular meshwork, partial steroid-induced component and smoldering inflammation can markedly elevate IOP. It is important to separate these components so that inflammation, IOP and optic nerve damage can be controlled or minimized.5

**CLASSIFICATION**

Several schemes have been used to classify uveitic glaucoma based on angle structure, course and specific causative agent of uveitis (Table 4). A useful diagnostic classification of uveitis is based on the predominant anatomic site of the inflammation as described by International Uveitis Study Group.74 The most appropriate approach is to classify uveitic glaucoma as a combination of these different schemes. Such a classification can be achieved, however, only after the uveitic entity has been diagnosed by careful history, physical examination and judicious use of ancillary tests.

**EVALUATION**

**History and Symptoms**

A detailed history, present and past, with specific questions regarding the symptoms, course, previous treatments, past ocular history, systemic disorders and/or medication, social history and family history is of utmost importance in a case of uveitic glaucoma. A thorough review of systems should be completed.

**Table 4: Classification of uveitic glaucoma**

<table>
<thead>
<tr>
<th>1. Angle structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Open-angle glaucoma</td>
</tr>
<tr>
<td>b. Angle-closure glaucoma</td>
</tr>
<tr>
<td>2. Course</td>
</tr>
<tr>
<td>a. Acute</td>
</tr>
<tr>
<td>b. Chronic</td>
</tr>
<tr>
<td>3. Severity</td>
</tr>
<tr>
<td>a. Hypertensive uveits</td>
</tr>
<tr>
<td>b. Postinflammatory glaucoma</td>
</tr>
<tr>
<td>4. Type of uveits</td>
</tr>
<tr>
<td>a. Pathology</td>
</tr>
<tr>
<td>• Nongranulomatous</td>
</tr>
<tr>
<td>• Granulomatous</td>
</tr>
<tr>
<td>b. Causes</td>
</tr>
<tr>
<td>• Infectious</td>
</tr>
<tr>
<td>• Autoimmune</td>
</tr>
<tr>
<td>• Systemic</td>
</tr>
<tr>
<td>• Idiopathic</td>
</tr>
</tbody>
</table>

**Visual Function**

It may be occasionally difficult to determine whether a decrease in the visual acuity is caused by the glaucoma, by the uveitis or its complications. Perimetry should be performed in patients with raised IOP.63 However, associated conditions affecting visual acuity and function can make interpretation of visual fields in uveitic patients difficult and unreliable.

**External and Slit-lamp Examination**

Detailed examination must be conducted to identify enlargement of the lacrimal gland, vitiligo or poliosis, conjunctival or episcleral injection, band keratopathy, epithelial dendrites or stromal scarring, corneal epithelia, keratic precipitates, cells or snowball opacities, vitreous strands, traction bands and cyclitic membranes.

**Gonioscopy**

Gonioscopy should be performed in all cases of uveitic glaucoma5 to determine the presence of peripheral anterior synechiae (PAS) and the extent of angle closure. It aids in differentiating appositional from synechial angle closure, distinguishing narrow angles which may be predisposed to angle closure, reveal angle neovascularization and the fine vessels crossing the angle in Fuchs’ heterochromic iridocyclitis.

**Fundus Examination**

The posterior segment should be examined with both direct and indirect methods for possible posterior segment lesions and the optic nerve head assessment.5 The optic nerve head should be assessed for excavation, hemorrhage, edema or hyperemia and retinal nerve fiber layer defects. The diagnosis of glaucoma
Laboratory and Ancillary Investigations

Careful history and physical examination help to initiate ‘tailored’ laboratory evaluation of uveitis patients to determine the cause of uveitis which may be potentially curable. Laboratory evaluation can be classified into noninvasive and invasive. Noninvasive techniques include serology, skin tests and radiography, such as chest radiographs, computerized tomography, magnetic resonance imaging and gallium scanning. Invasive tests include conjunctival biopsy, anterior chamber paracentesis, vitreous biopsy and chorioretal biopsy. With this array of tests, the etiology of uveitis may be determined in up to 60% of cases.

Other Investigations

Recent methods of improvement in evaluation of optic nerve head (scanning laser ophthalmoscopy) and of the angle [ultrasound biomicroscopy (UBM)] and optical coherence tomography] are as relevant to uveitic glaucoma as to other glaucomas. UBM also gives information on the morphology of the ciliary body which may show atrophic ciliary body in cases of chronic uveitis with hypertension and hence indicating high risk of phthisis in these patients after glaucoma surgery.

Laser flare photometry can rapidly detect changes in flare after modification of anti-inflammatory therapy; it is able to indicate before clinical changes whether or not the inflammation is active and might be a contributing factor to the hypertension.

MANAGEMENT

Treatment of uveitis aims at control of intraocular inflammation and normalization of intraocular pressure. In general, the treatment begins with control of the ocular inflammation, which itself may normalize the IOP. Medical and surgical therapy may be needed when the IOP does not respond to anti-inflammatory therapy. A number of factors influence the management of elevated IOP in uveitis including anatomic mechanism of elevated IOP, degree of optic nerve damage, response to steroids and so on.

Various studies have reported treatment profile in cohort of patients with secondary glaucoma in uveitis. In a study of 153 eyes of 120 patients with secondary glaucoma, all patients required one or more topical IOP lowering drug, 49% requires systemic CAIs, 10% had laser iridotomy done while filtering surgery was required in 31% patients. Another study from Japan, reported surgical therapy 38 eyes of 293 patients (12.7%) with uveitic glaucoma, where secondary glaucoma was defined as IOP greater than 21 mm Hg on two consecutive visits and 89.5% were controlled with IOP under 20 mm Hg with or without medication at mean follow-up duration of 71.6 ± 47.1 months with reduction in both mean IOP and number of ocular hypotensive drugs used. In another study by Herbert et al, nine out of 33 eyes (27.3%) with uveitic glaucoma underwent trabeculectomy with antimetabolite augmentation, one had broad iridectomy dome and the remaining 23 eyes were managed medically with six eyes requiring use of systemic CAI. In a retrospective review by Neri et al, 56 patients of chronic uveitis and five patients with acute uveitis developed SG defined by the criterion of IOP elevation alone. Seven patients (12.5%) required trabeculectomy and one underwent GDD implantation, laser iridotomy and cyclodiode laser treatment each in the former group while none required any surgery in patients with acute uveitis. Nearly half the patients in each group required use of systemic CAI.

In a cohort of 42 eyes of uveitic glaucoma, authors initiated treatment in patients with IOP greater than 25 mm Hg. At the end of 6 months of follow-up, there was significant reduction in mean IOP. Out of 42 patients, 30 patients (71.4%) were on medical treatment for glaucoma, 5 (11.9%) had undergone trabeculectomy with mitomycin C, while 7 (16.7%) patients were not on any treatment. None of the patients required systemic IOP lowering medication. Overall, there was decrease mean number of topical medication used in patients on either medical or surgical management. Two out of 42 patients continued with IOP greater than 25 mm Hg at the end of 6 months. Six patients (14.29%) had laser iridotomies done while one with absent perception of light underwent diode laser cyclophotocoagulation.

Management of Inflammation

Early anti-inflammatory therapy combined with mydriatics and cycloplegics is used to prevent irreversible consequences of uveitis, such as posterior and peripheral anterior synchiae, pupillary membrane or trabecular meshwork damage. Treatment of uveitis may consist of topical or systemic nonsteroidal anti-inflammatory agents, topical or periocular or systemic corticosteroids and systemic immunosuppressives. Infectious uveitis is treated with appropriate antimicrobials. Mydriatic-cycloplegic agents may be used to prevent or break posterior synchiae and to relieve the pain and discomfort of ciliary muscle and iris sphincter spasm.

Medical Management of Raised IOP

Topical beta-adrenergic antagonists are usually the first drug of choice. The choice of a second-line agent in uveitic glaucoma often depends on the level of the IOP. With high IOP levels, not reduced significantly by b-antagonists, the second-line therapy may be a systemic carbonic anhydrase inhibitor (CAI). Where IOP elevation is only moderate, in the absence of significant glaucomatous optic neuropathy the second-line of therapy may be either an adrenergic agonist or a topical CAI. In eyes with corticosteroid-induced glaucoma with recalcitrant inflammation, one may assist in the reduction of the intensity of corticosteroid therapy by substituting immunosuppressive agents.

The IOP-lowering effect of most ocular hypotensive agents is highly variable in uveitis, especially topical carbonic anhydrase inhibitors.
**Topical β-adrenergic Antagonist**

These reduce aqueous humor production and do not alter pupil size. A nonselective β-blocker, such as timolol, remains the first-line therapy in patients for whom there are no systemic contraindications. Levobunolol and Carteolol have similar efficacy and tolerability profile. Betaxolol is a cardioselective β-blocker with fewer pulmonary side effects, but is slightly less effective than timolol in lowering IOP. Metipranolol, a β-blocker with fewer pulmonary side effects, but is slightly efficacious and tolerability profile. Betaxolol is a cardioselective β-blocker with fewer pulmonary side effects, but is slightly less effective than timolol in lowering IOP.

**Adrenergic Agonists**

Their role in management of uveitic glaucoma is unclear. Nonselective topical adrenergic agonists are usually no longer used. Selective α-agonists are widely used which seem to act by a combination of aqueous suppression and increased uveoscleral outflow. Apraclonodine, a topical alpha-2 agonist, may be useful in controlling acute IOP elevations but has frequent local side effects and high risk of tachyphylaxis. Brominidine, specific for the a2-receptor, has a better ocular tolerance profile, although systemic side effects are more common. Byles et al reported granulomatous anterior uveitis caused by topical administration of brimonidine tartrate 0.2% for patients.

**Carbonic Anhydrase Inhibitors (CAIs)**

CAIs may be used when previously mentioned drugs are unable to control IOP or contraindicated because of potential side effects. These drugs reduce aqueous production through an alteration of ion transport mechanisms in the ciliary epithelium. CAIs can be administered orally, intravenously or topically. Systemic CAIs are used for short-term management of acute high IOP as prolonged use is associated with multiple side effects and need to monitor serum electrolytes. Systemic administration has the potential dual effect of reducing IOP and cystoid macular edema.

Minimal side effects occur with the use of topical CAIs. Dorzolamide also inhibits corneal endothelial carbonic anhydrase and may occasionally cause prolonged corneal edema and hence should be used with caution in those patients with uveitic glaucoma in whom corneal endothelial function is compromised.

**Hyperosmotic Agents**

These agents are used when IOP has to be lowered rapidly. They reduce the IOP primarily by reducing vitreous volume. Glycerine, mannitol or isosorbide may be used, the latter being preferable in diabetics. These agents are especially useful in patients with secondary angle-closure glaucoma due to pupillary block in whom a rapid drop in IOP is required to reduce corneal edema so that laser iridotomy can be performed.

**Miotics**

Cholinergic agents are generally avoided in uveitic glaucoma since they may potentiate formation of posterior synechiae or a pupillary membrane, cause discomfort by aggravating ciliary muscle spasm and increase inflammation by enhancing breakdown of the blood-aqueous barrier and accelerating the release of enzymes from polymorphonuclear lymphocyte lysozymes.

**Prostaglandin Analogues**

Schumer et al considered cystoid macular edema (CME) and iridocyclitis as putative but unproven side effects of prostaglandin analogues. Despite initial fears, it seems that prostaglandin receptor agonists have a propensity to increase the activity of uveitis in only a very small percentage of patients. However, prostaglandin agonists should still be used cautiously in uveitic glaucoma patients with a history of cystoid macular edema or herpetic keratouveitis.

**Interactions of Glaucoma Medication with other Anti-inflammatory Drugs**

There is evidence that the efficacy of prostaglandin agonists and α-adrenergic agonists may be partially blocked by the concurrent use of nonsteroidal anti-inflammatory drugs (NSAIDs). There is evidence that the efficacy of prostaglandin agonists and α-adrenergic agonists is compromised.

**Surgical Management of Raised IOP**

The decision to operate is based on the level of the IOP, the response to medication and the degree of optic nerve damage. Kok and Barton in their review proposed division of uveitic glaucoma patients with IOP elevation sufficient to require systemic CAI into three broad management groups. The first included those in whom the IOP could easily be brought under control with medical therapy, with a reasonable prospect that systemic CAI may be tapered off. Filtration surgery in this scenario was indicated only if the optic nerve shows significant glaucomatous damage as a consequence of repeated attacks of elevated IOP. The second group included patients with IOP control on a heavy regimen of systemic CAI combined with multiple topical agents. The long-term the likelihood of filtration surgery in this group was much higher; however, if the patient is reluctant to undergo surgery or prolonged medical therapy can be tolerated and there is reason to suspect a significant short-term corticosteroid-related component to the IOP elevation, then medical therapy was justified. In the third group, the IOP was uncontrolled and filtration surgery was indicated irrespective of existent damage to the optic nerve.

Irrespective of the type of surgical intervention, the inflammation should be as quiet as possible for a period of time before surgery. Good control of intraocular inflammation for a minimum of 3 months before surgery is ideal in elective cases; however, glaucoma surgery in uveitics is rarely performed on an elective basis. It is useful to consider pre- and postoperative topical corticosteroids. It also helps to reduce the conjunctival inflammatory cell population before any type of surgery that involves conjunctival filtration (trabeculectomy).
or drainage device implantation). In patients with severe inflammatory disease, a perioperative course of systemic or periocular steroid at the conclusion or surgery may be indicated. In cases of steroid-induced glaucoma, the management may be much more difficult requiring temporary immunosuppressive/cytotoxic therapy may need to be substituted to control inflammation in the perioperative period.

Management of Angle Closure with or without Pupillary Block

Acute pupillary block glaucoma in uveitis is often due to a secluded pupil and is a relative surgical emergency. Anti-inflammatory medication in combination with pupillary dilatation may reestablish normal aqueous flow. Intracameral tissue plasminogen activator (12.5 μg) may be used in severe fibrinous uveitis with pupillary membrane formation, such as in HLA B-27 associated iridocyclitis.

Angle closure due to iris bombe may be managed by laser iridotomy. Nd-YAG laser may have the advantage of inducing less postoperative inflammation and requiring considerably fewer applications with a marked reduction in total energy delivered as compared with the argon laser. In eyes with uveitis, the laser iridotomy has disadvantage of a smaller opening that is more prone to closure and worsening or reactivation of inflammation. For this reason, several iridotomies and aggressive topical corticosteroid therapy before and after the procedure are recommended. Nevertheless, it is a safer procedure than surgical iridectomy in eyes with intraocular inflammation and elevated IOP. Spencer et al reported high initial failure rate with significantly reduced mean survival rate of laser iridotomies in uveitic eyes with acute angle closure when compared with eyes with acute angle closure without uveitis. In another study of 67 eyes with uveitic closed-angle glaucoma that underwent laser iridotomy, 60% of the cases remained patent with normal intraocular pressures at final follow-up. Laser iridotomy should not be done in eyes with severe active anterior uveitis, corneal opacity or edema or iridocorneal touch.

In case laser is unsuccessful or contraindicated, a surgical iridectomy with or without synechiolysis should be performed in cases of uveitic acute angle-closure glaucoma. This procedure is successful only in eyes with peripheral anterior synechiae that involve less than 75% of the angle. The procedure can lead to severe surgically induced postoperative inflammation. Modern alternative treatments for pupillary block, such as iridoplasty, are not appropriate where pupil block is secondary to seclusion of the pupil because they have no influence on the causative mechanism. Mansouri et al, however, recently reported success with argon laser peripheral iridoplasty in one case of uveitis-associated acute angle-closure glaucoma which was unresponsive to medical management and repeated laser iridotomies.

In patients with angle closure without pupillary block, laser or surgical iridectomy may not be useful since inflammation of the ciliary body and anterior rotation of the lens-iris diaphragm cause the angle closure. Corticosteroids and aqueous suppressants can often reduce the IOP and help reverse the angle closure. Angle closure may not be reversed if PAS have formed. If medical therapy is unable to control the elevated IOP in the chronic form of angle closure without pupillary block, filtration surgery has to be considered. In the presence of extensive and fresh peripheral anterior synechiae, goniosynechiolysis has been reported to reestablish normal anatomy and to lower the IOP in some patients.

Trabeculectomy

Trabeculectomy is the surgical procedure of choice in phakic uveitic patients who have not undergone previous intraocular surgery and in whom there is no added risk of failure, like from anterior segment neovascularization (Table 5). Without antiproliferative agents, trabeculectomy survival after 5 years, in terms of IOP lesser than 21 mm Hg, has been reported to be 53 and 78% without and with medication respectively. In another study of 50 eyes with primary open-angle glaucoma controls without and with medication respectively.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patients (eyes)</th>
<th>Antiproliferative agent</th>
<th>Success (follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noble J et al</td>
<td>21 (21)</td>
<td>MMC</td>
<td>90% (1 year)</td>
</tr>
<tr>
<td>Park UC et al</td>
<td>23 (23)</td>
<td>MMC</td>
<td>91.3% (1 year)</td>
</tr>
<tr>
<td>Souissi K et al</td>
<td>14 (17)</td>
<td>None</td>
<td>64.7% (52 months)</td>
</tr>
<tr>
<td>Novak-Laus K et al</td>
<td>22 (22)</td>
<td>5-FU/MMC</td>
<td>78% (1 year)</td>
</tr>
<tr>
<td>Ceballos EM et al</td>
<td>44 (44)</td>
<td>5-FU</td>
<td>82% (2 years)</td>
</tr>
<tr>
<td>Towler et al</td>
<td>43 (50)</td>
<td>MMC</td>
<td>91.6% (10 months)</td>
</tr>
<tr>
<td>Prata JA et al</td>
<td>24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
follow-up of 52 months in 17 eyes. A study by Park et al reported favorable success rate of IOP control in patients with UG undergoing phacotrabeculectomy with MMC, 91.3% at 1 year and 84.8% at 2 years, but it was significantly lower than in the control group of primary OAG patients. Nevertheless, they concluded that with adequate inflammation suppression, procedure was an effective and safe therapeutic option for the management of secondary cataract and glaucoma in uveitic eyes. A lower surgical success rate of the uveitic group was attributed to the postoperative inflammation recurrence.

Uveitis has been reported to be a negative predictor of success in trabeculectomy when compared to primary open angle controls. Early postoperative complications include choroidal detachment, shallow anterior chamber, hyphema, macular edema and raised IOP. Late postoperative complications included exacerbation of uveitis, macular edema, cataract and raised IOP. The higher success rate of filtering surgery with modulation of wound healing is associated with an elevated risk for hypotony, bleb leaks and late bleb-related endophthalmitis.

Postoperative complications, such as choroidal effusion, choroidal hemorrhage, shallow anterior chamber and late ocular hypotension, may be higher in eyes with uveitic glaucoma than with primary open-angle glaucoma since adjunctive treatment with 5-fluorouracil, mitomycin-C or a drainage device is more commonly used in patients with uveitic glaucoma. Postoperative inflammation or reactivation of uveitis has been reported to occur in 5.2 to 31.1% of cases of uveitic glaucoma. This incidence can be lowered by treating the patients with pre- and postoperative corticosteroids.

**Glaucoma Drainage Devices (GDDs)**

The poor long-term success rate of repeat trabeculectomies in refractory uveitic glaucoma patients has led to the use of GDDs (Table 6). These have demonstrated improved efficacy of IOP control in patients with high risk for failure of trabeculectomy with antimetabolites and have the additional advantage of reducing the risk of bleb-related infection, due to the formation of a posterior bleb with a thick fibrous capsule. Studies report success rate ranging from 68.4 to 94.8% on short-term follow-up (1 to 2 years) and 50 to 87% at long-term follow-up (4 to 10 years) in uveitic glaucoma refractory to management. Hill et al reported 5-year life-table success rate of 79% in 11 patients who underwent Molteno implantation after failed trabeculectomy and higher success rate with Molteno implantation than standard trabeculectomy in patients with marked postoperative inflammation. Kuchty et al, in their review, reported no difference in IOP between patients with cataract and glaucoma surgery is not appropriate in patients with uveitis. A study by Park et al reported favorable success rate of IOP control in patients with UG undergoing phacotrabeculectomy with MMC, 91.3% at 1 year and 84.8% at 2 years, but it was significantly lower than in the control group of primary OAG patients. Nevertheless, they concluded that with adequate inflammation suppression, procedure was an effective and safe therapeutic option for the management of secondary cataract and glaucoma in uveitic eyes. A lower surgical success rate of the uveitic group was attributed to the postoperative inflammation recurrence.
UG undergoing trabeculectomy with MMC or AGV implantation. The cumulative success rates were 77 and 100% for the former and the latter respectively.27

Conflicting reports exist as to the benefits of MMC on IOP control after GDD implantation.129,130 However, Kok and Barton in their review stated widespread use of MMC in GDD surgery.6 In uveitic glaucoma associated with JRA, GDD implantation is an appropriate primary surgical procedure.131 Although the exact role of GDD implantation in uveitis has yet to be defined clearly, it is widely accepted that the threshold for GDD implantation is lower in patients with uveitis than in other glaucoma.6

Trabeculodialysis/Goniotomy

Trabeculodialysis is a modified goniotomy used in children and young adults with uncontrolled uveitic glaucoma (Table 7). Various series have reported success rate ranging from 56 to 75% over follow-up duration of 2.5 to 8 years.132-135 However, with the advent of antimetabolites to modify wound healing this procedure will probably be used less frequently. Goniotomy has been advocated as first-line surgery for young patients with refractory glaucoma associated with chronic uveitis.133

Nonpenetrating Glaucoma Surgery (NPGS)

There have been limited studies for role of NPGS in uveitic glaucoma (Table 8). Obstruction of TM, as with significant PAS, precludes use of this procedure.27 Auer et al first reported results of deep sclerectomy in uveitic glaucoma resistant to medical therapy. They reported 90% success rate at the end of 12 months.136 Another study reported success rate of 85.5% at mean follow-up of 42.2 months in 8 eyes without use of antimetabolites.137 Two recent studies have reported success rates of 66.67 and 92.3% at 12 months and 21 months follow-up respectively.138,139 Former used a reticulated hyaluronic acid implant, while later used MMC. Reported complications included hypotony, choroidal effusion, hyphema and cataract progression.136-139

In a recent article, Dupas et al have compared trabeculectomy with antiproliferative agent to deep sclerectomy with implant and have found equivalent IOP control with either method. While the former involved deeper invasion of the eye and resulted in more inflammation during first postoperative week, the latter required closer postoperative monitoring and more postoperative adjustments for successful outcome.146

**Table 6: Glaucoma drainage devices in uveitic glaucoma**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patients (eyes)</th>
<th>Valve type</th>
<th>Success (mean follow-up duration)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rachmiel R et al122</td>
<td>15 (15) (vs 53 OAG controls)</td>
<td>Ahmed</td>
<td>• 80% (vs 84.9%) (3 months) • 66.6% (vs 57%) (30 months)</td>
</tr>
<tr>
<td>Papadaki et al128</td>
<td>60 (60)</td>
<td>Ahmed</td>
<td>• 77% (1 year) • 50% (4 years)</td>
</tr>
<tr>
<td>Ozdal PC et al127</td>
<td>18 (19)</td>
<td>Ahmed</td>
<td>• 68.4% (26 +/- 9.7 months)</td>
</tr>
<tr>
<td>Kafkala C et al123</td>
<td>6 (7) pediatric</td>
<td>Ahmed</td>
<td>• 100% (36.8 months)</td>
</tr>
<tr>
<td>Ceballos EM et al124</td>
<td>24 (24)</td>
<td>Baerveldt</td>
<td>• 95.8% (3 months) • 91.7% (6/12/24 months)</td>
</tr>
<tr>
<td>Molteno AC et al126</td>
<td>35 (40)</td>
<td>Molteno</td>
<td>• 87% (5 years) • 76% (10 years)</td>
</tr>
<tr>
<td>Da Mata A et al125</td>
<td>19 (21)</td>
<td>Ahmed</td>
<td>• 94% (1 year)</td>
</tr>
</tbody>
</table>

**Cycloablation Therapy**

If all else fails to control the IOP Nd:YAG cyclophotocoagulation, cyclotherapy or ultrasonic cycloablation may be used to destroy the secretory ciliary epithelium. The main complication of cycloablation is the induction of uveitis in 100%.140 Cyclodestruction in an already compromised ciliary body may result in profound drop in IOP with risk of irreversible damage and phthisis. In a study of 18 eyes with medically uncontrolled chronic uveitis, IOP was controlled in 72.2% with transscleral diode laser cyclophotocoagulation but this should be reserved for patients with mild inflammatory disease who are unlikely to develop hypotony because of chronic inflammation.141

**Ab Interno Laser Sclerostomy**

To avoid the usual conjunctival dissection, several investigators have developed techniques of filtering surgery using ab internodisc sclerostomy. Wilson and Javitt, using a continuous wave Nd:YAG laser focused through a sapphire probe, reported a 60% success rate in five ab internodisc sclerostomies among patients with uveitic glaucoma and aphakia after 24 to 28 months of follow-up.142

**Complications**

Perioperative intraocular hemorrhage has not been reported to be a significant problem in trabeculectomy for uveitic glaucoma.107 Postoperative complications such as choroidal effusion, choroidal hemorrhage, shallow anterior chamber and late ocular hypotension may be higher in eyes with uveitic glaucoma than with primary open-angle glaucoma since adjunctive treatment with 5-fluorouracil, mitomycin-C or a
drainage device is more commonly used in patients with uveitic glaucoma.109,111,112,114 Postoperative inflammation or reactivation of uveitis has been reported to occur in 5.2 to 31.1% of cases of uveitic glaucoma.112,114 This incidence can be lowered by treating the patients with pre- and postoperative corticosteroids.5

Cataract progression is very common after filtration surgery for uveitic glaucoma. Phthisis bulbi may occur after any surgical procedure for uveitic glaucoma and is particularly common after cycloablation therapy and drainage device implantation.5 Late postoperative endophthalmitis can occur in up to 9.4% of eyes following 5-fluorouracil after trabeculectomy.142 Patients treated with mitomycin-C also develop this complication.5

REFERENCES


