### What’s New

**Recent Advances in Uveitic Glaucoma**

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**Core Concepts**

- Owing to the underlying disease sequelae and treatment with corticosteroid therapy, patients with uveitis have an increased risk of elevated intraocular pressure (IOP) and glaucoma.
- All forms of uveitis may be associated with raised IOP and glaucomatous optic neuropathy.
- Principles of management of uveitic glaucoma involve treating any identified underlying cause, controlling inflammation and managing any raised IOP by controlling its mechanisms.
- Rho-kinase inhibitors might prove to be a useful new class of anti-glaucoma topical medications for the treatment of uveitic glaucoma.
- Selective laser trabeculoplasty can be a minimally-invasive, effective and safe therapeutic procedure in uveitic glaucoma.
- Glaucoma drainage devices may afford clinicians an additional surgical option with high rates of success in patients with uveitic glaucoma.

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**Introduction**

Due to a combination of the pathogenesis of uveitis and the mainstay of therapeutic management (various forms of corticosteroids), patients with uveitis have an increased risk of glaucoma development.

Uveitic glaucoma is one of the most serious sequelae of intraocular inflammation. The pathogenesis and mechanisms of glaucoma associated with uveitis are incompletely understood and multidimensional. Uveitic glaucoma has been observed in all age groups and with most uveitic entities, with some disorders posing a more significant risk. The majority of uveitic glaucoma is open angle, and presumed to be due to irreversible damage to the trabecular meshwork and/or scar formation in the anterior chamber angle from chronic inflammation.

Management of uveitic glaucoma does not align exactly with the principles of therapy of primary glaucoma; the initial aim of treatment of uveitic glaucoma is always dependent upon the presence of underlying systemic disease. The key to preservation of vision and to control the glaucoma is durable, corticosteroid-free remission of uveitis. Oftentimes, treatment of inflammation will control intraocular pressure (IOP); pressure control outcomes are better with aggressive anti-inflammatory therapy.

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**Medical Management**

Topical first-line treatments for uveitic glaucoma include beta-blockers, carbonic-anhydrase inhibitors, and prostaglandin analogs. In the past prostaglandin analogs in uveitic glaucoma were avoided, owing to data purporting to show they increase risk for cystoid macular edema and worsening inflammation. In quiescent uveitis, no causal link and little additional risk have since been established in both prospective and retrospective trials, but long-term use has been cautioned in those patients already in need of trabeculectomy. Research and development continues with this class of medications (particularly prostaglandin analogs of the PGE₉ variant which are thought to increase the release of nitric oxide), as the effect is directed and potent. Selective alpha-2 adrenergic agonists, systemic carbonic anhydrase inhibitors, and hyperosmotic agents may be considered adjuvantly if the first-line topical agents are insufficient. Maximum medical management of uveitic glaucoma may encompass a topical prostaglandin analogue, a topical beta-blocker or topical carbonic-anhydrase inhibitor or alpha agonist, and an oral carbonic anhydrase inhibitor. As with other forms of glaucoma, uveitic glaucoma also demonstrates diminished returns with the addition of more than one therapy to the initial choice.

The newest drug class in glaucoma therapy inhibits rho-associated protein kinase; pre-clinical trials show promise with regard to both safety and efficacy in primary open-angle glaucoma. Rho-kinase inhibitors treat glaucoma by relaxing trabecular meshwork facilitating increased aqueous outflow, improving blood flow to the optic nerve, protecting the health of ganglion cells and acting as an anti-inflammatory agent in glaucoma surgery. Translation of this compound to patients with uveitic glaucoma will hopefully exhibit similar positive outcomes in IOP control and optic nerve damage prevention.

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**Surgical Management**

Approximately one quarter of uveitic glaucoma cases cannot be sufficiently managed medically and require surgery. Laser therapy is minimally invasive relative to other surgical procedures, and long-term outcomes in patients with uveitis are favorable with regards to minimizing glaucomatous damage. While Argon laser trabeculoplasty is not advised in uveitic glaucoma patients, recent data show selective laser trabeculoplasty (SLT) is not only appropriate, but can be regarded as a first-line therapy. SLT is effective, does not exacerbate inflammation, and does not damage the structural integrity of the trabecular meshwork.

Trabeculectomy, non-penetrating glaucoma surgery, and cycloablation techniques have been employed and reported in patients with uveitic glaucoma, but outcomes are either equivocal or...
Additional intraoperative applications of anti-metabolic and/or alkylating agents, and possible supplementation with additional doses postoperatively, increase success rates considerably. Carreño and associates reported a strong association between successful surgical outcomes in uveitic glaucoma patients and adequate pre- and postoperative inflammation control. Carreño and associates reported a strong association between successful surgical outcomes in uveitic glaucoma patients and adequate pre- and postoperative inflammation control.

Diode devices (Molteno, Baerveldt and Ahmed types) hold the most promise for surgical success in recalcitrant uveitic glaucoma. Improvements in design and implantation techniques, guided by clinical data, have rapidly advanced this treatment modality over the past decade. Rates of success in controlling IOP post-surgery with drainage devices (both short- and long-term in duration) range from 57–94%. Many different varieties are currently commercially available, and newer iterations are sure to materialize.

Future Direction

Although progress has been made, difficulty in treating and controlling uveitic glaucoma exists for uveitis patients and practitioners everywhere. Patient compliance with topical medications concerns uveitis specialists, especially when therapy choices are limited. As compared to prostaglandin analogs, other potential first-line treatments do not lower pressure nearly as impressively, in both quality and lasting effect. New topical combination products may increase compliance and lower costs, especially for an older patient population.

Not all advances in treatments for uveitis are beneficial for patients with uveitic glaucoma; drug delivery implants are one of the newest approaches to therapy for uveitis, but specific devices may contribute to and/or exacerbate pressure elevations and thus undermine control of the uveitic glaucoma. The Multicenter Uveitis Steroid Treatment (MUST) Trial aimed to compare conventional systemic immunosuppressive therapy with a fluocinolone acetonide implant (a corticosteroid) in patients with active uveitis; patients who received the implant experienced a 4-fold greater risk of developing elevated IOP; glaucomatous damage was reported in 23%, as compared with 6% in the systemic treatment group after 48 months. Available treatments for uveitis also need improvement, and such new treatment regimens should ideally be free of corticosteroids.

Implantable devices with a radiofrequency transceiver that monitor IOP are under study in vivo models for safety and efficacy. Future application to an intraocular lens and improvement in data transmission are pending prior to commercial availability.

The future of uveitic glaucoma care is moving in several directions, and is encouraging. Much work remains in the development of highly effective, corticosteroid-sparing medical and surgical therapies that control IOP long-term without side effects.

References