Treatment of Uveitic Glaucoma

Cigdem ALTAN[1]

ABSTRACT

Glaucoma is a common and serious complication of uveitis. In uveitic glaucoma treatment, goal is to control inflammation and reduce intraocular pressure; thus to prevent permanent structural changes in the anterior chamber angle and optic nerve damage. Treatment should be customized according to the patient. The first step in the treatment is the control of inflammation, and if necessary, anti-infectious treatment should be added. Miotic agents should not be used as anti-glaucomatous treatment. Prostaglandin analogs can be used carefully in the absence of macular edema and active inflammation; it should not be used in eyes with herpetic keratitis or keratouveitis. Glaucoma surgery is required in 25-30% of eyes with uveitic glaucoma. In uveitic glaucoma, surgery should be planned a few months after the patients' inflammation is controlled as much as possible; aggressive anti-inflammatory therapy should be applied before, during and after surgery.

Key words: Uveitis, Glaucoma, Uveitic glaucoma.

Intraocular pressure elevation or glaucoma is a common and serious complication of uveitis. In the literature, the term uveitic glaucoma, with no reference to glaucomatous optic disc anomaly or progressive visual field defect, is defined as secondary glaucoma causing intraocular pressure (IOP) >21 mmHg and requiring continuous anti-glaucomatous treatment which develops without previous history of glaucoma upon onset of uveitis. However, the term "ocular hypertension secondary to uveitis" is also used in the absence of pathological optic disc cupping or glaucomatous visual field defect.[1-3] In the literature, pathological IOP elevation incidence is reported as 20-40% and secondary glaucoma incidence as 4-40% and it has been reported as 10-20% in studies including all types of uveitis.[4-11] Major risk factors for uveitic glaucoma include duration of uveitis, anatomic type (more common in anterior uveitis), uveitis severity, presence of active inflammation, steroid use, time from diagnosis and advanced age.[1,2,4,8-11] Uveitis types most commonly associated with secondary glaucoma include viral anterior uveitis, Fuchs uveitic syndrome (FUS), juvenile idiopathic arthritis, Vogt Koyanagi Harada disease, sarcoidosis and HLA-B27 uveitis.[5, 11, 12]

In the uveitis, mechanisms involved in IOP elevation and/or glaucoma include cellular or biochemical changes in humor aqueous and morphological changes in anterior chamber angle. Uveitic glaucoma is generally open angle. Major mechanisms in open angle glaucoma are mechanical blockage of trabecular network by cell, protein, fibrin, debris and pigment and trabeculitis. In addition, steroids used in the treatment can cause iatrogenic open angle glaucoma in uveitic eyes by enhancing resistance against humor aqueous outflow.[2-4, 9, 10,12,13-17] In several studies, steroid-related IOP elevation rate has been reported as 10-65%.[6,18] Acute angle closure may develop due to anterior rotation of ciliary body or posterior synechia while chronic angle closure glaucoma may develop due to peripheral posterior synechia between iris and cornea, neovascularization or inflammatory membranes in some uveitic eyes.[2-4,9,10,19]

Although pathophysiology and mechanisms underlying uveitic glaucoma have been largely understood today, it remains to be a challenging clinical condition to manage. Its treatment is more difficult than primary open angle glaucoma since patients are younger; they generally have systemic diseases and ocular disorders other than glaucoma; serious structural injury can develop due

1- Assoc. Prof., University of Health Science Beyoglu Eye Training and Research Hospital, Istanbul, Turkey

Received: 29.02.2020
Accepted: 24.05.2020
Glo-Kat 2020; 15: 137-142
DOİ: 10.37844/glauc.cat.2020.15.25

Correspondence Adress:
Cigdem ALTAN
University of Health Science Beyoglu Eye Training and Research Hospital, Istanbul, Turkey
Phone:
E-mail: cigdem_altan@yahoo.com

to recurrent inflammation and uveitis; extremely high IOP values and IOP fluctuations may be present during attacks; response to anti-glaucomatous agents is variable; predictability is lower in glaucoma surgery; and visual prognosis is poorer.[10,14] Multidisciplinary approach is needed in management.

In uveitis, the treatment plan is often determined by mechanism underlying IOP elevation. In addition, uveitis type, clinical course and severity and angle status should be taken into consideration.[9, 20] Topical anti-glaucomatous treatment is helpful in open angle glaucoma while preferential treatment is laser or surgery in glaucoma secondary to pupillary blockage. In the absence of pupillary blockage, medical treatment is given initially; however, surgical treatment will often be required if large synechiae are present.[9]

In the treatment of uveitic glaucoma, the goal is to control inflammation and decrease IOP; thus, preventing permanent morphological changes in iridocorneal angle and optic nerve damage. Controlling inflammation is first step in the treatment. It was reported that prognosis of uveitic glaucoma is better in patients treated aggressively with anti-inflammatory therapy.[10,13] Corticosteroids are preferred anti-inflammatory agents in the treatment of uveitis. It is recommended to start with potent topical corticosteroids such as prednisolone acetate. Although less potent steroids such as rimexolone, fluorometholone or loteprednol decrease risk for steroid-related IOP elevation, they have weak anti-inflammatory effect and more potent steroids are needed in uveitic glaucoma.[13,20] Sometimes, IOP can be controlled by treatment of inflammation alone.[13] Periocular steroid injection and systemic steroids should be used in resistant cases. Systemic immunosuppressive/ immunomodulatory agents should be used when more potent and prolonged immunosuppression is needed or adverse effects of steroids are needed to be avoided.[20] The first way to prevent steroid-related glaucoma development is to minimize unnecessary steroid use. It is important being aware of risk groups, pretreatment IOP measurement, monitorization and being alert for steroid-related glaucoma.

Anti-microbial treatment should be added to anti-inflammatory treatment if needed. For instance, oral aciclovir or pro-drug valaciclovir in herpetic uveitis and ganciclovir or pro-drug valganciclovir treatment in cytomegalovirus anterior uveitis should be added to topical anti-inflammatory treatment in order to prevent viral replication. It should be kept in mind that the activity of topical anti-glaucomatous agents can be decreased due to reduced absorption in the presence of intensive inflammation. Generally, first choice of topical anti-glaucomatous agent is topical beta-blocker or carbonic anhydrase inhibitors (CAIs) or their fixed combinations. Oral CAI may be used if topical treatment is insufficient. The effect of hyper-osmotic agents can be limited due to disrupted blood-aqueous barrier in uveitic eyes.[13,20] Brimonidine, an alpha-2-adrenergic agonist, is generally second-line treatment and used in combination therapy. Granulomatous anterior uveitis was reported with brimonidine and apraclonidine use, which generally occurs following an allergic reaction at year one; it recovers by drug withdrawal and steroid therapy.[20-22]

Cholinergic agents are contraindicated in uveitic glaucoma since they increase vascular permeability; induce inflammation by disrupting blood-aqueous barrier; and cause ciliary spasm. They also trigger posterior synechia and pupillary blockage.[23]

Prostaglandin analogues (PGAs) are controversial in the treatment of uveitis due to increased risk for blood-aqueous barrier disruption, anterior uveitis (1-6.4%), HSV keratitis reactivation and cystoid macular edema (1-2%).[24,25] Ocular inflammation rate with latanoprost was reported as 1% in patients without history of uveitis and as 23% in those with uveitis; however, it was shown that there was no increases in anterior chamber flare values in a study using bimatoprost.[24, 26] Recent view is that PGAs can be used in uveitic glaucoma; however, it is recommended to use in cases in which other agents failed and in the absence of CME and active inflammation.[26,27] They are currently not recommended in patients with CME or previous history of complicated intraocular surgery and it should not be used in eyes with history of herpetic keratitis or keratouveitis.[20,28]

Laser peripheral iridotomy (LI) is indicated in uveitic glaucoma cases characterized by pupillary blockage and angle closure. LI may be closed due to inflammation over time; thus, more than one LI may be needed. It should be followed with aggressive anti-inflammatory treatment for introversion within first 20 days.[13] Argon laser peripheral iridoplasty may be effective in cases with uveitic glaucoma progressing with angle closure and pupillary blockage.[29] Argon laser trabeculoplasty is not recommended in open angle uveitic glaucoma since it may aggravate inflammation and cause synechia at angle. Role of selective laser trabeculoplasty is controversial in uveitic glaucoma; it is not preferred as it may trigger inflammation.[30] However, it was reported that selective laser trabeculoplasty is safe and effective in steroid-related glaucoma in well-controlled uveitic eyes.[31]

The role of cyclodestructive interventions such as diode laser cyclophotocoagulation is controversial due to risk for aggravation of inflammation, hypotonia and phthisis. It is

applied as the last option for eyes that have failed drainage surgery with low visual potential.[13, 32, 33]

In uveitic glaucoma, surgery is required in 25-30% of eyes. Surgical management is more challenging that other types of glaucoma as inflammation is highly effective in surgical success and other postoperative complications and patients are generally younger. Success rate has been reported as 50-100% in uveitic glaucoma surgery in recent years.[20, 34-37] Surgery itself may trigger inflammation and cause complications during and after surgery.[20] The passage of inflammatory mediators from humor aqueous to subconjunctival space during filtering surgery triggers fibroblast proliferation and collagen synthesis, resulting in increased risk for subconjunctival fibrosis. Use of anti-metabolites such as 5-Fluorouracyl or mitomycin C (MMC) during and after surgery inhibits fibroblast proliferation and improves success rate; they are warranted in trabeculectomy.[13,20,38,39] However, ciliary body toxicity caused by intraoperative MMC use and chronic and recurrent inflammation in uveitic eyes increases risk for hypotonia. In addition, one should be careful for intraoperative hemostasis, postoperative hyphema and fibrinous uveitis. Thus, surgery should be planned to a few months after control of inflammation, if possible, and aggressive anti-inflammatory treatment should be given before, during and after surgery.[4,20,35,40,41] Glaucoma drainage implant surgery is more commonly used in uveitic glaucoma when compared to other types of glaucoma as a result of subconjunctival scarring and high postoperative hypotonia and high success rate has been reported.[10,37,42-44] It should be preferred as first-line surgery; however, contradictory outcomes have been reported about superiority over trabeculectomy.[35, 45-47] It should be used in patients without well-controlled inflammation, those with anterior or posterior synechia, neovascular glaucoma, those with history of aphakic vitreoretinal surgery or filtering surgery and those with dense conjunctival scarring.[20, 48] It is considered as first choice in glaucoma secondary to juvenile idiopathic arthritis.[49] In addition, several surgical techniques are employed in the treatment uveitic glaucoma, including Xen implant,[50, 51] Ex-PRESS implant,[52] non-penetrating glaucoma surgery,[53,54] gonioscopy-assisted transluminal trabeculectomy (GATT),[55] trabectome and goniotomy in chronic childhood uveitis.[56]

Given lack of randomized, prospective, controlled, comparative studies in different uveitis subtypes, optimal surgical technique is controversial in uveitic glaucoma surgery. Timing of surgery, treatment selection and perioperative inflammatory control should be individualized. Treatment choice should be based on severity of glaucoma, inflammation level, chronic inflammation sequels (angle status, conjunctival scarring) risk factors for trabeculectomy failure, likelihood of re-operation, age, target IOP and preference of patient and surgeon. Regardless of surgical treatment modality selected, all patients should have to be monitored meticulously regarding preoperative inflammation control and postoperative reactivation.

REFERENCES

1. Neri P, Azuara-Blanco A, Forrester JV. Incidence of glaucoma in patients with uveitis. J Glaucoma.2004;13:461-5.
2. Panek WC, Holland GN, Lee DA, Christensen RE. Glaucoma in patients with uveitis. Br JOphthalmol. 1990;74:223-7.
3. Merayo-Lloves J, Power WJ, Rodriguez A, et al. Secondary glaucoma in patients with uveitis. Ophthalmologica. 1999;213:300-4.
4. Agnieszka G. Nagpal, Nisha R. Acharya. Uveitic Glaucoma. Ed. Grehn F, Stamper R. In Glaucoma (Essentials in Ophthalmology Progress III) Springer-Verlag Berlin Heidelberg; 2009: 49-58.
5. Kanda T, Shibata M, Taguchi M, et al. Prevalence and aetiology of ocular hypertension in acute and chronic uveitis. Br J Ophthalmol. 2014;98:932-6.
6. Takahashi T, Ohtani S, Miyata K, et al. A clinical evaluation of uveitis associated secondary glaucoma. Jpn J Ophthalmol 2002: 46: 556–62
7. Elgin U, Berker N, Batman A. Incidence of secondary glaucoma in Behcet's disease. J Glaucoma 2004; 13: 441-4.
8. Herbert HM, Viswanathan A, Jackson H, et al. Risk factors for elevated intraocular pressure in uveitis. J Glaucoma. 2004;13:96-9.
9. Kok H, Barton K. Uveitic glaucoma. Ophthalmol Clin North Am. 2002;15:375-87.
10. Kalogeropoulos D, Sung VC. Pathogenesis of Uveitic Glaucoma. J Curr Glaucoma Pract. 2018;12:125-138. Review.
11. Al Rubaie K, Al Dhahri H, Al Fawaz A, et al. Incidence and Risk Factors for Developing Glaucoma Among Patients with Uveitis in a University-based Tertiary Referral Center in Riyadh, Saudi Arabia. Ocul Immunol Inflamm. 2016; 24:571-8.
12. Baneke AJ, Lim KS, Stanford M. The Pathogenesis of Raised Intraocular Pressure in Uveitis. Curr 202 Eye Res. 2016;41:137-49.
13. Siddique SS, Suelves AM, Baheti U, et al. Glaucoma and uveitis. Surv Ophthalmol. 2013;58:1-10. Review.
14. Elgin U. Üveitik Glokom ve Güncel Tedavi Yaklaşımları. Glo-Kat 2016; 11:209-15
15. Wakefield D, Lloyd A. The role of cytokines in the pathogenesis of inflammatory eye disease. Cytokine 1992; 4:1–5
16. Hogg P, Calthorpe M, Batterbury M, et al. Aqueous humor stimulates the migration of human trabecular meshwork cells in vitro. Invest Ophthalmol Vis Sci 2000; 41:1091-98

17. Akyol N, Turgut B. Steroid Glokomu. Glo-Kat 2006; 1:239-44

18. Shrestha S, Thapa M, Shah DN. Pattern of intraocular pressure fluctuation in uveitic eyes treated with corticosteroids. Ocul Immunol Inflamm. 2014 ;22:110-5.

19. Moorthy RS, Mermoud A, Baervedt G, et al. Glaucoma associated with uveitis. Surv Ophthalmol. 1997; 41:361–94.

20. Muñoz-Negrete FJ, Moreno-Montañés J, Hernández-Martínez P, et al. Current Approach in the Diagnosis and Management of Uveitic Glaucoma. Biomed Res Int. 2015; 2015:742-92.

21. Byles DB, Frith P, Salmon JF. Anterior uveitis as a side effect of topical brimonidine. American Journal of Ophthalmology 2000; 130: 287–91.

22. Casado A, Cabarga C, De la Fuente MA, et al. Suspected granulomatous anterior uveitis associated with brimonidine tartrate 0.2% and timolol maleate 0.5% ophthalmic solution. Graefe's Archive for Clinical and Experimental Ophthalmology 2013; 251: 2659–60.

23. Kuchtey RW, Lowder CY, Smith SD. Glaucoma in patients with ocular inflammatory disease. Ophthalmology Clinics of North America 2005; 18: 421–30.

24. Smith SL, Pruitt CA, Sine CS, et al. Latanoprost 0.005% and anterior segment uveitis. Acta Opthalmol Scand. 1999;77:668-72.

25. Warwar RE, Bullock JD, Ballal D. Cystoid macular edema and anterior uveitis associated with latanoprost use. Experience and incidence in a retrospective review of 94 patients. Ophthalmology 1998;105:263-8.

26. Chang JH, McCluskey P, Missotten T, et al. Use of ocular hypotensive prostaglandin analogues in patients with uveitis: does their use increase anterior uveitis and cystoid macular oedema? Br J Ophthalmol. 2008;92:916-21.

27. Fortuna E, Cervantes-Castañeda RA, Bhat P, et al. Flare-up rates with bimatoprost therapy in uveitic glaucoma. Am J Ophthalmol. 2008;146:876-82.

28. Horsley MB, Chen TC. The use of prostaglandin analogs in the uveitic patient. Semin Ophthalmol 2011;26:285-9.

29. Mansouri K, Ravinet E Argon-laser iridoplasty in the management of uveitis-induced acute angle-closure glaucoma. Eur J Ophthalmol. 2009;19:304-6.

30. Koktekir BE, Gedik S, Bakbak B. Bilateral severe anterior uveitis after unilateral selective laser trabeculoplasty. Clin Experiment Ophthalmol 2013; 41: 305-7.

31. Maleki A, Swan RT, Lasave AF, et al. Selective laser trabeculoplasty in controlled uveitis with steroid-Induced glaucoma. Ophthalmology. 2016;123:2630-2.

32. Murphy CC, Burnett CA, Spry PG, et al. A two centre study of the dose-response relation for transscleral diode laser cyclophotocoagulation in refractory glaucoma. Br J Ophthalmol 2003;87:1252-7.

33. Schlote T, Derse M, Zierhut M. Transscleral diode laser cyclophotocoagulation for the treatment of refractory glaucoma secondary to inflammatory eye diseases. Br J Ophthalmol. 2000;84:999-1003.

34. Iverson SM, Bhardwaj N, Shi W et al. Surgical outcomes of inflammatory glaucoma: a comparison of trabeculectomy and glaucoma-drainage-device implantation. Japanese Journal of Ophthalmology 250, 2015; 59: 179–86.

35. Shimizu A, Maruyama K, YokoyamaY, et al. Characteristics of uveitic glaucoma and evaluation of its surgical treatment. Clinical Ophthalmology 2014; 8: 2383–9.

36. Kaburaki T, Koshino T, Kawashima H, et al. Initial trabeculectomy with mitomycin C in eyes with uveitic glaucoma with inactive uveitis. Eye (Lond). 2009; 23:1509-17.

37. Yakin M, Eksioglu U, Sungur G, et al. Short-term to Long-term Results of Ahmed Glaucoma Valve Implantation for Uveitic Glaucoma Secondary to Behçet Disease. J Glaucoma. 2017;26:20-6.

38. Wright MM, McGehee RF, Pederson JE. Intraoperative mitomycin-C for glaucoma associated with ocular inflammation. Ophthalmic Surg Lasers. 1997; 28:370-6

39. Yalvac IS, Sungur G, Turhan E, et al. Trabeculectomy with mitomycin-C in uveitic glaucoma associated with Behcet disease. J Glaucoma. 2004; 13:450-3

40. Sung VCT and Barton K. Management of inflammatory glaucomas. Curr Opin Ophthalmol. 2004;15:136-40.

41. Broadway DC, Bates AK, Lightman SL, et al. The importance of cellular changes in the conjunctiva of patients with uveitic glaucoma undergoing trabeculectomy. Eye 1993;7: 495-501.

42. Sungur G, Yakin M, Eksioglu U, et al. Assessment of conditions affecting surgical success of Ahmed glaucoma valve implants in glaucoma secondary to different uveitis etiologies in adults. Eye (Lond). 2017; 31:1435-42.

43. Satana B, Yalvac IS, Sungur G, et al. Ahmed Glaucoma Valve Implantation for Uveitic Glaucoma Secondary to Behçet Disease. J Glaucoma. 2015;24(8):607-12.

44. Papadaki TG, Zacharopoulos IP, Pasquale LR, et al. Longterm results of Ahmed glaucoma valve implantation for uveitic glaucoma. Am J Ophthalmol. 2007;144:62-9

45. Kwon HJ, Kong YXG, Tao LW, et al. Surgical outcomes of trabeculectomy and glaucoma drainage implant for uveitic glaucoma and relationship with uveitis activity. Clin Exp Ophthalmol. 2017;45:472-80.

46. Bettis DI, Morshedi RG, Chaya C, et al. Trabeculectomy with mitomycin C or Ahmed valve implantation in eyes with Uveitic glaucoma. J Glaucoma. 2015;24:591-9.

47. Esfandiari H, Loewen NA, Hassanpour K, et al. Fuchs heterochromic iridocyclitis-associated glaucoma: a retrospective comparison of primary Ahmed glaucoma valve implantation and trabeculectomy with mitomycin C. Version 2. F1000Res. 2018;7:876.

48. A. Kulkarni and K. Barton. Uveitic glaucoma in Glaucoma. Medical Diagnosis &Therapy, T. M. Shaarwy, M. B. Sherwood, R. A. Hitching, and J. G. Crowston, Eds., Elsevier Saunders, London, UK, 2015: 410–2

49. C. C. A. Sng and K. Barton. Mechanism and management of angle closure inuveitis. Current Opinion in Ophthalmology 2015; 26: 121–7.

50. Qureshi A, Jones NP, Au L. Urgent management of secondary glaucoma in uveitis using the Xen- 45 Gel Stent.
51. Sng CC, Wang J, Hau S, et al. XEN-45 collagen implant for the treatment of uveitic glaucoma. Clin Exp Ophthalmol. 2018;46:339-345
52. Lee JW, Chan JCh, Qing L, et al. Early Postoperative Results and Complications of using the EX- PRESS Shunt in uncontrolled Uveitic Glaucoma: A Case Series of Preliminary Results. J Curr Glaucoma Pract. 2014;8:20-4.
53. Mercieca K, Steeples L, Anand N; Medscape. Deep sclerectomy for uveitic glaucoma: long-term outcomes. Eye (Lond). 2017; 31:1008-19.
54. Lommatzsch C, Heinz C, Heiligenhaus A, et al. Canaloplasty in patients with uveitic glaucoma: a pilot study. Graefes Arch Clin Exp Ophthalmol. 2016;254:1325-30.
55. Aktas Z, Ucgul AY, Bektas C, et al. Surgical outcomes of prolene gonioscopy-assisted transluminal trabeculotomy in patients with moderate to advanced open-angle glaucoma. J Glaucoma. 2019 ;28:884-8.
56. Ho CL, Wong EY, Walton DS. Goniosurgery for glaucoma complicating chronic childhood uveitis. Arch Ophthalmol. 2004;122:838-44.