Review Article

A narrative review of ocular surface disease considerations in the management of glaucoma

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Background and Objective: Ocular surface disease (OSD) is a common yet often overlooked consideration in the management of patients with glaucoma. Although there have been several review articles summarizing the relationship between glaucoma medications and OSD, there is a relative absence of such articles on the effects of glaucoma surgical treatments. Here, we present a comprehensive review of the literature regarding the relationship of glaucoma management and OSD, with an emphasis on surgical considerations.

Methods: PubMed, Google Scholar, and Cochrane Review searches were performed using the following search terms: ocular surface, dry eye, minimally invasive glaucoma surgeries (MIGS), trabeculectomy, glaucoma medications. The titles and abstracts from those searches were screened for relevance to our review topics. Publications were included if the subjects included glaucoma patients, and if ocular surface outcomes were described. Non-English papers were excluded.

Key Content and Findings: Topical glaucoma medications frequently cause adverse effects on the ocular surface, both through direct action of the medications themselves as well as through toxicity from their associated preservatives. Optimization of the ocular surface may improve medication compliance rates. Traditional surgical treatments for glaucoma, such as trabeculectomy, can exacerbate OSD by disrupting the ocular surface but can also reduce the need for chronic medications. Optimization of ocular surface health is imperative in reducing trabeculectomy complication rates, while also potentially reducing the need for trabeculectomy in patients that are able to achieve intraocular pressure control through improved drop tolerability. The introduction of MIGS represents a promising alternative to existing therapies and has been shown to alleviate the overall medication burden. It would be reasonable to assume that decreasing the medication burden could reduce OSD prevalence and severity. However, more research is needed to directly assess the extent of improvement seen after MIGS.

Conclusions: A comprehensive understanding of the importance of OSD in medical and surgical management of glaucoma is essential in optimizing patient care and improving outcomes.

Keywords: Glaucoma; ocular surface disease (OSD); dry eye; minimally invasive glaucoma surgery (MIGS); trabeculectomy

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Introduction

Glaucoma is a leading cause of preventable blindness in the world, affecting more than 2 million people in the United State alone. One of the few proven ways of preventing glaucoma progression is by decreasing intraocular pressure (IOP), typically with the use of topical ocular hypotensive medications (1-3). However, the use of these IOP-lowering drops has been shown to worsen objective findings of ocular surface disease (OSD), initiate or exacerbate existing OSD-related symptoms, and consequently decrease long-term compliance with medications (4-8).

The correlation between OSD and glaucoma has been well-documented, with both diseases increasing in prevalence with advancing age. OSD prevalence has also been shown to correlate with glaucoma severity; Ocular Surface Disease Index (OSDI) scores tend to worsen in patients with higher drop requirements (9). This relationship appears to be reciprocal, with severe OSD likewise correlating with higher rates of glaucoma (10). Clinicians must have a low threshold in the diagnosis and treatment of co-existing, symptomatic OSD in glaucoma patients, particularly those that are initiating or escalating medical therapy.

One of the newer options in the management of glaucoma is the development of minimally invasive glaucoma surgery (MIGS), typically performed in combination with cataract surgery. There are currently a wide range of Food and Drug Administration (FDA)-approved MIGS procedures with varying mechanisms of action and efficacy. Several studies on various MIGS procedures have demonstrated a post-operative reduction in IOP as well as a reduction in the number of medications required for IOP control.

The goal of this review article is to summarize the current literature regarding the varying treatment options of glaucoma and its relation to OSD, with emphasis on surgical considerations and complications related to OSD. We present this article in accordance with the Narrative Review reporting checklist (available at https://aes.amegroups.com/article/view/10.21037/aes-22-59/rc).

Methods

PubMed, Google Scholar, and Cochrane Review searches were performed using the following search terms: ocular surface, dry eye, MIGS, trabeculectomy, glaucoma medications. The titles and abstracts from those searches were screened for relevance to our review topics. Publications were included if the subjects included glaucoma patients, and if ocular surface outcomes were described. Non-English papers were excluded (*Table 1*).

The adverse effects of glaucoma medications on the ocular surface

The Collaborative Initial Glaucoma Treatment Study (CIGTS) showed that initial management with medicine or surgery resulted in similar visual field outcomes after 5 years of follow-up (11). Given its relative safety and ease of use, medical therapy remains the preferred first choice of treatment for most forms of glaucoma in the United States. The side effects of the numerous topical hypotensive medications that are in common use have been well-explored to date. Broadly, these medications can worsen OSD either due to toxicity from the active medications themselves or from the preservative.

Prostaglandin analogs are widely considered as a first line option for the treatment of glaucoma due to their efficacy, favorable side effect profile, and simple once nightly dosing. Although they are generally well-tolerated, they have been found to increase prevalence and severity of meibomian gland disease and worsen subjective symptoms of OSD as measured through the OSDI (5,12-14).

Beta-blockers are another widespread ocular hypotensive medication utilized in the management of glaucoma. As one of the older agents, their efficacy and side effect profile have been well-established in the literature, including their potential negative effect on the ocular surface (8,15). Beta-blockers lower IOP through the proposed mechanism of inhibition of aqueous humor production in the ciliary epithelium. However, since their inhibitory effect on beta receptors is non-specific, they are also thought to act on the beta receptors within the lacrimal gland, resulting in decreased tear production. In addition, timolol specifically has been demonstrated to alter the composition of the tear film, leading to increasing toxicity to the ocular surface (16-18).

Brimonidine, an alpha-agonist, is also a proven topical IOP-lowering medication. However, it has also been shown to have elevated allergenicity, at a significantly higher rate than other topical preparations. Long-term intolerance to brimonidine is common due to this local adverse reaction. The allergic response associated with brimonidine use triggers an IgE cascade, which can also increase the likelihood of allergic reactions to other future topical medications (19).

In addition to the medications themselves, the

Table 1 The search strategy summary

Items	Specification
Date of search	May 12, 2022
Databases and other sources searched	Cochrane, PubMed, Google Scholar
Search terms used	Ocular surface, dry eye, MIGS, trabeculectomy, glaucoma medications
Timeframe	1980–2022
Inclusion and exclusion criteria	Inclusion criteria: Publications were included if the subjects included glaucoma patients, and if ocular surface outcomes were described.
	Exclusion criteria: non-English literature
Selection process	Conducted independently by all authors; discussed and reviewed prior to manuscript preparation

MIGS, minimally invasive glaucoma surgeries.

preservatives used in ophthalmic preparations are also well-known to adversely affect the ocular surface. Preservatives are a necessity in inhibiting contamination and bacterial growth in liquid medications; however, the same mechanism by which they prevent bacterial growth also causes toxicity to the ocular surface (20). Of note, most of the studies exploring these harmful side effects of topical glaucoma medications focus on a limited time window of approximately 1 to 5 years. However, when applied to a population level, it must be acknowledged that many of these patients will require lifelong use of topical hypotensive medication, likely amplifying the cumulative, chronic effects of these medications.

The most common preservative on the market is benzalkonium chloride (BAK), a quaternary ammonia compound used in approximately 70% of preserved ophthalmic solutions. Its biocidal properties prevent microbial contamination, and it can also enhance corneal penetration of some drugs by acting as a detergent and disrupting corneal epithelial tight junctions, thereby increasing permeability to water-soluble substances. However, it can also cause significant toxicity to various ocular tissues, including the corneal and conjunctival epithelium. The most significant known side effect of BAK is impaired corneal sensitivity. This impairment follows a dose-response curve, with studies showing a correlation between cumulative drop burden, duration of treatment, and severity of corneal sensation loss (21,22). Overall, BAK has been correlated with more severe OSD and worsened quality of life, which also contributes to decreased medication compliance.

Several studies have shown that OSD-related symptoms from topical glaucoma therapy interfere with patient compliance rates (4,5,23,24). One study found 27% of patients endorse side effects related to the drops affect adherence to glaucoma regimens (24). Another reported that 2% of patients cited medication side effects as the main reason for non-adherence (24,25). Lee *et al.* found an inverse relationship between meibomian gland function and rates of compliance of prostaglandin analogs (5). Alternative options exist for patients with severe BAK-related OSD, including preservative-free formulations or those that utilize gentler oxidizing preservatives. Preservative-free agents have been shown to decrease disturbances to the ocular surface and reduce OSD symptoms, leading to improved patient compliance (8,15,20,26). Although these preservative-free medications are better tolerated, they also are poorly covered by health insurance due to the lack of available generic formulations on the market, and therefore less economically viable for many patients.

The effect of MIGS on OSD

MIGS are one of the newer developments in the treatment of mild-to-moderate glaucoma and have steadily gained prominence as an alternative to traditional glaucoma surgeries such as trabeculectomy or glaucoma drainage device implantation. The term MIGS refers to a group of glaucoma procedures typically performed via *ab interno* approach and characterized by minimal disruption of normal anatomy, high safety profile, and rapid patient recovery. Studies have shown varying degrees of success among these procedures in achieving statistically significant decreases in medication burden, or complete independence from drops for a percentage of patients (27-32). Given the known correlation between the topical medication burden

and OSD, MIGS should be given significant consideration as a means of controlling IOP while simultaneously relieving or minimizing OSD symptoms.

iStent was the first MIGS device to receive FDA approval, and subsequently has the most published evidence regarding efficacy and safety amongst the MIGS procedures. iStent has been demonstrated to provide consistent short-term and long-term reduction in IOP, as well as a reduction in medication burden (28-30,33-38). To date, there has been one study assessing changes to the ocular surface in patients before and after cataract surgery with iStent (27). This study found significant improvement in OSDI, tear break-up time, and corneal and conjunctival staining up to 3 months post-operatively, as well as a notable decrease in medication burden and a 17% reduction in mean IOP. The improvement to the ocular surface, both in patient symptoms and objective data, was attributed to the overall decreased medication burden. This study was the first to directly assess the relationship between OSD and MIGS; however, given its relatively short-term 3-month follow-up period, further studies are needed to validate and reinforce these findings.

Other MIGS procedures, such as Trabectome, Hydrus, Xen Gel Stent, Kahook Dual Blade, Cypass, and Gonioscopy-Assisted Transluminal Trabeculotomy (GATT), have been proven to decrease mean IOP and have varying degrees of success in reducing the medication burden in patients with mild-to-moderate glaucoma (32). However, there is a lack of data directly assessing the effect of these MIGS procedures on OSD-related subjective symptoms or objective findings. As there is ample literature describing the correlation between decreased medication burden and improvement in OSD, it would be reasonable to presume that the aforementioned procedures would similarly improve the overall health of the ocular surface. Further research is needed on the long-term effect of MIGS procedures on the ocular surface, to better elucidate their role in the treatment of glaucoma patients with OSD.

The effect of trabeculectomy on OSD

Trabeculectomy is a standard, proven glaucoma surgery typically utilized in patients that have otherwise failed medical therapy (11). In this operation, an ostium into the anterior chamber is created through a partial-thickness scleral flap, which drains into the subconjunctival space resulting in a localized elevation of the conjunctiva, also known as a filtering bleb. An antimetabolite is typically used intraoperatively to prevent post-operative scarring and limit unintended closure of the ostium. Although the indications and complications associated with trabeculectomy have been well-established to date, there is a relative paucity of literature evaluating the effect of trabeculectomy on the ocular surface.

Anatomic disruption to the normal ocular surface anatomy can cause OSD or worsen pre-existing disease. The creation of an elevated conjunctival bleb may inadvertently cause mechanical friction of the bleb against the meibomian glands, leading to chronic irritation when blinking. This disruption can cause long-term meibomian gland loss over a median time span of 7 years, resulting in tear film instability and worsened OSD (39).

The net overall effect of trabeculectomy on the ocular surface health appears to vary depending on the time after surgery. Ono *et al.* found that patients can develop corneal epithelial defects at a median onset of 1.5 days, corneal dellen at a median onset of 5.5 days, and filamentary keratitis at median onset of 28.0 days (40). Another study found that trabeculectomy patients had more OSD symptoms than the phacoemulsification control group in the immediate and sub-acute post-operative period; however, by 3 months these objective measures had equalized between the two groups (41). In the subacute post-operative period, clinicians should remain vigilant for signs of ocular surface complications, as these typically occur within the first 60 days after surgery.

In contrast, trabeculectomy may confer an overall long-term benefit to objective measures of ocular surface health over 6 months to 1 year (42-44). The mechanism for this is not clear, but similar to MIGS, is thought to be a result of de-escalation of topical glaucoma drops leading to reduced pro-inflammatory gene expression on the ocular surface (45). Of note, however, Agnifili *et al.* reported a lack of correlation between these objective findings and patients' subjective symptoms (44).

Mitomycin-C and 5-fluorouracil (5-FU) are common anti-metabolites used as adjuvants during trabeculectomy, intended to inhibit closure of the partial-thickness scleral flap. As these anti-metabolites have non-specific activity, they also have adverse effects on the active replication of limbal stem cells, which can in turn prevent adequate replacement and healing of the corneal epithelium and subsequently cause or exacerbate OSD (46). Traverso *et al.* noted a dose-dependent corneal toxicity from 5-FU, specifically an absence of corneal epithelial defects and a significant reduction of punctate epitheliopathy 15 months

post-trabeculectomy using lower doses of 5-FU (47).

Overall, trabeculectomy can contribute to OSD due to disruption in normal anatomy and corneal sensation, adjuvant anti-metabolites administered during surgery, and post-operative complications. However, from the current literature, it appears there may be a net long-term benefit of trabeculectomy due to the decreased medication requirement in patients that undergo this surgery. Further research is needed to more directly assess this relationship.

The effect of OSD on trabeculectomy outcomes

In patients with comorbid glaucoma and OSD, the presence and severity of OSD can also significantly influence the outcomes of potential glaucoma treatments, particularly trabeculectomy. As mentioned, the chronic administration of topical glaucoma medications and their associated preservatives often have cytotoxic effects on the ocular surface. The effect of underlying OSD on glaucoma filtration surgery outcomes should always be considered prior to proceeding with trabeculectomy.

Boimer *et al.* performed a retrospective study evaluating the effect of BAK exposure on trabeculectomy outcomes and found a dose-dependent response between pre-operative BAK use and early surgical failure (48). In addition to the BAK preservative, topical medications themselves may also predispose to increased risk of surgical failure. The subclinical histologic inflammation induced by topical medications has been theorized to increase the risk of conjunctival bleb scarring, and thus surgical failure (49,50). However, the clinical correlation of this histological inflammation is controversial. Lavin *et al.* and Broadway *et al.* found that long-term topical combination therapy was a significant risk factor for trabeculectomy failure, with differences in histological inflammation seen on conjunctival biopsy (51,52). However, these findings may have been influenced by possible selection bias, due to poor randomization and lack of blinding in the study protocols. Johnson *et al.* also evaluated the effect of medical therapy on trabeculectomy outcomes, and found no significant correlation between long-term medication use and trabeculectomy failure rates (53).

Nonetheless, optimization of the ocular surface is an important step that should be taken into consideration prior to proceeding with glaucoma surgery, as successful outcomes may be facilitated by reducing inflammation and improving overall ocular surface health (54,55). Treatment of underlying OSD should include frequent administration of topical lubricants, appropriate lid hygiene, and avoiding the use of preservatives when appropriate.

In addition to optimizing the ocular surface pre-operatively, the continued management of OSD may be beneficial in minimizing risk of post-operative complications. Infection is a risk inherent to any surgery, and certain ocular surface findings can predispose to the development of post-operative infections. Chronic blepharitis has been found to be a significant risk factor for developing a bleb-related infection (56,57). The exact mechanism is unclear, but it is posited that alterations to the tear film composition may interfere with the ability of the ocular surface to eliminate bacteria. Rai *et al.* advocated for pre-operative screening of blepharitis, to properly assess and discuss the risk of infection with the patient prior to surgery.

Discussion

OSD is a prevalent, yet often undertreated condition in the management of glaucoma both medically and surgically. Given the well-known adverse effects of glaucoma medications on the ocular surface, patients on medical therapy for glaucoma should be regularly assessed for OSD, especially if escalation of medical therapy is being considered. Incisional glaucoma surgery, such as trabeculectomy, may cause an acute worsening of OSD due to anatomic alteration of the conjunctiva and subsequent mechanical disruption of the tear film. It is therefore important for clinicians to perform a thorough pre-operative evaluation of the ocular surface, and to maintain a high clinical suspicion for OSD exacerbations during the first 6 post-operative months. However, there may be an overall long-term net benefit of trabeculectomy on OSD, likely related to decreased medication burden. Similarly, numerous MIGS procedures have been shown in pilot studies to effectively reduce IOP as well as post-operative medication burden. Given their relatively minimal disruption of the ocular surface, the expanding role of MIGS in the surgical management of glaucoma may represent a promising development for the treatment of comorbid OSD. However, further studies are needed to assess the long-term impact of MIGS on the ocular surface.

This review has some limitations. First, there was a paucity of dedicated studies assessing the effect of MIGS procedures on the ocular surface. At this time, the study by Schweitzer *et al.* on the iStent's effects on the ocular surface remains the only study on this topic (27). However,

it is limited by its small sample size, single-arm design, and limited follow-up of only 3 months. Mathew *et al.* (32) provided a thorough review of MIGS to date; however, their Cochrane review was more focused on the efficacy of iStent relative to other proven therapies, rather than directly addressing the ocular surface. There remains a lack of dedicated randomized controlled trials assessing the effect of each glaucoma intervention on the ocular surface. The majority of the aforementioned studies were cross-sectional, observational studies, which are more susceptible to bias and confounding. Additionally, heterogeneity in study design on a given subject made it difficult to directly compare outcomes. For example, the studies assessing the effects of trabeculectomy on the ocular surface included an observational cross-sectional study, a retrospective case-control study, a case series, and a single-arm prospective cohort study. Conclusions drawn from these studies are in need of further support. Areas for further study include the effect of pre-operative OSD on trabeculectomy outcomes, the quantitative effect of MIGS on ocular surface health, and the long-term effects of trabeculectomy on the ocular surface beyond 1 year.

Conclusions

When managing glaucoma patients, clinicians must continually assess the ocular surface and maintain a low threshold to treat coexisting OSD. A comprehensive understanding of the importance of OSD in both the medical and surgical management of glaucoma is essential in optimizing patient care and improving outcomes.

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References

1. Anderson DR; . Collaborative normal tension glaucoma study. Curr Opin Ophthalmol 2003;14:86-90.
2. Leske MC, Heijl A, Hyman L, et al. Early Manifest Glaucoma Trial: design and baseline data. Ophthalmology 1999;106:2144-53.
3. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol 2002;120:701-13; discussion 829-30.
4. Chawla A, McGalliard JN, Batterbury M. Use of eyedrops in glaucoma: how can we help to reduce non-compliance? Acta Ophthalmol Scand 2007;85:464.
5. Lee TH, Sung MS, Heo H, et al. Association between meibomian gland dysfunction and compliance of topical prostaglandin analogs in patients with normal tension glaucoma. PLoS One 2018;13:e0191398.
6. Asiedu K, Abu SL. The impact of topical intraocular

pressure lowering medications on the ocular surface of glaucoma patients: A review. J Curr Ophthalmol 2019;31:8-15.
7. Fechtner RD, Godfrey DG, Budenz D, et al. Prevalence of ocular surface complaints in patients with glaucoma using topical intraocular pressure-lowering medications. Cornea 2010;29:618-21.
8. Nijm LM, De Benito-Llopis L, Rossi GC, et al. Understanding the Dual Dilemma of Dry Eye and Glaucoma: An International Review. Asia Pac J Ophthalmol (Phila) 2020;9:481-90.
9. Skalicky SE, Goldberg I, McCluskey P. Ocular surface disease and quality of life in patients with glaucoma. Am J Ophthalmol 2012;153:1-9.e2.
10. Tsai JH, Derby E, Holland EJ, et al. Incidence and prevalence of glaucoma in severe ocular surface disease. Cornea 2006;25:530-2.
11. Musch DC, Gillespie BW, Lichter PR, et al. Visual field progression in the Collaborative Initial Glaucoma Treatment Study the impact of treatment and other baseline factors. Ophthalmology 2009;116:200-7.
12. Mocan MC, Uzunosmanoglu E, Kocabeyoglu S, et al. The Association of Chronic Topical Prostaglandin Analog Use With Meibomian Gland Dysfunction. J Glaucoma 2016;25:770-4.
13. Zhu W, Kong X, Xu J, et al. Effects of Long-Term Antiglaucoma Eye Drops on Conjunctival Structures: An In Vivo Confocal Microscopy Study. J Ophthalmol 2015;2015:165475.
14. Arita R, Itoh K, Maeda S, et al. Effects of long-term topical anti-glaucoma medications on meibomian glands. Graefes Arch Clin Exp Ophthalmol 2012;250:1181-5.
15. Zhang X, Vadoothker S, Munir WM, et al. Ocular Surface Disease and Glaucoma Medications: A Clinical Approach. Eye Contact Lens 2019;45:11-8.
16. Thygesen J, Aaen K, Theodorsen F, et al. Short-term effect of latanoprost and timolol eye drops on tear fluid and the ocular surface in patients with primary open-angle glaucoma and ocular hypertension. Acta Ophthalmol Scand 2000;78:37-44.
17. Kuppens EV, de Jong CA, Stolwijk TR, et al. Effect of timolol with and without preservative on the basal tear turnover in glaucoma. Br J Ophthalmol 1995;79:339-42.
18. Coakes RL, Mackie IA, Seal DV. Effects of long-term treatment with timolol on lacrimal gland function. Br J Ophthalmol 1981;65:603-5.
19. Osborne SA, Montgomery DM, Morris D, et al. Alphagan allergy may increase the propensity for multiple eye-drop allergy. Eye (Lond) 2005;19:129-37.
20. Baudouin C. Detrimental effect of preservatives in eyedrops: implications for the treatment of glaucoma. Acta Ophthalmol 2008;86:716-26.
21. Van Went C, Alalwani H, Brasnu E, et al. Corneal sensitivity in patients treated medically for glaucoma or ocular hypertension. J Fr Ophtalmol 2011;34:684-90.
22. Roberti G, Tanga L, Manni G, et al. Tear Film, Conjunctival and Corneal Modifications Induced by Glaucoma Treatment. Curr Med Chem 2019;26:4253-61.
23. Tsai JC. A comprehensive perspective on patient adherence to topical glaucoma therapy. Ophthalmology 2009;116:S30-6.
24. Tsai JC, McClure CA, Ramos SE, et al. Compliance barriers in glaucoma: a systematic classification. J Glaucoma 2003;12:393-8.
25. Patel SC, Spaeth GL. Compliance in patients prescribed eyedrops for glaucoma. Ophthalmic Surg 1995;26:233-6.
26. Pisella PJ, Pouliquen P, Baudouin C. Prevalence of ocular symptoms and signs with preserved and preservative free glaucoma medication. Br J Ophthalmol 2002;86:418-23.
27. Schweitzer JA, Hauser WH, Ibach M, et al. Prospective Interventional Cohort Study of Ocular Surface Disease Changes in Eyes After Trabecular Micro-Bypass Stent(s) Implantation (iStent or iStent inject) with Phacoemulsification. Ophthalmol Ther 2020;9:941-53.
28. Craven ER, Katz LJ, Wells JM, et al. Cataract surgery with trabecular micro-bypass stent implantation in patients with mild-to-moderate open-angle glaucoma and cataract: two-year follow-up. J Cataract Refract Surg 2012;38:1339-45.
29. Fea AM, Consolandi G, Zola M, et al. Micro-Bypass Implantation for Primary Open-Angle Glaucoma Combined with Phacoemulsification: 4-Year Follow-Up. J Ophthalmol 2015;2015:795357.
30. Fea AM. Phacoemulsification versus phacoemulsification with micro-bypass stent implantation in primary open-angle glaucoma: randomized double-masked clinical trial. J Cataract Refract Surg 2010;36:407-12.
31. Otarola F, Virgili G, Shah A, et al. Ab interno trabecular bypass surgery with Schlemm´s canal microstent (Hydrus) for open angle glaucoma. Cochrane Database Syst Rev 2020;3:CD012740.
32. Mathew DJ, Buys YM. Minimally Invasive Glaucoma Surgery: A Critical Appraisal of the Literature. Annu Rev Vis Sci 2020;6:47-89.
33. Samuelson TW, Katz LJ, Wells JM, et al. Randomized evaluation of the trabecular micro-bypass stent with phacoemulsification in patients with glaucoma and

cataract. Ophthalmology 2011;118:459-67.
34. Fernández-Barrientos Y, García-Feijoó J, Martínez-de-la-Casa JM, et al. Fluorophotometric study of the effect of the glaukos trabecular microbypass stent on aqueous humor dynamics. Invest Ophthalmol Vis Sci 2010;51:3327-32.
35. Le JT, Bicket AK, Wang L, et al. Ab interno trabecular bypass surgery with iStent for open-angle glaucoma. Cochrane Database Syst Rev 2019;3:CD012743.
36. Hengerer FH, Auffarth GU, Riffel C, et al. Prospective, Non-randomized, 36-Month Study of Second-Generation Trabecular Micro-Bypass Stents with Phacoemulsification in Eyes with Various Types of Glaucoma. Ophthalmol Ther 2018;7:405-15.
37. Clement CI, Howes F, Ioannidis AS, et al. One-year outcomes following implantation of second-generation trabecular micro-bypass stents in conjunction with cataract surgery for various types of glaucoma or ocular hypertension: multicenter, multi-surgeon study. Clin Ophthalmol 2019;13:491-9.
38. Guedes RAP, Gravina DM, Lake JC, et al. One-Year Comparative Evaluation of iStent or iStent inject Implantation Combined with Cataract Surgery in a Single Center. Adv Ther 2019;36:2797-810.
39. Sagara H, Sekiryu T, Noji H, et al. Meibomian gland loss due to trabeculectomy. Jpn J Ophthalmol 2014;58:334-41.
40. Ono T, Yuki K, Ozeki N, et al. Ocular surface complications after trabeculectomy: incidence, risk factors, time course and prognosis. Ophthalmologica 2013;230:93-9.
41. Zhong S, Zhou H, Chen X, et al. Influence of glaucoma surgery on the ocular surface using oculus keratograph. Int Ophthalmol 2019;39:745-52.
42. Tong L, Hou AH, Wong TT. Altered expression level of inflammation-related genes and long-term changes in ocular surface after trabeculectomy, a prospective cohort study. Ocul Surf 2018;16:441-7.
43. Vaajanen A, Nättinen J, Aapola U, et al. The effect of successful trabeculectomy on the ocular surface and tear proteomics-a prospective cohort study with 1-year follow-up. Acta Ophthalmol 2021;99:160-70.
44. Agnifili L, Brescia L, Oddone F, et al. The ocular surface after successful glaucoma filtration surgery: a clinical, in vivo confocal microscopy, and immune-cytology study. Sci Rep 2019;9:11299.
45. Romano D, De Ruvo V, Fogagnolo P, et al. Inter-Eye Comparison of the Ocular Surface of Glaucoma Patients Receiving Surgical and Medical Treatments. J Clin Med 2022;11:1238.
46. Lam J, Wong TT, Tong L. Ocular surface disease in posttrabeculectomy/mitomycin C patients. Clin Ophthalmol 2015;9:187-91.
47. Traverso CE, Facino M, Murialdo U, et al. Decreased corneal complications after no-reflux, low-dose 5 fluorouracil subconjunctival injection following trabeculectomy. Int Ophthalmol 1994-1995;18:247-50.
48. Boimer C, Birt CM. Preservative exposure and surgical outcomes in glaucoma patients: The PESO study. J Glaucoma 2013;22:730-5.
49. Sherwood MB, Grierson I, Millar L, et al. Long-term morphologic effects of antiglaucoma drugs on the conjunctiva and Tenon's capsule in glaucomatous patients. Ophthalmology 1989;96:327-35.
50. Broadway DC, Grierson I, O'Brien C, et al. Adverse effects of topical antiglaucoma medication. I. The conjunctival cell profile. Arch Ophthalmol 1994;112:1437-45.
51. Broadway DC, Grierson I, O'Brien C, et al. Adverse effects of topical antiglaucoma medication. II. The outcome of filtration surgery. Arch Ophthalmol 1994;112:1446-54.
52. Lavin MJ, Wormald RP, Migdal CS, et al. The influence of prior therapy on the success of trabeculectomy. Arch Ophthalmol 1990;108:1543-8.
53. Johnson DH, Yoshikawa K, Brubaker RF, et al. The effect of long-term medical therapy on the outcome of filtration surgery. Am J Ophthalmol 1994;117:139-48.
54. Dubrulle P, Labbé A, Brasnu E, et al. Influence of Treating Ocular Surface Disease on Intraocular Pressure in Glaucoma Patients Intolerant to Their Topical Treatments: A Report of 10 Cases. J Glaucoma 2018;27:1105-11.
55. Batra R, Tailor R, Mohamed S. Ocular surface disease exacerbated glaucoma: optimizing the ocular surface improves intraocular pressure control. J Glaucoma 2014;23:56-60.
56. Ramakrishnan R, Bharathi MJ, Maheshwari D, et al. Etiology and epidemiological analysis of glaucoma-filtering bleb infections in a tertiary eye care hospital in South India. Indian J Ophthalmol 2011;59:445-53.
57. Rai PA, Barton K, Murdoch IE. Risk factors for bleb-related infection following trabeculectomy surgery: ocular surface findings-a case-control study. Br J Ophthalmol 2017;101:868-73.

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