Management of Ocular Surface Disease in Glaucoma: A Survey of Canadian Glaucoma Specialists

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Précis: Ocular surface disease (OSD) in glaucoma is an area for improvement in the management of patients with glaucoma. This study explores the knowledge of glaucoma subspecialists toward OSD in glaucoma, then provides a suggested treatment algorithm.

Purpose: To assess the attitudes, knowledge, and level of comfort of Canadian glaucoma specialists with respect to the assessment and management of OSD among patients with glaucoma.

Methods: Ophthalmologist members of the Canadian Glaucoma Society with fellowship training in glaucoma were contacted to participate in this cross-sectional survey study. Responses were recorded to statements regarding attitudes toward OSD in glaucoma, and assessment and management modalities. These were recorded primarily in the form of a Likert scale rated 1 to 7 from “strongly disagree” to “strongly agree.” Descriptive statistics were generated, and mean and SD for responses on Likert scales.

Results: Thirty-six responses were included. All respondents agreed that comprehensive management of OSD could improve quality of life, 97% agreed it could lead to better glaucoma outcomes, whereas only 22% agreed it is presently being adequately managed in glaucoma practices. Respondents were asked to list all treatment modalities they felt knowledgeable about, ranging from 100% for optimizing topical glaucoma therapies to 31% for serum tears. Nearly all respondents (92%) agreed that a suggested algorithm for the treatment of OSD in glaucoma could improve their approach to management.

Conclusion: OSD is a common comorbidity of glaucoma. Although respondents overwhelmingly agreed that comprehensive management of OSD may lead to improved quality of life and glaucoma-related outcomes, only a small percentage felt it was presently adequately managed. Increasing knowledge related to the assessment and management of OSD in glaucoma may in the future improve patient care.

Key Words: glaucoma, glaucoma therapy, dry eye, ocular surface disease, ocular surface disease in glaucoma, glaucoma surgery, cornea

ORIGINAL STUDY

METHODS

This cross-sectional survey-based study received prospective approval from the Ethics Committee of the Centre
Hospitalier de l’Université de Montréal and adhered to the tenets of the Declaration of Helsinki. Permission was sought to access the email list serve of the Canadian Glaucoma Society (http://cgs-scg.org), comprised of ophthalmologists in Canada providing subspecialty care in glaucoma. An expert panel of cornea and glaucoma subspecialists were sent a detailed summary of the objectives of the proposed study and a draft of the survey. They then reviewed the survey, and their suggestions were incorporated, to establish content and face validity. The electronic survey was distributed (see English Survey Form, Supplemental Digital Content 1, http://links.lww.com/IJG/A452), and responses were gathered on 23 prompts primarily in the format of a Likert scale rated 1 to 7 from “strongly disagree” to “strongly agree,” or a “select all that apply or none of the above” checkbox format. The survey could be submitted online through the survey platform Qualtrics (http://www.qualtrics.com) or printed and returned by mail. All data were collected anonymously. Responses were included for all participants who confirmed within the survey that they had completed glaucoma fellowship-level training. Responses for each other individual prompts were optional.

The survey was active for a period of 8 consecutive weeks after the initial invitation with 3 reminder emails sent at 2, 4, and 6 weeks.

Descriptive statistics were generated for the responses to each statement using the Qualtrics platform and Microsoft Excel 2016 (Microsoft Corp., Redmond, WA). For responses made on 7-point Likert scales, the median was generated by taking the numerical value of each response from 1 to 7. On each response scale, 1 represented “strongly disagree,” 4 represented “neither agree nor disagree,” and 7 represented “strongly agree,” whereas 2 and 3 or 5 and 6 represented varying levels of disagreement or agreement, respectively. The interquartile range (IQR) was calculated to measure the spread of the response data.

RESULTS

Demographics

Thirty-eight responses were collected from an email list serve of 117 recipients, representing a response rate of 32.5%. Two responses were excluded from analysis as the respondents indicated they had not completed glaucoma fellowship training. The mean rate of response for each individual prompt was 99.1% (x = 35.7 ± 0.6; n = 36; range, 34 to 36). Respondents reported their primary province of practice as Quebec (n = 8), British Columbia (n = 7), Ontario (n = 7), Nova Scotia (n = 5), Alberta (n = 4), Manitoba (n = 1), Newfoundland and Labrador (n = 1), and Saskatchewan (n = 1). No responses were gathered from New Brunswick, Prince Edwards Island, or the Canadian territories. Respondents reported that they had been in unsupervised practice for <5 years in 25.7% (n = 9), 5 to 14 years in 22.9% (n = 8), 15 to 24 years in 28.6% (n = 10), and ≥25 years in 22.9% (n = 8).

Disposition Regarding Management of OSD in Glaucoma

All respondents (100%, n = 36) agreed that comprehensive management of OSD could improve the quality of life of patients in tertiary glaucoma practices (median = 7, IQR = 1). Similarly, an overwhelming majority of respondents (97.1%, n = 34) agreed that comprehensive management of OSD in patients with glaucoma could lead to better glaucoma outcomes (median = 6, IQR = 2, n = 35). Furthermore, 91.7% (n = 33) agreed that a suggested algorithm for the treatment of OSD in glaucoma, including recommended timing and doses of therapies, could improve their approach to OSD in glaucoma (median = 6, IQR = 1.75, n = 36).

Present Management of OSD in Glaucoma

Responding to the statement “The ocular surface health of patients with glaucoma is presently being adequately managed in subspecialty (tertiary) glaucoma practices,” just 22.2% (n = 8) agreed, whereas 50.0% (n = 18) of respondents disagreed (median = 3.5, IQR = 2, n = 36). Similarly, a minority of respondents (13.8%, n = 5) agreed that patients were receiving adequate management of OSD while being treated in nonglaucoma ophthalmology practices before the referral, compared with 55.5% (n = 20) who disagreed (median = 3, IQR = 2, n = 36).

Assessment of the Ocular Surface in Glaucoma

Among respondents, 31 (86.1%) agreed with the statement “I routinely assess the ocular surface health of my patients with glaucoma,” whereas 5 disagreed (median = 6, IQR = 1.75, n = 36). The most frequently utilized OSD assessment methods reported were assessment of conjunctival health (91.4%, n = 32), assessment of lid health (88.6%, n = 31), assessment of lid position (80.0%, n = 28), and assessment of fluorescein staining (80.0%, n = 28). The reported frequencies of each response are shown in Figure 1.

Just one participant (2.9%) agreed with the statement “I routinely use a classification system [eg, Dry Eye Workshop (DEWS), National Eye Institute, etc.] to grade the ocular surface health of my patients with glaucoma,” whereas 33 (91.6%) disagreed (median = 2, IQR = 1, n = 36).

Treatment of OSD in Glaucoma

The majority of respondents agreed (83.3%, n = 30) that when considering further treatments for glaucoma, they often consider ocular surface health when choosing the next step (median = 6, IQR = 2, n = 35). Similarly, 66.7% (n = 24) of respondents agreed that when considering further treatments for glaucoma, they often anticipate their effects on the ocular surface health and take pre-emptive steps to mitigate them (median = 5, IQR = 2, n = 36).

When treating OSD in glaucoma, 66.7% (n = 24) of respondents agreed that their approach is highly individualized with respect to available treatment options, whereas 22.2% (n = 6) disagreed (median = 5, IQR = 2, n = 36). Respondents were asked to rate how frequently they consult with a specialist in ocular surface health (ie, cornea) as never, rarely, sometimes, often, and almost always, the results of which are summarized in Figure 2.

Treatment Modalities

Regarding specific treatments for OSD in patients with glaucoma, respondents were asked to select all treatment modalities they felt knowledgeable about with respect to their role and use. Responses ranged from 100% (n = 36) reporting they felt knowledgeable with respect to optimizing topical therapies, such as switching to combination drops or using nonpreserved or non–benzalkonium chloride (BAK) formulations, to just 11 respondents (30.6%) reporting they felt knowledgeable with respect to the role and use of serum tears. These results are summarized in Figure 3.

When asked to list the top 3 modalities used to first address OSD among patients with glaucoma, the most frequently utilized modalities were artificial tears (94.4%, n = 34), optimizing topical medications through the use of

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combination drops, preservative-free, or non-BAK formulations (66.7%, n = 24), and lid hygiene (ie, scrubs, 55.6%, n = 20). Further results are summarized in Figure 4.

When responding to statements about individual treatment modalities on a 7-point Likert scale, 94.4% of participants agreed that they felt knowledgeable with respect to the available non-BAK containing topical glaucoma medications (median = 7, IQR = 1.75, n = 36). They further agreed (83.3%, n = 30) that they felt knowledgeable with respect to the different topical steroid preparations available and their respective dosages for the use in OSD (median = 6, IQR = 1, n = 36). Fewer respondents (61.1%, n = 22) agreed that they felt comfortable identifying patients with glaucoma with OSD who may benefit from a course of topical steroids.
With regards to omega supplementation, only 48.6% (n = 17) agreed that they felt knowledgeable with respect to recommendations and specific dosages for the treatment of OSD, whereas 40% (n = 14) disagreed and 11.4% (n = 4) were neutral (median = 4, IQR = 3, n = 35). Just 30.5% (n = 11) agreed that they felt knowledgeable with respect to the use of serum tears for the treatment of OSD in glaucoma, whereas 58.3% (n = 21) disagreed (median = 2.5, IQR = 3.75, n = 36).

**DISCUSSION**

**OSD in Glaucoma Survey**

OSD is a common comorbidity of glaucoma therapy that has been shown to adversely affect the glaucoma-related quality of life and may adversely affect IOP control. In light of these findings, there has been greater attention to the assessment and management of OSD in glaucoma.
In this survey-based study, virtually all glaucoma specialists surveyed agreed that comprehensive management of OSD could improve the quality of life of patients with glaucoma and could lead to better glaucoma-related outcomes (100% and 97.1%, respectively). Surprisingly, responses suggest that the majority of glaucoma subspecialists in Canada do not feel that ocular surface health in patients with glaucoma is presently adequately managed in either glaucoma offices, or in nonglaucoma subspecialty practices before referral. This may represent an area for improvement in the comprehensive management of patients with glaucoma, which crosses the borders of traditional ophthalmology subspecialty practice.

With respect to the assessment of OSD in glaucoma, an overwhelming majority of respondents agreed that they routinely assess the ocular surface health of their patients with glaucoma, most commonly with an assessment of conjunctival health, lid health and positioning, and assessment of fluorescein staining, whereas a smaller majority utilized tear break-up time (TBUT) and meibomian gland health assessment and only 1 reported utilizing Schirmer testing. This indicates that respondents are routinely using several metrics to assess ocular surface health, which is a key step toward initiating appropriate therapy. Tests such as TBUT and Schirmer testing are commonly used in the setting of OSD practices to further individualize therapy toward primarily evaporative or aqueous deficient disease, however, it is now recognized that most patients suffer from a combination or “mixed-mechanism” OSD on a continuum between the 2.

Along those lines, only 2 respondents reported using a standardized assessment form such as the OSDI, whereas just 1 respondent (2.9%) agreed that they utilize a standardized classification system to grade the ocular surface health of patients with glaucoma. The use of standardized screening forms such as the OSDI, Symptom Assessment in Dry Eye, 5-item Dry Eye Questionnaire (DEQ-5), or Standard Patient Evaluation of Eye Dryness questionnaires among others offers valuable information regarding patient symptoms, which is another important metric by which response to treatment can be measured. Standardized OSD grading scores, such as the Delphi panel grading scale adopted by the 2007 DEWS Report, or the National Eye Institute/Industry Workshop scale offer greater consistency in assessment and measuring response to treatment. A thorough discussion of various questionnaires and grading scales is presented in the DEWS II Diagnostic Methodology report, along with comprehensive summaries of all aspects of OSD within the 10-chapter DEWS II report. Given the relative infrequency with which these were reported to be used, they may represent an avenue for improvement in an assessment that may be initiated on a case-by-case basis to aid in individualizing therapy and measuring treatment response.

While nearly 90% or more of respondents reported that they felt knowledgeable with respect to optimizing topical therapies, using artificial tears, lid scrubs, lid compresses and massage, only around 60% felt knowledgeable with regards to the deployment of topical immunomodulators, topical steroids, and omega supplements, and just over 30% felt knowledgeable with respect to the use of serum tears for the treatment of OSD in glaucoma. Although patients with glaucoma may be on multiple IOP-lowering drops, and greater use of these drops leads to an increasing likelihood of OSD, practitioners may be understandably reluctant to add further topical therapies to an already complex drop regimen. Nevertheless, after other therapies have been optimized to decrease the risk for OSD for at-risk or affected patients, medications such as immunomodulators, topical steroids, or serum tears can be considered in the appropriate circumstances.

Importantly, when considering further treatment for glaucoma, the majority of respondents agreed that they consider ocular surface health when choosing the next step, anticipate treatment effects on ocular surface health and take pre-emptive steps to mitigate them. The anticipation of the effects of further treatments offers an opportunity to mitigate potential adverse effects, which may in turn improve patient adherence to therapies.

In light of these findings, it is unsurprising that > 90% of respondents agreed that a suggested algorithm for the treatment of OSD in glaucoma may improve their approach to management. We present our suggested treatment algorithm in Figure 5 with a visual representation in Figure 6, and a further discussion of the proposed treatment steps and modalities below.

**Suggested Treatment Algorithm**

A suggested treatment algorithm for OSD in glaucoma is presented in Figure 5 in point form, and in Figure 6 as a flow diagram. The proposed steps in the algorithm are discussed in greater detail below.

Before initiating treatment, a careful assessment of the ocular surface and periorbital structures is paramount. Aggravating conditions, such as lid malposition, rosacea, blepharitis, allergies, or otherwise should be managed thoroughly. Further, local factors such as low environmental humidity or extended electronic device use should be addressed, such as with humidifiers, frequent breaks from device use, or blinking efficiency exercises. As soon as the earliest signs or symptoms of OSD are recognized, such as inferior punctate epithelial erosions or a dry, gritty sensation, treatment should be initiated promptly.

**Step 1: Optimize Glaucoma Therapy**

The first proposed treatment step is the optimization of topical therapies. Benzalkonium chloride, a commonly used preservative in topical IOP-lowering drops, has a long history of documented deleterious effects on the ocular surface, in addition to the effects of the active ingredients, which have been thoroughly reviewed by Baudouin et al. Clinical studies have corroborated that BAK administration in ocular hypertensive agents affects all layers of the tear film, leading to lower Schirmer testing scores implying increased aqueous tear deficiency, abnormal esthesiometry testing implying decreased corneal sensation and reflex tearing, and diminished TBUT indicating poorer tear quality. With each additional BAK containing drop administered, it has been estimated that the likelihood of demonstrating OSD increases 2-fold. Furthermore, chronic BAK exposure has been shown to adversely affect the outcomes of trabeculectomy surgery. In the setting of symptomatic OSD in glaucoma, or asymptomatic OSD with considerable changes in examination, every reasonable effort should be made to minimize the daily applied dose of BAK, and indeed all preservatives where possible while considering the increased cost associated with these formulations.

To accomplish this, one can consider combination drops, alternatively preserved drops or nonpreserved formulations. Combination drops containing 2 active ingredients have long...
When encountering a patient with glaucoma with symptomatic OSD*, or asymptomatic but considerable ocular surface changes on clinical examination/diagnostic testing that may be adversely affecting IOP control, a stepwise approach is recommended.

Prior to or concurrent with the initiation of OSD treatments, all aggravating conditions and factors should be managed aggressively, such as lid disorders (malposition, rosacea, blepharitis, etc.), other ocular surface conditions (allergy, contact lens wear, etc.), and local environmental factors such as low humidity (ie. by humidifier use) or extended electronic device use (ie. by frequent breaks or blinking exercises).

**Step 1: Optimize topical glaucoma therapies.**

a. Consider switching to combination drops where possible.

b. Consider switching to preservative free formulations where available.

c. Consider laser trabeculoplasty as a drop-alternative or as next step therapy.

d. Consider MIGS at the time of cataract surgery.

**Step 2: Promote ocular surface health.** Initiate topical lubricants, punctual occlusion therapies and/or warm compresses.

a. Artificial tears (non-preserved preferred) qid to q1h.

b. Tear gel (highly viscous) qhs minimum.

c. If drop fatigued or on a complex topical therapy regimen, consider early intervention with punctal plugs as an add-on or alternative.

d. Consider external eyelid heating, preferring non-wet devices (ie. rice-filled sock, TheraPearl, Bruder, or other commercial eye mask), with a recommended application of 5 minutes bid for a minimum of 1 month.

e. Consider oral omega-3 fatty acid supplementation at doses up to 2000mg of EPA and 1000mg of DHA daily.

**Step 3: Enhance ocular surface therapy.** If still symptomatic or considerable ocular surface changes are seen on exam with the above measures optimized:

a. Consider cyclopentolate A 0.05% bid. Lifitegrast 5% bid may be considered as an alternative.

b. Consider switching artificial tears to autologous or allogenic serum tears 20% qid minimum.

**Step 4: Stabilize the ocular surface (consider moving to surgery when appropriate).** If there remains significant OSD after the above measures, or they have been deemed unsuitable for an individual patient:

a. Consider washout of topical agents while stabilizing glaucoma with oral therapy where reasonable (ie. acetazolamide 125-250mg po bid-qid).

b. Consider a short course of topical steroids with lesser intraocular penetration, such as fluoromethalone 0.1%, loteprednol etabonate 0.2% or in cases of significant preservative toxicity, prednisolone 0.5% preservative-free minims qid, reducing the dosage by half every 4-7 days until completion (ie. qid x 4 days, bid x 4 days, qd x 4 days then stop).

c. Consider conjunctiva-sparing techniques if appropriate (ie. gonio-assisted trabeculotomy, trabectome, etc.) to minimize effects on ocular surface health.

d. When considering transscleral cyclophotocoagulation, micropulse techniques may have fewer ocular surface effects than continuous wave, if appropriate for the required degree of IOP reduction.

e. Manage OSD aggressively pre- and post-operatively, anticipating adverse effects on ocular surface health, particularly for filtering procedures.

**FIGURE 5.** Suggested algorithm for the treatment of OSD in glaucoma.

been available in various forms, simplifying patient drop regimens and decreasing the total dose of BAK administered when compared with the administration of 2 separate, preserved agents. Furthermore, an increasing number of formulations have been made available either with alternative preservatives or in nonpreserved variants, which have been shown to have fewer adverse effects on the ocular surface than BAK containing formulations.26-31 Recent reviews further explore the effects of topical glaucoma medications on the ocular surface, summarize the available topical agents along with their respective preservatives, and detail those available with alternative preservatives or in nonpreserved form.32,33 In the future, triple-agent combination drops may offer another alternative for decreasing the applied dose of preservatives while simplifying drop regimens.34 Similarly, sustained-release implants such as Bimatoprost SR (Allergan Inc, Dublin, ROI) are under investigation that may offer the IOP-reducing effects of topical agents with less toxicity to the ocular surface and surrounding tissues.35

To further optimize therapy in patients suffering from OSD before or after initiating topical glaucoma therapies, intervention with laser trabeculoplasty should be considered as drop-sparing therapy, either in place of topical therapies or as an add-on in place of further drops where lower IOPs are desired. This can be achieved with argon laser trabeculoplasty, selective laser trabeculoplasty, or more recently micropulse diode laser trabeculoplasty at the discretion of the treating physician.36 Selective laser trabeculoplasty has been shown in large trials and meta-analyses to be as effective as a first-line topical medication for IOP reduction, with the benefit of greater cost-effectiveness over eye drops.37-39 Similarly, if a patient is undergoing cataract surgery, then minimally invasive glaucoma surgeries (MIGS) can be considered early on in glaucoma.
management where clinically appropriate, which may further decrease the need for topical therapies. If a patient has previously undergone cataract surgery, MIGS may still be considered early on as drop-sparing therapy as appropriate. Further discussion of surgical intervention is found below.

### Step 2: Promote Ocular Surface Health

The second proposed step in treatment is the initiation of topical lubricants or punctal occlusion therapies, which may reasonably be started in conjunction with the optimization of topical agents. Artifical tears remain a mainstay of dry-eye therapy. Although preserved agents use alternative preservatives to BAK and may be considered because of the decreased cost, increased availability, and the convenience of standard multidose containers, nonpreserved agents are preferred and should be considered wherever possible. Dosing should be initiated qid-q1h, depending on a patient’s symptoms and willingness to apply throughout the day. The initiation of a highly viscous, nonpreserved tear gel should also be considered at qhs or up to qid as tolerated.

A recent randomized controlled trial of patients using topical prostaglandin analogs for glaucoma demonstrated the efficacy of the primary use of punctal plugs. When compared with the fellow control eye of each patient, eyes with nonabsorbable punctal plugs had increased TBUT, decreased Oxford Cornea Severity Score grading for signs of dry eye, and decreased tear osmolarity, with a favorable side-effect profile including an 8.5% rate of extrusion and symptomatic epiphora in 6.5%. Absorbable canalicular plugs are available in several materials and varying durations of effect, ranging from <1 week to \( \geq 6 \) months, but may not be as effective as nonabsorbable punctal plugs such as those made of silicone. Permanent punctal plugs, as opposed to intracanalicular plugs, are preferred as permanent intracanalicular plugs have a higher association with canaliculitis and pyogenic granulomas, in some cases requiring canaliculotomy and dacryocystorhinostomy. If plugs are well tolerated but repeatedly extrude, then permanent occlusion with punctal cautery can be considered. Given that increasing complexity of topical glaucoma therapy regimens has been shown to result in decreased adherence.

![FIGURE 6. Suggested algorithm for the treatment of OSD in glaucoma flow chart.](image-url)
medication adherence, punctal occlusion may represent an underutilized avenue of treatment for patients who are often on already complex drop schedules.42

External eyelid heating devices have demonstrated efficacy in reducing surface staining, improving TBUT and meibomian gland secretions, optimally with continued 2 times per day applications of ≥ 5 minutes.43,44 Because of evaporative cooling associated with wet devices such as facecloths, commercially available dry heating devices are preferred.43 Some examples include the Therapearls Mask (Bausch & Lomb, Rochester, NY) or Bruder Mask (Bruder Healthcare, Alpharetta, GA), both readily available online for under US$20 (US dollars, http://www.amazon.com, accessed February 22, 2019).

Omega-3 supplementation has long been believed to be beneficial in the treatment of OSD. Prospective randomized controlled trials have demonstrated conflicting results, with recent evidence from the National Institutes of Health-funded DREAM study showing no benefit to large doses of omega-3 over placebo for the treatment of moderate to severe OSD.45,46 A recent meta-analysis, however, indicated that omega-3 fatty acid supplementation significantly improved OSD symptoms and signs.47 Doses as high as 2000 mg of eicosapentaenoic acid and 1000 mg of docosahexaenoic acid daily were well tolerated with few adverse effects and may be considered for patients with treatment-resistant signs and symptoms of OSD.48

Step 3: Enhance Ocular Surface Therapy

For patients who remain symptomatic after the above modalities have been considered, and possibly require ongoing treatment with topical glaucoma therapies, the practitioner may consider the use of topical immunomodulators and/or serum tears. In a prospective comparative study of patients with glaucoma on IOP-lowering agents, all subjects received topical cyclosporine A 0.05% bid (Restasis, Allergan Inc) and were compared with healthy controls.49 Although significantly impaired at baseline and in follow-up compared with healthy controls by measures of TBUT, conjunctival and corneal sensitivity, and OSDI scoring, all measures were significantly improved after 6 months of therapy with few adverse effects. Lifitegrast 5% (Xiidra, Shire Pharmaceuticals, Lexington, MA) is an integrin antagonist that inhibits T-cell–mediated inflammatory pathways implicated in the pathogenesis of OSD.49 Studies specific to lifitegrast for the treatment of OSD in glaucoma may in the future define its role in this subgroup.

Autologous serum tears have increasingly been used as second-line therapy in treatment-resistant OSD and may similarly be considered for recalcitrant OSD in the setting of glaucoma. Controlled trials have shown the superiority of autologous serum tears compared with artificial tears in the setting of severe OSD.50–52 These are typically initiated at a concentration of 20% qid–q2h and are nonpreserved, containing essential tear components such as growth factors, fibronectin, and vitamin A.53–55 Allogenic serum tears, derived from blood products of donors, have been shown to be safe and may decrease the cost while increasing the availability of this therapy.56

Step 4: Stabilize the Ocular Surface (Consider Moving to Surgery When Appropriate)

In the next proposed step of the treatment pathway, should the above measures be unsuccessful or unsuitable for a patient suffering from OSD in the setting of glaucoma, the following should be considered. First, where clinically appropriate, a washout of topical agents may be considered while stabilizing glaucoma with oral therapy, such as acetazolamide (Diamoxx, Duramed Pharmaceuticals Inc, Cincinnati, OH) 125 to 250 mg po bid-qid for 2 to 4 weeks. This may be considered alone, along with measures to improve the ocular surface health as recommended above, or in conjunction with the initiation of a short course of the topical corticosteroid, used to break the cycle of inflammation and allow other ocular surface measures to take effect. Reasonable choices may include fluorometholone 0.1% qid (Flarex, Allergan, Inc), loteprednol etabonate 0.2% to 0.5% qid (Alrex 0.2%/Lotemax 0.5%, Bausch & Lomb), or in patients believed to be suffering significantly adverse effects to preservatives, prednisolone 0.5% qid in preservative-free minims. Topical corticosteroids used preoperatively for trabeculectomy have been shown to improve outcomes, possibly related to the reversal of medication-induced conjunctival inflammation.57,58 Specific recommendations for their use in glaucoma therapy-induced OSD, which may share similar pathophysiology, are lacking. A short course may include an initial application at 4 times daily (qid), reducing the dosage by half every 4 to 7 days until completion (eg, qid for 4 days, bid for 4 days, qdaily for 4 days, and then stop), with close monitoring of IOPs. Similarly, a pulse steroid application such as this may be considered in the absence of a washout period, ideally along with other measures to improve surface health.

Topical corticosteroids are a mainstay of OSD treatment, however, they present unique challenges among patients with glaucoma. Although the potential IOP-raising effects are well known even among normal eyes, studies have shown that >90% of eyes with primary open-angle glaucoma (POAG) responded with an IOP elevation of ≥ 6 mm Hg after a 4-week course of topical dexamethasone 0.1% 3 times daily.59,60 The IOP-raising effects differ by intraocular absorption and potency.61 Preparations such as fluorometholone or loteprednol etabonate have been shown to have lesser effects even among known steroid responders, which may be considered for short durations to disrupt the cycle of ocular surface inflammation, a key step in the pathophysiology of OSD.61–63 Nevertheless, these must be utilized with caution in patients with glaucoma, and in combination with long-term measures to improve the ocular surface health of the eye.

Step 5: Surgical Intervention

Finally, if the above measures are unsuccessful and the patient is suffering intolerable OSD-related effects from topical therapies, and/or requires further glaucoma treatment, then surgical intervention for glaucoma may be considered. If appropriate for the degree of IOP reduction required, MIGS procedures using ab interno, conjunctivaparating techniques may be preferred for ocular surface health. Procedures such as iStent or iStent Inject (Glaukos, San Clemente, CA), Hydrus Microstent (Ivantis Inc, Irvine, CA), Trabectome (Neomedix Corporation, Trustin, CA), or gono-assisted trabeculotomy have the advantage of delivery through clear-corneal incision, not requiring conjunctival dissection or antimetabolite use.64 Similarly, the Xen Gel Stent (Allergan Inc, Dublin), does not require a conjunctival incision, but does form a filtering bleb and is often accompanied by the use of mitomycin C, with promising results to date.65 Long-term studies will in the future define the
efficacy and safety of these devices compared with trabeculectomy or traditional glaucoma drainage devices, and their comparative effects on the ocular surface.

Micropulse trans-scleral cyclophotocoagulation (MP-TSCPC, Iridex Corporation) utilizes light at 810-nm wavelength delivered in an “on-and-off” manner, which is preferentially absorbed by the pigmented ciliary epithelium. Thermal energy delivered during the “on” cycle results in photocoagulative damage to the ciliary body, whereas the “off” cycle allows adjacent structures to cool, protecting them from collateral thermal damage. Although traditional CW-TSCPC was often considered therapy for patients with refractory glaucoma, in cases with limited visual potential or who were otherwise unsuitable for incisional surgery, MP-TSCPC is increasingly being used at earlier stages of the disease, in some cases before or as a bridge therapy to incisional surgery.66

Although some have advocated for judicious use among patients with poor ocular surface health or prior corneal transplantation because of the possibility of increased OSD, others specifically use it for patients with OSD to delay or obviate the need for incisional surgery with its associated ocular surface effects.67,68 Peer-reviewed publications of MP-TSCPC in the future may demonstrate its role in the treatment of earlier stages of glaucoma, and delineate its effects on ocular surface health in human eyes.

While improvements in pharmacotherapy, increasing adoption of laser trabecuoplasty, and the advent of MIGS procedures have decreased the number of trabeculectomies and glaucoma drainage implants such as the Ahmed or Baerveldt implants being performed, these procedures have yet to be supplanted, and trabeculectomy remains the gold standard for IOP reduction.69 It has long been recognized that filtering blebs from glaucoma surgery may interfere with lid function and cause impairment in the precorneal tear film, in some cases leading to Dellen formation.70 Filtering blebs have further been associated with increased symptoms of ocular pain, discomfort, burning, foreign body sensation, and tearing, termed glaucoma filtering bleb dysesthesia.71 More recently, increasing bleb height and the presence of bleb microcysts have been found to be associated with increasing signs and symptoms OSD among patients with post trabeculectomy.72 Mitomycin C, commonly used as an adjunct to filtering procedures (which may contribute to lower, more diffuse blebs), has been shown to decrease conjunctival goblet cell density, damage limbal stem cells, and cause direct ocular surface toxicity that may further impair ocular surface homeostasis.73-75 Given these findings, all reasonable steps listed in the proposed treatment algorithm to promote ocular surface health should be used both preoperatively and postoperatively, particularly in the setting of preoperative OSD.

Other Modalities

Many other treatments for OSD exist but have not been included in the above-mentioned treatment algorithm. Ciclosporine A, for example, is available in 0.1% concentration commercially in Europe and Canada (Verkazia, Santen, Osaka, JP) or through compounding pharmacies in concentrations typically ranging from 0.1% to 2%.76 These compounded drops are often reserved for more severe ocular surface disorders such as resistant vernal or atopic keratoconjunctivitis, rather than a failure of 0.05% CsA for OSD. Treatments targeting the meibomian glands, lids, or lashes, such as Lipiflow (Johnson & Johnson Vision Care Inc, Jacksonville, FL), intense pulsed light, and BlephEx (BlephEx LLC, Franklin, TN) among many others, may be considered for the management of OSD aggravating conditions such as significant meibomian gland dysfunction or blepharitis on an individualized basis. Finally, cryopreserved amniotic membrane (CAM) has been used for refractory DED/OSD, however, given the considerable cost of nonsurgical, self-retaining CAM rings such as PROKERA Slim (Bio-Tissue, Miami, FL) and limited data available for this subgroup, future studies of CAM for OSD in glaucoma may in the future define its use.77

Limitations of the present study include the relatively small sample size (n = 36), representing 32.5% of the Canadian Glaucoma Society membership. Furthermore, while providing a suggested treatment algorithm for OSD in glaucoma, we have made no distinction between the subtypes of glaucoma (ie, POAG, normal-tension glaucoma, etc.). Although much of the literature to date has focused on OSD in POAG, and indeed all forms of glaucoma may share pathogenic mechanisms for inducing OSD such as the use of BAK containing drops or through similar incisional surgical approaches, little is known about differences between glaucoma subtypes as far as the incidence of OSD, IOP control implications, or more individualized treatment modalities based on subtype. Given that this study represents exploratory research with a novel questionnaire, measurements of construct and concurrent validity will be more readily measured in future research with similar or related questionnaires in the future. Finally, knowledge and attitudes toward point-of-care diagnostic testing modalities such as matrix metalloproteinase 9 testing, tear osmolarity, and meibomography among others, and treatments such as Lipiflow thermal pulsation, intense pulsed light therapy, or microblepharoplasty were not probed in this survey, however, these newer modalities are finding more widespread use and may represent avenues for further research as they pertain to OSD in glaucoma.

CONCLUSION

In this cross-sectional, survey-based study of Canadian glaucoma subspecialists, it is evident that OSD is recognized by these glaucoma subspecialist respondents as an area for improvement in the comprehensive management of patients with glaucoma that crosses the borders of traditional glaucoma subspecialty practice. Although respondents in general felt knowledgeable with respect to many aspects of assessment and management, there remain areas for improvement. Increasing awareness of OSD in glaucoma will drive further research in the area, particularly with respect to new treatment modalities and modern surgical techniques. Future studies on medical and surgical glaucoma interventions should include OSD outcome measures to expand our understanding of their effects and further optimize the management of these frequently comorbid conditions.

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