Influence of Treating Ocular Surface Disease on Intraocular Pressure in Glaucoma Patients Intolerant to Their Topical Treatments: A Report of 10 Cases

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Purpose: The purpose of this study was to evaluate the effect of treating ocular surface disease (OSD) in patients with medically uncontrolled primary open-angle glaucoma (POAG) associated with OSD.

Methods: We compiled a retrospective observational case series of 10 patients with POAG that remained uncontrolled with topical treatments and who were referred for filtering glaucoma surgery. All patients underwent a complete assessment of their glaucoma and ocular surface for both eyes. The main treatments were change of topical antiglaucoma medications to preservative-free equivalents, removal of allergenic treatments or those identified as causing side effects, switch to another therapeutic class with the same efficacy but with a better safety profile and treatment of OSD.

Results: After a minimum follow-up of 6 months, we observed improved ocular surface in all patients, associated with an intraocular pressure (IOP) decrease or stabilization even if some antiglaucoma medications were removed. The mean IOP significantly decreased from 23.75 ± 9.98 mm Hg to 15.15 ± 4.75 mm Hg (−36.2%; $P = 0.0001$). The mean number of IOP-lowering medications was 3.7 ± 1.06 at presentation and 2.8 ± 0.63 after treatment ($P = 0.01$). The Oxford score also decreased from a mean 1.7 ± 0.67 to 0.4 ± 0.51 (−76.5%; $P < 0.001$). For 2 patients, IOP was not sufficiently reduced after treatment and they finally underwent filtering surgery.

Conclusions: The prevalence of OSD in POAG patients is very high, particularly in patients with uncontrolled glaucoma with multiple topical medications. Careful management of the ocular surface associated with a reduction of the toxicity of eyedrops may result in improvement of ocular surface health and better IOP control.

Key Words: glaucoma treatments, ocular surface disease, preservatives, trabecular meshwork inflammation

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Primary open-angle glaucoma (POAG) is a leading cause of blindness, defined as a progressive optic neuropathy with damage to the optic nerve and visual field loss. Abnormally elevated intraocular pressure (IOP) is the most critical risk factor for POAG and is related to an increase in trabecular meshwork outflow resistance to aqueous humor.[1] The current initial therapeutic strategy against POAG is based on reducing IOP, with IOP-lowering drugs that belong to various families depending on their pharmacological characteristics and modes of action. When a single drug is not efficient, associations of several drugs, either fixed or unfixed, are used, resulting in a large number of patients receiving topical drugs over the long term, that is, for decades and most often for the rest of their life.[2]

Although the overall safety/efficacy profile of these eyedrops appears satisfactory, real-life observational studies have clearly shown a high rate of side effects to the ocular surface caused by the long term use of topical drugs. Prevalence of ocular surface disease (OSD) in patients receiving antiglaucoma drugs over the long term has been shown to be as high as 40% to 50%, much higher than in the general population.[3–6] It mainly consists of dry eye, redness, symptoms of irritation, blepharitis or allergic reactions. Symptoms are more frequent and more severe in older patients receiving more drugs and presenting with more severe glaucoma.[7]

Subconjunctival fibrosis has also been described and several reports have pointed out the influence of conjunctival inflammation and preoperative use of eyedrops in glaucoma surgery failure, causing early subconjunctival fibrosis and poor surgical outcomes.[8,9] Indeed, chronic inflammation may affect not only the ocular surface but also deeper ocular structures, such as subconjunctival tissues and possibly the trabecular meshwork.[10,11] In is interesting to note that, in a large-scale study on OSD prevalence in glaucoma,[7] IOP was found higher in patients with severe OSDs compared with those with no or mild OSD, which remained an independent factor in multivariate analysis.

The causes of such chronic inflammation may be multiple and multifactorial: the role of preservatives has largely been emphasized,[12–14] but the toxicity of the active compounds, drug interactions, allergic reactions, as well as preexisting atopy, dry eye or meibomian gland dysfunction (MGD) may also play a role, either alone or within complex interactions. Aging and duration of treatments are also confounding factors that increase the risk of developing adverse reactions.[12] Long term treatments, mainly because of preservatives, have been shown to cause decreased goblet

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cell density[15,16] as well as increased tear film instability and osmolarity,[17] which are major components of dry eye disease. Most often, this ocular surface intolerance develops at a low-grade level, with slight symptoms and poor or misdiagnosed signs. This paucity of symptoms and signs may not initially influence the antiglaucoma therapeutic strategy of clinicians.

When dry eye symptoms develop, most ophthalmologists prescribe tear substitutes, an additive strategy, that is, adding a treatment for alleviating symptoms because of another treatment, rather than considering switching or removing some of the responsible drugs. In a study evaluating glaucoma patients, 37.7% used a mean of 3.3 ± 1.1 lubricant eyedrops per day and 4.7% were concomitantly treated with antiallergic drugs.[2] Among glaucoma patients with artificial tears, > 55% received preserved lubricants, intensifying preservative concentrations and acting as a toxic vicious circle responsible for OSD.[2] Another strategy could therefore be proposed, based on the known effects of preservatives on the ocular surface and growing development of preservative-free medications[14,16] and new safer preservatives,[18,19] namely the subtraction strategy, which consists in identifying and removing potentially toxic eyedrops, associated with dedicated ocular surface treatments.

In a retrospective study Batra et al[20] described 4 cases showing that interventions to improve the ocular surface (lid hygiene, preservative-free lubricants and antiglaucoma drops, doxycycline) resulted in a significant and sustained reduction in IOP. Both these observations and a large set of experimental data[11] support the theory of an increased outflow resistance and further IOP elevation caused by chronic ocular surface inflammation. This inflammation extending to the trabecular meshwork may also result from accumulation of the toxic, proinflammatory and prooxidative preservative benzalkonium chloride (BAK) in trabecular tissues, as shown in experimental pharmacokinetic studies.[21] Removal of preservatives and specific treatment of OSD might interrupt and partially reverse this phenomenon called OSD-exacerbated glaucoma.[20]

The present study describes another series of POAG patients presenting severe OSD and medically uncontrolled IOP, which improved dramatically after stopping most toxic eyedrops and treating the ocular surface. The aim was to further support the utility of treating OSD using a subtraction strategy instead of an addition strategy to improve IOP control or at least prepare eyes for glaucoma filtering surgery.

PATIENTS AND METHODS

A retrospective review of 10 patients with POAG uncontrolled with topical treatments and followed at the Centre National d'Ophtalmologie des Quinze-Vingts, Paris, France, between March 2016 and May 2017 was performed. Data from these 10 patients were extracted from those of 97 patients with severe glaucoma and referred to one surgeon (CB) for surgery during this period. General approval by an Ethics committee was previously obtained from the Comité de Protection des Personnes (Ile de France V, agreement number 10793) for all ocular surface investigations in our department. However informed consent was not collected initially when patients were referred, but at the end of the study period to obtain the patients' approval for collecting data for this case series. They had all been referred for filtering surgery as IOP was not controlled despite maximal therapy, and/or their glaucoma was progressing despite apparently appropriate treatment, and/or tolerance was poor and ocular surface severely affected. All patients declared having good compliance to treatments.

All patients had a complete glaucoma assessment with ocular and systemic medical history, IOP measurement, gonioscopy, central corneal pachymetry, dilated fundoscopy, and visual field evaluation. The ocular surface was also assessed, including as often as possible the tear breakup time (TBUT), the Oxford score (OXF), an evaluation of conjunctival hyperemia and signs of surface inflammation, and an eyelid examination.

Then all 10 patients underwent different treatments depending on their original treatments and ocular surface status. The main treatments were change in topical antiglaucoma medications to preservative-free equivalents whenever possible, removal of allergenic treatments or those identified or assumed to cause side effects after their introduction, switch to a therapeutic class with similar efficacy but with a better safety profile, treatment of the OSD with preservative-free tear substitutes, lid hygiene, and when necessary doxycycline, cyclosporine A, or nonsteroidal antiinflammatory (NSAID) agents.

All patients were followed for a minimum of 6 months and monitored for IOP, OSD clinical parameters and further need to perform glaucoma surgery.

Comparisons between continuous variables were made using a paired *t*-test and an ANOVA (Excel, Microsoft). $P < 0.05$ was considered statistically significant.

RESULTS

Of the 10 patients evaluated, there were 3 females and 7 males with a mean age of 74.9 ± 8.82 years. Seven (70%) of these patients had already had cataract surgery, 2 had undergone glaucoma filtering surgery and 1 selective laser trabeculoplasty. The mean duration of glaucoma was 16.9 ± 4.41 years and the mean deviation on the Humphrey visual field 24-2 was −11.85 db. At presentation, 9 patients were receiving a prostaglandin analog (90%), 9 had brimonidine (90%), 9 had topical carbonic anhydrase inhibitors (90%), 5 had β-blockers (50%) and 3 patients had oral acetazolamide. Moreover, 6 were on triple therapy, 2 had quadruple therapy, one was receiving 5 different drugs and another was being treated with 6. Table 1 shows the patients' personal information, ocular history, and glaucoma evaluation.

The mean IOP in these patients significantly decreased from 23.75 ± 9.98 mm Hg before OSD treatment to 15.15 ± 4.75 mm Hg (−36.2%; $P = 0.0001$) after 3 months and to 15.45 ± 3.60 mm Hg (−34.9%; $P = 0.01$) after a mean of 11 months (6 to 22). The mean number of IOP-lowering drugs also significantly decreased by almost one drop from 3.7 ± 1.06 to 2.8 ± 0.63 drops after treatment ($P = 0.01$). Four patients had the same number of IOP-lowering medications before and after OSD treatment, and in this group, IOP significantly decreased from 22.87 ± 8.11 mm Hg to 14.5 ± 3.82 mm Hg (−36.6%; $P = 0.01$) after 3 months and to 15.25 ± 3.92 mm Hg (−33.3%; $P = 0.01$) after a mean of 11.5 months (7 to 17). Six patients had fewer IOP-lowering medications after the intervention, with a significant mean IOP decrease from 24.33 ± 11.36 mm Hg to 15.5 ± 5.39 mm Hg (−36.3%; $P = 0.01$) after 3 months and to 15.58 ± 3.55 mm Hg (−35.9%; $P = 0.03$) after a mean of 10.6 months (6 to 22). All patients stopped brimonidine eyedrops, 7 were switched to unpreserved antiglaucoma eyedrops

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TABLE 1. Patient Information, Medical History and Glaucoma Evaluation

Case	Age (y)	Sex	Glaucoma Duration (y)	Humphrey Visual Fields 24-2 (MD)	Ocular History	Medical History	c/d Ratio	CCT (µm)
1	74	Female	15	−1.62/−1.29	None	Eczema Rosacea	0.7/0.6	585/600
2	74	Male	20	−18.92/−14.95	Monophthalmos OD GFS OD	None	0.9/0.8	534/540
3	61	Male	10	−19.82/−16.53	GFS OU 2014 ECCE + IOL OU 2014	High blood pressure	0.6/0.6	485/487
4	67	Male	13	−6.3/−2.3	ECCE+IOL OU 2006 Retinal detachment OD 2010	None	0.8/0.7	533/530
5	78	Female	22	−28.53/−17.96	ECCE+IOL OU	None	0.95 OU	511/517
6	90	Male	20	−14.10/−4.77	ECCE+IOL OU Intolerance for Brimonidine and oral acetazolamide	Kidney stone	0.5 OU	480/485
7	87	Male	15	−7.96/−9.17	PEX ECCE+IOL OU SLT OU	HTA	0.7/0.8	512/515
8	78	Male	20	−11.38/−14.56	None	None	0.7 OU	561/571
9	71	Male	22	−15.37/−10.50	NPG ECCE+IOL OU 2012	Diabetes OSAS Raynaud syndrome	0.9 OU	547/547
10	69	Female	12	−11.77/−9.12	ECCE+IOL+ISTENT OU 2010	High blood pressure	0.9 OU	524/527

c/d ratio indicates cup-to-disc ratio; CCT, central corneal thickness (microns); ECCE+IOL, extracapsular cataract extraction and intraocular lens; GFS, glaucoma filtration surgery; MD, mean deviation; NPG, normal-pressure glaucoma; OSAS, obstructive sleep apnea syndrome; PEX, pseudoexfoliation syndrome; SLT, selective laser trabeculoplasty.

(3 for preservative-free (PF) timolol, 6 for a PF timolol/dorzolamide fixed combination, 6 for PF latanoprost, and 1 for a PF bimatoprost/timolol fixed combination). Three patients had oral acetazolamide before intervention, which was stopped for 2 of them. Otherwise, 3 patients temporarily received oral acetazolamide for 1 month. Finally, 3 patients had dual therapy, 6 triple therapy and only 1 quadruple therapy (Figs. 1, 2).

All our observations also showed ocular surface improvement. The Oxford score significantly decreased from a mean 1.7 ± 0.67 before treatment to 0.4 ± 0.51 (−76.5%; $P < 0.001$) and conjunctival hyperemia significantly decreased from a mean 2.0 ± 0.82 before treatment to 0.65 ± 0.41 (−67.5%; $P = 0.0002$). All patients received preservative-free artificial tears and performed eyelid care. Furthermore, 5 patients had topical PF indomethacin, 1 cyclosporin A 0.05% BID, 1 received pulse azithromycin eyedrop therapy for MGD and three were treated with oral doxycycline 100 mg per day until inflammation decreased. Table 2 shows the ocular surface exams, treatments at presentation, variation in IOP during the treatment and treatment strategies to improve the ocular surface.

Since their IOP remained elevated, although improved compared to the inflammatory state, 2 patients finally underwent successful filtration surgery with a follow-up of 6 months.

DISCUSSION

In this case series, the IOP of patients with medically uncontrolled glaucoma was linked to the inflammatory status of the ocular surface. Its improvement with specific treatments, by removing preservatives and medicines suspected of causing allergy or intolerance, led to a paradoxical decrease in IOP or at least to a stabilization of IOP despite the removal of one or more treatments that were active but poorly tolerated.

This analysis supports the hypothesis already raised by Baudouin et al[11] and Batra et al[20] that inflammation of the ocular surface is associated with an increase in IOP and that the treatment of this inflammation has a beneficial action on IOP. Local inflammation may be associated with an inflammatory and/or toxic trabecular disease, which may be partially or totally resolved after the management of the ocular surface and by stopping or reducing all potentially toxic compounds. It can also be assumed that for those patients with uncontrolled glaucoma, the accumulation of eye drops over the years caused a major inflammation of the

FIGURE 1. Slit-lamp examination of right eye of patient number 8 before OSD treatment: high inflammation with conjunctival hyperemia and blepharitis, and IOP was 35 mm Hg.

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FIGURE 2. Slit-lamp examination of the right eye of patient number 8, 6 months after beginning OSD treatment: Substantial ocular surface improvement was observed with reduced inflammation, and IOP was 19 mm Hg.

ocular surface that may have extended to deeper tissues and affected trabecular filtration.

The prevalence of OSD is greatly increased in glaucoma patients, reaching 50% of patients in some studies.[3–7] Several factors are responsible for ocular surface inflammation including preservatives, in particular BAK, which causes ocular dryness as well as allergic and inflammatory reactions.[14,22] BAK has proapoptotic effects and causes oxidative stress similar to those found in the TM of glaucoma patients with accelerated aging, trabecular cell death and extracellular matrix accumulation.[11] Although the question of the presence of BAK in deep structures has long been debated and not fully recognized, BAK is a lipophilic molecule that accumulates deeply. Measurable levels of BAK can be found in the conjunctiva up to 1 week after administration of a single drop.[23] BAK has been retrieved using the mass spectrometry imaging technique in deep structures such as the trabecula or the lens in rabbit eyes treated with BAK for several months,[21] which was also confirmed in human tissues.[24] At higher concentrations, subconjunctival injection of BAK is capable of causing trabecular cell death, inflammatory infiltration, and increased IOP.[11]

In addition to preservatives, brimonidine also appears to have played an important role in this group of patients. Except for one patient who was already known to be intolerant to the drug and for whom the treatment had been stopped a few years before, all our patients were treated with this drug. Brimonidine is an α-2 adrenergic receptor agonist that decreases aqueous humor secretion and enhances aqueous humor resorption by the uveoscleral channels. In 9 patients, it participated by its allergenic and/or proinflammatory properties (associated with preservation with BAK) to considerably worsen the inflammation of the ocular surface. This deleterious effect has already been shown in other studies.[25,26] It may not be the only mechanism that contributes to the IOP rise, however. As we observed with one patient, several cases of granulomatous uveitis caused by brimonidine have been reported, with an IOP elevation of at least 5 mm Hg in 42% of cases in the series of 17 patients reported by Beltz et al.[27] In these uveitic phenomena, Byles et al[28] described the possible prolongation in the anterior chamber of the ocular surface inflammation caused by the allergic reaction. In addition, Mushtaq et al[29] described a case of iatrogenic hypertension with no evidence of associated uveitis but with a highly impaired ocular surface, ameliorated when brimonidine was stopped and an increase in IOP when brimonidine was reintroduced. Beyond the alteration of the ocular surface, we suggest that brimonidine could play an independent role by causing an isolated inflammation of the trabecula without necessarily presenting the symptomatology of uveitis.

Other factors helped us improve the ocular surface in this study. We treated MGD, which is present in 80% of glaucoma patients,[30] with eyelid care twice a day. In some cases, oral doxycycline reduced surface inflammation by helping treat associated blepharitis.[31] To treat dry eye disease, eyes were thereafter lubricated with unpreserved eye drops, in accordance with the recommendations of the Dry Eye WorkShop II for iatrogenic dry eye.[32]

Finally, it was also necessary for some patients to use anti-inflammatory drugs to break the vicious circle of ocular inflammation and dry eye syndrome. For instance, we used topical PF NSAIDs for 5 patients and topical cyclosporin A 0.05% for one patient. A study by Saini et al[33] showed the effectiveness of cyclosporin A for the treatment of dryness in glaucoma patients, with an enhancement in all ocular surface parameters. The use of topical corticosteroids should be avoided, however, because of the risk of corticosteroid-induced hypertension.

The transient administration of acetazolamide, as for 3 of our patients, temporarily decreased the toxic drug intoxication on the ocular surface and efficiently restored a healthy surface, in particular in severe ocular hypertension in which the removal of a hypotensive treatment is less stressful if associated with acetazolamide treatment. In all cases, acetazolamide was stopped after a few weeks without a further rise in IOP.

We can propose several hypotheses to explain this association between surface inflammation and uncontrolled IOP, such as the diffusion in deep tissues of inflammatory mediators present at the surface, the direct toxicity of drugs to the trabecula, but other hypotheses can be postulated. Superficial ocular inflammation could cause chronic inflammatory vasodilation of conjunctival vessels, which may increase resistance to the aqueous humor outflow through the episcleral venous network. It can also be hypothesized that this same vasodilation phenomenon can induce faster washout of eyedrops, rendering them less effective. Furthermore, although all patients reported good compliance, it cannot be ruled out that the initiation of a new treatment was accompanied by improved compliance and therefore lower IOP. However, the initial inflammatory state of the ocular surface was evidence of relatively reliable compliance. Finally, the change in treatments may have been accompanied by a decrease in the dilution phenomenon associated with multiple preinterventional treatments and excessive tearing related to irritation of the ocular surface. The main limit of the study is related to its retrospective design, with a restricted patient inclusion and a 6-month follow-up period. In addition, selection of cases induces a selection bias, which limits the generalization of the results. However, the follow-up period was at least 10 months for 5 patients and they still showed stable improvement over time. A larger prospective study on a larger scale would highlight the actual frequency of such scarce situations and the sustainability of these results over time.

In addition, the management of the ocular surface did not lead only to beneficial effects on IOP. It also had a positive impact on the tolerance of treatments by the patients and on their

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TABLE 2. Patients' Ocular Surface Exams, Treatments at Presentation, Variation of IOP During the Treatment and Interventions Done to Improve the Ocular Surface

Case	IOP at Presentation	Anterior Segment at Presentation	Treatment at Presentation	Intervention	Anterior Segment After Intervention	IOP M (mo) After Intervention
1	22/25	Hyperemia 1+	Bimatoprost 0.1 OD QD	Stop Bimatoprost 0.1	No hyperemia	M2 17/17
		OXF 2	Brimonidine +Dorzolamide BID	Stop Brimonidine	OXF 0	M7 18/17
		Blepharitis		Timolol PF BID	Reduced eyelid inflammation	M17 17/17
				Latanoprost PF QD		
				Dorzolamide BID		
				Lid hygiene		
				Lubricants QID		
2	14/14	Hyperemia 3+	Bimatoprost+Timolol QD	Stop Bimatoprost +Timolol	Hyperemia 1+	M3 14/13
		OXF 1	Preserved Timolol +Dorzolamide BID	Switch for Timolol +Dorzolamide PF BID	OXF 0	M6 15/13
		Flare 1+	Brimonidine BID	Stop Brimonidine	Flare 0	M18 11/12
			Acetazolamide 250 mg ½×3	Progressive stop of Acetazolamide 250 mg		M22 10/12
				Latanoprost PF QD		
				Indomethacin 0.1 PF BID		
				Lubricants PF QID		
				Lid hygiene		
3	21/13	Hyperemia 2+	Travoprost+Timolol OD QD	Travoprost+Timolol OD QD	Hyperemia 0.5+	M3 10/10
		OXF 2	Dorzolamide BID	Dorzolamide BID	OXF 1	M4 28/10
		Blepharitis	Brimonidine BID	Stop Brimonidine	Flare 0	M10 27/10 (GFS OD indicated)
		Flare 1+		Azithromycin QD 3 days every 15 days		M11 16/13
		No filtration bleb visible		Doxycycline 50 mg QD		
				Lid hygiene		
				Lubricants PF QID		
4	22/24	Hyperemia 3+	Brimonidine BID	Stop Brimonidine	Hyperemia 1+	M4 16/19
		OXF 2	Preserved Timolol +Dorzolamide BID	Switch for Timolol +Dorzolamide PF BID	OXF 0	M6 18/16
		MGD		Cyclosporin A 0.05% BID	TBUT 6 s	M7 14/15
		TBUT 2 s		Lubricants PF QID	Decreased neovascularization	M10 16/17
		Corneal neovascularization 360°		Lid hygiene		
				Indomethacin 0.1 PF BID		
				Acetazolamide 250 mg ½×3 for 1 month		
5	13/12	Hyperemia 2+	Brimonidine BID	Stop Brimonidine	Hyperemia 1+	M3 10/9
		OXF 2	Dorzolamide BID	Switch for Timolol +Dorzolamide PF BID	OXF 1	M8 9/9
		MGD	Latanoprost QD	Latanoprost PF QD	Decrease of neovascularization and RDP	M14 10/9
		Corneal Neovascularization 360°		Acetazolamide ¼×3 for 1 month		
		RDP		Doxycycline 50 mg QD		
				Lubricants PF QID		
				Lid hygiene		
6	34/31	Hyperemia 1+	Carteolol 2% QD	Stop Carteolol 2%	Hyperemia 0.5+	M1 19/16
		OXF 1	Bimatoprost+Timolol QD	Switch for Bimatoprost +Timolol PF QD	OXF 0	M4 12/14
		Blepharitis		Timolol+Dorzolamide PF QD	Decreased eyelid redness	M5 19/15

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TABLE 2. (*continued*)

Case	IOP at Presentation	Anterior Segment at Presentation	Treatment at Presentation	Intervention	Anterior Segment After Intervention	IOP M (mo) After Intervention
		Rosacea		Lid hygiene Doxycycline 50 mg QD Lubricants PF QID Indomethacin PF BID		M7 19/14 M8 17/14
7	40/45	Hyperemia 2+ OXF 1	Travoprost QD Brimonidine BID	Stop Travoprost Stop Brimonidine +Dorzolamide	Hyperemia 1+ OXF 0	M2 23/25 M3 GFS
		Blepharitis Flare 1+ Corneal edema RDP	Dorzolamide BID	Timolol PF QD Latanoprost PF QD Lubricants PF QID Lid hygiene Acetazolamide 250 mg ½×3 for 2 weeks	Flare 0 Decreased corneal edema	M4 9/10 M6 13/12
8	35/34	Hyperemia 3+ OXF 3 Blepharitis	Brimonidine BID Pilocarpine 1% BID Latanoprost QD	Stop Brimonidine Stop Pilocarpine Switch for Latanoprost PF QD	Hyperemia 1+ OXF 1 Flare 0	M3 19/18 M6 19/19 M8 21/19
		Flare 1+	Dexamethasone +Neomycin BID Timolol+Dorzolamide BID Acetazolamide 250 mg ½×3	Stop Dexamethasone +Neomycin Switch for Timolol +Dorzolamide PF BID Progressive stop of Acetazolamide 250 mg Lid hygiene Lubricants PF QID Indomethacin PF BID		
9	13/17	Hyperemia 2+ OXF 2 Blepharitis	Brimonidine BID Dorzolamide BID Bimatoprost 0.1 QD	Stop Brimonidine Dorzolamide BID Switch for Timolol PF 0.5 XE QD	Hyperemia 0.5+ OXF 1	M1 8/10 M3 9/10 M8 12/13
		Rosacea	Indomethacin PF BID	Lubricants PF QID Lid hygiene		
10	28/18	Hyperemia 1+	Latanoprost QD	Switch for Latanoprost PF QD	No hyperemia	M1 20/17
		OXF 1	Brimonidine +Dorzolamide BID	Stop Brimonidine	OXF 0	M3 19/18
		Blepharitis	Acetazolamide 250 mg ½×3	Switch for Timolol +Dorzolamide PF BID Acetazolamide 250 mg ½×3 Indomethacin PF BID Lubricants PF QID Lid hygiene		M7 20/18

GFS indicates glaucoma filtration surgery; IOP, intraocular pressure; MGD, meibomian gland dysfunction; OXF, Oxford score; PF, preservative-free; RDP, retrodescemetic precipitates; TBUT, tear break-up time.

quality of life, thus participating in better adherence to the treatment and glaucoma stability.[34] Moreover, as was done for 2 patients with high IOP despite maximum tolerated treatment, glaucoma filtering surgery was successfully performed on a cleaned, noninflammatory eye surface. As early as 1994, Broadway et al[35] showed the negative impact of an inflammatory conjunctiva on trabeculectomy results, which promoted early fibrosis of the filtering bleb. Management of the ocular surface may also improve postsurgical filtration. A recent study by Meziani et al[36] demonstrated a negative correlation between the accumulation of preoperative preservatives and the postoperative filtration rate through the study of the density of the conjunctival microcysts present on the surface of the filtering bleb, as demonstrated by en-face OCT. Boimer et al[37] also evidenced a treatment-dependent surgical failure rate correlated with the amount of preoperative BAK-containing drops in a retrospective study, the PESO study.

To try to estimate the number of patients presenting with such OSD influence, we looked at the number of patients referred for glaucoma surgery in the period: of a total of 97, 89 underwent surgery and 8 avoided surgery after taking care of their ocular surface. Therefore, we cannot draw conclusions that 8.2% of patients with severe glaucoma could avoid surgery just by adaptation of the medical treatment. Overall, these data encourage us to further consider the ocular surface of our patients in medical therapy failure before performing filtrating surgery. The result will be a reduction in ocular inflammation, sometimes with an improvement in IOP, making it possible to postpone surgery or at least prepare the conjunctiva to reduce local inflammation for more effective

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filtration surgery. This strategy is consistent with treating preoperatively with topical fluorometholone to reduce inflammation, as proposed >2 decades ago by Broadway et al,[38] which could be an alternative.

This study showed that the treatment of ocular surface irritation and inflammation may improve IOP control in patients with medically uncontrolled glaucoma associated with OSD. Taking care of the ocular surface also means taking care of the trabecular meshwork and therefore IOP. We consider that the management of these three entities should no longer be dissociated. Today, a subtractive and conservative approach to the ocular surface is therefore sometimes more suitable than an additive and iatrogenic approach.

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