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The impact of latanoprost glaucoma eyedrops with and without preservatives on the ocular surface parameters – a case series report

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HIGHLIGHTS

It is very important to minimize the negative impact of chronic glaucoma topical therapy on the ocular suface. This may be achieved by introducing preservative-free latanoprost in first line primary open angle glaucoma treatment.

ABSTRACT

Background: Preservatives and additives commonly found in ophthalmic solutions can aggravate the symptoms of dry eye disease, a condition that already affects a large percentage of the global population. These additives are also frequently present in topical medications for glaucoma, another widespread disorder impacting several millions of individuals worldwide being on a persistent anti-glaucoma therapy. With the continued aging of populations, the prevalence of both diseases is expected to rise.

Methods: Four patients diagnosed with glaucoma, who were on topical latanoprost monotherapy were switched from the preservative prescription to a preservative-free analogue. Lubricating eye drops were withdrawn 4 weeks prior and restrained from use during the 3 months observation period. Tear break-up time, interferometry, conjunctival redness, tear film osmometry, along with a dry eye disease questionnaire were performed at each timepoint to assess changes on the ocular surface condition. Standard ophthalmic examination was also performed.

Results: Conjunctival redness remained constant at all timepoints. Tear film osmolarity decreased in all patients and so did the Ocular Surface Disease Index. As for the tear break-up time and interferometry, tendencies of the results were inconclusive. Best corrected visual acuity and intraocular pressure remained stable throughout the study.

Conclusions: Preservative-free topical glaucoma therapies appear to be better tolerated and impose less burden on the ocular surface. Such formulations should be prioritized for glaucoma patients, who often require life-long treatment. Given the chronic nature of dry eye disease and the absence of regenerative options for the lacrimal and meibomian glands, preventive strategies are of critical importance.

Key words: latanoprost, osmometry, tear film, OSDI, McMonnies scale, preservatives

INTRODUCTION

The ocular surface represents a complex anatomical and functional unit, composed of the cornea, conjunctiva, tear film, meibomian glands, lacrimal glands and eyelids. Together, these structures maintain a stable refractive interface, providing a barrier against pathogens and preserving visual quality. Disruption of this homeostatic balance results in ocular surface disease (OSD), a broad term encompassing various pathological conditions such as dry eye disease (DED), allergic conjunctivitis, limbal stem cell deficiency, ocular surface inflammatory disorders, and sometimes a reflection of systemic or iatrogenic factors [1]. The complexity of molecular, immunological, and environmental factors are proportional to the struggle faced by healthcare professionals to provide solid long-lasting results of OSD treatment [2]. The aim of this study was to evaluate certain eye surface parameters as: non-invasive tear break-up time (NITBUT), interferometry, conjunctival redness according to the McMonnies scale, osmometry and the Ocular Surface Disease Index (OSDI) in a case series of glaucoma patients after replacing BAK-preserved latanoprost eye drops with preservative free (PF) latanoprost. Scientific studies show that avoiding preservatives in glaucoma eye drops in persistent therapy may have a beneficial effect on the eye, increase local tolerability of the treatment and improve the patient's quality of life.

METHODS

The patients from the glaucoma outpatient clinic of the Military Institute of Aviation Medicine in Warsaw being on topical therapy with latanoprost with preservatives for a minimum of 24 months were included in the trial. They were under regular, biannual follow-up, examined at a fully dilated eye fundus, OCT measurements with ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL) analysis, standard automated perimetry 30-2 threshold scanning for progression that would require escalating medical interventions.

Criteria of exclusion concerned administering other glaucoma eye drops (with the exception of lubricating eye drops), intraocular surgical/laser interventions 12 months prior or severe OSD. Patients were instructed to abstain (if taken) from instilling lubricating eye drops 4 weeks preceding the first measurements and if tolerated, continue without until the end of the study. In case of worsening of symptoms of the ocular surface, patients were invited to be examined additionally and if needed – they would be returned to lubricating drops/gels/ointments or prescribed antibiotics/antiseptics adequately to the diagnosis. Patients were also instructed they could retrieve voluntarily from the trial at any point and go back to their original latanoprost with preservatives treatment.

On the first visit, patients were tested on best corrected visual acuity (BCVA) and intraocular pressure (IOP). They filled in the FAST (fast assessment of ocular surface trouble) and OSDI (ocular surface disease index) questionnaires with help of the investigators. Then, using the IDRA (SBM Sistemi, Italy) device, they were assessed on NITBUT (fig. 1), interferometry (fig. 2) and redness of the ocular surface. NITBUT and interferometry measurements were repeated a few times in a row until three correct measurements were obtained. The amounts were calculated automatically and listed in the form of diagrams as presented (fig. 3). Lastly, the tear film osmolarity was measured by the TearLab (Bausch & Lomb, USA) osmometer (fig. 4).

FIGURE 1

Non-invasive tear break-up time.

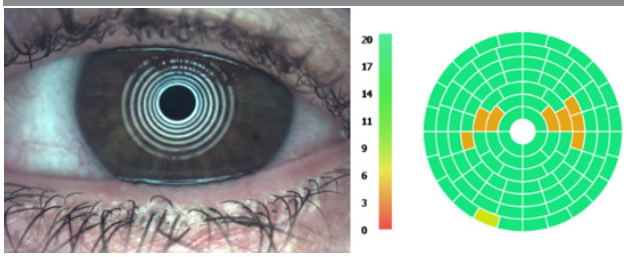


FIGURE 2

Interferometry.

After the first visit the patient's treatment was replaced with preservative-free latanoprost solution (Monoprost®, Thea). This topical medication is free both from BAK and from additional phosphates, which also may have a damaging impact on the ocular surface. This is the only BAK-free and phosphate-free latanoprost formulation accessible on the market. All tests were performed 3 times: before switching

FIGURE 3

Measurements shown on diagrams – separate and cumulative. Green indicates correct results, yellow shows borderline values and red stands for abnormal.

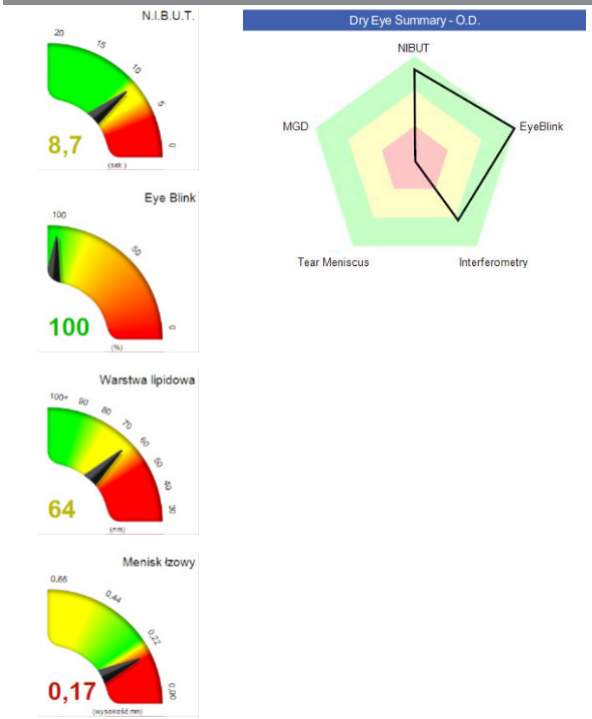
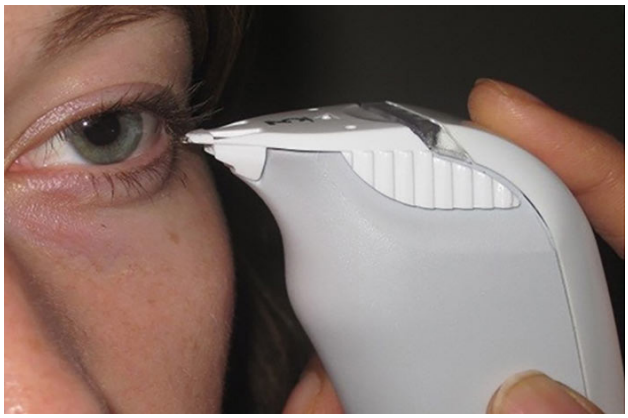


FIGURE 4

Osmometry measurement (source: https://www.opticianonline.net/cpd-archive/4750/).



the eye drops, 1 month after replacing the drug to preservative-free and the last time after another 2 months.

Out of 9 patients who fulfilled the criteria described above, 5 patients were recruited for the study. One patient was excluded after the second visit due to DED aggravation, probably resulting from no lubrication for several weeks. Eventually, four patients managed to conclude the study upon adhering to the protocol.

RESULTS

Results have been listed in table 1. The BCVA and IOP measurements remained stable throughout the whole observation period. Ocular redness assessed with the McMonnies scale didn't change at the control timepoints. Tear film osmolarity decreased in all patients after discontinuing latanoprost with preservatives, even in the 5th case with OSD aggravation. OSDI scores improved in all 4 patients who finished the entire study – they all indicated increased comfort of the ocular surface and did not feel the need to go back to lubricating eye drops. NIBUT showed a tendency to decrease in time, interferometry on the other hand did not provide conclusive results.

DISCUSSION

Unsurprisingly, the OSDI index improved in all patients. The fact that patients could spend weeks without need for lubricating eye drops, without a negative impact on the ocular surface, was what they were most content about. Using the McMonnies scale, we wanted to select patients with mild to moderate OSD, with a higher likelihood of compliance with the study protocol requiring not taking any lubricating drops for 4 months. Some unfavorable interferometry results overtime in our patients may be explained by the fact that patients discontinued using moisturizing drops for the entire study period. Osmolarity of the tear film, though generally improving, shows an increase of values at 3 months in the last two cases, suggesting the beneficial effect of discontinuing preservatives but also multi-year damage from previous drops. In addition, tear film osmolarity is not only influenced by local homeostasis, since cytokines from the bloodstream are also expressed in tears being essentially a blood plasma filtrate [3, 4]. Aside from the lack of preservatives, the instillation of single-dose containers minimized the possibility of contaminating the tip [5], which delimits another risk factor irritating the ocular surface.

Limitations of this study were a small group of patients and a relatively short period of observation, although this was a pilot study and expansion of the protocol regarding multimodal diagnostics of ocular surface disease is currently being implemented based on these preliminary findings. The number of patients taking latanoprost with preservatives as the only anti-glaucoma agent was very limited, since adhering to the guidelines of the European Glaucoma Society (EGS) [6], the majority of patients in the database were routinely prescribed the analogue without preservatives to prevent ocular surface disease. Although the group examined at our clinic is too small to draw conclusions, the findings align very well with reports from larger studies.

Preservatives present in ophthalmic eye drops have a negative effect on the ocular surface and fortunately this fact has

TABLE 1

Measurements taken prior to drug switching, 1 month and 3 months on new treatment, in the right and left eyes, respectively.

	BCVA	GAT	NITBUT (s)	Interferometry (nm)	Bulbar redness (McMonnies scale)	Osmometry	OSDI (mOsm/l)
Case 1	0.6, 0.6	17, 18	10.1, 8.4	78, 67	1, 1	297, 303	13.6
	0.6, 0.6	16, 18	10.5, 7.4	90, 89	1, 1	290, 291	2.3
	0.6, 0.6	17, 17	8.0, 8.5	92, 90	1, 1	281, 286	2.3
Case 2	1.0, 0.6	12, 11	17.9, 18.4	86, 100	2, 2	288, 290	50
	1.0, 0.6	11, 11	14.6, 15.0	90, 78	2, 2	279, 277	54.1
	1.0, 0.6	11, 12	8.2, 8.4	84, 82	2, 2	278, 254	37.5
Case 3	1.0, 1.0	16, 17	14.9, 10.4	78, 100	2, 2	296, 286	20.8
	1.0, 1.0	16, 17	10.3, 9.5	100, 100	2, 2	293, 276	20.8
	1.0, 1.0	15, 15	12.3, 10.1	95, 96	2, 2	308, 276	12.5
Case 4	0.9, 0.9	15, 15	14.2, 13.0	87, 87	1, 1	330, 308	55.6
	0.9, 0.9	15, 16	12.8, 12.4	80, 84	1, 1	284, 279	46.9
	0.9, 0.9	15, 15	12.5, 9.4	100, 86	1, 1	295, 288	33.3

BCVA – best corrected visual acuity; GAT – Goldmann applanation tonometry; OSDI – Ocular Surface Disease Index; NITBUT – non-invasive tear break-up time.

been getting stronger attention in the last few years [7–9]. This is particularly relevant to glaucoma patients, which have been shown to experience dry eye symptoms not only resulting from pharmacotherapy, but also worsening observed after surgical treatment such as the widely performed trabeculectomy, correlated with increased tear film osmolarity [10]. Inflammation upregulation is suspected to be implicated in the pathophysiology of glaucoma [11]. Importantly, the use of BAK-preserved in latanoprost eye drops can worsen this process since switching to preservative-free equivalents demonstrated a reduction of inflammatory biomarkers [12].

OSD is an inherent part of glaucoma patients in ophthalmic practice [13–15]. Hence preservatives should be avoided in all drug formulations administered to patients, to prevent inflammation leading to blepharitis, eye irritation and redness, globally reducing the quality of life [16, 17]. Discomfort concomitant to glaucoma pharmacotherapy may lead to decreased patient compliance, adherence to treatment and persistence in keeping with medical recommendations [18, 19]. Awareness should be drawn to the fact that preservatives contribute to meibomian glands damage due to cytotoxicity, which is currently irreversible and hugely contributes to the already prevalent OSD in non-glaucomatous patients [20, 21].

Diagnostic and therapeutic advances continue to refine patient management, but preventive strategies and individualized treatment remain essential. Deeper investigations of ocular surface biology and novel technological approaches hold promise for more durable solutions to this prevalent condition.

CONCLUSION

Preservative-free latanoprost without BAK and phosphates is a well-tolerated topical medication in primary open angle glaucoma patients on persistent therapy. Switching glaucoma eye drops to preservative-free and additive-free analogues should be always considered as it has beneficial influence on ocular surface parameters, especially on the very important tear film osmolarity. This change of medications is also reflected in improvement of OSDI which determines well-being and quality of life of glaucoma patients being on a chronic topical therapy.

Figures: from authors' own materials.

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Grzegorz Rotuski – conception and design of the study or data acquisition or data analysis and interpretation, critical corrections.
Marta Dubisz – conception and design of the study or data acquisition or data analysis and interpretation, critical corrections.
Magdalena Cichowska – patient recruitment.
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