ORIGINAL ARTICLE

Comparison of BAK free Travatan with BAK Preserved Xalatan in Terms of Ocular Surface Disease in Glaucoma patients in our population

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ABSTRACT

Objective: To assess symptoms of ocular surface disease (OSD) in patients treated with a BAK-preserved Xalatan (Latanoprost) to control their intraocular pressure, who either continued that medication or switched to a BAK-free therapy (BAK free Travatan),as well as patients newly placed on BAK free Travatan in our population.

Patients & methods: A prospective observational study was conducted at CMH Lahore. Eighty (80) cases 20 years of age or older, with open-angle glaucoma or ocular hypertension were consecutively recruited for the study. Baseline records were documented after taking written informed consent. Every patient completed an Ocular Surface Disease Index questionnaire and underwent evaluation by Schirmer test, corneal and conjunctival fluorescein staining, and tear break-up time. Cases were divided into two groups (A, B). Group A (40 patients) includes those patients who were already using latanoprost (Xalatan) and those who were put on Xalatan monotherapy for the first time. In group B (40 patients) were those who were on Xalatan therapy but now switched to BAK free Travatan and those who were placed on BAK free Travatan antiglaucoma therapy for the first time. Ocular symptoms by OSDI scores were assessed again after 4, 8 and 12 weeks. The patients were queried for ocular symptoms, and ocular signs were assessed by using tear break-up time, Schirmer's test, fluorescein staining and evaluation of conjunctival hyperemia.

Results: The study showed that the symptoms of ocular surface disease were significantly lower in the BAK-free travatan 0.004% group (35% of group) than in the BAK-preserved latanoprost (Xalatan)0.005% group (62.5%% of group) and a significantly larger percentage showed normal OSDI scores in the BAK-free travatan 0.004% group than in the BAK preserved latanoprost 0.005% group. Moreover patients on BAK-preserved latanoprost 0.005% who were switched to BAK-free travatan showed a better OSDI score after 12 weeks. In BAK preserved Latanoprost Group A (67.5%) had abnormal fluorescein staining of cornea, (77.5%) had conjunctival hyperaemia and abnormal Schirmer's test was present in (65%). In BAK free Travatan group B 45%, 52.5%, 37.5% respectively had abnormal results which were significantly less than latanoprost group. The tear break-up time was also better in Travatan group 7.6±4.9 seconds compared to latanoprost group 4.2±2.5 seconds.

Conclusion: Patients placed on BAK free Travatan showed less symptoms of ocular surface disease as compared to those placed on BAK preserved Latanoprost (Xalatan). Moreover Switching from BAK-preserved latanoprost 0.005% to BAK-free travatan 0.004% yielded significant improvements in symptoms of OSD in patients with glaucoma. Preservative-free travatan treatment resulted in increased patient satisfaction, drop comfort and vision related quality of life in terms of ocular surface disease.

Key words: Ocular surface disease, Travatan, Latanoprost, Glaucoma, OSDI, preservative, Xalatan

INTRODUCTION

Ocular surface disease (OSD) is a condition that results from inadequate tear film production and/or increased tear evaporation, tear film degradation resulting in poor quality of tears as well as damage to the ocular surface.[1]Now a days the large number of available topical medicines to control intraocular pressure (IOP), like Xalatan (Latanoprost) 0.005% are preserved with benzalkonium chloride (BAK)[2]. Individuals with repeated long term exposure to BAK-preserved anti glaucoma medications suffered from variety of ocular symptoms with varying severity, including burning/stinging, itching, irritation, tearing, photophobia, foreign body sensation, grittiness, redness, blurred vision and dry eye sensation[3,4].

Topical anti glaucoma drugs trigger or exacerbate ocular surface disease by inducing ocular surface damage, especially those containing benzalkonium chloride (BAK) preservative[3,5]. In humans, adverse effects of chronic exposure to BAK-preserved topical anti glaucoma medications on the ocular surface, includes instability of the tear film, reduced density of superficial epithelial cells, disruption of corneal epithelial barrier function, and conjunctival inflammation[6-8]. Ocular surface disease is prevalent in approximately 15% of the general elderly population[9]. However it has been reported to occur in 48% to 59% of patients who were on anti glaucoma therapy[10,11].

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Previous studies have documented the detergent effect of preservatives containing anti glaucoma therapy on the lipid layer of the tear film and decrease in the density of goblet cells in the conjunctival epithelium[12,13]. In animal studies, BAK free Travatan 0.004% did not affect goblet cell numbers or corneal epithelial cells, whereas back containing Xalatan 0.005% was shown to cause loss of goblet cells and pathologic changes in the corneal epithelium[14-16]. It was shown in literature that adverse reactions induced by BAK-preserved IOP lowering drugs may be reversible in glaucoma patients who are switched to BAK-free medications[4].

PATIENTS AND METHODS

A prospective observational study was conducted at CMH Lahore.80 cases 20 years of age or older, with open-angle glaucoma or ocular hypertension were consecutively recruited for the study. All participating patients signed a written informed consent form. Patients with a history of any lid/conjunctival surgery or ocular trauma; pterygium, ocular laser surgery, ocular allergy; corneal disease, progressive retinal or optic nerve disease, use of cyclosporine, steroids, topical ocular nonsteroidal anti-inflammatory drugs, any other anti glaucoma drugs or punctal plugs were excluded from the study.

Cases were divided into two groups (A, B). Group A (40 patients) includes those patients who were already using latanoprost (Xalatan) and those who were put on Xalatan monotherapy for the first time. In group B (40 patients) were those who were on Xalatan therapy but now switched to BAK free Travatan and those who were placed on BAK free Travatan antiglaucoma therapy for the first time.

Ocular examination was carried out, consisting of detailed history, visual acuity by snellen charts, slit-lamp anterior segment examination, tonometry and a dilated fundus examination. Baseline records of ocular surface disease were documented by using the Ocular Surface Disease Index (OSDI) questionnaire. The patients were questioned for ocular symptoms like burning, stinging, itching, irritation, tearing, photophobia, foreign body sensation, grittiness, redness, blurred vision/poor and dry eye sensation, any problem with reading, driving, working with computer, watching TV, any uncomfortable eyes in windy conditions, in areas of low humidity and areas that are air conditioned. The ocular signs were assessed by using tear break-up time, Schirmer's test, corneal fluorescein staining and evaluation of conjunctival hyperemia and blepharitis.

Follow up visits were scheduled at 4, 8 and 12 weeks. At each visit medical history and detailed ocular examination was repeated. Ocular symptoms were assessed by OSDI questionnaire form and ocular signs were reassessed by using tear break-up time, Schirmer's test, corneal fluorescein staining and evaluation of conjunctival hyperemia and blepharitis.

RESULTS

Eighty confirmed patients with open-angle glaucoma or ocular hypertension were included in the study. Patient age ranges from 20 to 75 years with mean value of 56 years. There were 52 (65%) males and 28 (35%) females (Table 1). Correctable visual acuity ranges from 6/6 to 6/18.

Table 1: Socio demographic profile of subjects

Sex	Frequency	Percentage
Male	52	65.0
Female	28	35.0

The study showed that significantly larger percentage on BAK preserved latanoprost 0.005% (Group A) showed abnormal OSDI score (62.5%) where as OSDI score is abnormal in only 35% of patients in BAK free Travatan (Group B). The study also indicated that greater percentage improved to better OSDI scores in the BAK-free travatan 0.004% group (65%) than in the BAK preserved latanoprost 0.005% group (37.5%) Table 2.

Abnormal Schirmer's test was observed in 65% of patients on BAK preserved latanoprost (Xalatan) and 37.5% of patients on BAK free Travatan. Corneal fluorescein staining was also significantly higher 67.5% in BAK containing latanoprost (Group A) compared with BAK free Travatan (Group B) 45%. More conjunctival hyperemia 77.5% was noticed in latanoprost group compared to BAK free Travatan group 52.5%. The tear break-up time was also better in Travatan group 7.6+/- 4.9 seconds compared to latanoprost group 4.2 +/- 2.5 seconds Table 2.

Table 2: Effect of BAK preserved and BAK free drops on ocular surface after 12 weeks

ocular surface disease	BAK preserved latanoprost 0.005% Group A	BAK-free Travatan 0.004% Group B
%of patients with abnormal OSDI score	25(40) 62.5%	14(40) 35%
% of patients with normal OSDI score	15(40) 37.5%	26(40) 65%
Abnormal Schirmer's test	26(40) 65%	15(40)37.5%
corneal fluorescein staining	27(40) 67.5%	18(40)45%
conjunctival hyperemia	31(40) 77.5%	21(40) 52.5%
tear break-up time	4.2 +/- 2.5 sec	7.6 +/- 4.9 sec

Moreover ocular symptoms like burning, stinging, itching, irritation, tearing, photophobia, foreign body sensation, grittiness, redness, blurred vision and dry eye sensation was found to be higher in BAK preserved Xalatan(latanoprost)group A compared to BAK free Travatan group B after 12 weeks of treatment as shown in Table 3.

Table 3: %age of Patient experiencing symptoms in BAK preserved and BAK free group after 12 weeks

Symptoms experienced by patients	**Group A n=40**	**Group B n=40**
	BAK-preserved latanoprost 0.005%	**BAK-free Travatan 0.004%**
irritation/burning/ stinging	(24)60%	(16)40%
Itching	(19)47.5%	(17)42.5%
Foreign body sensation	(21)52.5%	(15)37.5%
Tearing	(22)55%	(21)52.5%
Dry eye sensation	(27)67.5%	(23)57.5%
Blurred vision	(18)45%	(14)35%

DISCUSSION

Glaucoma affects an increasing number of populations worldwide and is the second leading cause of blindness. The aim of antiglaucoma therapy is to maintain a patient's visual function and quality of life. Prostaglandin analogues are first-line topical antiglaucoma therapy. Most of them like Xalatan (Latanoprost) 0.005% are preserved with benzalkonium chloride (BAK)[2]. Preservatives are added to ophthalmic products in order to increase their shelf life and decrease their risk of contamination.[17]Long-term instillation of preserved ophthalmic products may result in ocular surface damage caused by the preservative[18]. BAK is the most widely used preservative in ophthalmic preparations due to its broad spectrum of antimicrobial efficacy[19]. However, BAK has been shown to induce toxic effects on the cornea, conjunctiva and ocular tissues[20,21]. The damaging action of BAK is exerted by a direct cytotoxic mechanism. These toxic effects are dose dependent and are likely to be aggravated after repeated long term use of BAK-containing eye preparations for the treatment of such diseases as dry eye and glaucoma[22].

Preservative-free preparations (like BAK free Travatan) are likely to reduce such adverse effects and therefore improve patient compliance and quality of work. In our study symptoms and signs of ocular surface disease were higher (62.5%) among patients who were using BAK containing latanoprost (xalatan) topical treatment as assessed by OSDI questionnaire compared to group B patients (35%) who were put on BAK free Travatan anti glaucoma therapy. Symptoms of ocular discomfort including irritation, burning, stinging, itching, foreign body sensation, blurred vision and dry eye sensation were also greater in group A using latanoprost (xalatan) compared with group B on BAK free Travatan (Table 3).

We also found in our study that use of BAK containing eye drops like latanoprost was associated with a higher prevalence of abnormal results on tear break-up time, Schirmer's test, corneal fluorescein staining and conjunctival hyperemia indicating the presence of ocular surface disease (OSD) compared to using BAK free Travatan where they were present in significantly lower percentage. Our study agree with that of Pisella et al results showing that symptoms and signs of ocular surface disease(OSD) are more prevalent in patients using BAK preserved eye preparations compared with those using preservative free eye drops[4].

More over patients in our study who were switched to BAK-free travatan monotherapy from BAK preserved latanoprost (xalatan) yielded a better OSDI score after 12 weeks (Table 2). Our research thus supports the recommendation to switch to BAK-free therapy that has been advocated by previous researchers who have studied effects of BAK-containing medications in glaucoma patients[8, 23].

Our study is stretched over a short period. Glaucoma and ocular surface disease may coexist in some patients and old age further aggravates the condition. More over chronic damage takes longer to recover and response is varied among different patients and races affected by patient compliance, environmental factors and demographic features. The subject is very important and needs exhaustive studies and research to help eliminate the adverse effects and adopt such innovative methods to achieve more useful results for curing patients suffering from glaucoma and dry eye. This requires longer research with determination so as to gain positive results. Our this study is the beginning and the first step to move in this direction and we are confident that further research on the subject shall meet with better and useful results for service of humanity.

CONCLUSION

Patients placed on BAK free Travatan showed less symptoms of ocular surface disease as compared to those placed on BAK preserved Latanoprost (Xalatan). Moreover Switching from BAK-preserved latanoprost to BAK-free travatan yielded significant improvements in symptoms of OSD in patients with glaucoma or ocular hypertension. Preservative-free

travatan treatment resulted in increased patient satisfaction, drop comfort and vision related quality of life in terms of ocular surface disease.

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