

Original Research Paper

EFFECT OF BRIMOGUT ON OCULAR COMFORT

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Purpose: To investigate the Methods: 25 patients with use articial tear because of	e effect of Brimogutused as an antiglaucoma agent on ocular comfort. I glaucoma who use brimonidine (Brimogut, Turkey, Bilimilaç) and 25 patients with no glaucoma who dry eye (Evestil: SIELS, P.A. Italy) were included in the study as control group. Schirmer test was applied	

to the patients in each of the two groups on 1st day, in 1st week and 1st month. We applied Ocular Discomfort Scale (ODS) to all the patients in each group and we compared the results.

Results: 25 patients whose age average is 49.72 were included in the first group. 18 of them are male and 7 of them are female. In the second group, 25 patients whose age average is 46.44 were participated; 10 of them are male and 15 of them are female. It was not seen any statistically significant difference in the comparison for Schirmer tests and ODS.

Result: Consequently, when we compared brimonidinedrop (Brimogut) consisting ofbenzalkonium chloride (BAK) with artificial tear again consisting of BAK, we saw that there was no significant difference in terms of ocular comfort. However, there is a need for studies in which much more cases are included, and which are long-term.

KEYWORDS

Brimonidine, ocular comfort

INTRODUCTION

Glaucoma is the second greatest one of the reasons for blindness in the world (1). Glaucoma is a progressive disease which causes optic nerve damage and commonly progresses with high intraocular pressure(2,3). Before symptoms are clearly realized by the patient, permanent damages can occur(4). If it is not treated, progressive vision loss and contrast sensitivity loss occur. Finally, blindness may occur(5,6).

It was indicated that topical ophthalmic treatments decrease intraocular pressure and stop the progress of glaucoma. For glaucoma treatment, the effectiveness of the treatment which decreases intraocular pressure depends particularly on the patient's compliance to treatment. Especially when the patient does not realize the symptoms of the disease, the compliance to treatment can be thorny (7). Other factors influencing the compliance to treatment are the number of the applied topical treatments, the number of daily dose and side effects such as burning, stinging (8,9).

Experimental and clinical studies showed that long-term usage of the topical medicine can create effects such as ocular discomfort, tear film instability, conjunctiva inflammation, subconjunctival fibrosis, epithelial apoptosis and corneal surface disease. It can cause symptoms such as dry eye, burning, stinging, eye irritation, lacrimation, feeling of foreign body, red eye and blurring of vision(10). These side effects can be referred to preservatives in commercial medicine as well as active compounds. However, it has been still discussed the roles of active compounds and preservatives in inducing allergic, toxic or proinflammatory effects of the relevant mechanisms and ophthalmic solutions(11-14).

Since brimonidine 0.2% ophthalmic solution which is highly selective ₂-adrenergic agonist (Alphagan; Allergan, Irvine, CA) was presented in 1996, it has been approved that it is an effective and safe agent in glaucoma and ocular hypertension treatment(15). In a study conducted randomly, it was reported that the effectiveness of the usage of brimonidine 2% twice a day is sustained over 4 years and comparable to timolol 0.5%. In other studies, it was indicated the effectiveness of the usage of brimonidine 2% twice a day in monotherapy, in replacement

treatment and as an additional agent. It was commonly accepted the usage of brimonidine 2% twice a day as the only option or secondary option in long-term treatment of glaucoma and ocular hypertension (16-19).

Studies showed that brimonidine 2% has systemic side effects in lower rate comparing to topical -blockers. Depending on diagnostic criteria and length of treatment period, ocular allergy rates related to the brimonidine treatment was reported within the range of 4.2% and 12.7% (20).

Brimonidine 0.15% (Brimogut; Bilim, İstanbul, Turkey) was released in the year of 2013. It includes benzalkonium chloride as preservative. The purpose of this study is to investigate the effect of Brimogut used as antiglaucoma agent on ocular comfort.

METHODS

25 patients with glaucoma who use brimonidine (Brimogut, Turkey, Bilimilaç) and 25 patients with no glaucoma who use artificial tear because of dry eye (Eyestil; SIFI S.P.A. Italy) were included in the study as patient control group in our clinic in September 2016 – January 2017. The study was conducted in accordance with Helsinki Human Rights Statement. The patients were informed and their written consents were obtained.

In the first group using Brimogut, patients who have experienced ocular trauma, intraocular surgery or intervention; who use contact lens; who have eye lid or eyelash deformation; who have a history of ocular inflammation or infection; who receive artificial tear treatment, who have a history of autoimmune disease; and who have any ocular surface disease were not included in the study. Patients whose age is over 18 and who are diagnosed with glaucoma (primer open-angle glaucoma, pseudoexfoliative glaucoma, chronic narrow-angle and normal-pressure glaucoma) and ocular hypertension. In the control group, patients whose age is over 18 and who are healthy for other reasons but use artificial tear (Eyestil) because of eye dryness were included. Eyestil was chosen as preservative since it consisted of benzalkonium chloride. Glaucoma was defined as untreatable intraocular pressure's being over 21 mmHg, abnormal full threshold perimetry and abnormal

optic disc (increase in vertical and horizontal cup-disc rate, asymmetry of cup-disc rate between two eyes and peripapillary splinter haemorrhages). Normal-Pressure Glaucoma was defined as an open-angle glaucoma type in which intraocular pressure is not over 21 mmHg at any time of day although glaucomatous changes were determined in optic nerve and visual field.

Schirmer test was applied to all the patients in both groups on the 1st day, in the 1st week and in the 1st month. Topical anaesthesia was not performed before Schirmer tests. Schirmer paper strip is folded and put in outer conjunctival sac of 1/3. All patients were asked to close their eyes during the test. Paper strip was removed after 5 minutes and wet area on the paper strip was measured.

We also used Ocular Discomfort Scale (ODS) of Chan et al. for the patients in each group. Just after medicine was started, it was scored and recorded by means of Ocular Discomfort Scale on the 1st day, in the 1st week and in the 1st month. Patient problems were scored accordingly: 0- Normal, no discomfort; 1- Very milddiscomfort; 2- Mild discomfort; 3- Moderate discomfort; 4-Apparent discomfort; 5- Severe discomfort(21).

Statistical analysis

Statistical evaluations were performed with Statplus Pro statistical analysis program (Analysoft, the United States). Groups of Brimogut and artificial tear were compared with Mann Whitney U test. For the comparisons of each group in itself, Wilcoxon Matched Pairs Test was used. If duplex p value is below 0.05, this was evaluated as statistically significant difference.

RESULTS

Comparisons of two groups in terms of demography and averages of Schirmer test and ODS were presented in Table 1.

Table 1

	Brimogut group (n=25)	Artificial tear group (n=25)
Age (year)	49.72	46.44
Gender (M/F)	18/7	10/15
PretreatmentSch	9.98±8.45	9.74±7.55
1. w Sch	11.14±8.54	10.38±6.82
1. m Sch	10.56±8.15	10.06±7.04
1. d ODS	1.24±0.77	1.4±0.57
1. w ODS	1.04±0.67	1.08±0.57
1. m ODS	0.88±0.72	0.96±0.61

Sch: Schirmer test, ODS: Ocular Discomfort Scale, d: day, w:week, m: month

Statistical results of the comparisons for ODS and Schirmer test of each group in itself at the beginning of the treatment and at the end of the 1st month were presented in Table 2. While there was no significant difference for Schirmer test, there was a significant difference for ODS in each group.

Table 2*

	Brimogut group (p level)	Artificial tears group (p level)
Schirmer test	0,417304	0,498962
ODS	0,007661	0,004427

ODS: Ocular Discomfort Scale

*Wilcoxon Matched Pairs Test was used for statistical analysis.

Statistical results of the comparisons of each group for Schirmer tests and ODS were presented in Table 3. There was no statistically significant difference between two groups.

Table 3*

	P value	
PretreatmentSch	0,699457	
1. w Sch	0,939553	

1. m Sch	0,814682
1. d ODS	0,443431
1. w ODS	0,71963
1. m ODS	0,573651

Sch: Schirmer test, ODS: Ocular Discomfort Scale, d: day, w:week, m: month

*Mann Whitney U Test was used for statistical comparisons.

DISCUSSION

Cases that require continuous usage of topical medicine such as glaucoma can affect ocular surface negatively. However, action mechanisms of active compounds and preservatives which cause ocular surface damage in ophthalmic solutions have still been researched. (22).

Adverse effects of medicine used continuously in glaucoma treatment on tear functions decrease patients' compliance to treatment. Many researchers reported that antiglaucoma causes decrease in tear functions and leads some symptoms (23).

BAK is a preservative material commonly used in ophthalmic solutions. It was indicated that BAK causes tear film instability, loss of goblet cells, conjunctival squamous metaplasia, apoptosis, deformation of corneal epithelial barrier, and corneal nerve damage(22). Too few in vitro or in vivo comparative toxicological studies were reported. BAK, benzododecinium bromide, cetrimide, phenylmercuric nitrate, thiomersal, methyl parahydroxybenzoate, chlorobutanol and EDTA were scanned toxicologically. In another study, BAK, methyl paraben, sodium perborate, chlorobutanol, stabilized thiomersal and EDTA were tested. The authors stated that preservatives considerably cause conjunctival and corneal cell toxicity depending on all concentrations(10).

Decrease in Break up time test (TBUT) indicating tear film instability is a sign for ocular surface disease affected in supreme rate. Rossi et al. showed that increase in the usage frequency of drop by the patients who receive tropical glaucoma treatment causes abnormal TBUT and punctate keratitis. (22). Kuppens et al. showed that TBUT considerably decreases in patients who use timolol with preservative andfree from preservative. These changes in tear function can vary depending on the concentrations of medicine and preservatives, and the use frequency (24).

In the study conducted by Erb et al., it was showed that dry eye occurs more frequently in the patients with more severe glaucoma, in the patients whom a lot of antiglaucoma medicine is used, and in the patients who have had glaucoma disease for a long time. Similarly, in the United States, ocular surface effect in 101 patients with open-angle glaucoma and ocular hypertension was evaluated in a cross-sectional study. Dry eye symptoms were evaluated with Ocular Surface Index. While symptoms were reported at least in one eye in 59% of the patients, severe symptoms were reported in 27% of them. While there was a decrease in tear production at least in one eye in 61% of the patients, there was a severe effect in 35% of the patients in Schirmertest(10).

A study showed that prevalence of dry eye occurring in the patients with glaucoma is related to the number of drops used. While dry eye rates are 39% and 43% in the patients who use two or three drops, this rate is determined 11% in the patients who use one drop. In the scoring of ocular surface symptoms, it was reported that severe dry eye is 15% in the patients who use three drops while it is 8.7% in the ones who use two drops.(10)

In our study, any significant difference was not seen for Schirmer test when each group was compared in itself and when the beginning of the treatment and the end of the 1st month were considered as criteria. However, there were significant differences for ODS. It was seen that less symptoms occurred at the end of the

1st month in each group. When compared two groups in terms of pre-treatment Schirmer test levels and 1st month Schirmer test levels, any significant difference was not seen. Similarly, when compared values at the end of the 1st day and 1st month for ODS, there was no significant difference between two groups. We think that the difference between our study and other studies can be related to the patient follow-up periods.

Consequently, when we compared brimonidine drop(Brimogut) consisting of BAK with artificial tear drop again consisting of BAK, we saw that there was no significant difference in terms of ocular comfort. However, there is a need for studies in which much more cases are included, and which are long-term.

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