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A CROSS SECTIONAL OBSERVATIONAL STUDY TO EVALUATE THE PREVALENCE OF OCULAR SURFACE DISEASE IN GLAUCOMATOUS PATIENTS USING ANTIGLAUCOMA DRUGS ATTENDING IN A HOSPITAL.

Ophthalmology

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ABSTRACT

Purpose: Evaluation of Prevalence of Ocular Surface Disease in Glaucomatous Patients Using Antiglaucoma Drugs attending Out Patient. Department in a hospital. **Method:** This study was carried out in Index Medical College and Research Centre, Indore. Out of the total 210 eyes of 105 Adult Glaucomatous patients (30 -80 yrs) who were using topical anti-glaucoma drugs for more than a period of 3 months were included by OSDI questionnaire. A complete history with routine ocular examination with other necessary investigations was performed in all the patients. The prevalence of Ocular Surface Disease was assessed by noting the OSDI score, Schirmer's 1 test value and Tear film break up time value in both right and left eyes of the patients. **Results:** In our cross-sectional study of the 210 eyes of 105 patients, we found that majority 69.5% (73/105) were in the age group of 50- 70 years, Ocular Surface Disease was found to be highly significant ($p<0.001$) with preservative BAK medication in OSDI Score, Schirmer 1, TBUT than BAK free preservative medications. Ocular Surface Disease assessment by OSDI score with preservative BAK and BAK free preservative medications is (61.8%) and (12.5%) respectively, Difference was statistically highly significant ($p<0.001$, OR= 2.290, 95% CI= 1.659- 3.163) by Fisher's exact test. Ocular Surface Disease assessment in Right eye and Left eye by Schirmer's 1 test with preservative BAK and BAK free preservative medication is (74.2% & 70.8%) and (18.8% & 12.5%) respectively. Ocular Surface Disease assessment in Right eye and Left eye by TBUT test with preservative BAK and BAK free preservative medication is (76.4% & 82.0%) and (12.5% & 31.3%) respectively. As the number of IOP-lowering medication with BAK preservative increased from one or more than one drug, a strong positive correlation with OSD with Pearson Correlation 0.683 significant at <0.001 level.

KEYWORDS

Open Angle Glaucoma, Anti Glaucoma Drugs, Ocular Surface disease, Benzalkonium Chloride (BAK).

INTRODUCTION

Glaucoma is a group of disorder characterized by progressive irreversible optic neuropathy consistent with excavation and undermining of the neural and connective tissue elements of the optic disc and specific pattern of visual field defects that is associated frequently but not invariably with raised intraocular pressure.

It's a second leading cause of global blindness, and the leading cause of irreversible visual loss in the adult population worldwide, estimated to have affected 60.5million people in 2010 and projected to affect 79.6 million by 2020. It is characterized by the loss of retinal nerve fiber tissues, recognized clinically as visual field defect and loss of the neuroretinal rim of the optic nerve head, termed glaucomatous optic neuropathy (GON).

Many clinical researches have shown that damage to the optic nerve in glaucoma is associated with elevated intraocular pressure (IOP) **(1,2)**. Decreasing IOP by Medical and surgical treatments reduces both the incidence of glaucoma in individuals without optic nerve damage and the rate of new damage in individuals with glaucoma. Specifically, medications intended to lower intraocular pressure (IOP) are generally administered several times a day, and patients with chronic conditions like glaucoma and ocular hypertension require long-term use and/or multiple medications to achieve and maintain the desired IOP-lowering effects **(3).**

Glaucoma therapy is lifelong and topical agents used over long time are likely to cause changes in ocular surface like tearing, photophobia, burning and gritty sensation, redness and dry sensations which suggest inadequate tear production. On chronic administration they damage the mucin layer of tear film, decrease tear production and reflex tear secretion by decreasing corneal sensations. The symptoms on chronic administration like burning and itching, dry sensation, grittiness and erythema are mainly due to altered tear film. **(4)**

Affecting 15% of Individuals older than 65 years, ocular Surface disease is common **(5)** characterized by symptoms such as grittiness, burning, photophobia, OSD, foreign body sensation and transient visual disturbance. Age, ethnicity and sex influence OSD, it is more frequent in older subjects. **(6)**

OSD affects up to 59% of patients with glaucoma. **(7)** This high prevalence may result from both conditions being increasingly common one the elderly in addition. Preservatives containing topical medications, especially those used chronically, can exacerbate or contribute to OSD. Benzalkonium chloride (BAK) in particular reduces the stability of the precorneal tear film, with direct corneal toxicity. **(8)**

MATERIALS AND METHODS:

The present study "A Cross Sectional Observational Study to Evaluate the Prevalence of Ocular Surface Disease in Glaucomatous Patients Using Antiglaucoma Drugs Attending in a hospital." was an observational, cross sectional study conducted in department of ophthalmology at Index medical college and research Centre, Indore. A total number of 210 eyes of 105 patients were enrolled.

METHODOLOGY:

1. Written informed consent was taken.
2. OSDI Questionnaires
3. Visual acuity by Snellen's chart
4. Intraocular pressure by Goldmann's Applanation Tonometry
5. Gonioscopy by Goldmann's three mirror gonioscope
6. Visual field examination by Humphery Field Analyser
7. Optic disc examination by 90 D lens
8. Schirmer's 1 test using No 41 Whatmann filter paper strip
9. Tear film Break-up time using fluorescein staining strips

The following were the inclusion and exclusion criteria of study:

Inclusion Criteria:

Adult Glaucomatous patients (30 -80 yrs) using topical anti-glaucoma drugs (like topical beta-blockers, parasympathomimetics, sympathomimetics, carbonic anhydrase inhibitors and prostaglandins analogues) for more than a period of 3 months.

Exclusion Criteria:

1. Previous history of ocular surgery or trauma.
2. Treatment with other topical drugs.
3. Systemic disease affecting tear production like Sjogren's syndrome, Steven-Johnson's syndrome.
4. Uncontrolled IOP.
5. Contact lens wearer.
6. Inflammatory conditions like allergic conjunctivitis, pterygium etc.

RESULTS:

This study was conducted with 210 eyes of 105 patients considering both eyes. All of them undergone same procedure as described in materials and methodology section.

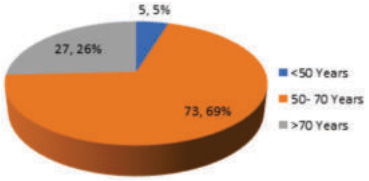

Fig 1: Age Wise Distribution Of Patients

Majority, 69.5% (73/105) were in the age group of 50- 70 years. 25.7% (27/105) were >70 years of age while only 4.8% (5/105) were <50 years of age.

Intra Ocular Pressure:

Table 1: Distribution Of Cases As Per IOP In Right And Left Eye

IOP	Right eye		Left eye	
	Frequency	Percent	Frequency	Percent
<18 mm	64	61.0	72	68.6
18- 24 mm	39	37.1	32	30.5
>24 mm	2	1.9	1	1.0
Total	105	100.0	105	100.0

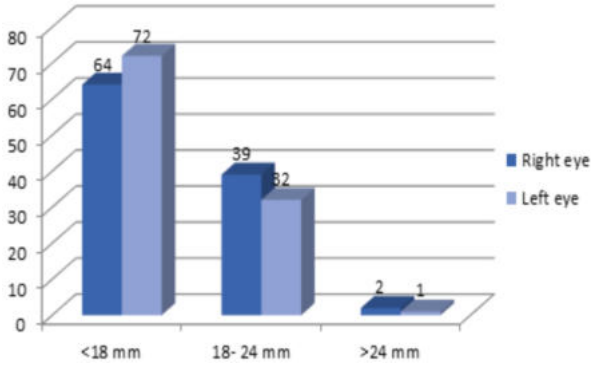

Fig 2: Distribution of cases as per IOP in Right and Left eye

Figure 2, table 1 represents distribution of cases as per IOP majority of cases had IOP <18mm, in right eye 61% cases and in left eye 68.6% cases.

MEDICATIONS USED:

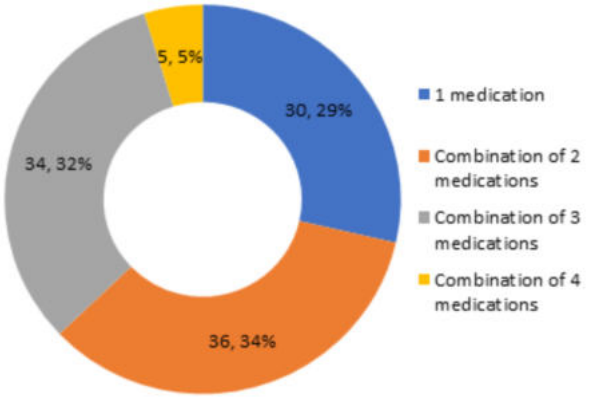

Fig 3: Distribution As Per Number Of Medications Used In Cases

Figure 3, represents distribution of cases as per the medications used, 28.6% (30/105) cases only one medication was used. For 34.3% (36/105) cases combination of two medications, for 32.4% (34/105) cases combination of three medications and for 4.8% (5/105) cases combination of four medications was used.

- **No. Of medications with BAK free preservatives:**

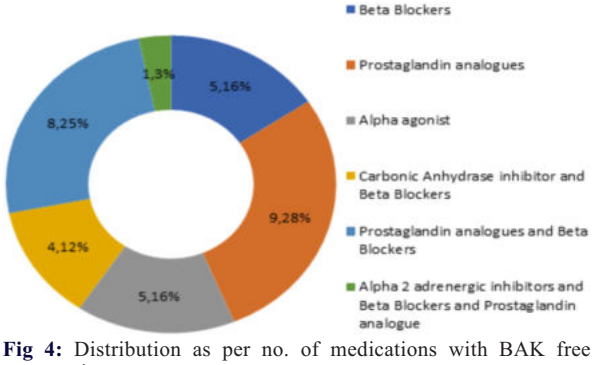

Fig 4: Distribution as per no. of medications with BAK free preservative

Figure 4 represents the distribution of cases as per number of medications with BAK free preservatives used.

In 5(16%) cases only Beta blocker was used, in 9 (28%) cases only prostaglandin analogues used, 5(16%) cases only alpha agonist used, in 4 (12%) carbonic anhydrase inhibitor and beta blocker combination were used while in 8 (25 %) cases prostaglandins analogues with beta blocker were used. All were BAK free preservative medications.

Number Of Medications With Preservative Containing BAK:

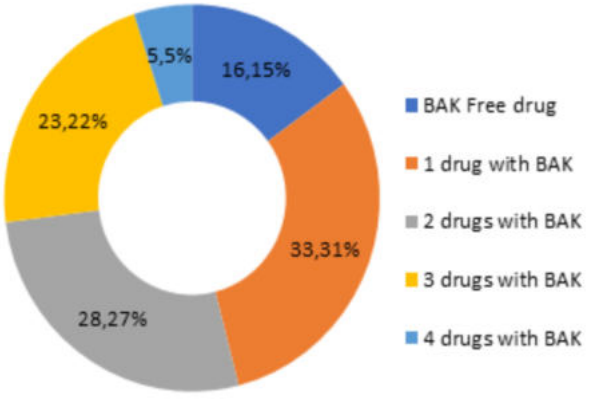

Fig 5: Distribution As Per Number Of Medications With Preservative Containing BAK

Fig.5 represents the distribution of cases as per number of medications used with preservative containing BAK were 33 (31%) cases used 1 medication, 28(27%) cases used 2 medications, 23(22%) cases used 3 medications and 5 (5%) cases used 4 medications. Out of these, 16(15%) cases used only medications which are BAK free.

Ocular Surface Disease Index Score

Table 2: Grades of OSD as per OSDI score

OSDI score	Grade	Frequency	Percent
≤ 12	Normal	48	45.7
13-22	Mild OSD	39	37.1
23-32	Moderate OSD	16	15.2
> 33	Severe OSD	2	1.9
	Total	105	100.0

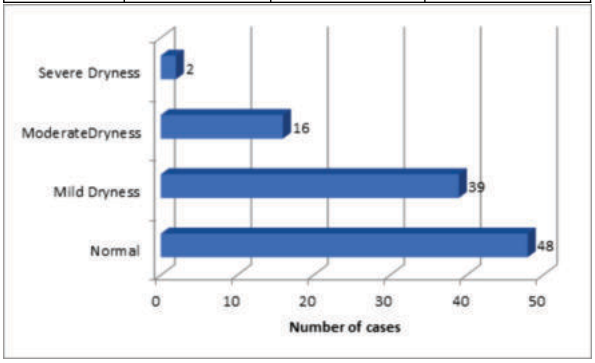

Fig 6: Grades of OSD as per OSDI score

Correlation with number of medications with BAK Preservative and OSD

Table 3: Number Of Medications With BAK Preservative And OSD

Number of medications with preservative BAK		Normal	OSD	Total
0	N	14	2	16
	%	87.5	12.5	100.0
1	N	25	8	33
	%	75.8	24.2	100.0
2	N	7	21	28
	%	25.0	75.0	100.0
3	N	2	21	23
	%	8.7	91.3	100.0

4	N	0	5	5
	%	0	100.0	100.0
Total	N	48	57	105
	%	45.7	54.3	100.0

(p<0.001, by likelihood ratio of Chi squared test).

0 is BAK free preservative medications. 33 cases were using 1 BAK preservative medications and out of it in 8 cases (24.2%) OSD was found, 28 cases were using 2 medications out of it in 21 cases (75%) OSD was found, 23 cases were using 3 medications out of it in 21 cases (91.3%) OSD was detected and 5 cases were using 5 medications with BAK preservative medications and in all (100%) OSD was found. Thus, there was a strong positive correlation between number of medications with BAK preservative medications and OSD with Pearson Correlation 0.683 significant at 0.001 levels. (Table 3)

OSD By Different Methods And In Cases With BAK and BAK Free Combinations

1. By Schirmer's 1 test -

Table 4: Assessment Of OSD By Schirmer 1 Test In BAK Preservative And Without BAK Preservative Medications:

Purely BAK preservative free combination		OSD by Schirmer for Right eye		Total	OSD by Schirmer for Left Eye		Total
		Normal	Dry		Normal	Dry	
Yes	N	13	3	16	14	2	16
	%	81.3	18.8	100.0	87.5	12.5	100.0
No	N	23	66	89	26	63	89
	%	25.8	74.2	100.0	29.2	70.8	100.0
Total	N	36	69	105	40	65	105
	%	34.3	65.7	100.0	38.1	61.9	100.0

Right eye: P<0.001, OR=3.144 (95%CI= 2.059- 4.801), Left eye: P<0.001, OR=3.144 (95%CI= 2.059- 4.801).

In Table 4, OSD is present in eyes having BAK preservative medication, RE (74.2%), LE (70.8%) than purely BAK free medication RE (18.8%), LE (12.5%). By using chi-square test p-value < 0.001 therefore OSD is significantly higher in the BAK medication than BAK free medications.

2.By Tear Break Up Time:

Table 5: Assessment Of OSD By TBUT In BAK Preservative And Without BAK Preservative Medications:

Purely BAK free combination		TBUT for Right eye		Total	TBUT for Left eye		Total
		Normal	Dry		Normal	Dry	
Yes	N	14	2	16	11	5	16
	%	87.5	12.5	100.0	68.8	31.3	100.0
No	N	21	68	89	16	73	89
	%	23.6	76.4	100.0	18.0	82.0	100.0
Total	N	35	70	105	27	78	105
	%	33.3	66.7	100.0	25.7	74.3	100.0

Right eye: P<0.001, OR=3.708 (95% CI=2.443- 5.628), Left eye: P<0.001, OR=3.824 (95% CI=2.199- 6.650).

In Table 5, OSD is present in eyes having BAK preservative medication, RE (76.4%), LE (82.0%) than purely BAK free medication RE (12.5%), LE (31 .3%). By using chi-square test p-value < 0.001 therefore OSD is significantly higher in the BAK medication than BAK free medications.

DISCUSSION:

This study was a cross-sectional hospital based observational study undertaken to evaluate the presence of ocular surface disease in Glaucoma patients who were on Antiglaucoma medications. 210 eyes of 105 adults with glaucoma or ocular hypertension who were using 1 or more topical IOP-lowering medications completed the Ocular Surface Disease Index (OSDI) questionnaire during a regularly scheduled clinic visit and were subjected to the following tests: Schirmer's 1 test, Tear film break up time.

The epidemiological analysis of present study showed Majority, 69.5% (73/105) were in the age group of 50- 70 years of age. Male (62%) are more than female (38%).

Similarly, David A Infeld et al **(9)** observed an Age-specific prevalence in the age group 55-59 years. Men had a more than three times greater risk of having POAG than women (odds ratio 3.6).

In the present study, significant OSD was found in cases with BAK preservative medication than in BAK preservative free medication respectively by OSDI score (61.8%) and (38.2%).

Similarly Simon E et al **(10)** investigated the relationship between ocular surface disease and glaucoma related quality of life by OSDI questionnaires, glaucoma severity and treatment in patients with open angle glaucoma observed that OSDI scores and the number of patients with OSD increased with increasing glaucoma severity.

In the present study, significant OSD in Schirmer's 1 test was observed. There is significant decrease in Schirmer's 1 value hence OSD is present in eyes having BAK preservative medication, RE (74.2%), LE (70.8%) than purely BAK free medication RE (18.8%), LE (12.5%). The p value is highly significant < .001.

Our finding was consistence with the results of Arici et al **(11)** observed a statistically significant decrease in the number of patients with normal Schirmer's test values after timolol administration for three years. Donocik et al**(12)** in their study of influence of beta adrenergic antagonist on tear secretion have observed significant decrease in Schirmer's test values in children treated with timolol twice daily for 12 months.

In our study there is significant decrease in TBUT thus, OSD is present in eyes having BAK preservative medication, RE (76.4%), LE (82.0%) than purely BAK free medication RE (12.5%), LE (31 .3%). By using chi-square test p-value < 0.001 therefore OSD is significantly higher in the BAK medication than BAK free medications

Similar results were found in following studies, Strempel et al **(13)** also observed significant decrease in break up time with topical beta blockers which may be due to influence on tear production and composition or a membrane stabilising effect or some unknown factor that leads to break up time alteration.

Similarly, J. Thygesen et al **(14)** investigated and compared the short-term effect of latanoprost and timolol eye drops on tear fluid and the ocular surface in patients with primary open-angle glaucoma and ocular hypertension.

In our study there was a strong positive correlation between number of medications with BAK preservative and OSD with Pearson Correlation 0.683 significant at p <0.001 level. 33 cases were using 1 BAK preservative medications out of it in 8 cases OSD was found (24.2%), 28 cases were using 2 medications in it 21 cases (75.0%), 23 cases were using 3 medications in it 21 cases (91.3%) and 5 cases used 4 medications and in it (100%) OSD was found. Hence Prevalence of OSD was significantly increasing as numbers of medications were increasing.

Similar correlations were found in the study conducted by Fechtner RD et al**(15)** who observed a positive correlation with the severity of OSD symptoms to the number of IOP-lowering medications used. Severe dry eye was found in 8.7% and 15% of patients using 2 or 3 topical antiglaucoma drops. **(16)**

Wong et al **(17)** compared tear protein profile in patients receiving long-term glaucoma medication and in those with primary dry eye. They suggested that duration of use of anti-glaucoma medications longer than 1 year might start to induce changes in ocular surface inflammation.

In this study the drugs used had benzalkonium chloride as preservative. Benzalkonium chloride is the most frequently used preservative in ophthalmic solutions today, and its concentration in glaucoma formulations ranges from 0.004 to 0.02%. The reasons for the frequent use of BAK as a preservative includes its extreme efficacy in combating microbial contamination of bottles, its ability to break cell–cell junctions in the corneal epithelium.

Many experimental and clinical studies have shown that the long-term use of topical ophthalmic medication, especially those containing benzalkonium chloride (BAK) as a preservative, may induce changes

of the ocular surface, tear film instability, epithelial apoptosis, conjunctival inflammation, fibroblast proliferation, corneal microvilli loss, and goblet cell loss in the conjunctival epithelium **(18-20)**.

So, we conclude that on long term therapy, topical anti glaucoma drugs cause changes on ocular surface in terms of increased OSDI score, decreased Schirmer's 1 test, decreased Tear film break up time and increased Rose Bengal staining score and decreased tear meniscus height.

Newer ophthalmic preservatives have been developed e.g. Purite, SofZia buffer system, and Polyquad preservative and have been used in reformulating BAK-preserved IOP-lowering medications. This advancement can help preserve ocular surface health of patients by providing alternate therapies that can reduce their exposure to BAK in patients who use mono drug therapy or multiple drug therapy over many years. **(21-22)**

CONCLUSION

Our study confirms that patients using antiglaucoma medications with BAK as preservative shared significant prevalence of OSD as compared to medications with preservatives other than BAK. We also confirm that as we increase the number of medications with BAK as preservatives for lowering the intraocular pressure, there is a significant increase in Ocular Surface Disease then in medications with preservative other than BAK.

REFERENCES

1. D. S. Friedman, R. C.Wolfs, B. J.O'Colmain et al. Prevalence of open-angle glaucoma among adults in the United States, Archives of Ophthalmology. 2004; vol.122, no. 4:532-38.
2. P. Martus, A. Stroux, W. M. Budde, C. Y. Mardin, M. Korth, and J. B. Jonas, Predictive factors for progressive optic nerve damage in various types of chronic open-angle glaucoma, American Journal of Ophthalmology. 2005; vol. 139, no. 6: 999– 1009.
3. Baudouin C, Labbe A, Liang H, Pauly A, Brignole-Baudouin F. Preservatives in eyedrops: the good, the bad and the ugly. Prog Retin Eye Res. 2010; 29(4):312–334.
4. Singh S.V, Pal V, Singh DC, Garg N. Ocular surface changes with topical anti-glaucoma drugs. AIOC Proceedings. 2004; 260-61.
5. Moss SE, Klein R, Klein BE. Prevalence of and risk factors for dry eye syndrome. Arch Ophthalmol 2000; 118(9): 1264-1268.
6. Brewitt H, Sistani F. Dry eye disease: the scale of the problem. Surv Ophthalmol 2001; 45(suppl 2): S199-202.
7. Leung EW, Medeiros FA, Weinreb RN. Prevalence of ocular surface disease in glaucoma patients. J Glaucoma 2008; 17(5) :350-55.
8. Baudouin C. "Detrimental effect of preservatives in eyedrops: implications for the treatment of glaucoma. Acta Ophthalmol 2008;86 (7): 716-26.
9. Dielemans I, Vingerling JR, Wolfs RC, Hofman A, Grobbee DE, de Jong PT. The prevalence of primary open-angle glaucoma in a population-based study in The Netherlands. The Rotterdam Study. Ophthalmology 1994; 101:1851-5.
10. Simon E. Skalicky et al. Ocular surface disease and quality of life in patients with glaucoma. American Journal of Ophthalmology. Jan 2012; vol 153: 1-9.
11. Arıcı MK, Arıcı DS, Topalkara A, Güler C. Adverse effects of topical antiglaucoma drugs on the ocular surface. Clinical & Experimental Ophthalmology. 2000 April; 2(28); 113–117.
12. Donocik ES, Koraszewska M. Influence of beta-adrenergic antagonist on tear secretion in children. Pol J Pharmacol. 2004; 56: 871-3.
13. Strempal I. The influence of topical beta-blockers on the breakup time. Ophthalmologica Basel. 1984; 189:110-5.
14. Thygesen J, Aaen K, Theodorsen F, Kessing SV, Prause JU. Short-term effect of latanoprost and timolol eye drops on tear fluid and the ocular surface in patients with primary open-angle glaucoma and ocular hypertension. Acta Ophthalmol Scand. 2000 Feb;78 (1): 37-44.
15. Fechtner R.D., Godfrey D.G., et al. Prevalence of ocular surface complaints in patients with glaucoma using topical intraocular pressure-lowering medications. Cornea. 2010;29: 618–21.
16. Rossi GC, Tinelli C, Pasinetti GM, Milano G, Bianchi PE. Dry eye syndrome-related quality of life in glaucoma patients. Eur J Ophthalmol 2009; 19:572-9.
17. Wong TT, Zhou L, Li J, et al., Proteomic profiling of inflammatory signalling molecules in the tears of patients on chronic glaucoma medication, Invest Ophthalmology Vis Sci, 2011;52(10):7385–91.
18. M. Y. Kahook and R. J. Noecker, Comparison of corneal and conjunctival changes after dosing of travoprost preserved with sofZia, latanoprost with 0.02% benzalkonium chloride, and preservative-free artificial tears, Cornea. 2008; vol. 27, no. 3: 339–43
19. M. Y. Kahook and R. Noecker, "Quantitative analysis of conjunctival goblet cells after chronic application of topical drops," Advances in Therapy. 2008; vol. 25, no. 8: 743–51,
20. W. S.Wilson, A. J. Duncan, and J. L. Jay, "Effect of benzalkonium chloride on the stability of the precorneal tear film in rabbit and man," British Journal of Ophthalmology. 1975; vol. 59, no. 11: 667–69
21. Noecker R. Effects of common ophthalmic preservatives on ocular health. Adv Ther. 2001; 18(5):205–15.
22. Yee RW. The effect of drop vehicle on the efficacy and side effects of topical glaucoma therapy: a review. Curr Opin Ophthalmol.2007; 18(2):134–39.