To Study Ocular Surface Morbidities among Glaucoma Patients on Anti-Glaucoma Drops

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Abstract:

Title : To study ocular surface morbidities among glaucoma patients on anti-glaucoma drops

Background : Glaucoma is a chronic, lifelong disease and it requires lifelong therapy as well. Topical anti-glaucoma drugs are often associated with symptoms and sign of toxicity.

Objective : We aimed to study the incidence, symptoms and signs of ocular surface disease among patients on different anti-glaucoma drops and control group and to compare effects of mono and combination therapy.

Materials and methods : In this case control study 105 patients of glaucoma on anti-glaucoma drops for at least 3 months who presented to us were examined and compared to 102 patients of glaucoma not on anti-glaucoma drops.

Observation/result : Mean age was 56.2 years with male to female ratio 1.25:1. 83.09% of the patients had primary glaucoma with PNAG being the most common diagnosis. DOV, redness and pain being the most common presenting complaint in study group. In both groups on application of different dry eye test, there was increased incidence of abnormal OSDI, corneal assessment, TBUT and schirmer's test in study group. Difference in incidence of abnormal OSDI, corneal assessment, TBUT and schirmer's test was not significant in mono therapy and combination therapy group.

Conclusion : there is higher incidence of ocular surface disease among patients on anti-glaucoma drops and the most commonly encountered problem is reduced tear film stability. Preservative free and combination drops along with use of lubricant is found to reduce the ocular surface toxicity.

Key words : anti-glaucoma, drops, glaucoma, ocular surface, tear film

Introduction :

Glaucoma is a chronic, lifelong disease which requires lifelong therapy in a regular and continuous manner. Topical anti-glaucomatous therapy is often associated with symptoms and signs of toxicity, inflammatory changes of the ocular surface and decrease of tear film break up time (TBUT).[1,2] The main causative factor for the toxicity and ocular surface disorders can be preservative or an active compound of the drug.[3,4] There are two main groups of preservatives, detergent and oxidative. Detergent preservatives like BAK can cause cell membrane lysis and accumulate in ocular tissue. They have dose dependent effect. They also interfere with the integrity of superficial lipid layer of the tear film, reduce the TBUT and may contribute to the ocular surface disease .[5,6] Second group are oxidative preservatives with Stabilized Oxochloro Complex (SOC) as the main representative. Their key component is sodium chloride and it has mild cytotoxic effect and excellent safety record.

Ocular surface disease (OSD) represents one of the major causes for ophthalmological consultation worldwide.[7] It involves all sorts of pathological alterations of conjunctiva and cornea from the minor such as punctate keratitis to the extreme such as symblepharon, or loss of limbal stem cells with corneal conjunctivalisation. Within this group, dry eye syndrome (DES) constitutes a well-defined, yet not completely explained entity, with multifactorial etiology but clearly defined symptoms like redness, itching, foreign-body sensation, tearing and pain. Ocular lubricants constitute the main treatment, but recently, advances in the understanding of the DES as an inflammatory condition have modified our view on the correct way to approach this problem. The clinical diagnosis of objective tests for DES includes: 1) the Schirmer test (ST), with or without anesthesia, which determines tear production; 2) tear break-up time (TBUT) that reflects tear film stability; and 3) dye staining tests for evaluating the tissue integrity .[8-10]

The purpose of this study is to evaluate the incidence of ocular surface disease and need for preservative free or combination drops among glaucoma patients under topical treatment, and to identify risk factors associated with it.

Material and methods :

Ocular surface morbidities are essentially a clinical diagnosis, assisted by information obtained from both the history and the examination and performing one or more tests to lend some objectivity to the diagnosis. No one test is sufficiently specific to permit an absolute diagnosis of dry eye.

We did a prospective observational study for a duration of 1 year on patients presenting to our OPD with symptoms of

discomfort and ocular irritation such as redness, pain, discharge, blurred vision itching, watering or tearing. All the selected patients were subjected to detailed history taking, clinical examination and investigation like Schirmer's test, Rose Bengal test and Tear-film Breakup Time. Patients were divided in to 2 groups.

Study Group : diagnosed Patients of glaucoma and on anti-glaucoma drops for at least 3 months.

Control : glaucoma patients (based on signs, symptoms and investigation) not on anti-glaucoma drops

Inclusion criteria :

1. Patients 40 years and above whom have been diagnosed as glaucoma and on anti-glaucoma drops for at least 3 months and age matched control group.
2. Patients of either sex and any age suffering from ocular surface disorder.

Exclusion criteria :

1. Patients suffering from any medical disorders that can cause ocular surface disease (like DM, arthritis, thyroid diseases etc.)
2. Recent history of surgeries and history of chemo or radiotherapy.
3. Patient having conjunctivitis of various etiology including allergic or other ocular diseases that can cause ocular surface disorders.

The demographic and clinical characteristics were represented by frequencies and percentage. Chi square test and Fischer exact test were used to calculate P-value. Significant p value was taken as <0.05.

Observation :

Out of total 207 patients in our study 115 (55.56%) were male and 92 (44.44%) female with sex ratio of 1.25:1. Maximum number of patients i.e. 41.55% (86) presented to us with primary narrow angle glaucoma (PNAG) closely followed by primary open angle glaucoma (PAOG) with 36.71% (76) patients whereas 15.94% (33) had secondary glaucoma, 0.97% (2) had ocular hypertension, 1.45% (3) patient presented with normal tension glaucoma. 7 patients in our study did not have glaucoma. POAG was diagnosed in a higher age group with mean age of POAG, PNAG and secondary glaucoma group were 59.68, 53.72 and 52.28 respectively.

Out of 207 patients in our study, 105 belonged to the study group whereas 102 belonged to control group. In the study group, out of total 105, 54 and 51 were male and female respectively where POAG was found to be more common in males (44.44%) and PNAG in females (58.82%). Similarly, out of 102 patients in control group, 61 and 41 were male and female respectively where POAG was found to be more common in females (60.97%) and PNAG in males (55.73%).

Diminution of vision was the most common presenting complaint (68%) followed by pain (47.5%) and redness (17.5%). Watering (4.5%) and other complaints (5%) were some of the less common presenting symptoms. 2 patients did not present with any symptom.

Both the groups when given OSDI questionnaire comprising 12 questions, 61% and 68.6% were normal in study and control group respectively with p value of 0.604. similarly, 16.2% and 18.6% showed mild symptoms, 10.5% and 5.9% showed moderate and 12.4% and 6.9% showed severe symptoms in study and control group respectively. More patients (41) showed symptoms in study group than control group (32) but the difference was not statistically significant.

SCHIRMER test showed higher incidence of abnormal result in study group (39%) than control group (24.5%) with p value of 0.049 which was statistically significant. Similarly, corneal assessment showed higher incidence of abnormal result (SPK) in study group (62.9%) than control group (37.3%) with statistically significant p value of 0.006.

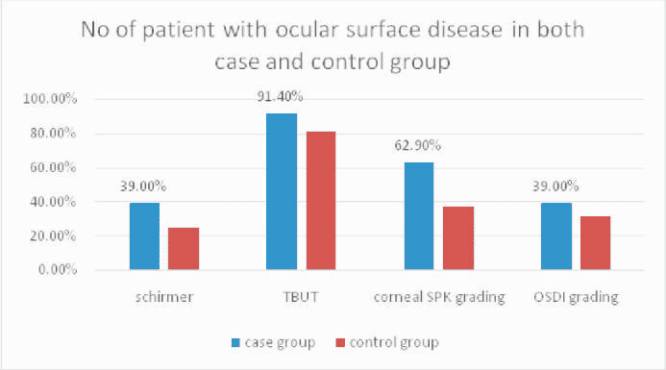

Figure 1 : No of patient with ocular surface disease in both case and control group

Out of 105 patients in study group on anti-glaucoma medication, 55 patients were on monotherapy while 60 were on combination therapy. Abnormal test for ocular surface disease was seen in both groups, more in combination therapy group.

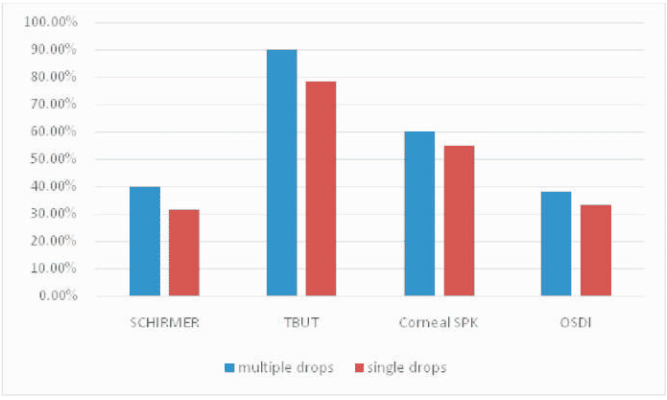

Figure 2 : Difference between ocular surface disease in single and multiple medication

but the difference was not statistically significant. In 55 patients on monotherapy, 18 were on preservative free drops

and 37 on BAK containing drops. All the test showed more no of patients with abnormal result in BAK group .

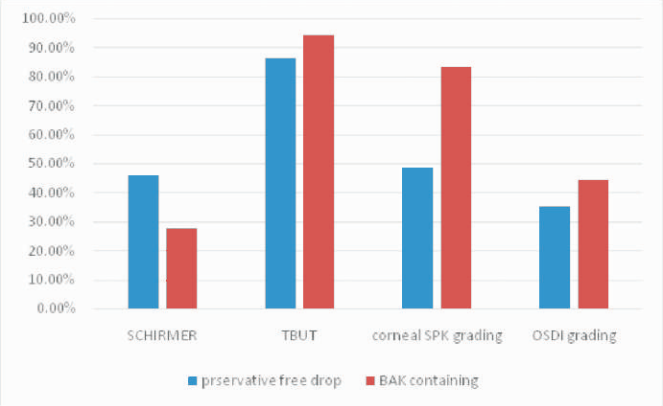

Figure 3 :Difference in ocular surface disease among patients using preservative free and BAK containing eye-drops

Discussion :

It is an established fact that OSD is more frequently observed in patients on anti-glaucomatous medication. During treatment it is necessary to consider not only the effect of medication on IOP but also the incidence and severity of drug-induced OSD as the most frequent side effect. Careful observation is particularly needed for the eyes that are treated with multiple eye drops and in the older age group.[3] Moderate or severe OSD affects 38% of patients who received a single topical therapy, 54% of those who received 2 topical therapies, and 71% of those who received 3 or more topical therapies.[11] It should however be emphasized that in daily practice the situation is probably even more difficult than which can be assessed using data available from clinical trials .[12,13]

In our study Patients on anti-glaucoma eye drops did not show presence of any significant lid abnormalities such as blepharitis or meibomitis. However, they suffered from reduced tear production (Schirmer test less than 10mm) as well as abnormal corneal punctate keratitis. In both groups, most of the patients had tear film instability which was reflected by the shortened tear break-up time. Based on the Ocular Surface Disease Index grading, in both groups less than 50% of patients experienced symptoms ranging from mild to severe.

In a national panel survey, dry eye was found to be more common among glaucoma respondents than non-glaucoma controls (16.5% vs 5.6%, P<0.0001), and there was a non-significant trend for glaucoma patients with dry eye to report higher rates of intraocular pressure-lowering medications than those without dry eye (44.2% vs 35.0%, P<0.076).[14] Interestingly, we found that the use of 2 or more anti-glaucoma medications (OR=1.92) and duration of treatment greater than 5 years (OR=2.92)

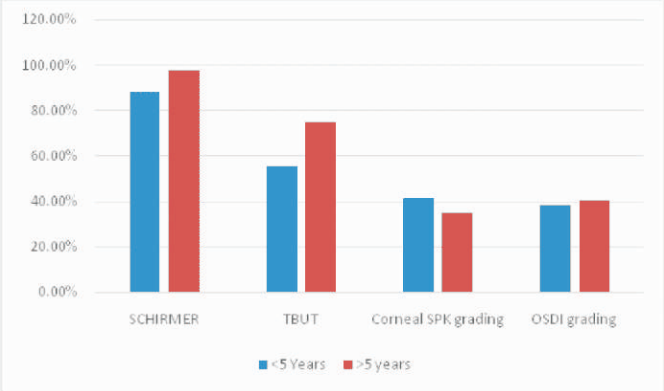

Figure 4 :comparison of ocular surface disease in duration more than or less than 5 years

were significantly associated with dry eye. We believe that this association is explained by the fact that longer treatments with more drops per day have a higher load of preservatives delivered to the ocular surface.

Martone et al,[15] in a comparative retrospective study using in vivo confocal microscopy,found lower density of superficial epithelial cells, higher density of basal epithelial cells, higher stromal keratocyte activation, less sub-basal nerves and higher tortuosity on glaucomatous patients with chronic treatment. Fechtner et al,[16] observed that the mean OSDI score significantly increased from 12.9 when one anti-glaucoma medication was used to 19.4 when three or more medications were used (p=0.0001). Rossi GC et al[17] investigated the occurrence of dry eye syndrome (defined as presence of punctuate keratitis or decreased tear break-up time) in 61 glaucoma patients divided according to the number of glaucoma drops instilled per day.[1,2, or 3] The prevalence of dry eye was 40% in patients using 3 drops/day, 39% in patients using 2 drops/day, and 11% in patients using one drop/day. Furthermore, OSDI questionnaires revealed that 15% of those using 3 drops/day and 8.7% of those using 2 drops/day showed severe OSD. Pisella et al,[18] observed that the prevalence of ocular symptoms and signs related to dry eye were dose dependent, increasing with the number of preserved anti-glaucoma drops. Although there is some evidence that glaucoma per se may be associated with decreased basal tear turnover, most of the studies blame the development of dry eye on the chronic use of anti-glaucoma medications, especially due to the presence of preservatives.

Conclusion :

In conclusion, there is higher incidence of ocular surface disease among patients on anti-glaucoma drops. The most commonly encountered problem is the tear film stability and this is most likely caused by deficiency of mucin production from conjunctival goblet cells. To curb this problem, the use of preservative containing drops should be minimized as much as possible. Preservative free or combination drops should be used to reduce the preservative load in the eye. In patients who

have to use multiple drops, eye drops with much gentler preservatives can be prescribed. All patients on anti-glaucoma drops should be screened for ocular surface disease during their follow up.

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Fluoxetine and AMD

An antidepressant best known as FLUOXETINE could offer the first treatment for the leading cause of blindness among people over 50, new research from the University of Virginia School of Medicine suggests.

UVA's Bradley D. Gelfand, PhD, and collaborators have found early evidence that the drug fluoxetine may be effective against atrophic (or "dry") age-related macular degeneration. The drug has shown promise in the scientists' lab tests and animal models, and the researchers bolstered by their results by examining two huge insurance databases encompassing more than 100 million Americans. That analysis concluded that patients taking fluoxetine were less likely to develop atrophic macular degeneration (AMD).

Based on their findings, the researchers are urging clinical trials to test the drug in patients with AMD. If successful, they believe the drug could be administered either orally or via a long-lasting implant in the eye.

The researchers believe fluoxetine works against AMD by binding with a particular agent of the immune system known as an inflammasome. This inflammasome, NLRP3-ASC, triggers the breakdown of the pigmented layer of the eye's retina.

Source : Journal reference :

Ambati, M., et al. (2021) Identification of fluoxetine as a direct NLRP3 inhibitor to treat atrophic macular degeneration. Proceedings of the National Academy of Sciences. doi.org/10.1073/pnas.2102975118.