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Research Article

The Effect of Active Management of Ocular Surface Disease in a Glaucoma Clinic: An Observational Study

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Abstract

Purpose: The objective of the study was to evaluate the effect of active management of ocular surface disease in our cohort of glaucoma patients treated in the outpatients department at a tertiary referral center.

Methods: A single centre, non-interventional, observational study designed to assess the effect of active management of ocular surface disease in a small cohort of patients getting treatment for chronic primary open angle glaucoma. Using the quality of life questionnaire – Ocular Surface Disease Index (OSDI) the severity of ocular surface disease was quantified. Other relevant parameters were analysed to find any correlation between OSD vs disease chronicity, disease duration, number of topical drops and associated use of lubricant therapy, tetracyclines and Omega 3 supplements.

Results: Severity of symptoms graded by OSDI questionnaire showed 89% of our patients were in the normal to mild range inspite of being on glaucoma treatment for an average of 10.52years. The number of antiglaucoma topical therapy was found to be 1.91 in our group, which is well known to cause ocular surface issues. In our cohort, practice of using oral supplements and oral tetracyclines was also found, and the OSDI scores were found to be less when compared to those not on these supplements.

Conclusion: Active management of ocular surface disease in patients on chronic antiglaucoma topical medication can reduce the burden of ocular surface disease and maintain a relatively low level of discomfort in the day-to-day lives of glaucoma patients.

Keywords: *Glaucoma; Ocular Surface Disease; Osdi; Dry Eye; Blepharitis; Dry Cornea*

Introduction

Glaucoma is a potentially blinding condition, afflicting around 67 million people worldwide, of whom about 10% or 6.6 million eventually lose their vision. This makes it the second most common cause of blindness worldwide, and the leading cause of irreversible blindness [1]. The majority of glaucoma patients are treated with medical therapy using eye drops to lower intraocular pressure.

Apart from the visual symptoms of glaucoma, other conditions may co-exist, further compromising the patient's quality of life. Ocular surface disease (OSD), a multifactorial condition that leads to tear film instability and subsequent predisposition to inflammation at the ocular surface [2] may potentially be one of them. Older studies show that approximately 15% of the general elderly population experiences some level of OSD [3]. However, OSD is becoming increasingly recognized as a highly prevalent entity in the general population with an incidence ranging from 5 to 30% in population aged 50 years and above [4].

Patients with ocular hypertension and primary open glaucoma have been shown to suffer from OSD at a higher prevalence than in the general population [5,6]. OSD has been shown to reduce quality of life in patients with and without glaucoma [7]. Patients with more severe glaucoma and those on multiple medications have been shown to have a very high prevalence of OSD [8].

The objective of our study was to determine the effect of active management of OSD in glaucoma patients treated in our practice. The intention was to compare our results with other published studies, identify differences in prevalence of OSD and discuss factors that may explain the difference.

Materials And Methods

This was a non-interventional, observational study, designed to determine the effect of managing OSD in patients suffering with glaucoma or ocular hypertension (OHT) and on topical medical therapy. Eligible patients included male and female patients over the age of 18 years who had a confirmed diagnosis of primary open angle glaucoma (POAG) or OHT, and were using drops to lower intraocular pressure. Prior to being seen by the ophthalmologist, the nurse specialist identified patients attending our clinic, who met our inclusion criteria. They were requested to complete the Ocular Surface Disease Index (OSDI) questionnaire. This questionnaire is one of the frequently used survey tools for assessment of ocular surface disease severity in dry eyes [14]. It consists of 12 questions that assess symptoms (OSDI - Symptoms), functional limitations (OSDI- Functional) and environmental factors (OSDI-Triggers) related to ocular surface disease divided into three subscales, with each response being recorded on a scale from 0 (none of the time) to 4 (all of the time). The OSDI outcome is a score on a scale of 0 to 100, with a higher score representing greater disease severity. An OSDI score of 0 - 12 indicates a normal ocular surface, of 13 - 22 indicates mild OSD, of 23 - 33 represents moderate OSD and a score of 33 - 100 indicates severe OSD, as shown in chart 1.

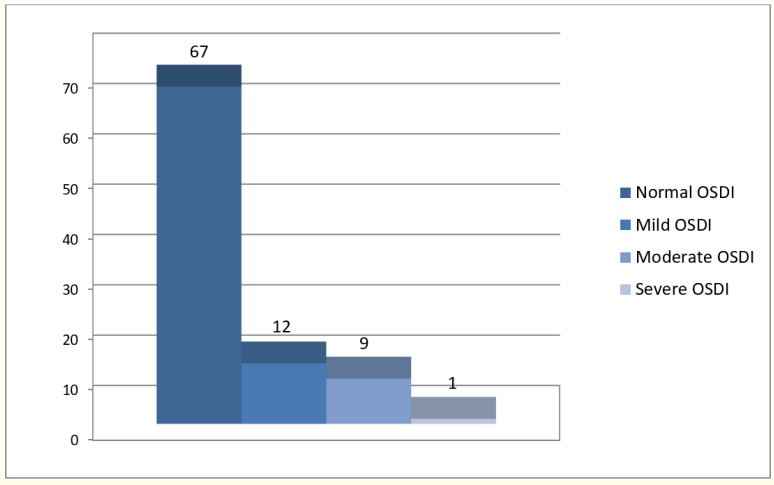

Chart 1: *OSDI score differentiation into 4 different groups. Maximum number of patients fell the Normal group.*

In addition to recording the OSDI score of each patient, the usual demographic data was collated (age, sex and ethnicity). The duration of the disease and severity of glaucoma classified into early, moderate and advanced based on global indices of Mean Deviation (MD) measured during the latest and most accurate Humphrey visual field assessment (24 - 2) were also recorded. A mean deviation (MD) of 0 to - 5 decibels (dB) was regarded as early glaucoma, an MD of - 5dB to - 10dB was classified as moderate and an MD of less that -10dB was classified as advanced glaucoma. Topical glaucoma therapy, topical lubricant therapy, oral tetracycline use and oral supplement use were recorded to observe their collective impact on severity of OSDI.

Statistical analysis

The statistical analysis was undertaken using Microsoft Excel 2011 (version 14.4.9; Microsoft Corporation) and Statistics Open for All (SOFA) (version 1.4.4; Paton-Simpson and Associates Ltd). The normality of the distribution of the sample was checked by the Wilcoxon signed rank test. The number and percentage of patients having normal, mild, moderate and severe OSD based on their OSDI score were analyzed. Correlations between the mean OSDI score and other independent variables that were identified were analyzed using the Spearman's test of linear correlation. The variables were compared using T-Test with one tailed distribution and heteroscedastic test (samples with unequal variance).

Results

A total of 93 patients were enrolled in the study. Four patients had incomplete data hence were excluded. The demographic data showed no gender bias, with equal male to female ratio and average age of the patients being 70.29 years (± 12.79 years, range 44 to 93).

Although the majority of our patients were of Caucasian descent (67/89, 75.3%), a significant proportion were non-Caucasian as expected in a tertiary referral hospital setting serving a large proportion of a cosmopolitan city. Seventy percent (70%) of our patients had Primary open angle glaucoma or OHT and the rest had secondary glaucomas.

Sixty-seven (75.3%) patients had OSDI scores falling in the normal range, 12 patients (13.5%) had an OSDI score in the mild OSD range and 9 patients (10.1%) had an OSDI score in the moderate range. We only had 1 (1.1%) patient who scored their OSDI questionnaire with values suggesting severe OSD (Chart 1).

Mean OSDI score for different age groups is shown in chart 2. The average age was noted to be 71 years (± 12.23) in the normal OSDI score group, 64.4 years (± 12.85) in the mild OSDI score and 72.5 (± 8.61) years in the moderate OSDI score group and 72 years of age for the patient in the severe OSDI score group. There was no statistically significant difference between the groups but a poor but positive correlation was noted between age and OSDI score (R = 0.29; p = 0.06).

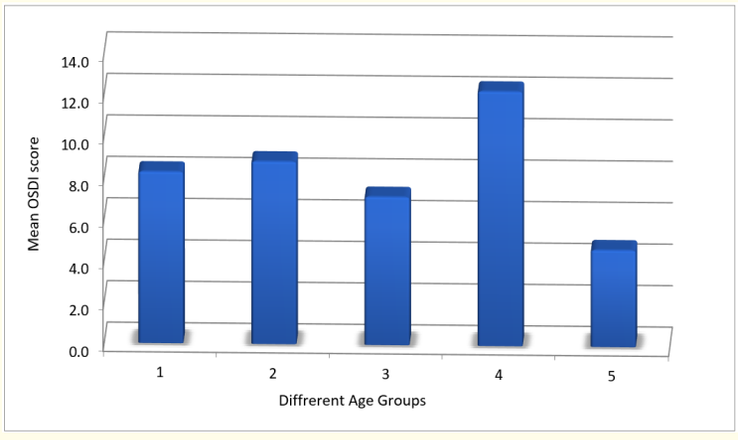

Chart 2: *Mean OSDI score based on age of population under study. The age was divided into 5 age group as given in the chart. Age Group (years) 1- 40-50; 2 -51-60; 3 - 61-70; 4 - 71-80; 5 > 81years.*

The mean time since glaucoma diagnosis for the whole group was 10.52 years ± 7.24 years, range 2 to 31 years. The mean time from diagnosis was found to be 11.12 (± 7.73) years for the normal OSDI score group, 7.2(± 3.7) years for the mild OSDI score group and 10.89 (± 6.71) years for the moderate OSDI score group and 7 years for the severe OSDI score patient. We did not find a statistically significant difference between the duration of anti-glaucoma treatment and OSDI scores (Chart 3) and a poor but positive correlation was noted between the two as well (R = 0.299).

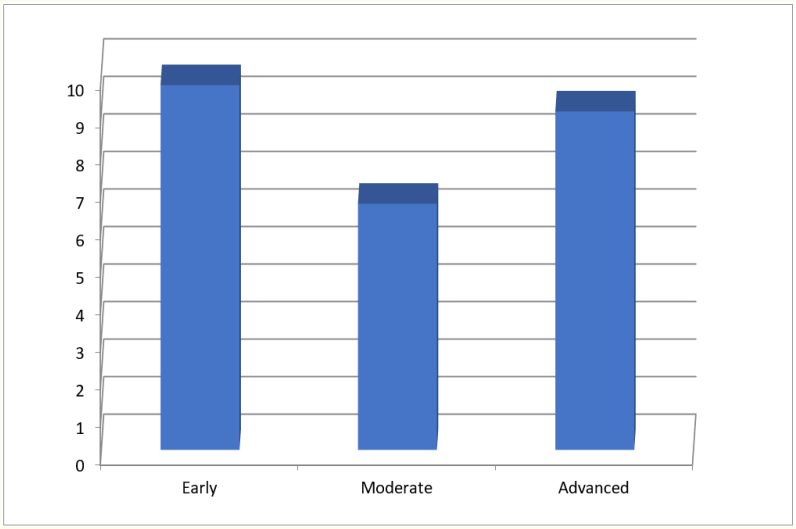

Chart 3: *Mean OSDI according to severity of glaucoma.*

On average patients used 1.91 anti-glaucoma medications. Thirty-six patients (40.4%) were using only 1 anti-glaucoma medication, 25 patients (28.1%) were on 2 medications and 28 patients (31.5%) were on 3 medications. The average number of medications used in the normal, mild and moderate group was 1.92, 1.42 and 2.33 respectively. There was no statistically significant difference on comparing the number of medications and OSDI score.

Out of 89 patients 44 (49.4%) had early glaucoma, 21 (23.6%) had moderate glaucoma and 24 (27%) had advance glaucoma. The mean OSDI scores for early, moderate and advanced groups were 9.72, 6.56 and 9.02 respectively. We could not show any correlation between the stage of glaucoma and ocular surface disease as shown in chart 3 and no statistical significance was found between each group on comparison.

In our group we used low dose oral tetracyclines (Doxycycline 50mg once daily or alternate day) to help improve OSD. Eight of eighty-nine patients (9%) were on oral Doxycycline and had mean OSDI score of 4.30 (± 4.41) and those not on Doxycycline had a mean OSDI score of 9.22 (± 9.71). As the number of patients who were on oral Doxycycline was too low as compared from those who were not, statistical significance was not calculated.

Oral Supplements were also given to patients to improve OSD. Forty-eight of eighty-nine (54%) were on oral supplementation (various vitamins and Omega 3 oil). The mean OSDI scores for those on oral supplementation were 7.34 (± 7.22) and those without was 10.47 (± 11.41). These differences were not found to be statistically significant (p = 0.13).

Twelve patients were taking oral supplements with topical unpreserved antiglaucoma therapy and no lubricating agents. Of these twelve, eleven (92%) had OSDI scores in the normal range, which do suggests that oral supplements in combination with preservative free medications may help in curtailing ocular surface inflammation.

Discussion

Ocular surface disease in glaucoma patients is under-recognized and undertreated [9]. The incidence of OSD in patients with glaucoma and OHT using topical anti glaucoma drops is much higher than in the general population as reported by Leung., *et al* [6], who found that 59% of patients with glaucoma or OHT had OSD symptoms. They also noted that 27% of their study population with primary open angle glaucoma (POAG) or OHT had severe symptoms of OSD. This is consistent with a study published by Erb., *et al* [10], in 2008 involving 20,000 glaucoma patients having an incidence of 53% of OSD based and a 20.3% prevalence of severe OSD [4]. In another multicenter study involving 448 glaucoma patients, Garcia-Feijoo., *et al* [11], reported an OSD prevalence of 59.2% using the OSDI questionnaire to identity OSD.

Our data shows that patients with glaucoma and OHT treated with topical anti-glaucoma medication and active management of OSD using the various strategies outlined above had lower OSDI scores. Prevalence of OSD among our cohort of patients was found to be 24.7% with only 1.1% having severe OSD.

In addition, in our population, OSD prevalence was not correlated with duration or severity of glaucoma or the number of anti-glaucoma medications used and only a weak correlation to the age of the patient was observed.

OSD is known to cause discomfort and fluctuating vision and in particular difficulty with reading and driving. It is therefore useful to incorporate the OSDI questionnaire into the routine examination of patients with glaucoma. We believe that the lower prevalence of OSD in our population is a reflection of our clinical approach. In our practice, management of the glaucoma patient involves meticulous attention to the care of ocular surface as well as controlling intraocular pressure.

We use various approaches to support ocular surface health. We start by asking the patient's subjective opinion on ocular comfort and visual problems related to OSD. We then actively look for the multitude of signs of OSD. Therapy is targeted for the individual by using various measures to support the ocular surface. These include using less toxic glaucoma medications, reducing Benzalkonium Chloride (BAK) exposure to the eyes, use of non BAK containing lubricants, use of low dose oral tetracyclines, advice on dietary measures thought to improve ocular surface health, use of targeted supplements, advising on lid hygiene using hot compresses and lid wipes (Blephaclean, Thea Pharmaceutical Ltd, Banbury, UK).

Therapeutic considerations stem from clinical experience. We know from much published earlier data that prolonged use of topical ocular medications preserved with BAK may exacerbate OSD. Preservatives in anti-glaucoma medications have been implicated in the development and worsening of ocular surface disease [12,13]. There is a demonstrated correlation between ocular surface disease and the presence of BAK and the number of concomitantly used eye drops containing BAK [6,8,10,14]. Preservatives cause a detergent effect on the lipid layer of tear film [15], and have been shown to decreases the density of goblet cells in the conjunctival epithelium [16]. The subsequent mucin reduction contributes to further instability of the tear film. Tear film instability is thought to lead to cytokine up regulation and a downstream activation of an inflammatory cascade [17]. In addition, the active ingredient in glaucoma medications also exerts an effect on the ocular surface [18]. The BAK molecules also alter the permeability of the ocular surface epithelium and are known to induce cell membrane lysis, putting the ocular surface at risk of dehydration and cause alterations in tight junctions and excessive stimulation of nociceptors and chronic pain [19].

The use of Tetracycline derivatives is useful in patients with OSD. Tetracycline compounds possess antibacterial as well as anti-inflammatory properties [20]; they have been shown to have immune-modulatory properties at lower doses and modulate the effects of inflammatory cytokines (IL-1B, IL-6, MMP-8 and -9) [21]. The anti-inflammatory benefits of orally administered tetracycline derivatives have been used in the treatment of chronic immune mediated diseases, including dry eye secondary to ocular rosacea and blepharitis [22,23]. A study conducted by Batra., *et al,* has shown marked improvement in ocular surface disease in patients with refractory glaucoma who had 3-month course of 50 mg daily oral doxycycline [24].

Some recent studies have shown a beneficial effect of a high intake of oral Omega 3 oils in patients with OSD [25]. In addition, we recommend a varied diet high in fruits and vegetables to ensure adequate intake of vitamins and other nutrients to ensure that the highly active process of tear production and regulation is appropriately supported.

Hot compresses and medicated lid wipes have been shown to be beneficial in improving tear film health [26]. We therefore also recommend these interventions in appropriate patients.

Study Limitations

We appreciate that our study has a small number of patients and is an observational study with multiple interventions but is undertaken in a pragmatic real world setting. Also, the samples were of unequal size and this may have an impact on the statistical analysis. However, it has shown baseline differences in OSDI scores in different intervention samples, opening horizons to further investigate these interventions through RCTs, eventually providing better evidence for practice.

We also understand the limitations of the OSDI as an instrument for accurately scoring OSD. Some of the parameters could be affected by the reduction in vision that occurs in patients with glaucoma. OSDI was designed as a screening survey to assess symptoms and their impact on vision related functions. However, this questionnaire does have excellent test-retest reliability and can effectively differentiate the ocular surface disease severity by giving it an objective composite score [8]. We also used it in our study as it is widely used and therefore our results are comparable to other studies.

The treatment of OSD in our patients is also varied and it is therefore difficult to draw conclusions on the best way to manage OSD. However, our paper was designed to only look at the effectiveness of these various strategies on the management of OSD in our population of glaucoma patients and the interventions are only of secondary significance. Further work in determining the most effective intervention in this group of patients is warranted.

Conclusions

Our study shows that if careful attention is given to ocular surface health of patients who are using anti glaucoma drops, it reduces the prevalence of OSD. This is likely to lead to an improvement in the quality of life of glaucoma patients. Ocular surface disease should not be accepted as a fact of life for glaucoma patients but rather clinicians should actively manage OSD in the glaucoma patient population.

Declaration of Competing Interests

No competing interests.

Declaration of Funding Sources

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