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Incidence and Risk Factors for Ocular Surface Disease in Patients Undergoing Glaucoma Medication: A Retrospective Analysis

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KEYWORDS

Ocular Surface Disease, Glaucoma, Benzalkonium Chloride, Intraocular Pressure, Quality of Life

ABSTRACT:

This research aims to examine the prevalence and the predisposing factors of Ocular Surface Disease (OSD) in glaucoma patients on long-term medication in the Department of Ophthalmology. The necessity of the presented research is explained in the context of the high rate of OSD among glaucoma patients, which negatively affects their quality of life and adherence to treatment. Major discoveries include the decrease in IOP after OSD treatment and a high proportion of the participants who had cataract surgery performed on them. The analysis reveals that the preservative agents in contact lenses including but not limited to benzalkonium chloride (BAK) are significant causal factors of OSD. The study reinforces the importance of preservative-free glaucoma medications and the necessity of the use of composite care models that would improve patients' prognosis and their adherence to therapy. Further, more extended follow-up and patient-depicted outcomes should be conducted in future to enhance the consequences of the treatment plans.

1. Introduction

1.1 Background of the Study

Glaucoma is a common and severe eye disease, which is currently classified among the most frequent causes of irreversible blindness. Here, it is mainly treated by using drugs that help to reduce Intraocular Pressure (IOP). Therefore, it has an important role in the development of the disease. Some of these drugs are prostaglandin analogues, beta-blockers, alpha agonists and carbonic anhydrase inhibitors that are useful in reducing IOP [1]. However, since glaucoma is a lifelong disease with continuous medication therapy, such treatment impacts the ocular surface unfavourably. Ocular Surface Disease (OSD) refers to disorders that affect the cornea, conjunctiva and eyelids and patients who suffer from the condition complain of dryness, irritation, burning sensation and blurring of vision. The issues concerning the prevalence and effects of OSD among glaucoma patients on long-term medication are becoming increasingly important in the field of ophthalmology.

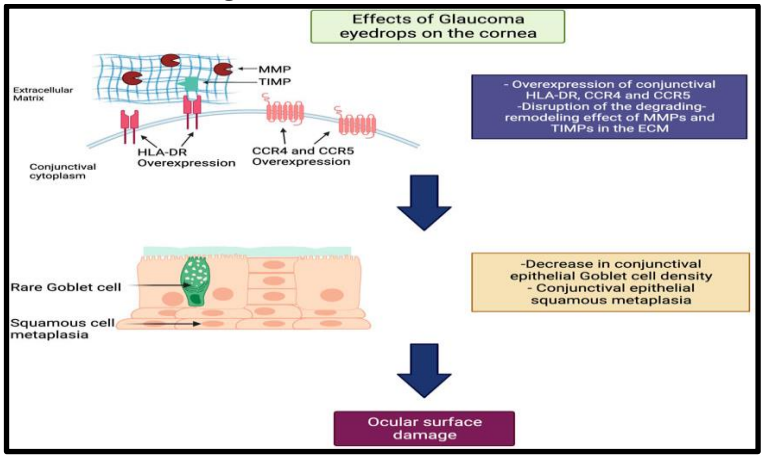

Figure 1.1: General Mechanism of Ocular Surface Damage

(Source: Influence by the study of MacIver *et al.* 2017)

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1.2 Problem Statement

However, there is limited information on the prevalence and risk factors of OSD in glaucoma patients despite the frequent use of glaucoma medications. It is crucial to research these aspects to minimise their effects on patients' ocular health and quality of life. Most patients with OSD stop taking their glaucoma medications or fail to adhere to the prescribed regimens, thereby experiencing a rise in IOP and worsening of glaucoma [2]. The purpose of this study is to investigate the incidence of OSD in patients using glaucoma medication and to identify the risk factors that may be associated with it.

1.3 Aims and Objective

The aim of this study is to establish the rate of development of OSD in glaucoma patients who are on medical therapy with glaucoma medication as well as establish the risk factors that lead to the development of OSD in the patient group. The specific objectives are

- To estimate the prevalence rate of OSD in the target population
- To control for age, gender and medication types and doses associated with the development of OSD
- To establish this relationship, the degree of OSD was compared with the types and periods of the use of glaucoma medication

1.4 Significance of the Study

It would be beneficial to comprehend how frequently this complication occurs in glaucoma patients and what contributed to the development of the disease. The outcomes of this study will add valuable evidence that can assist ophthalmologists in preventing patient compliance issues with glaucoma medications due to the occurrence of OSD, resulting in better management and treatment of this condition. Therefore, quicker recognition of patients who require special attention concerning OSD will help to introduce early intervention and more appropriate management of glaucoma patients' condition as well as contribute to enhancing their quality of life [3]. This will not only enrich the existing datasets but also help to empower clinicians in their efforts to deliver the best possible treatments for patient care with minimal interference to the patient's life.

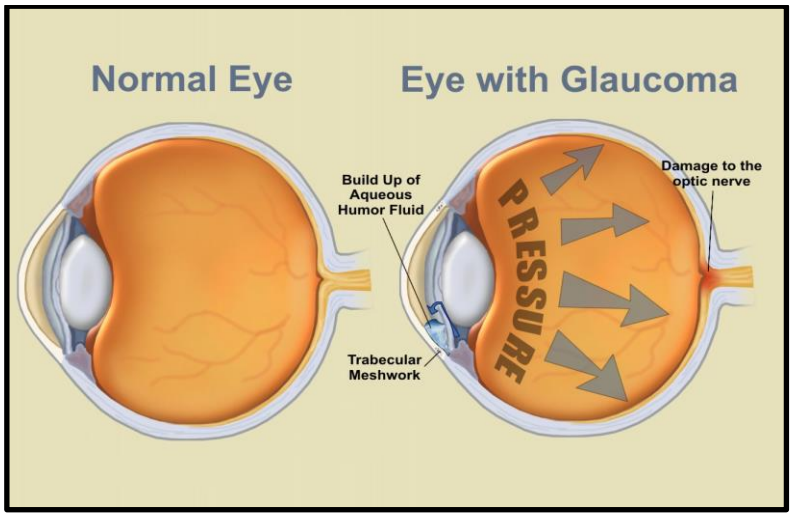

Figure 1.4: Normal Eye and Eye with Glaucoma

(Source: Influence by the Study of Kalouda *et al.* 2017)

2. Literature Review

2.1 Incidence of Ocular Surface Disease in Glaucoma Patients

A review of the literature concerning glaucoma and its complications discloses that Ocular Surface Disease (OSD) is a frequent occurrence among glaucoma patients, the rates of which differ significantly. Some surveys showed that the prevalence of OSD in patients using topical glaucoma therapy varies between 15% and 60%, proving that this is a serious issue [4]. These variability in the incidence rates can be due to the following factors, the study subjects, diagnostic procedures, and forms of glaucoma drugs administered. Glaucoma is a chronic

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condition, and hence, patients have to be on medication for an extended period, which is one of the significant causes of OSD in this population. These sustained exposures keep the eye surface exposed to medications, especially those with preservatives, which results in OSD.

2.2 Risk Factors for Ocular Surface Disease

Various factors predispose patients suffering from glaucoma to the development of OSD have been discovered. The type of medication is one of the independent variables, where prostaglandin analogues, beta-blockers, alpha agonists, and carbonic anhydrase inhibitors are somehow related to OSD. The introduction of preservative agents such as benzalkonium chloride (BAK) is seen to worsen the condition of OSD due to the toxicity of the former to the ocular surface [5]. Another interesting and, therefore, worthy of study type of material is drugs that are stored in the presence of BAK, as their use can lead to inflammation, instability of the tear film, and cellular damage [6]. In addition, they established that the period that participants are on medication increases with the worsening of OSD symptoms. This study revealed that patients on long-term glaucoma therapy experience cumulative toxic effects on their ocular surface thus manifesting more severe OSD. Moreover, in a study by Pérez-Bartolomé *et al.* (2017), it is seen that several factors contribute to the increased risk of OSD in glaucomatous patients. In particular, the OR of using BAK-containing medications is equal to 1.567, which is significant while eyedrops containing both BAK and PQ-1 reveal an OR of 5.09 It also reveals that a higher average OSDI score enhances the risks (OR 1.06).

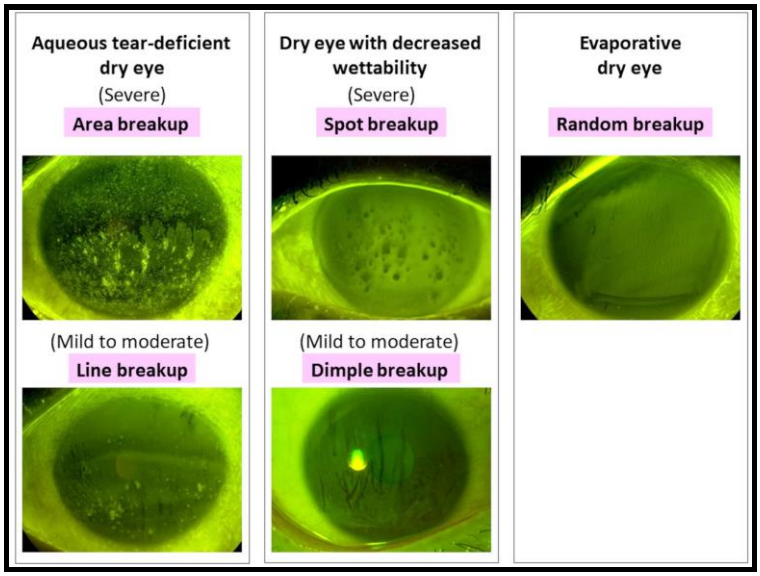

Figure 2.2: Effects of Tear film on quality of vision

(Source: Influence by the Study of Georgiev *et al.* 2017)

2.3 Impact of OSD on Quality of Life

It is imperative to state that OSD impacts the quality of life of glaucoma patients. These signs include dryness, itching, burning, and blurriness of vision which are quite agonising and hinder vision. Such manifestations cause poor compliance with glaucoma medications because the patient will decrease the dosage or stop using the medication altogether due to pain, which compromises the patient's glaucoma treatment. Failure to adhere to glaucoma medications entails elevation of the intraocular pressure (IOP) and progression of glaucoma which increases the risk to the patient's vision [7]. Treatment of OSD is therefore imperative because it helps provide comfort to the patients and at the same time manage the glaucoma, and reduce the rate of vision loss.

2.4 Literature Gap

There is still inadequate information regarding the identification of possible risk factors and their interfacing regarding the occurrence of OSD in glaucoma patients. The most common has been to investigate specific drugs or small groups of patients with no overall approach that takes into consideration demographic and clinical characteristics and their medications. Moreover, there are very few cross-sectional and comparative researches on

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the prevalence and severity of OSD under various glaucoma management modalities. These gaps are to be filled in this study by offering an extensive report on the prevalence and causes of OSD in a controlled patient population and thereby assist in more appropriate interventions for glaucoma patients vulnerable to developing OSD.

3. Methodology

3.1 Research Design

This study conducted at IGIMS Patna between March 2018 to February 2019, adopts an exploratory research design, which is particularly suitable for examining the complexities of OSD among glaucoma patients due to the varied and comprehensive interactions involved. This design enables the investigation of different factors and interactions prognostic to the incidence of OSD in patients with glaucoma receiving chronic glaucoma medication [8]. The exploratory feature of this design helps in the flexibility of the process of data collection and analysis, which allows for the consideration of new variables and correlations that may affect OSD outcomes. It is helpful when managing glaucoma in clinical practice because of the constant medication changes and patients' differential response. As a result of the structured approach, the study aims to establish causal relations and risk factors for OSD which will help to the dynamics of interaction between glaucoma medications and ocular surface condition.

3.2 Data Collection Method

Patients visiting tertiary eye care centres between April 2017 and March 2018 will form the sample population, and data will be obtained from their electronic medical records (EMRs). This particular secondary qualitative data collection technique involves identifying in-depth patient history, clinical notes, treatment plans, and instances of OSD recorded during clinical practice. Inclusion criteria will include patients, who are aged 18 years and above, had a diagnosis of primary open-angle glaucoma, pseudoexfoliative glaucoma, or normal-tension glaucoma and are on glaucoma medication for not less than six months [9]. Patients with a history of ocular surface diseases within one month before the study or those who undergo ocular surgeries during the study will be excluded to eliminate unrelated factors.

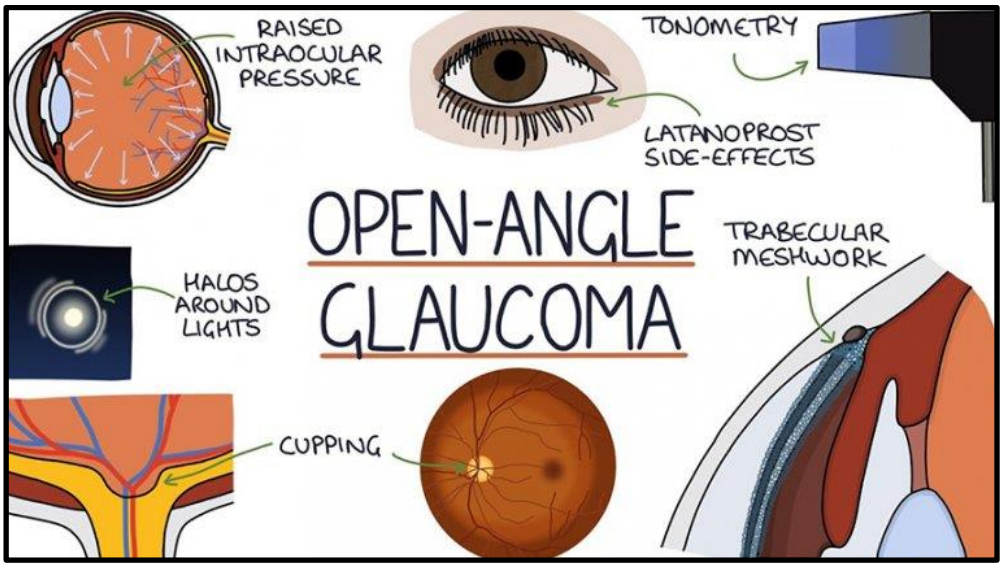

Figure 3.2: Open-angle glaucoma treatment

(Source: Influence by the Study of Sihota *et al.* 2018)

3.3 Data Analysis Method

Here, in this study, the thematic data analysis method has been selected to analyse the various factors and challenges associated with OSD amongst glaucoma patients on chronic medications. The thematic analysis involves codification, where one looks for patterns within qualitative data obtained from the EMRs. It entails data saturation, coding of information, formulation of themes from codes, refinement of themes to check on relevance and coherence, designation of each theme by definition and naming to give a clear insight into the discovery made [10]. Therefore, the analysis of findings in so far as the

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objectives of the research are concerned. This approach helps one to understand how various types of glaucoma medication as well as the lengths of time that they are used predict the incidence of OSD, thus explaining facts that can enable enhanced patient management of the disease.

3.4 Research Limitations

The practicable limitations that may affect the results of the study are one should also take into account that EMR data are retrospective, thus, they may indicate variability and completeness of documentation bias. Hence, the use of qualitative methods might not provide a correct insight into the entire spectrum of quantitative aspects of OSD incidence, which necessitates quantitative research. Generalisations of the findings obtained from the study done on the participants attending some tertiary eye care centres may not hold when compared to other demographically diverse populations or in other contexts of health care scenarios. However, the difference was largely carrying on the perception that study-specific inclusion and exclusion criteria might omit some cases and could affect the general range of the study. However, such an approach seems to provide some useful knowledge about OSD in glaucoma patients for subsequent research and clinical applications.

4. Data Analysis

4.1 Theme 1: Impact of Glaucoma Medication Types on OSD Development

Here, from the results of this study, one of many discovered problems amongst the glaucoma populace is the impact of the myriad categories of glaucoma medications on Ocular Surface Disease (OSD) [11]. This study has also been able to show the population evidence that prostaglandin analogues, beta-blockers, alpha-agonists, and carbonic anhydrase inhibitors are noticeable classes of medications that aggravate the symptoms of OSD. These are topical anti-inflammatory medications that are often prescribed in the control of IOP in glaucoma patients and are generally notorious for being damaging to the ocular surface, due to the inclusion of BAK as a preservative agent. Therefore, it has been disclosed that BAK can induce inflammation, compromise the tear film stability and exhibit toxic effects on the ocular surface cells which present as dryness, redness and discomfort which defines OSD.

Analysing factors, it was established that medication course and frequency are positively correlated and significantly affect the presence of OSD symptoms. In glaucoma patients, long-term medications including both preservatives and the active ingredient exert cumulative toxicity on the ocular tissues hence aggravating the OSD in patients [12]. This theme showed that the categorisation of medication and dosage must be taken into account more when evaluating Ocular Surface Disease in Glaucoma patients. This highlights the ophthalmologists to weigh the merits and demerits of the kinds of drugs to be used on the patients. Therefore, it seeks other forms of medications to be administered to the patients reducing the dosage of preservative to which the patient is subjected to minimise the development of the OSD.

4.2 Theme 2: Patient Compliance and Quality of Life Implications

The second major theme that emerged from the data analysis process is the ability of OSD to affect patient adherence to glaucoma medicines and the subsequent quality of life. Patients with OSD reported that symptoms such as dryness, itching, burning sensation, and blurred vision affected their quality of life and medication compliance [13]. Some of the patients complained of discomfort and reduced tolerance to their prescribed medicines due to OSD symptoms which may result in non-compliance or irregularity in taking glaucoma medications. Medication non-adherence is one of the biggest problems in glaucoma treatment because it leads to suboptimal control of intraocular pressure and progression of the disease with potential further loss of vision [14]. From the study, it emerged that OSD-related non-compliance is prevalent among glaucoma patients since many of them adjust their use of glaucoma medications to manage OSD symptoms with the possibility of affecting glaucoma therapy. In the study of Dubrulle *et al.* (2018), it is seen that the mean IOP in patients reduced considerably from 23.75±9.98 mmHg before OSD management to 15.15±4.75 mmHg. Compliance is effective in the management of the disease, as evidenced by the patients' reduction of BP to 75 mmHg after three months of treatment. Moreover, seventy per cent of patients in this study had previously had cataract surgery, indicating an interference of multiple operations on the quality of patients' lives. Therefore, the qualitative analysis suggests that aside from physical comfort, OSD symptoms interfere with the psychological well-being and overall quality of life of glaucoma patients. Here, OSD management is quite challenging and complicated with glaucoma, and patients have even complained of

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frustration and anxiety due to the inability to manage the two conditions.

5. Conclusion and Recommendations

5.1 Conclusion

Moreover, as an end to this retrospective analysis, it is realised that Ocular Surface Disease (OSD) is likely to pose a challenge for a good number of patients being treated for glaucoma. The study emphasises OSD symptoms such as dryness, irritation and blurred vision, all of which have severe effects on glaucoma patients' medication adherence, and interpersonal well-being. These results also highlighted the importance of adopting those treatment management approaches to manage both disorders at the same time, leading to better results in the patient's condition and compliance with therapy plans.

5.2 Recommendations

It is highly recommended that healthcare providers should aim at selecting glaucoma drugs that contain little or no preservatives at all or where this is impossible select formulations of glaucoma drugs in preservative-free formulations to minimise the impact of OSD. Healthcare practitioners managing glaucoma should incorporate screening and monitoring of the ocular surface as part of a glaucoma examination [15]. The patient education programs should also emphasise that despite the presence of OSD signs, the glaucoma treatment should be continued to reach the target IOP and halt the progression of the pathology. Eye care professionals and other healthcare professionals such as ophthalmologists, optometrists, and other primary care physicians who come across glaucoma patients should address the physical and psychological implications of OSD in this patient population.

5.3 Future Outlook

Future research regarding the subject should therefore entail follow-up studies to observe the condition of OSD in patients with glaucoma after the long-term use of fashionable medications for an extended period. New glaucoma medications clinical trials with different preservatives or formulated without preservatives are vital to provide better management of this condition and reduce the risks of OSD impact. The inclusion of patient-reported outcome measures and quality-of-life measures will give a deeper insight into how OSD affects patient's day-to-day existence and satisfaction with treatment. Disseminating knowledge about the ocular surface and its relevance within glaucoma healthcare policies will also contribute to enhancing the overall scale of care delivery by recommending standardised approaches to care.

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