



# Investigation of the Relationship Between Chronic Use of Topical Antiglaucomatous Drops and Ocular Demodex Infestation

## Topikal Antiglokomatöz Damlaların Kronik Kullanımı İle Oküler Demodeks Enfestasyonu Arasındaki İlişkinin Araştırılması

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### Abstract

**Aim:** To investigate the relationship between chronic use of topical antiglaucomatous drop and ocular Demodex infestation.

**Material and Method:** This cross-sectional study included a total of 226 eyes, as both eyes of 55 patients with bilateral glaucoma and 58 control subjects. A total of 8 eyelashes, 2 each from the lower and upper eyelids of all the study participants, were taken and the samples were sent to the parasitology laboratory for analysis.

**Results:** The mean age of the study participants was 66.48±15.19 years in the glaucoma patients, and 64.76±10.89 years in the control group. From analysis of the eyelash samples taken, ocular Demodex was positive in 55% of patients with glaucoma, and negative in 45%. In the control group, Demodex was positive in 34% and negative in 66%. Demodex infestation positivity was determined to be statistically significantly higher in patients with glaucoma (p= 0.042).

**Conclusion:** The rate of ocular Demodex infestation increases with age, and it is estimated that this rate is further increased by the use of chronic topical antiglaucomatous drops.

**Keywords:** Antiglaucomatous drops, demodex folliculorum, glaucoma, ocular demodex

### Öz

**Amaç:** Topikal antiglokomatöz damlaların kronik kullanımı ile oküler Demodeks infestasyonu arasındaki ilişkiyi araştırmak.

**Gereç ve Yöntem:** Bu kesitsel çalışmaya 55 bilateral glokomlu hasta ve 58 kontrol olgusunun her iki gözü olmak üzere toplam 226 göz dahil edildi. Tüm katılımcılardan alt ve üst göz kapaklarından 2'şer adet olmak üzere toplam 8 adet kirpik alındı ve örnekler analiz için parazitoloji laboratuvarına gönderildi.

**Bulgular:** Çalışmaya katılanların yaş ortalaması glokom hastalarında 66,48±15,19, kontrol grubunda 64,76±10,89 idi. Alınan kirpik örneklerinin analizinden, oküler Demodeks glokomlu hastaların %55'inde pozitif ve %45'inde negatifti. Kontrol grubunda Demodeks %34 pozitif, %66 negatifti. Demodeks enfestasyon pozitifliği glokomlu hastalarda istatistiksel olarak anlamlı derecede yüksek saptandı (p= 0,042).

**Sonuç:** Oküler Demodeks infestasyon oranı yaşla birlikte artmaktadır ve kronik topikal antiglokomatöz damla kullanımı ile bu oranın daha da arttığı tahmin edilmektedir.

**Anahtar Kelimeler:** Antiglokomatöz damlalar, demodeks follikülörüm, glokom, oküler demodeks



## INTRODUCTION

Glaucoma, a neurodegenerative disease, is the most common cause of irreversible, preventable blindness worldwide, although it usually progresses slowly.<sup>[1]</sup> The main treatment principle of the disease is to lower the intraocular pressure (IOP).<sup>[1,2]</sup> Even though lowering IOP is mostly achieved with antiglaucomatous drops (AGDs), laser, or surgical methods<sup>[1]</sup> the treatment becomes difficult due to the side effects of the AGDs used including redness, itching, burning, stinging, epiphora, and iris discoloration.<sup>[3,4]</sup> Ocular infections such as blepharitis and conjunctivitis may occur at any time during treatment with topical AGDs, especially those containing preservatives.<sup>[5-7]</sup>

The most common ectoparasite in humans is Demodex<sup>[8]</sup>, two medically important species of which are Demodex folliculorum and Demodex brevis, although the Demodex species found in different organisms can be seen incidentally. Demodex brevis is smaller and found deep in the sebaceous glands of the eyelids and the lobules of the meibomian glands. Demodex folliculorum is larger and typically found in clusters in the eyelash follicles.<sup>[8]</sup> Demodex lives in the anterior structures of the eye, including the eyelashes, eyelids, and ocular surface, causing ocular demodicosis. The mites were thought to be mostly innocuous, forming a normal component of the eyelid flora and causing allergic or immunological reactions only in rare cases. However, a number of ocular surface disorders, such as chronic blepharitis, ocular surface inflammation, and meibomian gland dysfunction, have been connected to Demodex infestation. Undiagnosed or neglected Demodex infestations may be among the causes of chronic blepharitis, conjunctivitis and chalazions.

To our knowledge, no research has been done in the literature examining the relationship between ocular Demodex, and chronic use of topical AGDs. The purpose of this study was to look into the relationship between Demodex and chronic use of topical AGDs.

## MATERIAL AND METHOD

This cross-sectional, observational study analyze the prevalence of ocular Demodex infestation in patients with glaucoma was conducted between May 2022 and August 2022. The study included a control group of 58 individuals without glaucoma and 55 bilateral glaucoma patients who were being followed up in the Ophthalmology Department of Bolu Abant İzzet Baysal University Training and Research Hospital. Approval for the study was granted by the Local Ethics Committee (No: 2022/132). Patients signed informed consent forms, and all procedures followed the principles of the Helsinki Declaration.

All patients underwent detailed eye examinations. The control group comprised healthy subjects with the exception of refractive disorders within  $\pm 3.0$  diopters. Patients using

topical AGDs with preservatives for at least 2 years were included in the glaucoma group, and patients were excluded from the study if they were using topical drugs other than topical AGDs, had any known eye disease other than glaucoma, or any known systemic disease.

A total of eight eyelashes per person were taken from each study participant, two from each eyelid. Eye forceps were used to remove the eyelash samples, which were then fixed on slides with cellophane tape, and examined under a light microscope at x5 and x10 magnification in the laboratory of the Department of Medical Parasitology, Bolu Abant İzzet Baysal University Faculty of Medicine. Patients with Demodex infestation in their eyelashes were treated.

## Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA) for Windows software. The Independent Samples t-test was used to evaluate parametric data, and the Chi-square test was used for non-parametric data. Data were calculated as mean  $\pm$  standard deviation values, number and percentage. A value of  $p < 0.05$  was considered statistically significant.

## RESULTS

Evaluation was made of a total of 226 eyes of 55 bilateral glaucoma patients and 58 control subjects. The glaucoma group comprised 29 males and 26 females with a mean age of  $66.48 \pm 15.19$  years, and the control group comprised 31 males and 27 females with a mean age of  $64.76 \pm 10.899$  years. No statistically significant difference was observed between the two groups in terms of gender and age ( $p = 0.742$ , and  $p = 0.097$  respectively). In the eyelash samples taken, ocular Demodex positivity (Demodex+) was determined in 30 (55%) and ocular Demodex negativity (Demodex-) in 25 (45%) of the glaucoma patients. In the control group, Demodex+ was determined in 20 (34%) patients and Demodex- in 38 (66%) patients. When the glaucoma and control groups were compared, the rate of Demodex+ was found to be statistically significantly higher in the glaucoma group ( $p = 0.042$ ). In the glaucoma patients with Demodex+, involvement was bilateral in 14, in the right eye only in 10, and in the left eye only in 6. On the other hand, in the control group with Demodex+, involvement was bilateral in 5, in the right eye only in 7, and in the left eye only in 8. In the samples taken from the eyelashes of all the patients with Demodex+, D. Folliculorum was present in 38 eyes, D. Breves in 5 eyes, and both parasite species were found in 7 eyes.

## DISCUSSION

In this cross-sectional study, the rate of ocular demodicosis was found to be higher in patients with glaucoma than in the control group without glaucoma (55 % and 34 %, respectively).

Antiglaucomatous drops still take the first place in the treatment of glaucoma, which is an insidious disease. In addition to the therapeutic properties of these drops, the frequent occurrence of side-effects, known as ocular surface disease (OSD), is a negative situation for the patient.<sup>[3,5]</sup> In previous studies, it has been observed that OSD disrupts the normal flora in the cornea and conjunctiva, changes the inflammatory and anti-inflammatory balance, and increases the risk of ocular infection.<sup>[6,7,9,10]</sup> Schwartz et al. stated that although most of the preservatives used in AGDs are bactericidal and fungicidal, when they are used for a long time bacterial resistance increases and the risk of bacterial and fungal infections increases.<sup>[10]</sup> Geyer et al. reported that eye infections due to contamination increased after the use of AGDs in patients with glaucoma.<sup>[6]</sup> Azari et al. also reported that toxic and infectious conjunctivitis is more common in patients using topical drugs.<sup>[7]</sup> Baudouin et al., however, found that glaucoma itself triggers inflammation in many areas of the eye, from the anterior segment to the posterior segment, and can disrupt the anti-inflammatory response.<sup>[11]</sup> The results of the current study demonstrated that the rate of ocular Demodex infestation was higher in patients with glaucoma compared to the control group. It was thought that the AGDs used disrupt the ocular flora, disrupt the structure of the ocular surface, damage ocular immunity, and thus, the associated infection rate is higher.

It is known that ocular demodicosis increases with age and may be associated with OSD and especially blepharitis.<sup>[8,9,12]</sup> Bonnar et al found ocular Demodex+ at a rate of 53 % preoperatively in 100 cataract patients.<sup>[13]</sup> However, most of those patients were asymptomatic. Many studies have shown that ocular Demodex is closely related to ocular infections (such as blepharitis, conjunctivitis, and keratitis).<sup>[8,12,14]</sup> The aforementioned studies have revealed that sometimes demodicosis causes OSD and ocular infection, and sometimes in contrast, these primary ocular disorders create a predisposition to demodicosis.<sup>[8,12,14]</sup> In other words, it is thought that both situations contain complex mechanisms that are intertwined.

From a literature search only one article was found which had examined the relationship between ocular demodicosis and glaucoma.<sup>[4]</sup> In that study by Polit et al., glaucoma patients using Prostaglandin analogue with preservatives and control subjects were compared. Interestingly, the prevalence of Demodex+ patients was found to be lower in the glaucoma group.<sup>[4]</sup> In this study, Demodex+ was reported 52% with latanoprost; 42% with travoprost; 7% with bimatoprost.<sup>[4]</sup> On the contrary, in our study, regardless of the type of AGDs, all patients with glaucoma were included in the study and the rate of demodicosis was found to be statistically significantly higher in the glaucoma group than in the control group. The mean age of the patients with glaucoma was higher than that of the patients in the current study (70.34±9.7 years, and 66.48±15.19 years, respectively).<sup>[4]</sup> Together with the factors mentioned above, many multifactorial causes, which are

as yet unknown, may have affected the results of the study. However, according to the literature information obtained, the use of topical AGDs may increase the risk of many bacterial and fungal infections, including ocular Demodex, by disrupting the structure of the ocular surface and flora.<sup>[6,7,9-11]</sup>

One of the important drawbacks of this study was the limited number of patients included. More comprehensive results could have been obtained if the patients were classified separately according to the type of AGDs used and according to age groups. However, despite these limitations, this study can be considered of value as statistically significant results were obtained, there were significant differences compared to other studies, and it is one of the very few studies on this subject.

## CONCLUSION

It should be known that the rate of ocular Demodex increases with age, and this rate may increase with chronic use of AGDs with preservatives in patients with glaucoma. However, there is a need for more comprehensive studies including more patients and different age groups to clarify the subject.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of the Bolu Abant İzzet Baysal University Clinical Researches Ethics Committee (2022/132).

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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