

Does proptosis effect the meibography in patients with thyroid eye disease?

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ABSTRACT

Objective: The study aimed to compare the meibographies of the eyes of patients with thyroid eye disease who have varying degrees of proptosis.

Materials and Methods: Charts of patients with thyroid eye disease between January 2019 to January 2022 were retrospectively reviewed. Patients with mild and inactive thyroid eye disease, and with 1 mm or more difference in measurements of Hertel exophthalmometer between the eyes were included in the study. The eye of each patient with higher proptosis was included in the study group while the other eye with lower proptosis was included in the control group. The area of meibomian gland loss was evaluated using meibography (Sirius; CSO, Florence, Italy).

Results: Total of 28 eyes of 14 patients were evaluated. Mean meibomian gland dropout area for the upper eyelid was $17.91 \pm 15.37\%$ in the study group and $14.43 \pm 8.61\%$ in the control group. Mean meibomian gland dropout area for the sum of upper and lower eyelid was $44.76 \pm 23.16\%$ in the study group and $43.03 \pm 21.59\%$ in the control group. Mean meibomian gland dropout area for the upper eyelid and also for the sum of upper and lower eyelid were higher in the study group than the control group; however, these results were not significant ($p=0.540$ and 0.865 , respectively). On the other hand, the Pearson correlation test results suggested a significant correlation between the two groups; for the upper eyelid ($p<0.001$, $r=+0.670$) and also for the sum of upper and lower eyelids ($p<0.001$, $r=+0.768$).

Conclusion: This study showed differences regarding meibographic changes between control and study group. Further studies with larger series are needed to confirm these results.

Keywords: Meibography, meibomian gland morphology, thyroid eye disease

INTRODUCTION

Thyroid eye disease (TED) is one of the most common orbital inflammatory disease, moreover it is the most common cause of unilateral and bilateral proptosis seen in adults [1]. The clinical presentation of TED includes proptosis, lid retraction, lid lag, lagophthalmus, restrictive extraocular myopathy, optic neuropathy, and inflammatory changes of the ocular surface [2]. Dry eye is often the primary culprit behind ocular surface discomfort in these individuals [3]. Prior research has suggested that, alongside inflammation, factors such as tear film evaporation and osmolarity due to proptosis and widened lid fissures could contribute to dry eye symptoms in these patients [4]. However, the precise mechanism detailing the connection between TED and dry eye remains incompletely understood.

The study was designed to compare the meibographies of the eyes of patients with TED who have varying degrees of proptosis in between the eyes. Thus, it was aimed to investigate one of the factors contributing to the pathophysiology of dry eye in TED patients.

MATERIALS and METHODS

Charts of patients with TED who were admitted to our hospital between January 2019-January 2022 were retrospectively reviewed. Patients with mild and inactive TED, and with 1 mm or more difference in measurements of Hertel exophthalmometer (Handaya, Tokyo, Japan) between the eyes were included in the study. The eye of each patient with higher proptosis was included in the study group while the other eye with lower proptosis was included in the control group. The area of meibomian gland loss was evaluated using meibography (Sirius; CSO, Florence, Italy). The upper and lower eyelids' tarsal conjunctival surfaces were inverted, and a minimum of eight images of meibomian

glands were captured to choose the most distinct image. All the measurements were done by the same physician. The study was approved by the Ankara Bilkent City Hospital Ethics Committee (E1-23-4564) and conducted in accordance with the principles of the Helsinki Declaration.

The distribution of the data was evaluated with the Kolmogorov–Smirnov test. Student's T-test and Mann-Whitney U test were used for differences between the groups. Pearson correlation coefficients were used to study the association between study and control groups. A value of $P \leq 0.05$ was considered significant. Statistics were made using SPSS 25.0 program.

RESULTS

A total of 28 eyes from 14 patients were assessed, comprising 9 (64.3%) women and 5 (35.7%) men. The mean age of the patients was 49.30 ± 11.25 years. The mean Hertel exophthalmometry value was 19.36 ± 4.22 mm for the study group and 17.79 ± 3.87 mm for the control group.

The mean meibomian gland dropout area for the upper eyelid was $17.91 \pm 15.37\%$ in the study group and $14.43 \pm 8.61\%$ in the control group, while for the sum of upper and lower eyelids, it was $44.76 \pm 23.16\%$ in the study group and $43.03 \pm 21.59\%$ in the control group. Although the mean meibomian gland dropout area for both the upper eyelid and the sum of upper and lower eyelids was higher in the study group compared to the control group, these differences did not reach statistical significance ($p=0.540$ and $p=0.865$, respectively) (Table 1).

On the other hand, the results of the Pearson test indicated a significant correlation between the two groups: for the upper eyelid ($p < 0.001$, $r = +0.670$) and also for the sum of upper and lower eyelids ($p < 0.001$, $r = +0.768$).

Table 1. Meibomian gland dropout area in eyes with greater proptosis (study group) and lesser proptosis (control group)

	Study Group	Control Group	P
Meibomian gland loss area (upper eyelid) (%)	17.91 ± 15.37	14.43 ± 8.61	0.540
Meibomian gland loss area (lower eyelid) (%)	26.85 ± 12.75	28.60 ± 15.80	0.788
Meibomian gland loss area (sum of lower and upper eyelid) (%)	44.76 ± 23.16	43.03 ± 21.59	0.865

DISCUSSION

TED is one of the most common orbital inflammatory disease, moreover it is the most common cause of unilateral and bilateral proptosis seen in adults [1]. The clinical presentation of TED includes proptosis, lid retraction, lid lag, lagophthalmus, restrictive extraocular myopathy, optic neuropathy, and inflammatory changes of the ocular surface [2]. Dry eye is often the primary cause of ocular surface discomfort in individuals with TED [3]. Prior studies suggest that, apart from inflammation, tear film evaporation and osmolarity due to proptosis and widened lid fissures may contribute to dry eye symptoms [4]. However, the exact mechanism elucidating the link between TED and dry eye remains incompletely understood.

Earlier investigations examining the correlation between dry eye and TED found notable distinctions in meibography scores between individuals with TED and healthy individuals [5-7]. Moreover, the meibography scores of TED patients had a positive association with exophthalmos and palpebral fissure height in some studies [7, 8].

Recent studies have identified a link between meibomian dysfunction caused by systemic and ophthalmologic conditions and inflammation. TED is recognized as an inflammatory disorder, with previous research indicating inflammation in both the ocular surface and eyelids [9]. Is the pathogenesis of the dry eye seen in TED patients due to inflammation or does the degree of proptosis also contribute to the pathophysiology?

The investigation of mechanical effects revealed that blinking exerts shearing forces, reducing tear viscosity and facilitating the ejection of lipid from the meibomian orifices [10]. Consequently, incomplete blinking due to proptosis and eyelid retraction in TED patients may lead to obstructive meibomian gland disease. This obstruction could be one among multiple factors contributing to dry eye in individuals with TED.

In the lights of aforementioned; this study examined the attributes of the meibomian glands in mild-inactive TED patients who had different levels of proptosis in between the eyes. Thus, it was aimed to investigate one of the factors contributing to the

pathophysiology of dry eye in TED patients. In the study, it is found that the mean meibomian gland dropout area for both the upper eyelid and the sum of upper and lower eyelids was higher in the more proptotic eyes of the patients with TED compared to the less proptotic eyes; however, these differences did not reach statistical significance. On the other hand, the results of the Pearson test revealed a significant correlation between the two groups: for the upper eyelid ($p < 0.001$, $r = +0.670$) and also for the sum of upper and lower eyelids ($p < 0.001$, $r = +0.768$). Consequently, the importance of these findings deserves to be confirmed in larger-scale studies.

The study has several limitations. To start, the study followed a retrospective design and had a limited sample size. Another limitation is the lack of data on diagnostic tests for dry eye and blinking mechanism. However this study was designed considering that there may be meibographic differences between the eyes of TED patients who have different amounts of proptosis in between the eyes that are exposed to different biomechanical conditions with each blinking movement. The study revealed meibography changes through a comparison among more proptotic eyes and less proptotic controls. It is believed that this finding warrants further investigation.

CONCLUSION

This study identified differences in meibographic changes between the eyes of TED patients with varying degrees of proptosis between both eyes. Further studies with larger series are necessary to validate these findings.

Author contribution

Study conception and design: SBE; data collection: SBE and DS; analysis and interpretation of results: SBE and DS; draft manuscript preparation: SBE. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the Ankara Bilkent City Hospital Ethics Committee (E1-23-4564/27.12.2023).

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Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

- [1] Bahn RS. Graves' ophthalmopathy. *N Engl J Med.* 2010; 362:726-8.
- [2] Bartalena L, Pinchera A, Marcocci C. Management of Graves' ophthalmopathy: reality and perspectives. *Endocr Rev.* 2000; 21(2): 168-99.
- [3] Nowak M, Marek B, Kos-Kudla B, et al. [Tear film profile in patients with active thyroid orbitopathy]. *Klin Oczna* 2005; 107: 479–482.
- [4] Eckstein AK, Finkenrath A, Heilingenhaus A, et al. Dry eye syndrome in thyroid-associated ophthalmopathy: Lacrimal expression of TSH receptor suggests involvement of TSHR-specific autoantibodies. *Acta Ophthalmol Scand.* 2004; 82:291-7.
- [5] Inoue S, Kawashima M, Arita R, et al. Investigation of Meibomian Gland Function and Dry Eye Disease in Patients with Graves' Ophthalmopathy. *J Clin Med.* 2020; 9(9):2814.
- [6] Park J, Kim J, Lee H, et al. Functional and structural evaluation of the meibomian gland using a LipiView interferometer in thyroid eye disease. *Can J Ophthalmol.* 2018; 53(4):373–379.
- [7] Kim YS, Kwak AY, Lee SY, et al. Meibomian gland dysfunction in Graves' orbitopathy. *Can J Ophthalmol.* 2015;50(4):278–282.
- [8] Sheppard JD, Nichols KK. Dry Eye Disease Associated with Meibomian Gland Dysfunction: Focus on Tear Film Characteristics and the Therapeutic Landscape. *Ophthalmol Ther.* 2023; 12(3): 1397–1418.
- [9] Yilmaz Tuggan B, Ozkan B. Evaluation of Meibomian Gland Loss and Ocular Surface Changes in Patients with Mild and Moderate-to-Severe Graves' Ophthalmopathy. *Semin Ophthalmol.* 2022; 37(3):271-276.
- [10] Knop E, Knop N, Millar T, et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. *Invest Ophthalmol Vis Sci* 2011; 52:1938–1978.