

The impact of smoking on ocular surface health in patients with Graves' ophthalmopathy

Abstract

Graves' ophthalmopathy is associated with a reduced blinking frequency, eyelid retraction, proptosis, incomplete eyelid closure. Smoking significantly increases the incidence and severity of GO in patients with Graves' disease.

Objective: To assess the influence of smoking on the development of dry eyes in patients with Graves' ophthalmopathy (GO) and to determine the properties of tear secretion and ocular surface in these patients.

Methods: A cross-sectional study was conducted at the outpatient department of the Eye Diseases Clinic of the Lithuanian University of Health Sciences. The study included 52 patients with a mean age of 47.3 (17.4–69.6) years. The study included 25 smokers and 27 non-smokers with Graves' ophthalmopathy (a total of 52 patients). Their mean age was 47.3 (17.4–69.6) years.

Patients underwent ophthalmological examination, ocular surface disease index (OSDI) assessment, Schirmer test without local anesthesia (<5 mm was abnormal), slit-lamp biomicroscopy (tear break-up time (TBUT) under blue light illumination).

Statistical analysis was performed using SPSS for Windows software (SPSS Inc., Chicago, IL, USA). Statistical significance was determined at $p < 0.05$.

Results: The mean OSDI score in smoking GO patients was significantly higher (28.79 ± 15.29) compared to non-smoking patients (10.58 ± 7.41), ($p < 0.05$).

The mean Schirmer test value in smoking GO patients was significantly lower (4.21 ± 3.07 mm) compared to non-smoking patients (11.74 ± 6.24 mm). The difference was statistically significant ($p < 0.04$), indicating insufficient tear production. The mean tear film break-up time (TBUT) was lower in smoking GO patients (7.04 ± 2.25 s) compared with non-smoking patients (10.93 ± 3.12 s), ($p < 0.04$), indicating an unstable tear film.

Conclusion: The study found statistically significantly increased OSDI scores, shorter Schirmer scale and tear film breakup time measurements in smokers with GO. These data may indicate a predisposition to dry eye syndrome in smokers.

Keywords: Graves' ophthalmopathy, dry eye, smoking

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Introduction

Graves' ophthalmopathy (GO) is the most common extrathyroidal manifestation of Graves' disease, characterized by several ocular symptoms, such as eyelid retraction, eyelid lag, proptosis, extraocular muscle restriction, compressive optic neuropathy, exposure keratopathy, conjunctival hyperemia, and chemosis.^{1–3}

More than half of people with hyperthyroidism develop eye symptoms during their illness, which can be unilateral or bilateral, mild or severe. 25–50% of patients with Graves' disease (GD) have eye involvement, of which 3–5% may develop severe disease.^{4–6}

The clinical presentation of GO includes eyelid retraction in 80–90% of patients, wide palpebral fissure, exophthalmos, limitation of eye movements, and diplopia.^{7–10} The correlation between thyroid disease and dry eye symptoms has been established for a long time. Previous studies have shown that Graves' ophthalmopathy increases the risk of dry eye.^{8,11–16} Patients with Graves' disease and Graves' ophthalmopathy are often associated with dry eye syndrome.^{17–20} Patients with GO often complain of ocular discomfort, redness, and foreign body sensation. Dry eyes are more common in patients with Graves' disease. Rarely, it can occur in patients with hypothyroidism and euthyroidism.^{21–23} Dry eye symptoms may impair the quality of life of patients with GD and ophthalmopathy and affect the psychological

their state.²⁴ In order to improve the quality of life of patients with GO, ophthalmologists must determine the cause of dry eye disease. The exact mechanism of the relationship between GO and dry eye syndrome is unknown. Internal and external factors can increase the lack or decrease in tear production, increase tear evaporation, and disrupt the function of the tear film.^{25,26}

Tear film osmolarity may increase (hyperosmolarity) and superficial corneal inflammation may develop.^{27,28} Studies show that the tear gland may be involved in the pathogenesis of dry eye disease. In GO, when inflammation occurs, tear production may decrease.^{29,30} The thyroid and lacrimal glands stimulate specific thyroid-stimulating hormone receptor antigen, which triggers an autoimmune response in the thyroid and orbit. Therefore, these mechanisms may be synergistic. Autoantibodies against thyroid hormone receptors formed in the lacrimal gland in GO disrupt the function of the lacrimal gland, resulting in reduced tear production and dry eyes.^{4,17,31}

The main causes of dry eyes in patients with GO are wide eyelid fissure, lagophthalmos, exophthalmos, decreased blink rate, lack of tear production, and tear evaporation.^{32–34} Magnetic resonance imaging shows enlarged lacrimal glands in patients with GO. Patients with GO also have altered tear protein composition, which is associated with decreased tear production.¹⁷ Many published studies have found that approximately 45–85% of patients with GO may experience dry

eye symptoms.^{15,18,35,36} Authors noted that in GO most often patients have dry eye and ocular surface changes. They described that showed that patients with GO have been found to have a higher incidence of significant ocular surface abnormalities and dry eye symptoms compared to healthy people.^{17,32,37}

Studies have noted meibomian gland dysfunction in patients with thyroid disease and GO.^{6,37,38} Some authors noted that in patients with GD even in the absence of exophthalmos or in early stages of GO, the tear film and cornea may be damaged and sensitivity of the cornea may decrease.^{18,39} The association between GO and dry eye and smoking syndrome has long been shown. Studies have reported that T lymphocyte-dependent inflammation is associated with tear production dysfunction, evaporation of tear film, and hyperosmolarity of tear film due to proptosis and eyelid retraction, which may cause dry eye signs and symptoms.^{17,33,37} In response to these TSHR-specific autoantibodies present in thyroid tissue, T cells infiltrate the orbital tissues and external ocular muscles. Inflammation often leads to glycosaminoglycan deposition, fibrosis of extraocular muscles, and adipogenesis of orbital microsoft tissues.^{4,5,40}

The authors noted that dysfunction of the meibomian gland is the important cause of tear film evaporation and dry eye syndrome.^{41,42} Smoking is a common habit associated with GO. Cigarettes smoke contains nicotine and complex harmful chemicals and particles that affect not only lungs, but eye and orbital tissues. Smoking causes oxidative stress and reduces antioxidant levels, which complicates the GO process.⁴³ Smokers develop Graves' ophthalmopathy more often than nonsmokers. The authors reported that smoking increased the development of Graves' ophthalmopathy in patients with GD. The frequency of smoking also correlates with the severity of the eye disease. Those who smoke more often have more severe GO. Smoking is a risk factor for Graves' disease, but its association with the development of Graves' ophthalmopathy and disease progression is significant.⁴⁴⁻⁴⁶

Smoking significantly increases the incidence and severity of GO in patients with Graves' disease. The authors determined that smoking may affect the course of GO in dynamic of the treatment and reduce the effectiveness of treatment.⁴⁷ Smokers are at higher risk of developing more advanced ophthalmopathy than non-smokers. The authors studied patients with Graves' ophthalmopathy and found that patients with Graves' ophthalmopathy who smoked had more advanced inflammatory responses than those with Graves' ophthalmopathy who did not smoke.^{14, 44,48-50} Ocular surface studies in smokers and patients with GO are lacking.

Studies have shown that smokers develop dry eye symptoms more quickly and have lower tear film break-up time than nonsmokers. Cigarette smoking is a significant modifiable risk factor for GO and dry eye syndrome.⁵¹

The exact mechanisms of the association between smoking and dry eye symptoms in Graves' ophthalmopathy are not enough understood. They may involve increased tear evaporation, inflammation, and changes in tear film composition due to toxicants in cigarette smoke. Smoking affects oxidative stress, the immune system, causes inflammation, may involve vascular reactions.

In this study, we aimed to evaluate symptoms of dry eye, the tear secretion and ocular surface properties in smoking and non smoking patients with GO.

Objective

To assess the influence of smoking on the development of dry eyes

in patients with Graves' ophthalmopathy (GO) and to determine the properties of tear secretion and ocular surface in these patients.

Methods

A cross-sectional study was conducted at the outpatient department of the Eye Diseases Clinic of the Lithuanian University of Health Sciences. The study included 52 patients with a mean age of 47.3 (17.4–69.6) years. The study included 25 smokers and 27 non-smokers with Graves' ophthalmopathy (a total of 52 patients). Their mean age was 47.3 (17.4–69.6) years.

Patients underwent ophthalmological examination, ocular surface disease index (OSDI) assessment, Schirmer test without local anesthesia (<5 mm was abnormal), slit-lamp biomicroscopy (tear break-up time (TBUT) under blue light illumination).

Statistics

Statistical analysis was performed using SPSS for Windows software (SPSS Inc., Chicago, IL, USA). Statistical significance was determined at $p < 0.05$.

Results

The mean OSDI score in smoking GO patients was significantly higher (28.79 ± 15.29) compared to non-smoking patients (10.58 ± 7.41), ($p < 0.05$). Results are presented in Table 1.

Table 1 Comparison of dry eye parameters between smokers and non-smokers GO patients

Dry eye parameters	Smokers (mean \pm SD)	Non smokers (mean \pm SD)	P
OSDI	28.79 \pm 15.29	10.58 \pm 7.41	< 0.05
Schirmer test mm	4.21 \pm 3.07	11.74 \pm 6.24	< 0.04
TBUT s	7.04 \pm 2.25	10.93 \pm 3.12	< 0.04

SD: Standard deviation, OSDI: Ocular Surface Disease Index, TBUT: Tear breakup time

The mean Schirmer test value in smoking GO patients was significantly lower (4.21 ± 3.07 mm) compared to non-smoking patients (11.74 ± 6.24 mm). The difference was statistically significant ($p < 0.04$), indicating insufficient tear production. The mean tear film break-up time (TBUT) was lower in smoking GO patients (7.04 ± 2.25 s) compared with non-smoking patients (10.93 ± 3.12 s), ($p < 0.04$), indicating an unstable tear film.

Discussion

Dry eye syndrome is a common condition that increases in patients with autoimmune thyroid diseases.^{25,26} Studies have shown that dry eyes cause eye discomfort and may lead to anxiety and negative emotions.^{26,52} It has been found that T lymphocytes cause inflammation of the eye, reducing tear production, which determines the pathogenesis of dry eye syndrome.³⁰ Several studies have shown that patients suffered from thyroid diseases have signs of dry eyes.

Abusharaha et al.³⁴ reported that the mean OSDI score was higher in patients with hyperthyroidism compared to individuals with hypothyroidism.³⁴ Turkyilmaz et al.²⁸ showed that patients with thyroid diseases had signs of dry eyes compared to healthy people. The mean OSDI score of patients with thyroid diseases was higher than that of healthy people. The mean TBUT test score in both eyes of the study group with thyroid diseases was lower compared to the control group of healthy people. The mean Schirmer test value in patients with thyroid diseases was lower than that of healthy people.²⁸

Another study found that the mean Schirmer's test score in patients with thyroid disorders was significantly lower at compared to normal subjects.¹² Reduced tear drainage or corneal evaporation and tear film instability cause ocular discomfort and impaired vision. Reduced corneal sensitivity has been observed in the early stages of thyroid disease. Patients with GO develop changes in the surface of the eye that cause dry eyes.^{12,18,33}

Eckstein et al.¹⁷ showed that fluorescein staining was more frequently observed in patients with dry eye syndrome and GO compared with healthy subjects. The authors found that in patients with GO, there is a relationship between ocular surface dryness and ocular surface damage and decreased tear production and tear gland dysfunction.¹⁷

A cohort study was conducted in patients with dry eye syndrome and GO, the vast majority (97%) of patients had dry eye symptoms: tearing (65%), grittiness and irritation (70%), and photophobia (55%).⁵³ Another study showed reduced Schirmer test values than thus in control group. Authors suggest that Schirmer test values <8 mm may be classified as pathological in patients with GO. The Schirmer test results obtained in this study were lower than in the control group. Gupta et al. suggest that Schirmer test values less than 8 mm in patients with GO may indicate signs of dry eye syndrome.³²

Patients who develop early signs of GO also experience decreased corneal sensitivity.¹⁸ A confocal microscopy study by the authors showed that patients with GO had a lower number of corneal nerve fibers than healthy people.²⁰

The study of Garza-León et al. found that dry eye symptoms occurred majority of students (70.4%), these symptoms were in relation with gender, smoking and ocular drops.⁵⁴ The researchers noted that there is strong evidence of a link between smoking and the development of GO.^{44,55,56} Smokers are at higher risk of developing more advanced forms of GO, and there is a correlation between cigarette smoking and disease symptoms. This is related to tissue hypoxia, modulation of circulating proinflammatory and antiinflammatory cytokines and expression of fibroblast HLA-DR.⁴⁸

We could objectify the symptoms of dry eyes as a common feature of GO. Our study showed that GO smoking patients had a higher mean OSDI score (28.79 ± 15.29) compared with non smokers (10.58 ± 7.41), ($p < 0.05$). Dry eye syndrome has many causes and is characterized by changes in the ocular surface that weaken the tear film and cause itching, redness, sensitivity to light, blurred vision, and/or other symptoms. These may include chronic inflammation of the ocular surface, decreased sensitivity of the cornea and conjunctiva, decreased tear production and/or tear film stability, and epithelial damage. Smoking is a modifiable risk factor for dry eye syndrome that can alter tear film stability and reduce corneal and conjunctival sensitivity.¹¹

In our study, the results of the Schirmer test showed a statistically significant difference between smokers and non-smokers with GO. Tear secretion was statistically significantly lower compared to non-smokers (Schirmer test value 4.21 ± 3.07 mm vs. 11.74 ± 6.24 mm, $p < 0.04$). The ocular inflammation resulting from smoking in patients with GO causes ocular surface damage. The average TBUT score of our GO smoking patients was significantly lower (7.04 ± 2.25 s) than that of the non-smoking group (10.93 ± 3.12 s), $p < 0.04$). Instability of tear film may lead to dryness because tear film stability depends on several factors, such as tear flow interval, adequate blinking, normal tear function, and maintenance of a normal ocular surface.

This result suggests the severity of dry eye in these patients with GO and may be due to insufficient tear secretion, high tear evaporation, and tear film instability. The evaluation of dry eyes, including ocular surface assessment, tear secretion, and TBUT, should be evaluated to properly treat GO patients.

These data on insufficient tear secretion, high tear evaporation and tear film instability have shown the occurrence of dry eyes in smokers with GO. To start treating GO patients, it is necessary to collect a medical history, ask if the patient is a smoker, assess for signs of dry eye syndrome, evaluate the condition of the ocular surface, tear secretion and tear break-up time.

Cessation of smoking is of great importance in the treatment of GO and dry eyes, as it reduces dry eye symptoms and improves tear film function. Smokers should be advised to quit smoking as soon as possible to prevent disease progression and complications of dry eye syndrome in GO patients. To further investigate the symptoms of dry eyes in smokers with GO, further and more detailed studies of tear production and the ocular surface are needed.

Conclusion

The study found statistically significantly increased OSDI scores, shorter Schirmer scale and tear film breakup time measurements in smokers with GO. These data may indicate a predisposition to dry eye syndrome in smokers. We recommend that ophthalmologists, in collaboration with other healthcare professionals, educate patients about the harmful effects of smoking on their eye health.

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Conflicts of interest

The author declares that there are no conflicts of interest.

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