Original Article

Ocular Surface Assessment in Patients with Obstructive Sleep Apnea Syndrome

Reza Ghaffari[1], Hamed Ghassemi[1], Khosro Sadeghniiat Haghighi[2], Mehran Zarei-Ghanavati[1], Golshan Latifi[1], Karzan Nebi Kheder[1], Ahmad Masoumi[1], Pedram Afshar[1]

[1]Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran, [2]Occupational Sleep Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Purpose: To evaluate the prevalence of dry eye, meibomian gland dysfunction (MGD), and conjunctivochalasis in patients with obstructive sleep apnea (OSA).

Methods: We included 37 patients diagnosed with OSA according to polysomnography. The control group comprised 31 subjects. The study participants underwent a complete ophthalmic examination and ocular surface assessment. Meibography was done using infrared imaging. Furthermore, tear meniscus height was measured using anterior segment optical coherence tomography.

Results: The mean age of the OSA and control groups were 50.3 ± 9.0 and 50.3 ± 8.0, respectively ($P = 0.77$). The mean scale for meibomian gland expression, meibomian gland plugging, and lid margin telangiectasia was similar in both groups. The meiboscores of the upper and lower eyelids were similar in both groups (upper meiboscores of 0.67 ± 0.48 and 0.37 ± 0.49 in OSA and control group, $P = 0.180$ and lower meiboscores of were 0.47 ± 0.57 and 0.22 ± 0.42 in OSA and control group, $P = 0.179$). The mean tear break-up time (TBUT) was significantly lower in the OSA group (8.17 ± 3.70 compared to 11.47 ± 4.52, $P < 0.001$). Upper and lower tear meniscus height were 186.14 ± 40.11 µm and 199.59 ± 37.22 µm and 237.25 ± 82.86 µm and 218.59 ± 68.8 µm in OSA and control group, respectively ($P = 0.221$, $P = 0.166$). The mean conjunctivochalasis grading score was 0.92 ± 0.72 and 0.81 ± 0.65 in the OSA and control groups, respectively ($P = 0.143$).

Conclusions: Despite decreased TBUT in patients with OSA, other dry eye parameters are not altered in these patients. Moreover, the frequency of MGD and conjunctivochalasis is not higher in OSA patients.

Keywords: Dry eye, Meibomian glands, Ocular surface, Sleep apnea

Address for correspondence: Hamed Ghassemi, Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran.
E-mail: hamedghasemi@yahoo.com
Submitted: 19-Aug-2023; **Revised:** 10-Mar-2024; **Accepted:** 10-Mar-2024; **Published:** 16-Oct-2024

Introduction

Obstructive sleep apnea (OSA) is characterized by disruptive snoring, daytime sleepiness, and nocturnal hypoxemia caused by periodic partial or complete obstruction of airway passages during sleep.[1] The first line of treatment for OSA is continuous positive airway pressure. This condition increases the risk of systemic hypertension,[2] cardiovascular disease,[3] and stroke.[4] Various ocular disorders are associated with OSA, including floppy eyelid syndrome, nonarteritic anterior ischemic optic neuropathy, glaucoma, and central serous chorioretinopathy.[5] OSA is thought to be associated with an increased risk of dry eye syndrome (DES).[6,7] Meibomian gland dysfunction (MGD) is the most common cause of DES. Meibomian glands are a type of sebaceous glands with holocrine function that are located in superior and inferior tarsal plates. The secreted meibum helps stabilize the tear film and protects the ocular surface against microbial invasion. MGD often results in tear film instability and damage to the ocular surface epithelium.[8]

Access this article online

Quick Response Code:

Website: https://journals.lww.com/joco

DOI: 10.4103/joco.joco_173_23

How to cite this article: Ghaffari R, Ghassemi H, Sadeghniiat Haghighi K, Zarei-Ghanavati M, Latifi G, Nebi Kheder K, *et al*. Ocular surface assessment in patients with obstructive sleep apnea syndrome. J Curr Ophthalmol 2024;36:42-5.

Meibomian glands are located superficially in the tarsal plates and thus diagnostic tests such as meibography can be used to define the anatomic features of these glands in the eyelids.

In this study, we aim to evaluate ocular surface changes related to MGD in patients with OSA and compare them to normal subjects.

Methods

In this cross-sectional study, people who complained of symptoms related to sleep disorders such as loud snoring, witnessed apnea, and daytime sleepiness were evaluated by a single sleep medicine physician. The patients were selected from the Sleep Disorders Clinic of Imam Khomeini Hospital and underwent in-laboratory polysomnography (Alice 5 Diagnostic Sleep System, Philips, Respironics, USA). The control group was selected from people who presented to the Farabi Eye Hospital. The subjects in the control group were visited by the same sleep medicine physician to ensure that they had no sleep disorders. Patients with any ocular surface disease, keratoconus, history of ocular trauma or surgery, recent contact lens wear, and topical drug use were excluded from the study. The risks and benefits of participating in the study were explained to the patients who fulfilled the inclusion criteria. Permission to conduct this study was approved by the Ethics Committee of the Farabi Eye Hospital. This work is adherent to the ethical principles of the Declaration of Helsinki. The patients signed an informed consent if they agreed to be part of the study. The participants were examined in the Farabi Eye Hospital and the ophthalmic examination was performed before initiation of lifestyle modification and medical interventions. The examiners were masked about the presence of OSA.

The subjects underwent complete ophthalmologic examination including visual acuity, slit-lamp examination of the conjunctiva and cornea before and after instillation of 2% fluorescein, and funduscopy. The presence of conjunctivochalasis, lid margin telangiectasia, and plugging in the orifices of meibomian glands was recorded. Patients underwent infrared meibomiography and measurement of tear meniscus height.

Conjunctivochalasis was graded according to the method proposed by Höh *et al*.[9] and later modified by Meller and Tseng:[10] Grade 0 (no persistent fold), Grade 1 (a single small fold), Grade 2 (two or more folds not higher than lower tear meniscus), and Grade 3 (multiple folds higher than lower tear meniscus). Lid margin telangiectasia was evaluated on a scale from 0 to 3 according to Arita *et al*.:[11] 0 = No redness of lid margin with no lid margin telangiectasia, 1 = Redness of conjunctiva on lid margin with no lid margin telangiectasia, 2 = Redness of lid margin conjunctiva accompanied by lid margin telangiectasia involving less than half of full length of the eyelid, and 3 = Redness of lid margin conjunctiva accompanied by lid margin telangiectasia involving more than half of full length of the eyelid. Plugging of meibomian gland orifices was also assessed on a scale of 0–3 according to Arita *et al*.:[11] 0 = No plugging of meibomian gland orifices, 1 = Plugging in fewer than 3 meibomian gland orifices, 2 = Plugging of 3 or more meibomian gland orifices involving less than half of the eyelid length, and 3 = Plugging of 3 or more meibomian gland orifices involving more than half of the eyelid length. Oxford scheme was used to grade ocular surface staining on a scale of 0–5.[12] Meibomian gland expression was performed by pressing the middle third of the upper eyelid. The quality of expressed meibomian gland secretions was assessed on a scale of 0–3 for each gland: 0 = Clear, 1 = Cloudy, 2= Cloudy with debris, and 3 = Inspissated. Tear break-up time (TBUT) was measured by averaging the time to appear the first dry spots on the cornea after staining the ocular surface with fluorescein 2% for 3 consecutive times. The Schirmer I test was performed by placing a 5 mm × 30 mm strip of standard filter paper in the lateral third of the lower lid. The distance wetted after 5 min was recorded.

Infrared images of the meibomian glands were captured using the Keratograph 5M (Oculus, Weltzar, Germany). Partial or complete atrophy of meibomian glands was recorded in Grade 0 (no atrophy of meibomian glands), Grade 1 (atrophy of <1 / 3 of total meibomian glands), Grade 2 (atrophy of 1 / 3–2 / 3 of total meibomian glands), and Grade 3 (atrophy of >1 / 3 of total meibomian glands).

Tear meniscus height was measured using visante optical coherence tomography (OCT) (Carl Zeiss Meditec, Inc.). The OCT light beam was focused on the cornea and a 10-mm long vertical scan was performed. The images of the upper and lower tear meniscus were analyzed to calculate the tear meniscus height on the upper and lower eyelid.

Statistical analysis was executed using SPSS 21.0 (SPSS Inc., Chicago, IL, USA). The right eye of both patients and the control group was chosen for statistical analysis. Mann–Whitey test was used to compare the means between the two groups. Mean ± standard deviation was reported for continuous variables. Percentages were used for categorical variables. P <0.05 was considered statistically significant.

Results

Thirty-seven patients with OSA and 31 control subjects were included in the study. Meibomiography and tear meniscus height in four eyes in the OSA group and one eye in the control group did not have the adequate quality to be included in data analysis. The mean age was 50.3 ± 9.0 in the OSA group (range, 26–74) and 50.3 ± 8.0 (range, 30–65) in the control group (P = 0.77). The male-to-female ratio was 21–16 in the OSA group and 18–13 in the control group. The mean body mass index was 30.5 ± 5.7 in the OSA group (range, 20.4–52.0), which was significantly higher than the control group (27.4 ± 4.3, range, 20.2–35.9) (P < 0.05).

The mean scale for meibomian gland expression, plugging of meibomian gland orifices, and lid margin telangiectasia was similar between patients with OSA and the control group (meibomian gland expression: 1.89 ± 0.77 in the OSA and

2.10 ± 0.83 in the control group [$P = 0.256$], meibomian gland plugging 1.35 ± 0.35 in the OSA and 1.29 ± 0.34 in the control group [$P = 0.941$], and lid margin telangiectasia 1.27 ± 0.65 in the OSA and 1.39 ± 0.92 in the control group [$P = 0.556$]).

Evaluation of meibomian glands with infrared meibography revealed that there is no significant difference between upper and lower meiboscores in OSA patients and the control group ($P = 0.180$ and $P = 0.179$, respectively). Upper meiboscores were 0.67 ± 0.48 and 0.37 ± 0.49 and lower meiboscores were 0.47 ± 0.57 and 0.22 ± 0.42 in OSA patients and the control group, respectively.

The mean TBUT score was 8.17 ± 3.70 and 11.47 ± 4.52 in the OSA and control group ($P < 0.001$). The mean Schirmer I test values were 9.56 ± 6.08 and 10.11 ± 8.09 in OSA and control patients ($P = 0.658$). Measurement of tear meniscus height using Visante OCT showed that upper and lower tear meniscus heights were similar in OSA patients and normal subjects. Upper tear meniscus height was 186.14 ± 40.11 µm and 199.59 ± 37.22 µm in the OSA and control group ($P = 0.221$). Lower tear meniscus height was 237.25 ± 82.86 µm and 218.59 ± 68.87 µm in the OSA and control group ($P = 0.166$).

Corneal fluorescein staining stage scores using the Oxford scheme were 0.26 ± 0.53 and 0.13 ± 0.46 in the OSA group and control subjects, respectively ($P = 0.144$). The rate of conjunctivochalasis was 70.3% (26 of 37) in OSA patients and 67.7% (21 of 31) in normal subjects ($P = 0.514$). The mean conjunctivochalasis grading score was 0.92 ± 0.72 and 0.81 ± 0.65 in the OSA and control groups, respectively ($P = 0.143$). Table 1 provides a summary of the comparison between patients with OSA and the control group.

Discussion

OSA is characterized by nocturnal pharyngeal collapse, which leads to partial airway obstruction and hypopneic episodes during sleep. The long-term intermittent hypoxia causes a chronic ischemic and inflammatory state. Intermittent hypoxia and local mechanical factors such as eye rubbing and sleeping face down may lead to ocular complications in this syndrome.[1,7]

Table 1: Comparison of lid margin abnormalities, dry eye tests, and anterior segment optical coherence tomography parameters in obstructive sleep apnea patients and control group

	Patients with OSA	Control group	*P*
Meibomian gland expression	1.89±0.77	2.10±0.83	0.25
Meibomian gland plugging	1.35±0.35	1.29±0.34	0.94
Lid margin telangiectasia	1.27±0.65	1.39±0.92	0.55
Upper meiboscore	0.67±0.48	0.37±0.49	0.18
Lower meiboscore	0.47±0.57	0.22±0.42	0.18
TBUT (s)	8.17±3.70	11.47±4.52	<0.001
Schirmer I test (mm)	9.56±6.08	10.11±8.09	0.66
Upper tear meniscus height (µm)	186.14±40.11	199.59±37.22	0.22
Lower tear meniscus height (µm)	237.25±82.86	218.59±68.87	0.17
Corneal fluorescein staining score	0.26±0.53	0.13±0.46	0.14

OSA: Obstructive sleep apnea, TBUT: Tear break-up time

Dry eye is a debilitating disease, which severely affects the quality of life of patients. Increased tear film osmolarity in dry eye patients leads to the secretion of proinflammatory cytokines by lacrimal glands and ocular surface inflammation. It is postulated that increased levels of proinflammatory cytokines such as tumor necrosis factor, interleukin 1, and interleukin 6 in OSA patients may predispose these patients to dry eye.[7,13,14]

In the present study, we evaluated ocular surface findings and dry eye parameters in patients with OSA. Although the mean TBUT was significantly reduced in patients with OSA, Schirmer test results, ocular surface staining, and tear meniscus height assessed by anterior segment OCT (AS-OCT) were similar in both groups. Moreover, we did not find a higher prevalence of meibomian gland plugging, lid margin telangiectasia, and meiboscores in OSA patients. Previous studies reported a higher prevalence of abnormal dry eye tests, lid margin abnormalities, and conjunctivochalasis in patients with severe OSA.[6,7] Our study, however, shows that when all patients with OSA, regardless of the apnea-hypoxia index (AHI), are evaluated, the previous findings are not confirmed. This implies that MGD, conjunctivochalasis, and punctate epithelial keratopathy are not more prevalent in milder stages of OSA. Mojon *et al*. also found that TBUT is reduced in patients with OSA. However, they did not report a higher prevalence of punctate epithelial keratopathy in these patients. Although signs of corneal involvement were present in about half of the patients, few patients complained of symptoms of ocular irritation.[15]

Schirmer test is widely used by clinicians to assess tear production in patients who are suspected to have dry eye. This test indicates the adequacy of tear production. Karaca *et al*. reported decreased Schirmer test values in moderate-to-severe OSA.[7] However, in our study, the results of the Schirmer test were similar in both groups. We believe that this contradictory finding is due to the lack of patient classification in our study.

Staining of the ocular surface with vital dyes is a critical component for the diagnosis of dry eye disease. It helps the clinician with the diagnosis of the disease, assess its severity, and monitor the response to therapy. Acar *et al*. reported that the ocular surface staining score according to the Oxford scheme is increased in patients with OSA. This score increases as AHI increases in these patients.[6] However, we did not find any difference in ocular surface staining in patients with OSA compared to the control group. Again, this might be because we did not classify the patients based on the severity of OSA, potentially including those with lower stages of the disease in our study.

Obstructive MGD is the main reason for evaporative dry eye, where clinical signs of blepharitis might be absent. Expression

of meibomian gland secretions is the most important test to diagnose obstructive MGD.[16] It is well established that meibomian gland dropout as identified by meibography is inversely correlated with the number of expressible meibomian glands and therefore, meibomian gland atrophy indicates loss of meibomian gland function.[17] In this study, we found no difference in meiboscores of the OSA group compared to normal subjects. Increasing age is a known risk factor for the development of MGD. However, even when accounted for the effect of age, no difference was observed between the two groups. This is in contrast to Karaca *et al*. who reported a higher meiboscore in patients with severe OSA.[18] Moreover, the authors identified morphological alterations in the meibomian glands of patients with severe OSA. They reported a higher prevalence of meibomian duct distortion, thinning, and dilation in this subgroup of patients. We believe that this discrepancy is because we included all patients with OSA and not only patients who suffered from the severe stage of this syndrome.[18]

Acar *et al*. reported a higher prevalence of conjunctivochalasis in patients with OSA. The authors postulated that intermittent hypoxia in OSA patients triggers inflammations. The resultant increase in matrix metalloproteinase-1 (MMP-1) and MMP-3 may lead to the separation of conjunctiva from underlying episclera.[19] However, we found no difference in the rate of conjunctivochalasis in OSA patients and the control group.

AS-OCT can be a useful tool in the diagnosis and management of dry eye by measuring tear meniscus parameters such as tear meniscus height, width, and curvature.[20] In this study, we evaluated tear meniscus height by Visante AS-OCT in OSA patients and the control group. However, we found no difference in tear meniscus height between the two groups. This indicates that the tear volume of OSA patients is similar to healthy subjects.

The limited sample size might have diminished the study's statistical power, potentially impacting the accuracy of the results. Lack of OSA grading is the main limitation of our study which interferes with comparing the results of the present study with the previous one; however, in conclusion, our study shows that despite decreased TBUT in patients with OSA, other dry eye parameters are not altered in these patients. Furthermore, the prevalence of lid margin abnormalities was similar to normal subjects.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Osman AM, Carter SG, Carberry JC, Eckert DJ. Obstructive sleep apnea: Current perspectives. Nat Sci Sleep 2018;10:21-34.
2. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378-84.
3. Leung RS, Bradley TD. Sleep apnea and cardiovascular disease. Am J Respir Crit Care Med 2001;164:2147-65.
4. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. N Engl J Med 2005;353:2034-41.
5. Santos M, Hofmann RJ. Ocular manifestations of obstructive sleep apnea. J Clin Sleep Med 2017;13:1345-8.
6. Acar M, Firat H, Acar U, Ardic S. Ocular surface assessment in patients with obstructive sleep apnea-hypopnea syndrome. Sleep Breath 2013;17:583-8.
7. Karaca EE, Akçam HT, Uzun F, Özdek Ş, Ulukavak Çiftçi T. Evaluation of ocular surface health in patients with obstructive sleep apnea syndrome. Turk J Ophthalmol 2016;46:104-8.
8. Chhadva P, Goldhardt R, Galor A. Meibomian gland disease: The role of gland dysfunction in dry eye disease. Ophthalmology 2017;124:S20-6.
9. Höh H, Schirra F, Kienecker C, Ruprecht KW. Lid-parallel conjunctival folds are a sure diagnostic sign of dry eye. Ophthalmologe 1995;92:802-8.
10. Meller D, Tseng SC. Conjunctivochalasis: Literature review and possible pathophysiology. Surv Ophthalmol 1998;43:225-32.
11. Arita R, Minoura I, Morishige N, Shirakawa R, Fukuoka S, Asai K, *et al.* Development of definitive and reliable grading scales for meibomian gland dysfunction. Am J Ophthalmol 2016;169:125-37.
12. Bron AJ, Evans VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. Cornea 2003;22:640-50.
13. Lemp MA, Foulks GN. The definition and classification of dry eye disease. Ocul Surf 2007;5:75-92.
14. Ciftci TU, Kokturk O, Bukan N, Bilgihan A. The relationship between serum cytokine levels with obesity and obstructive sleep apnea syndrome. Cytokine 2004;28:87-91.
15. Mojon DS, Goldblum D, Fleischhauer J, Chiou AG, Frueh BE, Hess CW, *et al.* Eyelid, conjunctival, and corneal findings in sleep apnea syndrome. Ophthalmology 1999;106:1182-5.
16. Tomlinson A, Bron AJ, Korb DR, Amano S, Paugh JR, Pearce EI, *et al.* The international workshop on meibomian gland dysfunction: Report of the diagnosis subcommittee. Invest Ophthalmol Vis Sci 2011;52:2006-49.
17. Arita R, Itoh K, Inoue K, Amano S. Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population. Ophthalmology 2008;115:911-5.
18. Karaca I, Yagci A, Palamar M, Tasbakan MS, Basoglu OK. Ocular surface assessment and morphological alterations in meibomian glands with meibography in obstructive sleep apnea syndrome. Ocul Surf 2019;17:771-6.
19. Acar M, Firat H, Yüceege M, Şanal Doğan A, Çalişkan S, Gürdal C. The presence of conjunctivochalasis in obstructive sleep apnea patients. Eye Contact Lens 2018;44 Suppl 1:S163-6.
20. Ibrahim OM, Dogru M, Takano Y, Satake Y, Wakamatsu TH, Fukagawa K, *et al.* Application of visante optical coherence tomography tear meniscus height measurement in the diagnosis of dry eye disease. Ophthalmology 2010;117:1923-9.