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Original Article

Dry Eye and Meibomian Glands in Vitiligo

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Abstract

Objectives: To evaluate aqueous and lipid tear film parameters and the meibomian glands (MGs) with non-contact meibography in patients with vitiligo.

Materials and Methods: This case-control study was conducted in the right (OD) and left (OS) eyes of 43 patients with vitiligo and 43 controls in Birjand, Iran. In addition to demographic information and skin disease characteristics, the Ocular Surface Disease Index (OSDI) questionnaire was completed for each patient, followed by eye examinations including slit lamp examination, Schirmer test, strip meniscometry (SMTube), and tear break-up time (TBUT) measurement. The MGs were also imaged using a non-contact meibography system (SBM System, Italy). The data were analyzed using SPSS version 22.0 with a significant level of less than 0.05.

Results: Patients had higher OSDI score than controls but it was not significant (10.90±13.03 vs. 5.57±6.85; p=0.07). There were significant differences between the groups in mean Schirmer test values for both eyes (OD: 8.07±5.47 vs. 17.37±6.52; OS: 7.60±5.00 vs. 17.30±6.44, p<0.001) and mean SMTube results (OD: 4.49±2.40 vs. 9.74±3.67; OS: 4.30±2.81 vs. 9.65±4.52; p<0.001). However, mean TBUT did not differ between the groups (OD: 9.14±3.17 vs. 10.12±2.08, p=0.27; OS: 9.16±3.30 vs. 10.05±2.10, p=0.25). Meibography also showed no significant difference in MG dropout between the groups (OD: 20.86±9.79 vs. 21.05±12.07; p=0.74; OS: 18.16±8.83 vs. 19.53±10.30; p=0.51).

Conclusion: Vitiligo is associated with a reduction in the production of aqueous tear film, but does not affect the structure and function of the MGs.

Keywords: Vitiligo, dry eye, meibomian glands

Introduction

Vitiligo is an acquired depigmentation disorder of the skin and mucous membranes affecting approximately 0.5-1% of individuals worldwide. It is characterized by well-circumscribed white macules and patches that may appear at any age. Vitiligo can be divided into two major subgroups: non-segmental (NSV), which is more common and often symmetrical, and segmental (SV), which occurs in a unilateral distribution.[1] NSV is a multifactorial skin disorder with an immune-mediated melanocyte destructive mechanism. In contrast, SV is presumably a mosaic genetic skin disorder.[2]

The main hypotheses proposed for the pathogenesis of vitiligo are the autoimmune theory, the neural theory, and the cytotoxic theory. The autoimmune mechanism is believed to play a main role in the pathogenesis of NSV, while the neural mechanism has been implicated in SV. The autoimmune theory, which involves autoimmune-mediated destruction of melanocytes, is the most accepted mechanism for the pathogenesis of generalized vitiligo. The coexistence of vitiligo with several systemic and cutaneous

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autoimmune diseases supports this theory.[3] A cross-sectional study revealed that nearly 20% of patients with vitiligo had at least one comorbid autoimmune disease, with the most common being thyroid disease and alopecia areata.[4] The coexistence of vitiligo and Sjögren's syndrome, which includes dry eye as a diagnostic criterion, has also been reported.[5]

Melanocytes are present in other organs such as the eyes, ears, heart, and nervous system. As a result, these organ systems may be involved in pigmentation disorders. Vitiligo has been associated with systemic disorders such as Vogt-Koyanagi-Harada disease and Alezzandrini syndrome. Therefore, since the uveal tract and retinal epithelium are rich in melanocytes, it is not surprising that vitiligo has ocular comorbidities.[6]

Several studies have been conducted on the visual manifestations of vitiligo and have reported findings such as retinal hypopigmentation, retinal pigment epithelial atrophy, and impaired retinal electrophysiological function.[7] However, few studies have investigated ocular surface alterations and tear film abnormalities in people with vitiligo, particularly those with periocular involvement.[8]

Dry eye disease is one of the most common ocular morbidities, with as many as 4.3 million Americans older than 65 years affected to some degree. The impact of dry eye on quality of life was rated to be equivalent to unstable angina using utility assessments.[9] The meibomian glands (MGs) are large sebaceous glands located in the tarsal plates of the eyelids that secrete the lipid layer of the tear film, which plays a key role in retarding tear evaporation.[10] The assessment of MGs in various conditions such as dermatologic disorders has become a research topic since the recent introduction of infrared technology for MG imaging.

We hypothesize that tear film parameters worsen in vitiligo patients. Accordingly, we evaluated tear film parameters and MGs with non-contact meibography in vitiligo and compared these results with healthy individuals in the Iranian population.

Materials and Methods

Population and Study Design

This case-control study was conducted on both the right (OD) and left (OS) eyes of 43 patients with vitiligo and 43 controls in Birjand, Iran. The study protocol and examinations were reviewed and approved by the Ethics Committee of Birjand University of Medical Sciences (Ir.BUMS.REC.1396.302), and written informed consent was obtained from all subjects. Patients with vitiligo diagnosed clinically by a dermatologist (A.R.T.) were included. Subjects with a systemic or ocular disease, recent use of drugs affecting the lacrimal unit, or current use of contact lenses were excluded.

In addition to demographic information and skin disease characteristics, the Ocular Surface Disease Index (OSDI) questionnaire was completed for each patient. This was followed by eye examinations including slit lamp examination, tear break-up time (TBUT) measurement, Schirmer test, and strip meniscometry (SM) using the SMTube (Takagi Seiko Co., Nakano City, Japan). None of the patients used topical artificial tear drops within 2 hours before the examinations. The MGs were also imaged using BG-4M non-contact meibography system (SBM System, Turin, Italy). All ophthalmic examinations were done by the same ophthalmologist (M.N.).

Ocular Examinations

The OSDI questionnaire includes 12 questions related to experiences during the previous week, which are subdivided into 3 domains related to ocular symptoms, how these symptoms disturb visual function, and ocular reactions to environmental triggers. The OSDI is scored on a scale of 0 to 100, with higher scores demonstrating greater disability.[11]

TBUT was measured as the time (in seconds) between the last blink and the appearance of a dry spot in the fluorescein-stained tear film viewed under a cobalt blue filter. The mean of 3 measurements was recorded as the final result. Lower TBUT indicates tear film instability. Ten seconds or longer is considered normal. According to the study protocol, TBUT was performed first, followed by SM and Schirmer tests. A 30-min interval was applied between each examination to prevent disruption of the results.

In the Schirmer test, a strip is placed at the junction of the middle and lateral thirds of the lower eyelid and the length of tear wetting is measured in millimeters after 5 minutes.[11] We performed Schirmer test I without topical anesthesia.

SM is a promising new and non-invasive method that is expected to find application in the diagnosis and evaluation of treatment outcomes in dry eye patients.[12] The SMTube was shown to have acceptable sensitivity and specificity for assessing tear meniscus volume.[13]

Meibography is the visualization of the glands through trans-illumination of the eyelid with infrared light. The SBM System detects the length and width of MGs imaged by infrared meibography without requiring any input from the user. The images are then automatically classified. We performed lower eyelid meibography for the convenience and cooperation of patients (Figure 1 and 2).

Statistical Analysis

The collected data were entered into SPSS 22 software (IBM Corp, Armonk, NY, USA) and analyzed using appropriate statistical tests. The normality of distribution was assessed using the Shapiro-Wilk test. The Mann-Whitney U test was used to compare the means in non-normal distributions and independent t-test for normal distributions. Chi-square and Fisher's Exact tests were used to compare categorical data. Pearson correlation analysis was performed to evaluate the relationships between vitiligo duration and facial involvement and the patients' ocular parameters. The significance level was accepted as a p value less than 0.05.

Results

The mean age was 31.51±13.30 years in the vitiligo group and 33.23±12.46 years in the control group. In the group of patients with vitiligo, 10 (23.3%) were men and 33 (76.7%) were women, and the control group consisted of 17

men (39.5%) and 26 women (60.5%). The two groups were similar in age (p=0.47) and gender distribution (p=0.10). The mean duration of vitiligo was 7.26±5.03 years, and the mean involvement area was 11.70±9.49% of the total body surface area. There were 31 patients (72.1%) with facial involvement, 3 of whom had bilateral upper and lower eyelids lesions.

The results of ocular examinations are outlined in Table 1. Patients had higher OSDI score than controls but the difference was not significant (10.90±13.03 vs. 5.57±6.85; p=0.07). There were significant differences between mean Schirmer test (OD: 8.07±5.47 vs. 17.37±6.52 mm; OS: 7.60±5.00 vs. 17.30±6.44 mm; p<0.001) and SM results (OD: 4.49±2.40 vs. 9.74±3.67 mm; OS: 4.30±2.81 vs. 9.65±4.52 mm; p<0.001) in both eyes of the vitiligo and control groups. The mean TBUT of both eyes did not differ significantly between groups (OD: 9.14±3.17 vs. 10.12±2.08 s; p=0.27; OS: 9.16±3.30 vs. 10.05±2.10 s; p=0.25).

Meibography also showed no significant difference in MG atrophy rate between the groups (OD: 20.86±9.79% vs. 21.05±12.07%; p=0.74; OS: 18.16±8.83% vs. 19.53±10.30%; p=0.51).

Participants with OSDI higher than or equal to 13 and TBUT lower than 10 s were categorized as having dry eye. According to this new definition of dry eye, the prevalence of dry eye did not differ significantly between the vitiligo and control groups (11.6% vs. 9.3%, respectively; p=0.73). Finally, Pearson correlation test showed that facial involvement and disease duration had non-significant correlations with OSDI score, Schirmer test, SM, TBUT, and MG loss in the studied patients (Table 2).

Discussion

The concurrence of vitiligo and ocular abnormalities has been investigated in several studies, some of which have focused on ocular surface and dry eye evaluation in vitiligo. We employed Schirmer test and SM to assess the aqueous tear film and TBUT to evaluate tear film stability. In addition, we studied the structure of the MGs using SBM System.

Diagnosing dry eye presents many challenges to the medical practitioner due the absence of a gold standard protocol for diagnosis, the poor reliability of many common tests, and lack of well-defined cut-off values to distinguish disease from normal. The new definition of dry eye assigns an essential role to TBUT assessment in addition to the importance of visual impairment. According to the new definition, dry eye disease is diagnosed by the combination of symptoms (OSDI ≥13) and unstable tear film (TBUT <10 s).[14]

In this study, we observed that patients with vitiligo might have reduced production of aqueous tear film; however, there

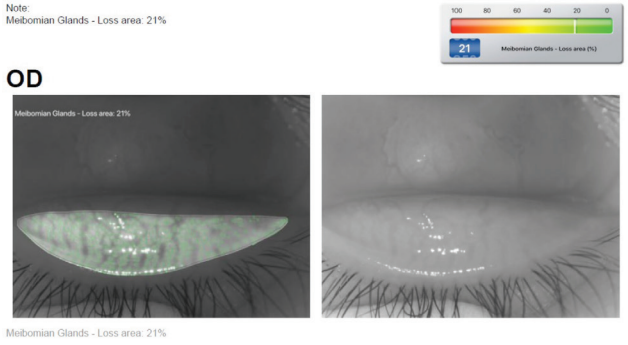

Figure 1. Meibography imaging of the right lower lid using SBM System in a normal control that shows minimal loss (21%) of meibomian glands

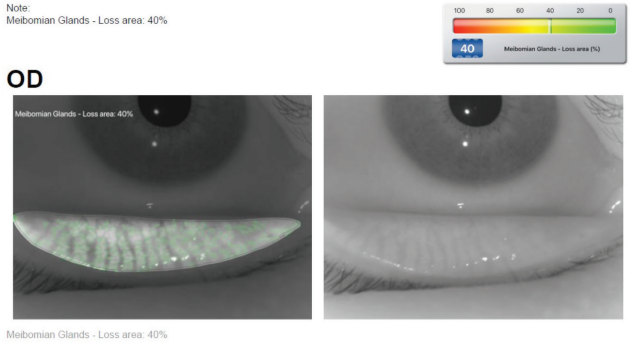

Figure 2. Meibography imaging of the right lower lid using SBM System that shows meibomian gland atrophy and dropout (40% loss) in a patient with vitiligo

Table 1. Dry eye parameters and meibography results of the groups

	Control group		Vitiligo group		p-value
	Mean ± SD	Range (min-max)	Mean ± SD	Range (min-max)	
OSDI score	10.90±13.03	52.08 (0-52.08)	5.57±6.85	29.17 (0-29.17)	0.07
Schirmer test (mm)	OD: 17.37±6.52 OS: 17.30±6.44	22 (5-27) 24 (6-30)	OD: 8.07±5.47 OS: 7.60±5.00	26 (0-26) 25 (0-25)	<0.001* <0.001*
SM (mm)	OD: 9.74±3.67 OS: 9.65±4.52	12 (3-15) 17 (3-20)	OD: 4.49±2.40 OS: 4.30±2.81	12 (1-13) 14 (2-16)	<0.001* <0.001*
TBUT (s)	OD: 10.12±2.08 OS: 10.05±2.10	11 (4-15) 11 (4-15)	OD: 9.14±3.17 OS: 9.16±3.30	13 (2-15) 13 (2-15)	0.27 0.25
MG loss (%)	OD: 21.05±12.07 OS: 19.53±10.30	64 (4-68) 48 (3-51)	OD: 20.86±9.79 OS: 18.16±8.83	37 (4-41) 30 (4-34)	0.74 0.51#

OSDI: Ocular Surface Disease Index, SM: Strip meniscometry, TBUT: Tear film break-up time, MG: Meibomian gland, SD: Standard deviation, *Mann-Whitney U test, #Independent t-test

Table 2. Association of vitiligo facial involvement and disease duration with OSDI score, Schirmer test, SM, TBUT, and MG loss, presented as Pearson correlation coefficients followed by p-values in parentheses

	OSDI score	Schirmer test		SM		TBUT		MG loss	
		OD	OS	OD	OS	OD	OS	OD	OS
Facial involvement	0.28 (0.07)	-0.26 (0.09)	-0.18 (0.25)	-0.13 (0.43)	-0.15 (0.34)	0.23 (0.14)	0.22 (0.16)	-0.19 (0.23)	-0.10 (0.53)
Disease duration	-0.11 (0.48)	-0.10 (0.51)	-0.09 (0.56)	0.14 (0.37)	0.05 (0.73)	-0.03 (0.84)	0.003 (0.98)	-0.13 (0.42)	0.01 (0.94)

OSDI: Ocular Surface Disease Index, SM: Strip meniscometry, TBUT: Tear film break-up time, MG: Meibomian gland

was no significant difference between patients and controls according to the new dry eye diagnostic criteria. This result is reasonable considering the key role of OSDI and TBUT in the new definition of dry eye and the lack of a significant association between these parameters and vitiligo in our study.

Studies investigating tear film parameters in vitiligo have yielded different and sometimes contradictory results. Karadag et al.[15] evaluated only Schirmer test as a tear film parameter in vitiligo and similarly showed a statistically significant difference between the vitiligo and control groups.

Güngör et al.[16] investigated TBUT and Schirmer test in 34 patients with different types of vitiligo. They found that the Schirmer test values in patients with vitiligo were insignificantly lower than those in the control subjects. However, the TBUT values of patients with vitiligo were significantly lower. A study by Dogan et al.[17] showed higher OSDI score, shorter TBUT, and shorter Schirmer test distance in vitiligo patients but the results were not statistically significant. Recently, Erdur et al.[18] evaluated ocular surface and tear film parameters in vitiligo patients with and without periocular involvement and compared them with controls. They showed that patients with vitiligo had higher OSDI score, lower TBUT, and higher tear osmolality, but there was no significant difference in Schirmer test and ocular surface staining between the groups. Moreover, they concluded that ocular involvement was associated with higher tear osmolarity values. The results of these studies were inconsistent with our results. However, we also performed SM, a novel test for tear production assessment, which showed significantly lower tear meniscus volume in vitiligo.

Palamar et al.[19] reported that OSDI score was higher while mean TBUT and Schirmer values were lower in vitiligo. The latter finding is similar to our results. To our knowledge, that is the only study investigating MG morphology in vitiligo patients. They showed significant differences in MG morphology in patients with vitiligo when compared to those without vitiligo. They evaluated the upper and lower eyelids using infrared biomicroscope images (Topcon, SL-D701, IJssel, Netherlands) and their morphologic results contradict our findings. Notably, we examined only the lower eyelid and employed a different device (SBM System, Turin, Italy), and the sample size in our study was twice as large. The mean extent of MG atrophy in the eyes of our vitiligo patients was greater than in the control group but the difference was not statistically significant.

Facial involvement in vitiligo might affect the eye, but this issue is more significant in patients with eyelid lesions. The association of periocular involvement with ophthalmic parameters was not assessed in this study due to small number of patients with eyelid lesions.

Study Limitations

The limitations of this study were a small sample size and lack of more comprehensive ocular surface investigations. Moreover, our meibography findings were limited to the lower eyelids. Despite these limitations, we believe that this study has the potential to guide future studies.

Conclusion

Vitiligo is associated with a reduction in the production of aqueous tear film, but does not affect MG structure and function.

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Ethics

Ethics Committee Approval: The study protocol and examinations were reviewed and approved by the Ethics Committee of Birjand University of Medical Sciences (Ir.BUMS.REC.1396.302).

Informed Consent: Obtained.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: A.R.T., B.H.R., M.N., Concept: A.R.T., E.A., B.H.R., M.N., Design: A.R.T., E.A., B.H.R., M.N., Data Collection or Processing: A.R.T., E.A., B.H.R., M.N., Analysis or Interpretation: A.R.T., E.A., B.H.R., M.N., Literature Search: A.R.T., E.A., B.H.R., M.N., Writing: A.R.T., E.A., B.H.R., M.N.

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