



Evaluation of dry eye disease and meibomian gland dysfunction with meibography in seborrheic dermatitis

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ARTICLE INFO

Keywords:

Meibomian gland dysfunction
Meibography
Dry eye disease
Seborrheic dermatitis

ABSTRACT

Purpose: To evaluate the dry eye disease and meibomian gland dysfunction with meibography of Seborrheic Dermatitis patients.

Methods: A hundred-ten of 50 patients with Seborrheic Dermatitis (group 1) and 100 eyes of 50 healthy individuals (group 2) were enrolled in this prospective study. All subjects were performed a comprehensive ophthalmic examination including lid margin alterations and meibomian gland obstruction assessment, Ocular Surface Disease Index assessment, tear film break-up time test, corneal and conjunctival fluorescein staining assessment, Schirmer test. In addition, upper and lower lids were evaluated for meibomian gland loss with non-contact meibography. The Meibomian glands were graded from grade 0 (no loss of Meibomian glands) to grade 3 (gland loss > 2/3 of the total Meibomian glands).

Results: The mean ages of Group 1 and Group 2 were 29.1 ± 9.1 (range, 18–48) and 30.6 ± 6.3 (range, 20–49) years, respectively. MGD (n = 19, %34.5), Meibum gland loss (%36.4 \pm 18.1), upper meiboscore (0.7 \pm 0.8), lower meiboscore (0.6 \pm 0.7) and DED (n = 10, %18.2) were significantly higher in the SD patients compared with the control participants (p = 0.002, p < 0.001, p = 0.011, p = 0.005, p = 0.048, respectively). There was significant relationship between age with Meibomian gland loss, MGD and DED (p = 0.017, p = 0.004, p = 0.002, respectively).

Conclusions: Seborrheic Dermatitis may influence meibomian gland morphology and as a result causing meibomian gland dysfunction and dry eye disease. For this reason, patients with Seborrheic Dermatitis should be evaluated for meibomian gland dysfunction and dry eye disease, and start treatment when needed.

1. Introduction

Seborrheic dermatitis (SD) is an inflammatory, chronic relapsing skin disease that affects 2–8% of the population [1,2]. Men are more likely to be affected and the peak incidence in the third and fourth decades. Various factors such as genetic predisposition, skin sebum levels, malassezia yeast, male sex, light skin color, winter season, androgens, immunological mechanisms have been defined as contributing factors of SD etiology [3–5]. The areas of sebaceous glands such as scalp, eyebrow, eyelid, nasolabial folds, lip, ear, sternal region, axilla, belly, inguinal and gluteal folds are often affected [6]. The diagnosis is mainly made with clinic [7]. Although the image varies according to the region, SD presents with erythematous, yellowish, greasy, scaly plaques.

Meibom glands (MG) are specific sebaceous glands in the eyelids. There are 20–30 glands in the lower eyelid and 30–40 glands in

the upper eyelid [8]. The Meibomian glands are responsible for the secretion of lipids that play a significant role in ocular surface tension and preventing evaporation of tear [9]. Meibomian gland dysfunction (MGD) is a chronic disease that characterized with terminal duct obstruction and/or quantitative-qualitative changes in the secretion [10]. Various parameters have used for diagnose of MGD in previous studies; for example, plugging of meibomian glands, telangiectasia, meibum secretion, collarettes, gland dropout, as well as combination of some of these parameters [11–14]. The prevalence of MGD is range from 3.5% to 74.5% [15,16] and there is no study on the relationship between SD and MGD. MGD is most common cause of dry eye disease (DED) and it is responsible for approximately 2/3 of the DED [17,18]. Decreased tear production, tear film imbalance and significant degeneration of the ocular surface epithelium had been demonstrated in a study with SD patients [19].

To date MGD has not been investigated in SD with meibography.

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<https://doi.org/10.1016/j.clae.2019.03.005>

Received 21 February 2019; Accepted 19 March 2019

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Therefore we investigated dry eye disease and meibomian gland dysfunction with meibography in SD patients.

2. Materials and methods

A hundred-ten eyes of 55 patients with SD (group 1) and 100 eyes of 50 healthy individuals (group 2) were included in this prospective study. All of the study procedures were performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all subjects before examination. The Ethical Committee approval was obtained from Kayseri Erciyes University. This prospective study was conducted between June 2018 and September 2018 in Aksaray Training and Research Hospital.

Exclusion criteria for both groups were a presence of ocular infection or allergy, a history of ocular surface disorder (Any other type of conjunctivitis, keratitis or ocular cicatricial pemphigoid), use of topical or systemic drugs that may affect the ocular surface, a history of ocular surgeries or ocular injury, contact lens wear, a history of systemic disease affecting the ocular surface and meibomian gland such as Sjögren, Rozacea, Psoriasis, Stevens-Johnson syndrome.

Eight seborrhic region (scalp, eyebrow, bridge of nose, beard, nasolabial folds, ear canal and posterior aspect of ear and chest) was evaluated in terms of included erythema, scaling, infiltration and pruritus for SD diagnosis [20]. The control group was also checked for the dermatological findings of seborrhic dermatitis.

The examination was performed sequentially as follows: Upper and lower eyelids were evaluate with biomicroscop for telangiectasia, irregular lid margin (notching), mucocutaneous junction shift and meibomian gland orifices for obstruction. Then fluorescein staining of the ocular surface, tear film breakup time (TFBUT) testing, Schirmer test and meibography were performed and recorded.

The diagnostic criteria recommended by the MGD Study Group in Japan were used for the diagnosis of MGD [21]. MGD was diagnosed when meibomian gland occlusion and lid margin abnormalities findings were both present. MG occlusion was considered to be present when at least one eye had meibum secretion that were decreased when moderate pressure was performed with the thumb to the middle-third region of the upper eyelid and ≥ 2 gland orifices appeared to be occluded. Lid margin abnormalities were considered to be present when at least two of the following were present in at least one eye: ≥ 2 telangiectasias, notching and mucocutaneous junction shifts. BG-4 M Non-Contact System was used for meibography (Sirius, Costruzione Strumenti Oftalmici, Firenze, Italy). Evaluation of the MG was carried out with the help of infrared imaging of a slit-lamp biomicroscopy and video camera. The ratio of meibomian gland loss area to the total area of the glands (Meibomian Gland Loss [MGL]; %) was calculated using software. With this software, the observer marks the total area and loss of area and the percentage of the MG loss is calculated by the software. MG loss was recorded as grade 0 (no loss of MG), grade 1 (0–1/3 of the total MG), grade 2 (1/3–2/3 of the total MG), and grade 3 (> 2/3 of the total MG) [22]. Grading of MG loss was performed by the same researcher blindly (E.Y). MG distortion was recorded as 0 (less than 50% changes) or 1 (more than 50% of the changes). The meiboscores and MG distortion for the upper-lower eyelids were evaluated for right eye

The dry eye diagnosis was ascertained using modified TFOS DEWS II Criteria: OSDI > 13 plus one among TFBUT < 10 s, Schirmer test score < 10 mm, or corneal and conjunctival staining > 0 [23]. TFBUT, corneal-conjunctival staining and Schirmer test were performed on the right eyes of the participants. TFBUT were evaluated by placing a single fluorescein strip over the inferior tear meniscus after instilling one drop of normal saline. Time from the last blink to the first appearance of a randomly distributed dry spot on the cornea was recorded in seconds. The mean time for three measurement was recorded. The ocular surface was divided into 3 sections as corneal, nasal conjunctival and temporal conjunctival to obtain fluorescein staining score. Each section was graded (0 = no staining, 3 = severe staining). The Schirmer test was

performed by placing a standard paper strip in the mid-lateral portion of the lower fornix without topical anesthesia. The wetted paper quantity was recorded after 5 min.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 23.0 for Windows (SPSS Inc., Chicago, IL). The normality of the data distribution was evaluated by the Shapiro-Wilk test. Student's *t*-test and Mann-Whitney test were used to compare the mean of numeric variables between the two groups. χ^2 test was used to compare the mean of categorical variable between the two groups. Spearman correlation analysis and multiple regression analysis were used to estimate the linear relationship between continuous variables. The *p*-value was statistically significant at 0.05 or smaller. The *p*-value was statistically significant at 0.05 or smaller.

3. Results

The mean ages of Group 1 (21 women and 34 men) and Group 2 (23 women and 27 men) were 29.1 ± 9.1 (range, 18–48) and 30.6 ± 6.3 (range, 20–49), respectively ($p = 0.547$). There was no significant difference in sex ratio or mean age between SD and control groups ($p > 0.05$).

MGD of group 1 and group 2 were 19(34.5) and 4(8), respectively. There was significant difference between groups ($p = 0.002$). Comparison of telangiectasia, mucocutaneous junction shifts, lid margin irregularity (notching) and meibomian gland occlusion in terms of group 1 and group 2 are presented Table 1.

MG loss of group 1 and group 2 were 36.4 ± 18.1 and 12.2 ± 10.8 , respectively. There was significant difference between groups ($p < 0.001$). Comparison of upper and lower meiboscore in terms of group 1 and group 2 are presented Table 1. No differences were found MG distortion between groups ($p > 0.05$).

DED of group 1 and group 2 were 10(18.2) and 2(4), respectively. There was significant difference between groups ($p = 0.048$). Comparison of OSDI, Schirmer test, TFBUT and corneal staining score in terms of group 1 and group 2 are showed Table 2.

Spearman correlation test was performed between MG loss with age and duration of the SD. There was significant positive relationship between age ($p = 0.017$, $r = 0.232$), in contrast there was no significant relationship between SD duration ($p > 0.05$, $r = 0.190$).

The relationship of MGD and DED with age, sex and SD duration was evaluated with binomial logistic regression test. There was significant relationship with age ($p = 0.004$, $p = 0.002$, respectively) between groups and there was no significant relationship with sex and SD duration ($p > 0.05$) (Table 3).

Table 1
Comparison of Meibomian gland Abnormalities Between Seborrhic Dermatitis patients and control groups.

	SD patients (n = 55)	Control Patients (n = 50)	p value
Meibomian gland dysfunction n(%)	19(34.5)	4(8)	0.002*
Telangiectasia n(%)	31(56.4)	14(28)	0.002*
Mucocutaneous junction shifts n (%)	15(27.3)	4(8)	0.021*
Lid margin irregularity (notching) n(%)	14(25.5)	3(6)	0.015*
Meibomian gland occlusion n (%)	19(34.5)	4(8)	0.002*
Meibomian gland distortion n (%)	10(18.5)	6(12)	> 0.05
MG loss(%) - Mean \pm SD	36.4 \pm 18.1	12.2 \pm 10.8	< 0.001*
Upper Meiboscore - Mean \pm SD	0.7 \pm 0.8	0.3 \pm 0.4	0.011*
Lower Meiboscore - Mean \pm SD	0.6 \pm 0.7	0.3 \pm 0.4	0.005*

Table 2
Ocular surface parameters in the Seborrheic Dermatitis patients and control groups.

	SD patients (n = 55)	Control Patients (n = 50)	p value
Dry eye disease n %	10(18.2)	2(4)	0.048*
Ocular symptoms (OSDI) - Median -(IQR)	20.5(0–25)	9.5(0–13)	< 0.001*
Schirmer test score(mm) - Median -(IQR)	12(5–21)	17(7–25)	0.046*
Tear film break up time(sec) - Median -(IQR)	8.5(4–17)	12(7–19)	< 0.001*
Staining score - Median -(IQR)	0.9 ± 1.3	0.4 ± 0.8	0.042*

Table 3
Results of the Binomial logistic regression model for Seborrheic Dermatitis patients.

	<i>Meibomian Gland Disease</i>		<i>Dry Eye Disease</i>	
	p	odds ratio	p	odds ratio
Age	0.04 *	1.20	0.02*	1.28
Sex	> 0.05	0.70	> 0.05	0
SD duration	> 0.05	0	> 0.05	1.34

4. Discussion

The morphologic changes in the meibomian glands associated with SD was investigated using non contact meibography imaging technique. The results of this study demonstrated that MGD, MG loss and dry eye disease were significantly higher in the SD patients compared with the control participants ($p = 0.002$, $p < 0.001$, $p = 0.048$, respectively). Eyelid telangiectasia, mucocutaneous junction shifts, notching and MG occlusion were significantly higher in the SD group ($p < 0.05$). Additionally corneal staining and OSDI scores were significantly higher and Schirmer and TFBUT values were significantly lower in the SD group ($p < 0.05$).

MGD is related to conjunctivitis [24], contact lens wearing [25], topical and systemic drugs [26,27], chemical burn [28], Dermatological diseases such as Rozacea, Psoriasis, Vitiligo, Lamellar Ichthyosis, Stevens-Johnson syndrome [29–33]. However, MG have not been evaluated with meibography in SD patients to date. To the best of our knowledge, this is the first study MGD with meibography objectively in SD. In the our study MGD (%34.5), MG loss(%36.4), upper (0.7 ± 0.8) and lower (0.6 ± 0.7) meiboscores were found statistically higher in SD patients than in the normal individuals. ($p = 0.002$, $p < 0.001$, $p = 0.011$, $p = 0.005$, respectively).

Several studies have reported the changes in the meibomian glands with aging [22,34]. In our study, the MG loss from the SD patients had association with age in the spearman linear regression analysis ($p = 0.017$, $r = 0.232$). There was no relationship between MG loss and SD duration ($p > 0.05$, $r = 0.190$) between groups. Also there was significant relationship between MGD with age in the binomial logistic regression($p = 0.04$, odds ratio = 1.20) and there was no relationship between MGD with SD duration and sex ($p > 0.05$).

Previously, conjunctival cytology and ocular surface changes were investigated in SD patients and were found to have higher corneal staining, OSDI scores and shorter Schirmer-TFBUT scores than in controls [19]. The present study is also supporting these findings with Schirmer and TFBUT values were found to be statistically lower in patients with SD than in controls. Also higher corneal staining and higher OSDI scores were more frequent in patients with SD than in controls ($p < 0.05$). As a result, DED (%18.2) was detected more higher in SD patients than in the control group ($p = 0.048$).

Dry eye disease is more common in women and the elderly after menopause [35]. In this study there was significant relationship between DED with age in the binomial logistic regression($p = 0.02$, odds ratio = 1.28) and there was no relationship between DED with sex ($p > 0.05$). This may be related to the relatively low mean age of the

patients. Also there was no relationship between DED with SD duration ($p > 0.05$).

SD is affect the areas of sebaceous glands in the body [6]. Meibomian glands are specific sebaceous glands that are responsible for lipid secretion that plays major role to build the ocular surface tension and prevent tear evaporation [9]. This situation can also explain why MGD and MG loss are both higher significantly in SD groups. MGD is major cause of DED and it is responsible for approximately 2/3 of the dry eye disease [17,18]. Hence this situation may also explain why DED is higher significantly in SD groups.

In this study, it was detected that SD should be kept in mind in the etiology of patients with MGD. In addition, it was concluded that patients presented with the diagnosis of SD in dermatology clinics should be questioned in terms of MGD and DED.

A limitation of our study is that the meibography method only demonstrates morphologic changes in the meibomian glands and cannot detect quality changes in the meibum. Another limitation of our study was the relatively low number of patients.

Our results demonstrate that SD may affect meibomian gland morphology and causing structural changes in the meibomian glands. These findings can help expand our knowledge of the etiology of MGD and may be contribute to the treatment of this condition. Also our results show that SD may cause reduction of tear production and tear film instability with MGD. So It seems to necessary to evaluate these patients for dry eye disease.

Funding

None.

Declaration of interest

The authors report no conflicts of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. Instution review board/Ethics Committee has approved the study.

Informed consent

Informed consent was obtained from all individual participants included in the study.

The article has not been presented in any conference or meeting.

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