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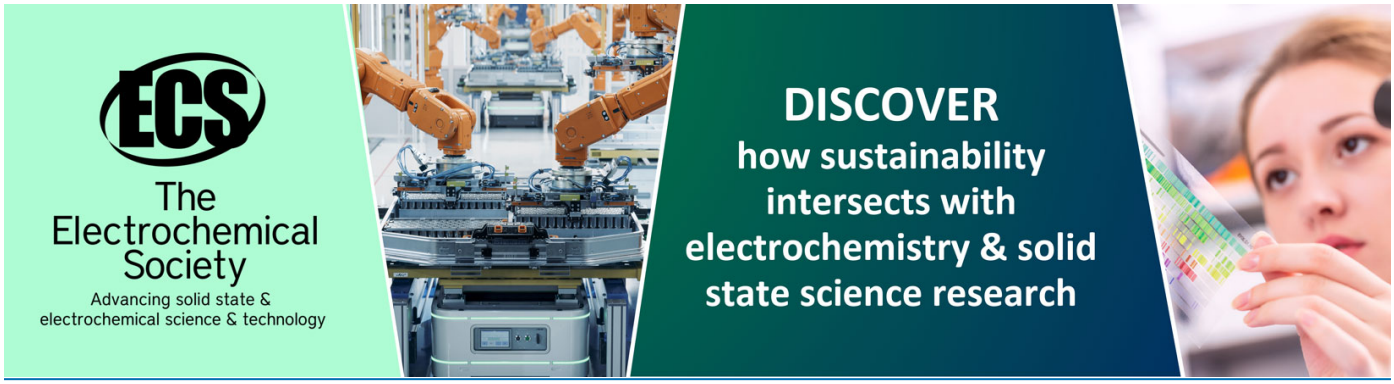

Meibomian gland loss area and its relationship with eyelid margin hyperemia and meibomian gland orifice plugging

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Abstract. Purpose: The aim of the present study was to state a relationship between the meibomian gland loss area (MGLA), eyelid hyperemia and meibomian gland (MG) orifices plugging in a sample of university students. Material and methods: A total of 74 participants were recruited. Meibography images were obtained with the OCULUS® Keratograph 5M and MGLA was calculated using the ImageJ software; also, MGLA was categorized following the Meiboscale into 4 groups: group 1 (<25%), group 2 (25-50%), groups 3 (50-75%), and group 4 (>75%). An exhaustive slit lamp examination of both eyelids was performed. Eyelid margin hyperemia and MG orifices plugging of each eyelid were categorized following Arita et. al grading scales. Results: A significant statistical relationship was found between MG orifices plugging and MGLA for both eyelids (Fisher's exact test; both $p < 0.019$). Also, correlations were obtained between lower MGLA and lower MG orifices plugging (Cramer-V = 0.583, $p \leq 0.001$); and between upper MGLA and upper eyelid margin hyperemia (Cramer-V = 0.418, $p = 0.023$), and upper MG orifices plugging (Cramer-V = 0.413, Fisher's exact test: $p = 0.042$). Conclusion: MGLA varies depending on MG orifices plugging in upper and lower eyelids; also, in upper eyelids MGLA was correlated with eyelid hyperemia.

1. Introduction

The Meibomian Glands (MG) are large sebaceous glands that produces the meibum which is the main component of the tear film lipid layer [1]. A principal tear film lipid layer function is to avoid the tear evaporation so changes on meibum delivery could alter ocular surface homeostasis [2, 3]. The most prevalent dry eye disease type is the evaporative dry eye, which main caused by the meibomian gland dysfunction [4]. Dry eye disease is defined as "a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles" [4]. The meibomian gland dysfunction use to present specific signs like eyelid margin alterations that include eyelid margin hyperemia and MG orifices plugging [3, 5]. Also, MG status can be examined with infra-red illumination obtaining meibography images [2]. Meibography images allow clinicians to calculate the Meibomian Gland Loss Area (MGLA) to grade the disease severity [6-8]. Although the meibomian gland dysfunction signs were identified there is not clear how they influence each other. The aim of the present study was to state a relationship between MGLA, eyelid margin hyperemia and MG orifices plugging in a sample of university students.

2. Material and Methods

2.1. Participants

A sample of 74 participants (50 woman and 24 men) of mean age 23.66 ± 2.50 (from 20 to 33 years old) were recruited from the Optometry Clinic in the Optics and Optometry Faculty of the Universidade de Santiago de Compostela, Spain. Participants were excluded from the study if have a history or active ocular disease, diabetes mellitus, thyroid disease, systemic inflammatory/autoimmune disease, undergone prior eye surgery, or were pregnant, breast-feeding, wore contact lenses, or were following any pharmacological treatment that can disturb the normal function of the ocular surface. Every participant has signed an informed consent to be included in this study, which is concerned with the tents of the Declaration of Helsinki and is approved by the Ethics Committee of the Universidade de Santiago de Compostela.

Participants were scheduled for an ocular surface exam, which included eyelid margin exploration under slit lamp and MG observation under OCULUS Keratograph 5M [9, 10].

2.2. Eyelid margin exploration

The exploration of both eyelid margins was performed under Topcon SL-D4 slit-lamp with a DC-4 video camera attached, 16x magnification and diffuse white light [11]. A video of each eyelid margin was recorded for the posterior analysis by a masked observer. Eyelid margin hyperemia and MG orifices plugging were categorized following Arita et al. grading scale [5]. Eyelid margin hyperemia was categorized into 4 levels: Grade 0 (No or slight redness and no telangiectasia crossing MG orifices), Grade 1 (Redness and no telangiectasia crossing MG orifices), Grade 2 (Redness and telangiectasia crossing MG orifices, less than half of the full length of the lid), and Grade 3 (Redness and telangiectasia crossing MG orifices, half or more of the full length of the lid). MG orifices plugging was categorized into 3 levels: Grade 0 (No plugging), Grade 1 (Fewer than 3 pluggings), Grade 2 (Three or more pluggings, less than half of the full length of the lid), and Grade 3 (Three or more pluggings, half or more of the full length of the lid.

2.3. Meibography Images evaluation

Meibography was performed using the OCULUS Keratograph 5M topographer that have and infra-red camera that allows to observe the MG [3, 6, 8, 12]. Upper and lower eyelids were everted for the meibography image capturing. Eyelids images were analysed by a second masked observer and MGLA was calculated with the open-source software ImageJ (Wayne Rasband, Research Services Branch, National Institute of Mental Health, Bethesda, Maryland, USA) (12). MGLA was categorized following the Meiboscale proposed by Pult et al.[13] into 4 groups: group 1 (<25%), group 2 (25-50%), groups 3 (50-75%), and group 4 (>75%).

2.4. Statistical Analysis

Data analysis was performed with the IBM SPSS Statistics v.23 software (SPSS Inc., Chicago, IL) and significance was set at $p \leq 0.05$ for all tests. Kolmogorov-Smirnov test was performed to check if the data followed parametric or non-parametric distribution [14]. All parameters followed non-parametric distribution as they were categorical variables. Therefore, contingency tables were elaborated, Fisher's exact test and Cramer-V were performed.

3. Results

As data followed a non-parametric distribution, non-parametric descriptive statistics (median and inter-quartile range (IQR)) were displayed in Table 1; also, maximum and minimum were included.

Table 1. *Descriptive statistics. n = 74 participants. IQR: Inter-quartile Range. MG: Meibomian gland. MGLA: Meibomian gland loss area.*

	Median	IQR	Minimum	Maximum
Lower eyelid margin hyperemia	1	0 – 2	0	3
Lower MG orifices plugging	0	0 – 1	0	3
Lower MGLA	2	2 – 2	1	4
Upper eyelid margin hyperemia	0	0 – 1	0	3
Upper MG orifices plugging	0	0 – 1	0	3
Upper MGLA	2	1 – 2	1	4

The relationship between MGLA, eyelid margin hyperemia and MG orifices plugging are showed in the two contingency tables, one for each eyelid, lower (Table 2) or upper (Table 3). A significant statistical relationship was found between MG orifices plugging and MGLA for both eyelids (Fisher's exact test; both $p < 0.019$). No statistical relationship between MGLA and eyelid margin hyperemia were found for both eyelids (Fisher's exact test; both $p > 0.172$).

Table 2. *Distribution of the lower MGLA according to lower eyelid hyperemia and MG orifices plugging. n = 74 participants. p-values were determined by Fisher's exact test. *Statistically significant (p < 0.05). MG: Meibomian gland, MGLA: Meibomian gland loss area.*

		Lower MGLA				Total	p
		Group 1	Group 2	Group 3	Group 4		
Lower eyelid hyperemia	Grade 0	3	18	7	0	28	0.453
	Grade 1	3	14	4	0	21	
	Grade 2	4	11	2	2	19	
	Grade 3	0	4	1	1	6	
Lower MG orifices plugging	Grade 0	6	32	11	0	49	0.001*
	Grade 1	4	14	3	0	21	
	Grade 2	0	1	0	0	1	
	Grade 3	0	0	0	3	3	

Table 3. *Distribution of the upper MGLA according to upper eyelid hyperemia and MG orifices plugging. n = 74 participants. p-values were determined by Fisher's exact test. *Statistically significant (p < 0.05). MG: Meibomian gland, MGLA: Meibomian gland loss area.*

		Upper MGLA				Total	p
		Group 1	Group 2	Group 3	Group 4		
Upper eyelid hyperemia	Grade 0	18	22	1	0	41	0.172
	Grade 1	12	8	1	0	21	
	Grade 2	4	4	0	0	8	
	Grade 3	0	1	0	1	2	
Upper MG orifices plugging	Grade 0	25	22	1	0	48	0.019*
	Grade 1	9	11	0	0	20	
	Grade 2	0	1	0	0	1	
	Grade 3	0	1	1	1	3	

Correlations were obtained between lower MGLA and lower MG orifices plugging (Cramer-V = 0.583, $p \leq 0.001$); also, between upper MGLA and upper eyelid margin hyperemia (Cramer-V = 0.418, p = 0.023), and upper MG orifices plugging (Cramer-V = 0.413, p = 0.042).

4. Discussion and Conclusion

Technology improvements made on the MG observation techniques have boosted investigations in the dry eye field. The meibography images capturing and MGLA measurement is an easy and fast procedure that supplies useful information about the MG anatomy. Nevertheless, analyzing other eyelid abnormalities that could influence the MG status should be implemented in a dry eye routine assessment.

The meibomian gland disease in its obstructive form is the most prevalent type of the disease [1]. Also, obstructive meibomian gland dysfunction is the principal cause of the evaporative dry eye. In the present study, it was found a statistical association between MG orifices plugging and MGLA on both eyelids. These findings are in concordance with the hypothesis that support the destruction of the MG by its orifice obstruction [15]. Also, a moderate correlation between MG orifices plugging and MGLA was obtained. Maybe the changes in meibum composition from being mostly non-polar lipids to presenting more concentration of polar lipids could stopple meibum secretion [16, 17]. Moreover, a thicker meibum is more difficult to be spread over the ocular surface, and therefore could not reach its anti-evaporative function, which is the main purpose of the lipids secreted by the MG.

Dry eye disease is defined as a chronic disease that includes inflammation of the ocular surface. Focusing on the obstructive meibomian gland dysfunction, an inflammation and keratinization procedure may occur, but it can be also presented without inflammation which is known as non-obvious meibomian gland dysfunction [18]. This reason could explain why specific inflammation signs like eyelid hyperemia sometimes were present. The present study showed a moderate correlation between upper eyelid hyperemia and MGLA but no association between eyelid hyperemia severity and MGLA groups. Also, no correlation between the MGLA and the eyelid margin hyperemia in the lower eyelid was found. This could occur because of the distribution of the managed data, not many participants of the MGLA Group 4 were included being a limitation of the present study. Further research into the inflammation signs of the meibomian gland dysfunction and its relationship with eyelid margin abnormalities is needed.

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