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Research Article

The Relationship Between the Activity of the Meibomian Gland and Pupil Diameter

Haci Keles[1], Erkut Kucuk[2], Zeki Baysal[2], Levent Dogan[2], Fatih Cicek[1], Faruk Gazi Ceranoglu[1]

[1]Niğde Ömer Halisdemir University, Faculty of Medicine, Department of Anatomy, Niğde, Türkiye
[2]Niğde Ömer Halisdemir University, Faculty of Medicine, Department of Ophthalmology, Niğde, Türkiye

Abstract

Aim: The meibomian glands are modified sebaceous glands that line the inner surface of the eyelids. The aim of this study was to investigate the relationship between the autonomic nervous system and meibomian gland activity based on pupil diameter values.
Material and Method: 55 volunteers (27 patients and 28 controls) aged 16-41 years participated in the study. Patients with dry eye and a visual acuity of 10/10 according to the Snellen visual threshold were included in the study. Participants underwent static measurements at different light intensities and dynamic measurements to measure the rate of pupil dilation.
Results: Static measurements (scotopic, mesopic ve photopic) in the patient group averaged 5.93±1.21, 4.70±0.86 and 3.99±0.97 mm, while measurements in the control group averaged 5.82±0.99, 4.87±0.83 and 3.87±0.90 mm. Pupillary velocity was 0.14±0.04 in the patient group and 0.12±0.03 mm/sec in the control group.
Conclusion: This is the first study to investigate the relationship between meibomian gland function and pupillary function. The present study contributed to the literature by showing that there is no relationship between meibomian gland function and pupillary function.

Keywords: Dry eye, meibomian gland, pupillometry, pupil diameter

INTRODUCTION

The meibomian glands (glandula tarsales) are modified sebaceous glands with a tubuloacinar structure and holocrine function, arranged in a single row between the conjunctiva and the tarsus on the inner surface of the eyelids. These glands can be seen as elevations under the conjunctiva when the eyelids are rotated (1,2). There are 25 to 40 meibomian glands on the upper eyelids and 20 to 30 on the lower eyelids (3). The meibomian glands, which are located in the furrows on the inner sides of the tarsus, are arranged as diverticula around a single excretory duct that opens into the limbus posterior palpebrae of the eyelids (1,2). These glands are largely parasympathetically innervated. The source of the parasympathetic fibers is the pterygopalatine ganglion. The sympathetic fibers of the glands, which also contain sympathetic and sensory fibers, originate from the superior cervical ganglion and the sensory fibers from the trigeminal ganglion (4).

The tarsal glandules in the upper and lower eyelids release lipid secretions, the so-called meibum, to the ocular surface. These lipids, which they secrete, form the outermost layer of the tear film and protect the tear from evaporation (5). Reduced or absent meibomian secretion impairs tear film formation, leading to rapid evaporation of tears and thus evaporative dry eye disease (EDE). Although the factors causing meibomian gland dysfunction (MGD) are not well understood, it is reported to be influenced by hormonal, microbial, environmental and metabolic causes. MGD is the leading cause of dry eye disease (DED) worldwide (4). In epidemiologic studies conducted worldwide, the prevalence of DED is reported at rates between 5% and 50%. Studies have shown that up to 87% of DED is caused by MGD (5,6). There are two forms of DED, one with low tear production (lack of water) and the other with rapid evaporation of tears. Of these, underproduction of tears is related to the lacrimal gland (which accounts for a small proportion of DED), while EDE is related to the meibomian

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Corresponding Author: Haci Keles, Niğde Ömer Halisdemir University, Faculty of Medicine, Department of Anatomy, Niğde, Türkiye
E-mail: hacikeles@ohu.edu.tr

glands (the main cause of DED) (5-7). MGD, which causes rapid evaporation of tears, can be detected in clinics by a tear break-up test (8).

Pupil dilation and constriction as well as pupillary function are controlled by the autonomic nervous system. Pupil dilation (mydriasis) is caused by dilator pupils, which are innervated by sympathetic nerve fibers, while constriction (myosis) is caused by sphincter pupils, which are innervated by parasympathetic nerve fibers. Some data obtained from the pupil (pupillary reflex, pupillary symmetry, pupil size, shape and diameter) provide information used in the diagnosis of neuro-ophthalmologic diseases and intracranial pathologies. Since pupillary changes provide important information about diseases, they are used among the objective measurement methods. In recent years, pupillary functions have been objectively measured with devices and the data obtained from these measurements have been evaluated with the data of diseases such as COVID-19, diabetes, oculomotor nerve palsy, bipolar disorder and pseudoexfoliation syndrome (9-11).

In this study, we aimed to investigate the relationship between meibomian gland activity and pupil width, which is automatically measured and provides information about the autonomic nervous system. In addition, this study will be the first to reveal whether there is an autonomic nervous system-related cause in the etiology of MGD according to the literature review. According to the literature review, this is the first study to show the relationship between the meibomian glands and pupil diameter, which provides information about the autonomic nervous system.

MATERIAL AND METHOD

Fifty-five volunteers aged 16-41 years (27 patients and 28 control subjects), who were admitted to the Department of Ophthalmology at Niğde Ömer Halisdemir University Training and Research Hospital, participated in the study. The control group consisted of patients who came to the ophthalmology outpatient clinic for routine check-ups and had no eye disease other than myopia and hyperopia of less than 3 diopters and astigmatic refractive error of less than 1 diopter. The patient group consisted of patients who came to the outpatient clinic and were diagnosed with evaporative dry eye. Patients with a visual acuity of 10/10 according to the Snellen visual threshold and those with evaporative dry eye were included in the study. Patients with systemic diseases, pregnant and breastfeeding women, patients with myopia and hyperopia of more than 3 diopters and astigmatism of more than 1 diopter, patients with a history of heart disease, trauma, eye diseases other than refractive error and dry eye, patients with a history of eye surgery, smokers and alcohol or chronic drug users were excluded. Pupillary parameters and tear refraction times were determined using Sirius Topography (CSO, Firenze, Italy). The study was approved by the Niğde Ömer Halisdemir University Non-Interventional Clinical Research Ethics Committee with protocol number 2023/17.

Data Collection Tools

The pupillometry device automatically evaluates and measures the pupil diameter at different light intensities. The device performs pupil measurements in two ways: statically and dynamically. Static measurements are performed scotopically, mesopically and photopically at three different light intensities. Scotopic measurements were calculated at a light intensity of 0.4 lx from the LED light source in the pupillometry device, mesopic measurements at a light intensity of 4 lx and photopic measurements at an ambient light intensity of 40 lx. Dynamic measurements were then carried out at an illuminance of 500 lx. In the dynamic measurements, the speed of pupil dilation was measured. For this purpose, the pupil widths were calculated at 0 and 18 seconds at a light intensity of 500 lx. The pupil speed was then calculated by dividing the difference between the values at 0 and 18 seconds by 18. As the participants had the longest adaptation time of 18 seconds, the data were analyzed during this period. Measurements were taken at the same time of day (09:00-10:00) by the same researchers to minimize pupil effects. Measurements were taken after a 5-minute adaptation period to the dark environment. Subjects were asked to abstain from caffeinated food and drink 24 hours prior to the measurements.

Data Analysis

The Shapiro-Wilk test was used to check whether the variables correspond to a normal distribution. Numerical variables were summarised with mean±standard deviation and minimum-maximum values. The independent t-test was used for comparisons between two groups. Analyses were performed using IBM SPSS version 22 (SPSS, Inc., Chicago, IL, USA). $p<0.05$ was accepted as the statistical significance level.

RESULTS

Fifty-five subjects (27 patients and 28 controls) with a mean age of 29.78±8.34 years participated in this study. Of all participants, 60% were female and 40% were male. Mean±standard deviation and minimum-maximum values of the parameters of all participants are shown in Table 1.

Table 1. Descriptive statistics of the parameters of the whole study group

	N	Mean±Sd	Min-Max
Age (year)	55	29.78±8.34	16-41
TBUT (sec)	55	9.07±6.42	1.20-17.00
TBUT Average (sec)	55	10.31±5.49	2.70-17.00
Scotopic (mm)	55	5.87±1.10	4.07-8.24
Mesopic (mm)	55	4.79±0.84	3.18-6.66
Photopic (mm)	55	3.93±0.93	2.43-6.70
Dynamic 0th second (mm)	55	3.73±0.81	2.46-5.86
Dynamic 18th second (mm)	55	6.09±0.94	3.95-8.21
Pupilla speed (mm/sec)	55	0.13±0.04	0.040-0.193

N: number of participants, SD: standard deviation, Min: minimum, Max: maximum, TBUT: tear film breakup time

Table 2 shows that the mean age of patients with EDE was 29.33±8.80 years and 30.21±8.01 years in the control group. The mean tear film break-up time (TBUT) and TBUT were 3.10±1.43 and 5.14±1.45 seconds, respectively, in EDE, while the same parameters were 14.81±3.27 and 15.29±2.43 seconds, respectively, in the control group. The difference between these two parameters was statistically significant (p<0.001 for both parameters). The static measurements (scotopic, mesopic and photopic) were 5.93±1.21, 4.70±0.86 and 3.99±0.97 mm in the subjects with EDE, while they were 5.82±0.99, 4.87±0.83 and 3.87±0.90 mm in the control group. When analyzing the dynamic measurements, the pupil aperture at 0 and 18 seconds was 3.66±0.77 and 6.17±0.95 mm, respectively, in EDE, while these data were 3.79±0.85 and 6.02±0.94 mm, respectively, in the control groups. Pupillary velocity was 0.14±0.04 mm/sec in the EDE group and 0.12±0.03 mm/sec in the control group. No statistically significant difference was found when comparing the static, dynamic and pupillary velocity parameters between the patient and control groups (p>0.05).

Tablo 2. Comparison of patient and control group data

	EDE	N	Mean±SD	Min-Max	p
Age (year)	Patient	27	29.33±8.80	16-41	0.699
	Control	28	30.21±8.01	20-40	
TBUT (sec)	Patient	27	3.10±1.43	1.20-5.70	<0.001
	Control	28	14.81±3.27	6.20-17.00	
TBUT Mean (sec)	Patient	27	5.14±1.45	2.70-8.70	<0.001
	Control	28	15.29±2.43	10.30-17.00	
Scotopic (mm)	Patient	27	5.93±1.21	4.16-7.77	0.708
	Control	28	5.82±0.99	4.07-8.24	
Mesopic (mm)	Patient	27	4.70±0.86	3.27-6.37	0.464
	Control	28	4.87±0.83	3.18-6.66	
Photopic (mm)	Patient	27	3.99±0.97	2.56-6.70	0.635
	Control	28	3.87±0.90	2.43-5.89	
Dynamic 0th second (mm)	Patient	27	3.66±0.77	2.46-5.86	0.530
	Control	28	3.79±0.85	2.51-5.44	
Dynamic 18th second (mm)	Patient	27	6.17±0.95	4.30-7.51	0.563
	Control	28	6.02±0.94	3.95-8.21	
Pupilla speed (mm/sec)	Patient	27	0.14±0.04	0.04-0.189	0.121
	Control	28	0.12±0.03	0.072-0.193	

EDE: evaporative dry eye disease, N: number of participants, SD: standard deviation, Min: minimum, Max: maximum, TBUT: tear film breakup time

DISCUSSION

DED is a corneal surface disease that results in damage to the cornea and conjunctiva caused by the absence or rapid evaporation of tears. DED is aggravated by advanced age, gender, medication, wearing contact lenses, low humidity environments, prolonged reading or screen time (e.g. phones, tablets, computers). Phones, tablets, computers), smoke, windy environments, Asian ethnicity, air-conditioned rooms, rheumatoid arthritis, sarcoidosis, Many factors such as Sjögren's syndrome, Parkinson's disease, thyroid abnormalities, bell's palsy, hepatitis C infections, rosacea, seasonal or persistent allergies, allergic conjunctivitis caused by Demodex mites, diabetes, and eye surgery or trauma can cause DED (7,12-16). There are two forms of DED, categorised as low tear production (aqueous deficiency) and rapid tear evaporation (7). In EDE, rapid evaporation of the tear film occurs in the absence or deficiency of meibum secretion (4). The diagnosis of EDE can be made by evaluating the TBUT parameter (8). TBUT is calculated as the time interval between the first dry area that appears in the tear film after complete eye closure (17). Deterioration of the tear film below 10 seconds is considered abnormal (18). In our study, the TBUT value in patients with EDE was calculated as 3.10±1.43 seconds, while the TBUT parameter in the healthy control group was calculated as 14.81±3.27 seconds.

The pupil is the hole in the center of the iris. Its task is to regulate the amount of light that reaches the retina. Midriasis means dilation of the pupil and miosis means constriction. These functions are carried out with the help of smooth

muscles. While the dilator pupils dilate the pupil under the action of the sympathetic nervous system, the sphincter pupils constrict it under the action of the parasympathetic nervous system (1,2). A device that measures pupil function under different light sources is called a pupillometry device. Pupillometry measures pupil diameter non-invasively and provides important information about the sympathetic and parasympathetic nervous system. It also measures pupil diameter statically and dynamically under different light intensities and provides quantitative and objective results on pupil functions (9-11). The relationship between pupillometry, which has become increasingly important in recent years, and diseases such as COVID-19, diabetes, oculomotor nerve palsy, bipolar disorder, pseudoexfoliation, depression, autism, Graves' disease, sepsis-related encephalopathy, pain classification, Alzheimer's disease and Chagas' disease has been investigated (9-11,19-23). In this study, patients with dry eye and MGD were compared with healthy individuals in terms of pupillary function. According to the literature review, this study was the first to find a correlation between meibomian gland function and pupil diameter. In this study, pupil functions of healthy subjects were calculated as follows: scotopic 5.82±0.99 mm, mesopic 4.87±0.83 mm, photopic 3.87±0.90 mm, dynamic 0th second 3.79±0.85 mm, dynamic 18th second 6.02±0.94 mm and pupillary velocity 0.12±0.03 mm/sec. In a study conducted on 30 healthy subjects aged 19-40 years, pupil functions were scotopic 5.63±0.459 mm, mesopic 4.47±0.574 mm, photopic 3.47±0.519 mm, dynamic 0th second 3.68±0.661 and pupil velocity 0.128±0.029 mm/sec. These data are consistent with the data we measured in healthy volunteers. In our study, no statistically significant difference was found between the measurements we made between the healthy and patient groups.

Limitations of the Study

This study has some limitations. Our study only covers one region and the number of participants is relatively small. Studies with a larger number of participants are needed.

CONCLUSION

Therefore, the relationship between meibomian gland function and pupillary function was discussed in this study and it is the first study to investigate this. The present study contributed to the literature by showing that there is no relationship between meibomian gland function and pupillary function.

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