



Research Article

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Clinical Features of Lid Margin, Meibomian Gland and Tear Film Changes in Patients with Primary Pterygium

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Abstract

Introduction: The aim of this study was to clinically evaluate lid margin abnormality, meibomian glands expression and tear function changes in patients with primary pterygium.**Methods:** Fifty normal and 50 primary pterygia participants without other ocular pathologies were randomly selected from patients who attended an ophthalmology visit. The lid margin abnormality, meibomian gland expression, tear break-up time, Schirmer's test results and ocular surface disease index (OSDI) were evaluated. Multiple tear meniscus values include the lower tear meniscus height (TMH), tear meniscus depth (TMD) and tear meniscus area (TMA) were also measured using time-domain ocular coherence tomography. Comparative analyses between groups were performed for all parameters. A statistical significance level of $P < 0.05$ was considered. Association of ocular surface disease index with lid margin abnormality scores, meibomian gland expression and tear break-up time were evaluated.**Results:** Ocular surface disease index, lid margin abnormality and meibomian gland expression scores were significantly higher in primary pterygium patients than in normals ($P < 0.001$). Tear break-up time, Schirmer's test results, lower TMH, TMD and TMA values do not differ between the two groups ($P > 0.05$). Correlation analysis demonstrated that lid margin abnormality, meibomian gland expression and tear break-up time were significantly correlated with ocular surface disease index ($P < 0.05$).**Conclusions:** Primary pterygium may cause alteration of lid margin and meibomian glands expressions, which is associated with ocular discomfort. Early detection of lid margin and meibomian gland changes seem to be important to understand the relationship between pterygium, tear film functions and changes of the ocular surface.

Keywords

Pterygium, Ocular surface, Meibomian gland, Tear function, Ocular coherence tomography

Abbreviations

OSDI: Ocular Surface Disease Index; TBUT: Tear Break-Up Time; SIT: Schirmer's Test; TMH: Tear Meniscus Height; TMD: Tear Meniscus Depth; TMA: Tear Meniscus Area; Secs: Seconds; Mm: Millimetres; μ m: Micrometres

Introduction

Pterygium is benign abnormal fibrovascular growth which is commonly found in countries near the equator [1,2]. It originates from bulbar conjunctiva and progresses towards central cornea [1-3]. Pterygium can be characterised based on its translucence appearance which gives rise to its morphology [4]. Pterygium patients are commonly had similar signs and symptoms such as ocular discomfort, itchiness, excessive tearing and foreign-body sensation [5] and reduction in vision acuity [6,7].

Previous works reported that inadequate tear film stability [8] or reduced tear function [9] are common in

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pterygium patients, although a recent study reported tear functions are normal in pterygium patient [10]. There is an unresolved issue with regards to the association of pterygium and abnormal tear function such as in dry eye. If they are related, what are the mechanisms of the association and could one factor aggravate the progression of pterygium. Information on the association of pterygium and dry eye is scarce. Based on the literature search, lack of evidence that addresses on which components of the pre-corneal tear film is more affected in pterygium. Tear film comprises of three layers known as lipid as the outermost, aqueous and mucin as the innermost layer. With regards to dry eye, it can be due to a lack of aqueous production or excessive evaporative due to lipid layer instability.

To date, information on the association of pterygium with tear film deficiency and instability is still poorly understood. Moreover, the relationship between dry eyes induced limbal/stem cell pathology [11] such as in pterygium are still unexplored. Hence, based on these shreds of evidence, we are embarking at assessing the objective relationship between pterygium and dry eyes by establishing their clinical manifestations. This study aims to evaluate the changes on multiple ocular surface features between normal and primary pterygium.

Materials and Methods

This prospective study comprised of 50 patients (50 eyes) with primary nasal pterygium and 50 normal patients (50 eyes) as a control group. The diagnosis of primary pterygium was made clinically using a high-definition white light digital slit-lamp performed by a consultant ophthalmologist (KMK). The diagnosis of pterygium is confirmed based on Tan's classification of pterygium [12,13]. The pterygium is classified into three grades. Grade I (atrophy) was defined as the pterygium growth in which the underlying episcleral vessels are unobscured and distinguished. Grade II (intermediate) pterygium was defined as the appearance of episcleral vessel are indistinct or partially obscured, and Grade III (fleshy) pterygium was defined as the underlying episcleral vessels are completely obscured.

All participants in this study were selected based on inclusion criteria including an established diagnosis of primary pterygium, patients of either gender with ages between 20 to 70 years, and no history of ocular trauma, ocular surgery and contact lens wear [1,14-16]. Patients with significant ocular surface diseases, such as recurrent pterygium, corneal irregularity, and opacity due to diseases other than pterygium were excluded [13]. Patients for whom corneal topography could not provide reproducible measurements due to obstruction of the central cornea by pterygium were also excluded.

Each patient had undergone a comprehensive optometric examination comprises of visual acuity (VA) testing, slit-lamp examination and anterior eye imaging using anterior segment ocular coherence tomography (AS-OCT). Dry eye symptoms were assessed using the ocular surface disease index (OSDI) questionnaire, which represents the quality of life related to

dry eye disease [17,18]. The study was conducted according to the recommendation of the tenets of the Declaration of Helsinki and approved by the International Islamic University Malaysia (IIUM) research ethical committee (IIUM/310/G13/4/4-125). Written informed consent was obtained from all participants prior to all procedures performed.

Meibomian gland expression

Meibomian gland expression (MGE) was conducted to evaluate meibomian gland dysfunction by assessing the clarity and ease of meibum expression in the eyelid region via slit-lamp observation. The quality of meibum expression was graded based on its degree of opacity and viscosity on a 0-4 scale [19], in which 0 indicates normal viscosity; 1, opaque with normal viscosity. Scale of 2 indicates opaque with increased viscosity, while 3 indicates severe thickening (toothpaste-like consistency) and 4, no expression which indicates the meibomian glands are completely obstructed. Lid margin abnormalities were subjectively evaluated, and scored either as 0 (absent) or 1 (present) for the following four parameters: vascular engorgement, plugged meibomian gland orifices, anterior or posterior displacement of the mucocutaneous junction, and irregularity of lid margin [20].

Tear-break-up time

Tear film stability was measured via tear-break-up time (TBUT), which is defined as the time taken for the first dry spots to appear on the corneal surface after a blink. TBUT was assessed by placing a drop of normal saline on a single fluorescein strip over the inferior tear meniscus. Patients were asked to blink three times and look straightforward. The pre-corneal tear film was evaluated objectively using Oculus keratograph 5 M (OK5M; Oculus Optikgeräte GmbH, Wetzlar, Germany), and the elapsed times between blinking to the formation of first dry spots were recorded [21]. Three measurements were recorded and the mean was taken as the TBUT value. Tears production was measured via non-anaesthesia Schirmer's test by placing the Schirmer's tear test filter strip in the mid-lateral portion of the lower fornix. The test was set at 5 minutes and the amount of wetting in millimetres (mm) was recorded [22].

Lower tear meniscus

The lower tear meniscus status was measured using time-domain optical coherence tomography (TD-OCT) Zeiss Visante™ OCT (Zeiss Meditec Inc., Dublin, United States). The middle of the lower eyelid was scanned via a vertical 2 mm scan mode three times per eye [22-24]. All participants were examined in an air-conditioned room with a temperature of 25 °C and humidity between 40%-50% [22,23]. These scans provide three additional parameters which are tear meniscus height (TMH), tear meniscus depth (TMD) and tear meniscus area (TMA). TMH was defined as the distance from the upper meniscus of the cornea and lower meniscus of the lid. TMD was defined as the distance from the midpoint of the meniscus interface to the cornea/lower eyelid. TMA was defined as the tears-covering areas which comprise of the cornea, lower eyelid and tear meniscus. TMH, TMD and TMA

were also measured three times and the average value was taken as variable for analysis.

Data analysis

All data were expressed as the mean ± standard deviation. A paired *t*-test was employed to evaluate repeated measurements of continuous values (OSDI score, TBUT, SIT, TMH, TMD and TMA). Pearson’s correlation analysis was employed to assess repeated measurements of non-continuous values (Lid margin abnormalities and meibum expression). Comparative analyses between primary pterygium and control group in tear film function were performed using independent T-test. Statistical analyses were performed using IBM SPSS (Predictive analytics software) Version 24 (IBM Corp, Armonk, NY, USA). *P* < 0.05 was set as the level of significance.

Results

The mean age of patients with primary pterygium was 55.2 ± 6.0 years (N = 50), which are comparable with control group 54.5 ± 4.7 years (N = 50). There were 35 patients (70%) with primary pterygium Type I and the others were Type II. Normality testing revealed that all data were normally distributed (*p* > 0.05). The mean OSDI score in the primary pterygium group was significantly higher than in the control group (mean difference ± SD; *P* < 0.001). TBUT was significantly lower in the primary pterygium than in the control group. (mean difference +/- SD; *P* < 0.001). Whereas, the values of TMH, TMD, TMA and SIT measured were not significantly different between the two groups (*P* > 0.05) (Table 1). Pearson correlation analysis indicates that the OSDI scores was significantly correlated with lid margin abnormality scores (*r* = 0.354, *P* < 0.001), meibomian gland expression (*r* = 0.625, *P* < 0.001) and TBUT (*r* = -0.748, *P* < 0.001). All parameters were found significantly correlated with primary pterygium group (*P* < 0.05).

Discussion

Pterygia are characterised as abnormal proliferative fibrovascular growth which involves inflammatory infiltrates

with prominent vascular reaction. It is an established fact that pterygium is highly associated with prolonged exposure to ultraviolet (UV) light radiation. Excessive UV stimulation was found inducing changes in pterygium fibroblast cells which further provoke pterygium development [1-4]. Recent study [25] had shown that pterygium was associated with alteration in limbal cells which caused hyperproliferative epithelial of the lid margin, which then cause structural changes of the meibomian glands.

Meibomian gland inflammation is often associated with ocular surface inflammation conditions such as blepharokeratoconjunctivitis, ocular rosacea and keratoconjunctivitis sicca. Not to mentioned inflammation associated with meibomian gland known as meibomian gland dysfunction (MGD) is one of the most common ocular surface inflammations. Previous works [26,27] reported that the inflammatory process is aggravated due to excessive production of cytokines and growth factors which involves complex regulatory pathway. Recent report [28,29] commented that the mean inflammatory cell density was found higher in MGD patients compared to controls, which indicates direct inflammatory damage to the eyelid due to release of series of inflammatory cytokines including tumor necrosis factor causing changes in meibomian gland. Long-term inflammation might cause blockage of meibomian gland (meibum stagnation) and may lead to keratinization of meibomian glands orifices.

This present study revealed that primary pterygium patients had significantly higher OSDI scores, lid margin abnormalities and meibum expression compared to the control group. However, changes in SIT and TMH were found not significant. Previous studies had shown debatable results with number of studies [30-32] showed that SIT was significantly reduced in primary pterygium patients, while few authors [10,33] commented no significant changes were found.

Variations of the results could be explained due to how tears evaluation was made. Objective and quantitative assessment using AS-OCT had proved that the measurements

Table 1: Mean ± standard deviation of the ocular surface parameters that were measured between two groups.

Parameters	Pterygium Group (N = 50)	Control Group (N = 50)	P-value
OSDI score	13.7 ± 0.8	9.8 ± 0.8	< 0.001 ^a
Lid margin abnormality	1.2 ± 0.7	0.7 ± 0.6	< 0.001
Meibum expression	1.4 ± 0.5	0.4 ± 0.5	< 0.001
TBUT (Secs)	4.4 ± 0.6	6.6 ± 1.2	< 0.001
SIT (mm)	10.3 ± 0.4	10.1 ± 0.3	0.076 (> 0.05)
Lower tear meniscus evaluated by TD-OCT			
TMH (µm)	225.12 ± 14.24	228.78 ± 14.00	0.198 (> 0.05)
TMD (µm)	197.08 ± 13.21	201.44 ± 27.81	0.319 (> 0.05)
TMA (10 ⁻⁹ mm ²)	25631.02 ± 456.60	25777.28 ± 477.87	0.121 (> 0.05)

^aIndependent t-test showed a significant difference between primary pterygium and control groups (*p* < 0.05);

^bCorrelation/MLR showed a significant difference between OSDI score and other tested variables (*p* < 0.05) suggest to include these Table or any graph for correlation or MLR???

are consistent and reliable [34], rather than relying on slit-lamp examination only. Likewise, this study found that TMH and SIT were found not significantly different compared to the control group. It showed that aqueous productions remain intact while the tear film quality is compromised particularly the lipid component. As this study samples are majority from pterygium of Type I (atrophy), this could mask the difference in TMH and SIT. Thus, that could lead to no significant changes between pterygium and normal patients studied in this current study.

The decrease in tear volume is shown to be corrected by a compensatory response to maintain the ocular surface homeostasis. Previous works [35,36] had shown that changes in ocular surface homeostasis could trigger reflex production of aqueous and lipid components of the tear film which indirectly improves the tear film. It could be another possible reason why SIT and TMH were found no difference between the primary pterygium and control groups.

This current study also found that TBUT was significantly reduced in the primary pterygium group. Shorter TBUT is known as associated with tear film stability [22]. Tear film comprises of three layers known as the lipid, aqueous and mucin layers, the lipid layer must be adequate to prevent evaporation and lowering surface tension in maintaining a good tear stability [23]. From this current TBUT findings, we speculate that the quantity of tear production is normal, but the tear quality is compromised as meibomian glands responsible to produce the lipid layer which is not well functioned in patients with primary pterygium.

Several works had postulated that abnormal tear function is a risk factor of the development of pterygium [37-39]. It is suggested that changes of conjunctiva, cornea, eyelid and tear film function due to pterygium leads to abnormal tear function [40]. Few studies [41,42] reported that density of conjunctival goblet cell counts which give rise to tear quality and quantity was found lower in pterygium patients. In addition, recent study [40] showed that the density of conjunctival goblet cell count increased subsequent to excision. These current results postulated that pterygium does cause changes on the ocular surface [43]. Alterations of meibomian glands in primary pterygium patients could exacerbate the tear instability and damages the ocular surface, by inducing changes on the lipid layer of tear film. Lid margin and meibomian gland changes could be the evidence of the presence of dry eye symptoms in pterygium patients.

This current study suggests that clinicians should pay attention to the changes in the lid margin and meibomian gland when examining pterygium patients with dry eye signs and symptoms. Proper treatment should be employed to treat dry eye condition in pterygium patient. For instance, different severity of pterygium would require specific physical properties of artificial tears [44,45]. Further research is needed to evaluate how different types of pterygium affect the ocular surface, and how dry eye symptoms related to the types of pterygium.

Conclusion

Alterations of the lid margin and meibomian glands in primary pterygium patients could exacerbate the tear stability and damaging the ocular surface.

Conflicts of Interest

Principal researcher and all co-researchers have no conflict of interest and financial gain from any companies involved in this study.

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