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Comparison of Clinical Features of Lid Margin and Tear Film Changes between Normal and Primary Pterygium Patients

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Abstract

Introduction: The goal of this study was to clinically evaluate meibomian glands and tear function changes in patients with primary pterygium.

Methods: Combinations of normal (n = 100) and primary pterygium (n = 100) participants without ocular pathologies were selected from patients who visited an ophthalmology clinic. Comprehensive assessment includes the ocular surface disease index, meibomian gland expression, lid margin abnormalities, tear break-up time and Schirmer's test scores were evaluated. Multiple tear meniscus values includes the lower tear meniscus height, tear meniscus depth and tear meniscus area 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 examined.

Results: Ocular surface disease index, lid margin abnormality and meibomian gland expression scores were significantly higher in primary pterygium patients than in controls ($P < 0.001$). However, tear break-up time scores, Schirmer's test scores, the lower tear meniscus height, tear meniscus depth and tear meniscus area values did not revealed a significant difference 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 scores ($P < 0.05$).

Conclusions: Pterygium may cause alteration of meibomian glands, which is associated with ocular discomfort. Early detection of meibomian gland changes seems 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

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 characterized based on its translucence appearance which gives rise to its morphology. Excessive or prolonged exposure to Ultraviolet (UV) light [4] is a known risk of developing pterygium. Pterygium patients are commonly had similar signs and symptoms such as ocular discomfort, itchiness, excessive tearing and foreign-body sensation [5], not to mentioned unfavourable cosmetic appearance and reduction in vision acuity [6,7].

Previous works reported that inadequate tear film stability [8] or reduced tear function [9] are common in pterygium patient, although a recent study reported tear

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functions are normal in pterygium patient [10]. Thus, 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 association of pterygium and dry eye is scarce. Based on the literature search, lack of evidence that address on which components of pre-corneal tear film is more affected in pterygium. Tear film comprise 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 lack of aqueous production or excessive evaporative due to lipid layer instability.

To date, information on association of pterygium with tear film deficiency and instability is still poorly understood. Moreover, relationship between dry eyes induced limbal/stem cell pathology [11] such as in pterygium are still unexplored. Hence, based on these evidences, 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 one hundred patients (100 eyes) with primary nasal pterygium and one hundred patients (100 eyes) of normal patients. 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], a clinical grading which clinical grading based on the translucence of the growth. Tan's classification of pterygium divides pterygium into types of atrophy, intermediate, and fleshy. Grade I (atrophy) pterygium is defined as growth in which the underlying episcleral vessels are unobscured and clearly distinguished. Grade II (intermediate) pterygium is defined as a growth in which details of the episcleral vessel are indistinct or partially obscured. Finally, Grade III pterygium (fleshy) is defined as growth in which 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 and 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 to ensure no corneal abnormalities other than pterygium were also excluded.

Each patient underwent 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 represent the vision-related quality of life related to dry eye disease [17,18]. Sample size was calculated by using mean difference in corneal astigmatism between preoperative and postoperative (3 months) of pterygium surgery as reported by previous study [1] using Power and Sample Size Calculation software (version 3.1.2) (PS software, Nashville, TN, USA). 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 (IREC) (IIUM/310/G13/4/4-125). Written and informed consent was obtained from all participants prior to any procedures performed.

Meibomian gland expression (MGE)

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. The quality of meibum expression was graded based on its degree of opacity and viscosity on a 0-4 scale [19], in which 0 indicate normal viscosity; 1) Opaque, normal viscosity; 2) Opaque, increased viscosity; 3) Severe thickening (toothpaste consistency); and 4) No expression which indicate the glands are completely obstructed. Lid margin abnormalities were subjectively evaluated, and scored 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 (TBUT)

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 precorneal tear film was evaluated objectively using Oculus keratograph 5 M (OK 5 M), and the elapsed times between blinking to 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 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, USA). The middle of the lower eyelid was scanned via vertical 2 mm scan mode three times per eye [22-24]. All participants were examined under controlled conditions 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 are (TMA). TMH was defined as the distance from the upper meniscus of the cornea and the 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. All images obtained were measured and analysed using Image J software (U. S. National Institutes of Health, Bethesda, Maryland, USA, https://imagej.nih.gov/ij/).

Data analysis

All data were expressed as the mean ± standard deviation. 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 analysis 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, SPSS Inc., Chicago, IL, 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 (N = 100), which are comparable with control group (N = 100). Based on Tan's classification of pterygium, 35 patients (70%) were in Type I (atrophy) with remaining are in Type II (intermediate). None of the samples are from Type III. Normality testing was conducted and all data were normally distributed. The mean OSDI scores of patients with primary pterygium were 13.7 ± 0.76, which was significantly higher than in control group (9.84 ± 0.76; $P < 0.001$). Tear break-up time (TBUT) was 4.36 ± 0.63 seconds (95% confidence interval (CI): -2.65 - -1.91) in primary pterygium group while 6.64 ± 1.2 seconds (95%: -2.66 - -1.91) in control group. The difference between the two groups was statistically significant ($P < 0.001$). However, the values of TMH, TMD, TMA and SIT measured were not significantly different between the two groups (all $P > 0.05$) (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 (all $P < 0.05$).

Discussion

This current study aimed to investigate the differences in clinical features of lid margin and tear film in between normal and pterygium patients. Pterygia are characterized 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. Recent study [25] had shown that pterygium was associated with alteration in limbal cells which caused hyperproliferative epithelial of the lid margin, which then causing structural changes of the meibomian glands.

Meibomian gland inflammation is often associated with ocular surface inflammation conditions such as blepharokeratoconjunctivitis, ocular rosacea and dry eye. 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. A study [21] commented that different type of pterygium also could leads to variation in tear function. An attempt [30], was made to correlate inflammation in form of pterygium redness as indicator for pterygium evaluation and the study found that different type

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

Parameters	Pterygium group (N = 100)	Control group (N = 100)	P-value
OSDI score	13.7 ± 0.8	9.8 ± 0.8	< 0.001
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)

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: Millimeters; µm: Micrometres

of pterygium based on its translucence appearance provides different amount of pterygium redness [31] in which does signify inflammation.

This present study revealed that primary pterygium patients had significantly higher OSDI score, lid margin abnormalities and meibum expression compared to control group. However, changes in SIT and TMH were found not significant. Previous studies had shown debatable results with number of studies [32-34] showed that SIT were significantly reduced in primary pterygium patients, while few authors [10,35] 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 anterior segment OCT had proved that the measurements are consistent and reliable [36], rather than relying on slit-lamp examination. Likewise, this study found that TMH and SIT were found not significantly different compared to normal group. This mean that aqueous productions are 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), in which the less severe compared to Type III (fleshy), this could masked the difference in TMH and SIT. Thus, that could leads to no significant changes between pterygium and normal patients studied in this current study.

Decrease in tear volume is shown to be corrected by a compensatory response in order to maintain the ocular surface homeostasis. Previous works [37,38] 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. Hence, it could be another possible reason on why SIT and TMH were found no difference between primary pterygium and normal group. In this study, TBUT was found significantly reduced in primary pterygium group. Shorter TBUT is known associated with tear film stability [22]. Tear film comprises of three layers known as the lipid layer (most superficial), aqueous and mucin layer. In order to have good tear stability, the lipid layer must be adequate to prevent evaporation and lowering surface tension [23]. Hence, based on TBUT findings, it can be postulated that the quantity of tear film production is normal in patients with primary pterygium, however the tear quality is compromised as meibomian glands which is responsible to produce the lipid layer is not-well functioned.

Several works had postulated that abnormal tear function is a risk factor of development of pterygium [39-41]. It is suggested that changes of conjunctiva, cornea, eyelid and tear film function due to pterygium leads to abnormal tear function [42]. Few studies [43,44] reported that density of conjunctival goblet cell counts which give rise to tear quality and quantity was found lower in pterygium patient. In addition, recent study [42] showed that the density of conjunctival goblet cell count increased subsequent to excision. Based on these evidences, it could be postulated that pterygium does caused changes on the ocular surface. Hence, 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 presence of dry eye symptoms in pterygium patients. Moreover, based on the current findings, as supported by previous literature [27,45], damage on the eyelid region could be more prominent in pterygium patients as lipid components could be more affected than aqueous. This indicates possibility of ocular surface inflammation due to increased roughness surface of the ocular surface or abrasion due to excessive rubbing between the lid margin and the ocular surface.

This study suggests that clinicians should take into consideration on 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 requires specific physical properties of artificial tears [46,47]. Further research are needed to evaluate how different types of pterygium affects the ocular surface, and how dry eye symptoms related to the types of pterygium [48,49].

Conclusion

Alterations of meibomian glands in primary pterygium patients could have 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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