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ORIGINAL PAPER

Dry eye and meibomian gland dysfunction in pseudophakic bullous keratopathy

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Abstract
Purpose To evaluate dry eye tests and meibography of patients with pseudophakic bullous keratopathy (PBK).
Materials and Methods Thirty-seven patients with PBK were included. The eyes with PBK were compared with the normal pseudophakic fellow eyes. All patients had undergone a detailed ophthalmic examination including corneal and conjunctival fluorescein staining and Oxford scoring, tear film breakup time, Schirmer 1 test, Ocular Surface Disease Index (OSDI) score assessment, lid margin abnormalities, upper and lower eyelid Meibomian gland evaluation using infrared captures of a biomicroscope. Partial or complete loss of the Meibomian glands (Meibomian dropout) was scored for each eyelid from grade 0 (no loss) through grade 3 (lost area was $>$ 2/3 of the total meibomian gland area).
Results The mean age of the patients was 73.2 $\pm$ 8.9 (range, 50–93). Mean tear film breakup time value was statistically lower in PBK eyes ($P \leq 0.001$). OSDI, Oxford, lid margin abnormalities, inferior meibography, total meibography score were significantly higher in PBK eyes ($P \leq 0.001$). The comparison of Schirmer 1 and superior meibography scores of the groups was insignificant ($P = 0.143$, $P = 0.793$, respectively).
Conclusion The Meibomian gland morphology of the PBK eyes demonstrates significant differences when compared with normal fellow eyes and might be related to evaporative dry eye. For this reason, patients with PBK should be monitored for Meibomian gland dysfunction and when needed start prompt treatment in order to prevent further disturbance of the ocular surface.

Keywords Bullous keratopathy · Dry eye · Evaporative dry eye · Meibography · Meibomian gland dysfunction · Pseudophakic bullous keratopathy

Introduction

Pseudophakic bullous keratopathy (PBK) is an undesired problem following cataract surgery. It is caused by corneal endothelial decompensation ending up with irreversible stromal edema causing foreign body sensation, lachrymation and ocular pain [1]. Although some treatment methods for PBK have been proposed, keratoplasty still seems to be the best treatment option for many patients [2, 3].

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It was reported that even after uneventful cataract surgery Meibomian gland dysfunction (MGD) causing decreased tear break up time (T-BUT) and ocular discomfort might be detected [4]. Long operation time, operation microscope light, the use of topical medications, reduced corneal sensitivity or conjunctival goblet cell loss are the accused mechanisms of this problem [5, 6]. In PBK additional to these factors an ongoing stress on the ocular surface is also evident. Moreover, chronic preservative containing eye drop use such as artificial tears, hypertonic solutions and corticosteroids in PBK might also trigger MGD.

Meibography is a relatively new technique enabling visualization of the Meibomian glands which are responsible for lipid secretion that plays a significant role to build the ocular surface tension and prevent tear evaporation [7]. MGD causes lipid tear layer abnormalities and results with chronic ocular irritation and ocular surface disorders, finally dry eye [8, 9].

The ocular surface problems of PBK patients are usually underestimated and overlooked. The aim of this study is to evaluate the ocular surface, to reveal dry eye tests and to demonstrate the rate of MGD. To the best of our knowledge, this is the first study to evaluate the ocular surface problems of PBK eyes and to display MGD with meibography.

Materials and methods

In this study, the PBK positive 37 eyes of 37 patients (PBK group) and 37 contralateral healthy pseudophakic eyes (Control group) were evaluated. The duration of PBK was at least 6 months in PBK group. The cataract surgeries of the Control group were performed at least 6 months prior to this study. Patients with any other corneal problems other than PBK (epithelial defect, ulceration, vascularization, scarring, etc.), glaucoma, contact lens use, previous ophthalmic surgery besides phacoemulsification and smoking history were excluded.

Upon a detailed ophthalmological examination for both eyes, tear film breakup time (T-BUT), Schirmer 1 score, Ocular Surface Disease Index (OSDI) score assessments, and corneal and conjunctival fluorescein staining (Oxford scoring) were performed.

Lid margin abnormalities were also scored as 0 (absent) or 1 (present) for vascular engorgement, plugged Meibomian gland orifices, anterior or posterior displacement of the mucocutaneous junction and irregularity of lid margin [8]. The sum was recorded as 0 through 4.

After everting both upper and lower eyelids, Meibomian gland evaluation was made by using infrared captures of a biomicroscope (Topcon, SL-D701, Netherlands). Partial or complete loss of the Meibomian glands was graded for each eyelid as grade 0 (no loss of Meibomian glands), grade 1 (the area characterized by gland dropout was $< 1/3$ of the total Meibomian glands), grade 2 (the area characterized by gland dropout was 1/3–2/3 of the total Meibomian glands) and grade 3 (the area characterized by gland dropout was $> 2/3$ of the total Meibomian glands) [9]. Meiboscore grading was performed blinded by the same researcher (AY). The meiboscores for the upper and lower eyelids, and total (upper + lower) eyelids were summed for each eye.

Written informed consent was obtained from each subject. This study adheres to the tenets of the Declaration of Helsinki. The Statistical Package for the Social Sciences version 11.5.0 was used for statistical analysis.

Results

The mean age of the patients was 73.2 ± 8.9 (range, 50–93). Mean T-BUT of PBK Group and Control Group was 8.81 ± 4.53 (3–20) seconds and 14.48 ± 3.4 (5–20) seconds, respectively ($P < 0.001$) (Table 1). Mean Schirmer 1 scores of PBK and Control Groups were 15.75 ± 6.33 (3–30) mm and 17.79 ± 5.51(5–30) mm, respectively ($P = 0.143$).

Mean Oxford staining scores and mean OSDI scores of the PBK and Control Groups were 1.27 ± 1.04 (0–3) and 0.21 ± 0.41 (0–1), and 57.44 ± 21.53 (10.4–93.7) and 13.48 ± 7.53 (2.1–29.1), respectively ($P < 0.001$ for both comparisons).

Lid margin abnormalities were significantly higher in PBK Group than Control Group ($P < 0.001$). Vascular engorgement was observed in 26 (%70.3) eyes of PBK Group and 5 (%13.5) eyes of Control Group ($P < 0.001$). Plugging in Meibomian gland orifices was observed in 28 (%75.7) eyes of PBK and 7 (%18.9) eyes of Control Groups ($P < 0.001$). The mucocutaneous junction displacement was observed in 29 (%78.4) eyes of PBK Group and 9 (%24.3) eyes of Control Group ($P < 0.001$). Lid margin irregularity

Table 1 The demographics, dry eye tests and meiboscores of PBK and fellow pseudophakic (Control) eyes

	PBK group (mean, SD, range)	Control group (mean, SD, range)	*P* value
Schirmer 1 (mm)	15.75 ± 6.33 (3–30)	17.79 ± 5.51(5–30)	0.143
T-BUT (s)	8.81 ± 4.53 (3–20)	14.48 ± 3.4 (5–20)	< 0.001
Oxford score	1.27 ± 1.04 (0–3)	0.21 ± 0.41 (0–1)	< 0.001
OSDI score	57.44 ± 21.53 (10.4–93.7)	13.48 ± 7.53 (2.1–29.1)	< 0.001
Upper meiboscore	1.05 ± 1.07 (0–3)	0.43 ± 0.64 (0–2)	0.793
Lower meiboscore	1.1 ± 0.8 (0–3)	0.29 ± 0.51(0–2)	< 0.001
Total meiboscore	1.08 ± 0.77 (0–3)	0.36 ± 0.53 (0–2)	< 0.001

SD standard deviation, *T-BUT* tear film breakup time, *OSDI* Ocular Surface Disease Index

was noted in 28 (%75.7) eyes of PBK Group and 9 (%24.3) eyes of Control Group ($P < 0.001$).

Upper and lower meiboscores of PBK and Control Groups were 1.05 ± 1.07 (0–3) and 0.43 ± 0.64 (0–2), and 1.1 ± 0.8 (0–3) and 0.29 ± 0.51(0–2), respectively ($P = 0.793$, $P < 0.001$, respectively). Total meiboscore of PBK and Control Groups was 1.08 ± 0.77 (0–3) and 0.36 ± 0.53 (0–2), respectively ($P < 0.001$).

Discussion

As PBK develops as a result of endothelial decompensation following endothelial injury caused by cataract surgery, pathological changes are most apparent at the level of the corneal endothelium and the neighboring posterior stroma [1]. Besides these posterior changes in endothelial decompensation, it was demonstrated that more anterior parts of the cornea—even the epithelium is effected to some degree [1, 3, 10]. As the cause of corneal endothelial damage in PBK—except Fuchs dystrophy and exfoliation syndrome—is not continuous, pathological changes at the posterior cornea are not expected to be progressive. However, the structural problems at the anterior segment of the cornea caused by epithelial erosion seem to be progressive [1]. Thus, as reported earlier, management of the condition of the corneal epithelium in PBK may be important for the outcome of subsequent endothelial keratoplasty [1].

In PBK, there is a vicious circle of tearing and ocular surface problems, such as epithelial disintegration. It is well known that tear fluid possesses many cytokines and growth factors. Among these, transforming growth factor-β is the most important one as it controls the initiation and resolution of inflammatory responses that can worsen the changes detected at the anterior layers of the PBK cornea and Meibomian glands [11–14] Supporting this, it was earlier shown that amniotic membrane transplantation reduces inflammation and pain in PBK eyes by suppressing transforming growth factor-β0 [15]. Herein, we demonstrated that the PBK eyes have signs of evaporative dry eye, significant lid margin abnormalities as well as significant MGD as detected by meibography. These changes might be due to the ongoing stress on the ocular surface and additional chronic preservative containing eye drop use (artificial tears, hypertonic solutions and corticosteroids)—all causing a cluster of never ending problems. Unfortunately, the more symptomatic the patient is, the more medications are prescribed in these miserable cases. Although not previously investigated, a decrease in corneal sensitivity in PBK cornea might also play a role in dry eye formation. This issue needs to be investigated in future studies.

The more significant changes in the lower eyelid meiboscores might be due to the continuous contact of tear film—loaded with many inflammatory mediators—with the lower Meibomian gland orifices. Moreover, the Meibomian glands are anatomically different in upper and lower eyelids. Upper eyelids move more prominently by blinking than the lower eyelids [16]. This causes the meibum to more easily and continuously be secreted from the upper eyelids. This functional difference may prevent stagnation and hyperkeratinization of the Meibomian glands located in the upper eyelids. Furthermore, the direction of meibum delivery in the lower eyelids has to overcome the gravity [16]. These changes might also be a result of the continuing preservative containing eye drop use,

such as artificial tears, hypertonic solutions and corticosteroids in PBK. One might also accuse the prior cataract surgery; however, it was reported that the effects of cataract surgery vanish in most of the patients after a few months [13]. The minor cases who tend to have symptoms for longer time are assumed to have multiple preoperative risk factors such as preexisting subclinic dry eye [13].

As a result, the lid margin and Meibomian gland morphology in PBK seems to be disrupted when compared with normal fellow eyes. The signs of evaporative dry eye are also more common in these eyes, probably due to these changes in Meibomian gland morphology. However, it is not clear if the PBK causes MGD or it induces dry eye to end up with MGD. Whatever the reason, patients with PBK should be monitored for MGD, dry eye and when needed start prompt treatment in order to prevent further disturbance of the ocular surface.

Compliance with ethical standards

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 Declaration of Helsinki and its later amendments or comparable ethical standards.

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

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