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Original Article

Corneal and conjunctival sensitivity in rosacea patients

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Abstract

Purpose: To assess corneal and conjunctival sensitivity in rosacea patients.
Methods: A total of 55 patients with rosacea and 37 control subjects participated in the study. Corneal and conjunctival sensitivity was determined by Cochet-Bonnet esthesiometer. Subjective symptoms of ocular dryness were evaluated using Ocular Surface Disease Index (OSDI). Schirmer's I test (ST), tear breakup time (tBUT) and ocular surface staining with fluorescein were carried out to measure objective signs.
Results: The mean corneal and conjunctival sensitivity did not differ significantly between rosacea patients and controls (all $p > 0.05$). Schirmer's I test and tBUT were significantly reduced ($p = 0.004$ for OD and $p < 0.001$ for OS) and grade of ocular surface staining was significantly high ($p = 0.018$ for OD and $p = 0.038$ for OS) in rosacea patients. Corneal and conjunctival sensitivity did not show significant correlation with ST, tBUT, ocular surface staining (Oxford Schema), duration of rosacea and OSDI score.
Conclusions: Corneal and conjunctival sensitivity did not change significantly in rosacea.

Keywords: Corneal sensitivity, Conjunctival sensitivity, Rosacea

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Introduction

Rosacea is a common chronic disease with unknown pathogenesis. It is characterized by inflammation and vascular abnormalities of the central facial skin.[1] Previous studies demonstrated upregulation of genes involved in vasoregulation and neurogenic inflammation and suggested that dysregulation of mediators and receptors implicated in neurovascular and neuroimmune communication may be important at early stages of the disease.[2–4]

Although considered as a skin disease, rosacea may affect eye in up to 58–72% of the patients. Superficial punctate keratitis, peripheral neovascularization associated with subepithelial marginal infiltrates, stromal ulceration, corneal perforation, recurrent corneal epithelial erosions, pseudodendritic ulcer, pseudokeratoconus, and infectious keratitis have been previously reported. Conjunctival manifestations are chronic conjunctivitis, chronic papillary reaction, cicatricial conjunctivitis, pinguecula, conjunctival fibrosis and symblepharon. Blepharitis and meibomian gland dysfunction are also common findings. Dry eye with abnormal Schirmer's I test (ST) and shorter tear breakup time (tBUT) has also been reported in a majority of patients with ocular rosacea.[5–9]

Up to now, no studies have been conducted to see the effects of rosacea on corneal and conjunctival sensitivity. In this study, in order to contribute in the clarification of the involvement of tear function in rosacea, we evaluated both the incidence of subjective symptoms and objective signs of dry eye and measured corneal and conjunctival sensitivity

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in rosacea patients. We also assessed the relationship among the symptoms and signs of dry eye and corneal and conjunctival sensitivity in these patients.

Materials and methods

Fifty-five patients (43 women and 12 men) diagnosed as rosacea at the Department of Dermatology by an expert dermatologist between August 2012 and November 2013 were enrolled into this prospective study. Thirty-seven healthy subjects (30 women and 7 men) from the Ophthalmology Department outpatient clinic served as control group. Written informed consent was obtained from all the participants. The study was approved by the Institutional Review Board and was conducted in accordance with the Declaration of Helsinki.

Subjects with previous ocular surgery and trauma, manifest anterior segment infection, history of refractive surgery and contact lens wear, diabetes mellitus, hepatitis and those using systemic and topical therapeutic agents that may affect ocular surface sensitivity were excluded from the study.

Each participant underwent a complete ophthalmological examination including best-corrected visual acuity, measurement of intraocular pressure and slit lamp examination. Schirmer's test was done with test strips. The strip was positioned behind the lower lid between the temporal and middle thirds, and the patient kept his/her eyes closed for 5 min, after that the strips were removed and the length of the moistened area was measured.

One drop of 1.25 mg/ml of sodium fluorescein was instilled in the lower conjunctival sac, and corneal, nasal conjunctival and temporal conjunctival staining was graded from 0 to 5 according to the Oxford Schema.[10] The mean of these three quadrants was used for statistical analysis. The tear breakup time was the average duration between the last complete blink and the first appearance of randomly distributed dry spot under cobalt blue filtered light.[11] Dry eye was diagnosed if a symptomatic patient had abnormal tBUT ($\leqslant$5 s) and ST ($\leqslant$10 mm in 5 min).

All subjects filled out the OSDI report which assessed the symptoms of ocular irritation consistent with dry eye disease and their impact on vision-related functioning. OSDI questionnaire with 12 items was graded on a scale from 0 to 4, where 0 indicated none of the time; 1, some of the time; 2, half of the time; 3, most of the time; and 4, all of the time. The total OSDI score was then calculated with the following formula: OSDI = (sum of scores for all questions answered) $\times$ 100/(total number of questions answered) $\times$ 4. OSDI is assessed on a scale of 0–100, with higher scores representing greater disability.[12]

Corneal and conjunctival sensitivity was measured using the Cochet-Bonnet esthesiometer which mechanically stimulates the ocular surface with a nylon filament of diameter 0.08 mm. All measurements were done by a single observer between 9 AM and 4 PM. The tactile sensitivity was assessed close to the center of the cornea and at temporal and nasal bulbar conjunctiva, 3–4 mm away from the limbus along the horizontal meridian as judged by simple inspection. The patients were asked to redirect their gaze prior to the stimulus cycle. The test was started at the maximal length of 60 mm. If no response was obtained at 60 mm, the length was reduced by 5 mm until a positive response was obtained. Assessment of the tactile threshold was made by defining the length of the filament which was detectable by the subject in two of three randomly repeated trials.

Statistical analysis was done by SPSS statistical software (SPSS for windows 10.0, Inc., Chicago, USA). All data were expressed as mean ± standard deviation (±SD). One way analysis of variance (ANOVA) and Student's *t*-test were used for the analysis. Statistical significance was defined at a level of 5% ($p < 0.05$) and correlation was significant at the 0.01 level (2-tailed).

Results

Fifty-five rosacea patients (43 women, 12 men; mean age: 47.2 ± 11.9 years; range, 14–74) and 37 controls (30 women, 7 men; mean age: 48.7 ± 12.6 years; range, 14–74) involved in this study. There was no statistically significant difference between the groups in terms of age and sex ($p = 0.5$, $p = 0.4$, respectively). Mean duration of the disease was 7.6 ± 6.1 (maximum 30; minimum 0.5) years.

Dry eye was diagnosed in 50.9% ($n = 28$) of rosacea patients according to ST and tBUT results. Grade of ocular surface staining was significantly higher in rosacea patients than controls according to Oxford Schema ($p = 0.018$ for OD and $p = 0.038$ for OS). And ST and tBUT tests' results were significantly shorter in rosacea patients than controls ($p = 0.004$ for OD and $p < 0.001$ for OS versus $p < 0.001$ for OU). OSDI scores were higher in rosacea patients than in controls but this was not statistically significant (20.18 ± 15.4 vs 16.4 ± 11.9, $p = 0.2$) (Table 1).

Although mean central corneal sensitivity decreased and conjunctival (temporal and nasal) sensitivity increased in rosacea patients, the change was not statistically significant in both eyes, except for nasal conjunctival sensitivity of right eye (Table 2).

Table 1. Characteristics of rosacea patients and controls.

		Rosacea group ($n = 55$)	Control group ($n = 37$)	p value*
Age (years)		47.2 ± 11.9	48.7 ± 12.6	0.5
OSDI (0–100)		20.18 ± 15.4	16.4 ± 11.9	0.2
Ocular surface staining	OD	1.67 ± 1.9	0.86 ± 1.0	0.018
	OS	1.51 ± 1.7	0.86 ± 0.9	0.038
Schirmer's I test (mm)	OD	12.56 ± 4.4	15.57 ± 5.5	0.004
	OS	12.18 ± 5.1	17.05 ± 5.5	<0.001
tBUT (seconds)	OD	7.16 ± 2.7	10.19 ± 2.9	<0.001
	OS	8.15 ± 3.1	10.59 ± 3.0	<0.001

* p=<0.05.

Table 2. Corneal and conjunctival sensitivity of rosacea patients and controls.

		Rosacea group ($n = 55$)	Control group ($n = 37$)	p value*
Corneal sensitivity (mm)	OD	56.9 ± 7.7	58.7 ± 2.8	0.1
	OS	57.2 ± 6.1	58.8 ± 2.7	0.1
Temporal conjunctival sensitivity (mm)	OD	12.7 ± 6.3	11.2 ± 4.9	0.2
	OS	12.6 ± 6.4	11.1 ± 4.9	0.2
Nasal conjunctival sensitivity (mm)	OD	11.6 ± 6.3	9.2 ± 4.0	0.039
	OS	12.0 ± 6.6	10.5 ± 4.7	0.2

* p=<0.05.

Table 3. Correlation of corneal and conjunctival sensitivity of the right eye with objective tests and subjective symptoms of dry eye and duration of rosacea.

	Corneal sensitivity (mm)	Temporal conjunctival sensitivity (mm)	Nasal conjunctival sensitivity (mm)
Schirmer's I test (mm)	−0.043 ($p = 0.7$)	0.094 ($p = 0.4$)	0.107 ($p = 0.4$)
tBUT (s)	−0.156 ($p = 2$)	0.012 ($p = 9$)	−0.027 ($p = 0.8$)
Ocular surface staining	0.077 ($p = 0.5$)	−0.112 ($p = 0.4$)	−0.197 ($p = 0.1$)
OSDI	0.081 ($p = 0.5$)	0.32 ($p = 0.01$)	0.231 ($p = 0.1$)
Rosacea duration (years)	0.052 ($p = 0.7$)	−0.073 ($p = 0.5$)	−0.139 ($p = 0.3$)

* p=<0.05.

No significant correlation was detected between corneal and conjunctival sensitivity of the right eye and ST, tBUT, ocular surface staining (Oxford Schema), rosacea duration and OSDI score, except for temporal conjunctival sensitivity and OSDI score (Table 3).

Discussion

Rosacea is a chronic inflammatory skin disease. The prevalence of ocular involvement in rosacea is probably higher than assumed but it varies considerably between ophthalmological and dermatological studies.[5,6] The incidence of dry eye in rosacea is higher than the normal population (39–62% versus 15–34%).[8,9,13,14] Most of the ocular symptoms and signs in rosacea are related to dry eye which is closely associated with inflammation and dysfunction of the meibomian glands. The dysfunction could be secondary to increased production of free fatty acids due to bacterial lipases or facial and angular venous dilation.[15–17] These changes cause abnormal lipid composition of the tear film leading to shorter tBUT and dry eye. Normal corneal sensitivity is necessary for maintenance of basic tear secretion.[18,19] The etiology of dry eye may change, but an underlying cytokine-/receptor-mediated inflammatory process is common to all ocular surface diseases.[20] Dry eye is frequently associated with inflammatory changes both in the lacrimal glands and on the ocular surface.[21] Treating this could normalize the ocular surface/lacrimal neural reflex. Anti-inflammatory drugs have been beneficial in the treatment of dry eye.[22] Schechter et al. have shown that Cyclosporine-A is more effective than artificial tears for the treatment of rosacea-associated eyelid and corneal changes.[23]

In our study, despite high incidence (50.9%) of dry eye, corneal and conjunctival sensitivity did not reveal any significant difference in rosacea patients. As known mechanical sensitivity of cornea and conjunctiva to tactile stimulus is reduced in dry eye.[24] Alterations in corneal nerve morphology and increased number of antigen-presenting cells, implicating the role of inflammation, may be responsible for the reduction.[25] On the other hand, we know that rosacea patients are susceptible to certain stimuli.[26] The modification of cutaneous sensitivity indicates the relevance of the sensory and/or autonomic nervous system in the pathogenesis of the disease.[4] Schwab et al. have shown increased number of myelinated nerves which are ultimately involved in pain transmission in rosacea.[3] Therefore, basal ocular surface sensitivity may be increased in rosacea patients, but coexisting dry eye reduces ocular surface sensitivity and brings it to normal levels.

While grade of ocular surface staining was significantly higher, subjective symptoms measured by OSDI were only slightly higher in rosacea patients. Patients with dry eye often present with ocular surface epithelial disease and complain of irritation symptoms, but weak correlation in our study suggests that factors other than ocular surface staining may play a role in OSDI scores.[27] Pult et al. also reported weak correlation between dry eye symptoms and objective tests and corneal staining.[28] Ünlü et al. showed absence of correlation between OSDI and ST scores and blamed reflex tearing that developed during ST.[29] Our results are in accordance with their findings. Thus, we may conclude that subjective symptoms may not correlate with the objective test results of dry eye in rosacea.

We did not find any significant correlation between corneal/conjunctival sensitivity and ST, tBUT, ocular surface staining, rosacea duration and OSDI score (except for temporal conjunctival sensitivity and OSDI score). Change in ocular surface sensitivity may be caused by rosacea itself. Although the pathophysiology of the disease is still poorly understood, dysfunction of neurovascular regulation and the innate immune system seems to be the driving forces.[30] Normal ocular sensitivity and a high rate of dry eye in our patients may be the consequences of neural dysfunction in rosacea.

Corneal and conjunctival sensitivity values may have clinical implications for rosacea patients who may require anterior segment surgery such as LASIK, keratoplasty, and cataract surgery. Visual function is an important role of tear film. Abnormalities in tear function tests may negatively impact visual quality leading to blurred vision and may also predispose to corneal erosions or other associated complications in rosacea patients.

There are some limitations to this study. First, we did not evaluate subtypes of rosacea. Second, we did not measure the amount of proinflammatory cytokine secretion which could help to understand the effect of inflammation on corneal sensitivity and fluorescein staining, as correlation between corneal fluorescein staining and focal inflammation has been demonstrated in Sjögren syndrome.[31,32] Finally, Cochet-Bonnet esthesiometer measures only mechanical sensitivity and has limitations in reproducibility and sensitivity. Changes in the tear film might have affected the intensity of the mechanical stimulus.

To conclude, the dry eye experienced in rosacea was found to be not associated with changes in the sensitivity of ocular surface that was measured with Cochet-Bonnet esthesiometer. The findings of current study constitute only preliminary data on ocular surface sensitivity and rosacea and further studies would be necessary to better understand the relationship.

Conflicts of Interest

The authors declared that there is no conflict of interest.

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