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ORIGINAL ARTICLE

Corneal sensitivity in patients with lamellar ichthyosis

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Abstract

Purpose: The purpose of the study was to evaluate the ocular surface and corneal sensitivity in patients with lamellar ichthyosis (LI).

Methods: Eleven eyes of 11 patients with LI (Group 1) and 11 eyes of 11 healthy individuals (Group 2) were enrolled into this cross-sectional study. Detailed ophthalmological examination along with ocular surface fluorescein staining with Oxford scoring, tear film break-up time, Schirmer 1 test, ocular surface disease index (OSDI) score assessment, and evaluation of corneal sensitivity with Cochet-Bonnet esthesiometer was performed.

Results: The mean ages of Group 1 and Group 2 were 24.54±10.22 years (range, 11–37) and 26±7.53 years (range, 16–40), respectively (p=0.764). Male/female ratio was 5/6 in Group 1 and 4/7 in Group 2. Mean tear film break-up time and the corneal sensitivity of the superior and inferior region of cornea were lower (p=0.00008; p=0.019; and p=0.006, respectively), and OSDI and Oxford scores were significantly higher in Group 1 (p<0.00001 and p=0.002, respectively). No significant difference in terms of Schirmer 1 test and corneal sensitivity of central, temporal, and nasal regions was detected (p>0.5).

Conclusion: LI is not only associated with evaporative type dry eye but also decreased corneal sensitivity of peripheric cornea. Therefore, to prevent uninvited complications, LI patients should be examined for dry eye regularly, even if they do not have any complaints.

Keywords: Cochet-Bonnet esthesiometer; corneal sensation; dry eye; lamellar ichthyosis; ocular surface.

The ichthyoses are a heterogeneous and large group of genetically transmitted skin disorders characterized by abnormal keratinization or cornification of the skin that causes dry, thickened, scaly, or resembling fish skin.[1,2] Lamellar ichthyosis (LI), a rare and autosomal recessive form of ichthyoses, presents at birth including a collodion membrane and continues throughout the lifetime.[3,4] LI is characterized by generalized scales, which range from thin and white to thick dark and plate-like, and involve the whole skin.[1] Cicatricial ectropion is the most common eyelid abnormality, which may lead to corneal exposure, ulceration, and even corneal perforation.[5–9] Dry eye is also

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one of the most important ophthalmological problems in these patients.[10,11]

Ocular surface sensitivity has been used to demonstrate sensory function in systemic and corneal diseases such as diabetes, dry eye, and neurotropic keratitis.[12–15] Cochet-Bonnet (CB) esthesiometer is a relatively objective device, which enables measuring mechanical ocular surface sensory function.[16,17]

The purpose of the present study is to evaluate the corneal sensitivity with CB esthesiometer in patients with LI.

Materials and Methods

Eleven eyes of 11 patients with LI (Group 1) and 11 eyes of 11 healthy individuals (Group 2) were evaluated in this cross-sectional study. The drier eyes of LI patients were included in the study. All LI patients were diagnosed based on clinical and histopathological findings. All patients provided written informed consent to participate in the study. The study protocol complied with the Declaration of Helsinki and was approved by the Ege University, Faculty of Medicine Ethics Committee.

In addition to detailed ophthalmologic examination, Schirmer 1 test, tear film break-up time (T-BUT) measurements, ocular surface staining with fluorescein 2% (graded according to Oxford scale), and ocular surface disease index (OSDI) score assessment were performed. Patients with any other ocular diseases, contact lens use, ophthalmic surgery history, or other systemic diseases were excluded from the study.

CB esthesiometer was used to assess the corneal sensitivity. This instrument consists of a nylon monofilament of 0.12 mm diameter which can give pressure based on its length. The length of the monofilament ranges from 60 mm to 5 mm. As the length of the filament is reduced, the pressure transmitted to the cornea is increased. Therefore, decreasing the length of monofilament indicates decreased corneal sensitivity. A table on the CB esthesiometer reveals the length of the monofilament and its equivalent pressure. After clearly explaining the procedure, the subjects were instructed to look straight in a semi-reclined position. The tip of the filament was applied perpendicularly to the patient's cornea with enough force to make a slight deflection. The central, superior, nasal, inferior, and temporal regions of the cornea were measured, respectively. The peripheral parts of the cornea were measured 2 mm away from the limbus. The measurement was started with the fully extended filament and decreased by 5 mm each time until the participant felt the stimulus. The principle for a positive response was the participants' subjective report of the sensation. Therefore, each measurement was repeated at each region of the cornea to confirm the corneal touch threshold. All measurements with CB esthesiometer were performed by the same ophthalmologist (R.Y.K.) at normal ranges of room temperature (21–24°C) and ambient humidity (40–60%) between 13:30 and 16:00 pm to avoid diurnal variation. The nylon filament was cleaned with 70% of ethanol before each measurement.

The Statistical Package for the Social Sciences version 15.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Numerical variables are given as mean and standard deviation and median (min-max). Comparisons between continuous variables were performed by Mann–Whitney U-test. To examine relationship between numeric variables, Spearman correlation analysis was performed. $P<0.05$ was considered statistically significant.

Results

The mean age was 24.54±10.22 years (range, 11–37) in Group 1 and 26±7.53 years (range, 16–40) in Group 2 (p=0.764; [Table 1]). Male/female ratio was 5/6 in Group 1 and 4/7 in Group 2. No significant difference was noted between groups in terms of best-corrected visual acuity (p=0.49). None of the patients had corneal exposure due to eyelid malposition. Mean Schirmer 1 test scores of Group 1 and Group 2 were 21.18±8.34 (10–35) mm and 25.09±6.35 (9–30) mm, respectively (p=0.2). Mean T-BUT of Group 1

Table 1. The demographics, dry eye tests of the groups

	Group 1 (LI group)	Group 2 (control group)	p-value
	(Mean±SD, range)	(Mean±SD, range)	
Age (years)	24.54±10.22 (11–37)	26±7.53 (16–40)	0.764
Best-corrected visual acuity (LogMAR)	0.02±0.04 (0–0.09)	0	0.49
Schirmer 1 (mm)	21.72±7.42 (10–35)	25.86±6.33 (10–35)	0.087
Tear film break-up time (s)	3.45±2.18 (1–8)	11.05±2.44 (6–15)	<0.00001
Oxford scale	0.73±0.77 (0–2)	0	0.002
Ocular surface disease index score	26.3±19.88 (4.16–66.7)	4.18±6.89 (2.1–6.25)	<0.00001

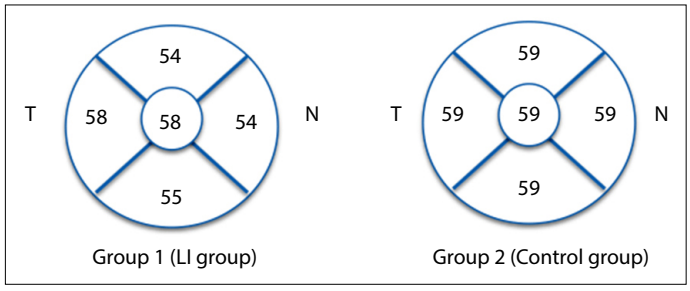

Fig. 1. Average corneal sensitivity values (mm) of Groups 1 and 2 (T: Temporal and N: Nasal).

and Group 2 was 3.36±2.16 (1–6) s and 11.27±2.49 (7–15) s, respectively. Mean T-BUT was significantly lower in Group 1 (p=0.00008). The mean superficial punctate staining according to the Oxford scale in Group 1 and 2 was 0.73±0.79 (0–2) and 0.0±0.0 (0), respectively (p=0.03). Mean OSDI scores of Group 1 and 2 were 26.3±19.88 (4.16–66.7) and 4.18±6.89 (2.1–6.25), respectively. The Oxford scale and OSDI scores were significantly higher in Group 1 (p=0.002 and p<0.00001, respectively). All LI patients who were diagnosed with dry eye syndrome were prescribed such as preservative-free artificial tear drops to protect the ocular surface as the severity of the disease.

The average corneal sensitivity values measured from five corneal regions through CB esthesiometer are shown in Figure 1. The corneal sensitivities of the superior and inferior region of the cornea were lower in Group 1 (p=0.04 and p=0.008, respectively). However, no significant difference in the corneal sensitivities of the central, temporal, and nasal regions of the cornea was noted between two groups (p=0.53, p=0.69, and p=0.57, respectively) (Table 2).

Discussion

LI affects the entire body and is seen approximately in 1 in 300,000 live births.[3] The most common ocular problem among LI patients is eyelid abnormality due to cicatricial ectropion.[6,8,11] In addition, recent studies showed the importance of evaporative dry eye in LI patients.[10,11] Palamar et al.[10] reported normal Schirmer 1 and Oxford staining scores, decreased T-BUT values, and increased OSDI scores. They also demonstrated Meibomian gland loss in both eyelids with meibography. Similarly, in the present study, despite normal Schirmer 1 test scores, T-BUT values were significantly decreased, and OSDI scores were significantly increased. Furthermore, Oxford staining scores were noted higher in LI patients. The effect of the dry eye should also be considered in the formation of keratopathy, which may lead corneal perforation in these patients.

Table 2. Mean corneal sensitivity (mm) of the five corneal regions, which were measured by the Cochet-Bonnet esthesiometer

	Group 1	Group 2	p-value
	(Mean±SD, range)	(Mean±SD, range)	
Central	58.5±3.37 (50–60)	59.09±3.02 (50–60)	0.535
Superior	54.09±5.39 (45–60)	59.09±3.02 (50–60)	0.004
Nasal	54.55±6.5 (40–60)	59.09±2.02 (55–60)	0.574
Inferior	55±3.16 (40–60)	59.09±2.02 (55–60)	0.008
Temporal	58.18±3.37 (50–60)	59.09±2.02 (55–60)	0.696

Corneal sensitivity is essential for a healthy ocular surface.[13] The previous studies showed that corneal sensitivity varies across the corneal surface and the center of the cornea is the most sensitive part.[18,19] Lack of corneal sensation may stop the afferent limb of the corneal blink reflex and can cause basal epithelial morphology change, or neurotropic epithelial defect formation.[20] In the present study, it is demonstrated that there is a significant decrease in the superior and inferior region of the corneal sensitivity in LI patients. To the best of our knowledge, the present study is the first report that evaluates corneal sensitivity in LI patients. In LI patients, decreased corneal sensitivity may be a cause or a result. The most important limitations of the present study are the small sample size and the absence of confocal microscopy findings. To make any absolute conclusion on the issue, it is a must to investigate the epithelium, stroma, and sub-basal corneal nerves with confocal microscope and to evaluate the correlation of these findings with corneal sensitivity.

Conclusion

In LI patients, decreased corneal sensitivity, dry eye disease, and eyelid abnormalities can cause ocular surface problems that can result in corneal perforation. Accordingly, to prevent destructive ocular surface problems, LI patients should be examined for dry eye disease regularly, even if they do not have any complaints.

Ethics Committee Approval: This study was approved by Ege University Faculty of Medicine Ethics Committee (date: 29.05.2019; number: 19-5.2T/46).

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References

1. Oji V, Traupe H. Ichthyosis: Clinical manifestations and practical treatment options. Am J Clin Dermatol 2009;10:351–64.
2. Oji V, Traupe H. Ichthyoses: Differential diagnosis and molecular genetics. Eur J Dermatol 2006;16:349–59.
3. Victor F, Schaffer JV. Lamellar ichthyosis. Dermatol Online J 2005;11:13. [CrossRef]
4. Fischer J. Autosomal recessive congenital ichthyosis. J Invest Dermatol. 2009;120:1319–21. [CrossRef]
5. Jay B, Blach RK, Wells RS. Ocular manifestations of ichthyosis. Br J Ophthalmol 1968;52:217–26. [CrossRef]
6. Cruz AA, Menezes FA, Chaves R, Coelho RP, Velasco EF, Kikuta H. Eyelid abnormalities in lamellar ichthyoses. Ophthalmology 2000;107:1895–8. [CrossRef]
7. Turgut B, Aydemir O, Kaya M, Türkçüoğlu P, Demir T, Çeliker Ü. Spontaneous corneal perforation in a patient with lamellar ichthyosis and dry eye. Clin Ophthalmol 2009;3:611–3. [CrossRef]
8. Singh AJ, Atkinson PL. Ocular manifestations of congenital lamellar ichthyosis. Eur J Ophthalmol 2005;15:118–32. [CrossRef]
9. Cinar Y, Selcuk CT, Cingu AK, Turkcu FM, Yuksel H, Yildirim A, et al. Spontaneous bilateral corneal perforation in a patient with ichthyosis. Int Ophthalmol 2014;34:919–21. [CrossRef]
10. Palamar M, Karaca I, Onay H, Ertam I, Yagci A. Dry eye and Meibomian gland dysfunction with meibography in patients with lamellar ichthyosis. Contact Lens Anterior Eye 2018;41:154–6.
11. Palamar M, Onay H, Ertam I, Ates EA, Dereli T, Ozkinay F, et al. Genotype and anterior segment phenotype in a cohort of Turkish patients with lamellar ichthyosis. Ophthalmic Genet 2015;36:229–33. [CrossRef]
12. Brennan N, Bruce A. Esthesiometry as an indicator of corneal health. Optom Vis Sci 1991;68:699–702. [CrossRef]
13. Sitompul R. Corneal sensitivity as a potential marker of diabetic neuropathy. Acta Med Indones 2017;49:166–72.
14. Cousen P, Cackett P, Bennett H, Swa K, Dhillon B. Tear production and corneal sensitivity in diabetes. J Diabetes Complicat 2007;21:371–3. [CrossRef]
15. Hsu HY, Modi D. Etiologies, quantitative hypoesthesia, and clinical outcomes of neurotrophic keratopathy. Eye Contact Lens 2015;41:314–7. [CrossRef]
16. Golebiowski B, Papas E, Stapleton F. Assessing the sensory function of the ocular surface: Implications of use of a non-contact air jet aesthesiometer versus the Cochet-Bonnet aesthesiometer. Exp Eye Res 2011;92:408–13. [CrossRef]
17. Chao C, Stapleton F, Badarudin E, Golebiowski B. Ocular surface sensitivity repeatability with Cochet-Bonnet esthesiometer. Optom Vis Sci 2015;92:183–9. [CrossRef]
18. Mirzajan A, Khezri F, Jafarzadehpur E, Karimian F, Khabazkhoob M. Normal corneal sensitivity and its changes with age in Tehran, Iran. Clin Exp Optom 2015;98:54–7. [CrossRef]
19. Roszkowska AM, Colosi P, Ferreri FM, Galasso S. Age-related modifications of corneal sensitivity. Ophthalmologica 2004;218:350–5. [CrossRef]
20. Kumar RL, Koenig SB, Covert DJ. Corneal sensation after descemet stripping and automated endothelial keratoplasty. Cornea 2010;29:13–8.