

Pathogenesis of Dry Eye in Leprosy and Tear Functions¹Sheena Koshy, Ebenezer Daniel, Nisha Kurian, and Paramanandam Yovan²

Dry eye is characterized by the ocular surface disease that results from any condition or circumstance that decreases tear secretion or increases tear film evaporation. Early literature (⁴) cited leprosy as one such disease, but the possible risk factors and mechanisms have not been fully explored.

A few studies (^{6, 9, 10}) done on dry eyes in leprosy did not have controls for demographic or other factors. Studies conducted by Hodges, *et al.* (⁶) indicate that a patient with leprosy is at risk for developing keratoconjunctivitis sicca, and they suggest that the aqueous layer of the tear film may be decreased due to reduced secretion of tears from the accessory lacrimal glands of the conjunctiva. The decrease could also be due to a diseased afferent arc to the lacrimal gland or to a diseased lacrimal gland. Previous studies (¹⁰) have shown that low tear production is the main cause of dry eye in leprosy and just lubrication prevents dryness in the majority of them. In this paper, the findings from a prospective study of pathogenesis of dry eye in leprosy using

tear function tests carried out at this institution are presented.

MATERIALS AND METHODS

Both eyes of 75 leprosy patients who attended the Ophthalmology department of the Schieffelin Leprosy Research and Training Center (SLR&TC) hospital in Karigiri, India, during November 1998 to October 1999 were studied and compared with 75 age- and sex-matched controls, who were selected from patients without leprosy who attended the eye outpatient department. Eyes were carefully examined in the following order: 1) ocular history; 2) visual acuity; 3) external examination; 4) Schirmer's test 1 (without anesthesia); 5) corneal sensation (using cotton wisp); 6) slit-lamp examination; 7) break up time; 8) tonometry; 9) lacrimal drainage system irrigation. A Schirmer test was done using standardized Schirmer's tear strips measuring 5 mm × 35 mm. A notch is present 5 mm from one end, the strip is bent at the notch and the 5 mm section of the strip is inserted at the lower fornix between the medial two-thirds and the lateral one-third of the eye lid of each eye. The 30-mm segment is left to hang over the lower lid. In 5 min the strip is removed and the wetted length from the notch is measured.

A value of <5 mm is suggestive of true dry eye, 5–15 mm is borderline and >15 mm is regarded as normal tear production. Corneal sensation was measured qualita-

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TABLE 1. Schirmer's values by type of leprosy and controls.

| Schirmer value (mm) | MB leprosy cases | | Controls | | PB leprosy cases | | Controls | |
|---------------------|------------------|-------|----------|-------|------------------|-------|----------|-------|
| | No. | % | No. | % | No. | % | No. | % |
| <5 | 3 | 3.9 | 7 | 9.2 | 3 | 4.1 | 3 | 4.1 |
| 5–15 | 18 | 23.7 | 6 | 7.9 | 13 | 18.9 | 14 | 18.9 |
| >15 | 55 | 72.4 | 63 | 82.9 | 58 | 77 | 57 | 77 |
| Total | 76 | 100.0 | 76 | 100.0 | 74 | 100.0 | 74 | 100.0 |
| Significance | NS | | | | NS | | | |

TABLE 2. Tear break up time (BUT) by type of leprosy and controls.

| Tear BUT (secs.) | MB leprosy cases | | Controls | | PB leprosy cases | | Controls | |
|------------------|------------------|-------|----------|-------|------------------|-------|----------|-------|
| | No. | % | No. | % | No. | % | No. | % |
| <10 | 24 | 31.6 | 9 | 11.8 | 21 | 28.4 | 16 | 21.6 |
| ≥10 | 52 | 68.4 | 67 | 88.2 | 53 | 71.6 | 58 | 78.4 |
| Total | 76 | 100.0 | 76 | 100.0 | 74 | 100.0 | 74 | 100.0 |
| Significance | p < 0.01 | | | | NS | | | |

tively with a sterile cotton wisp. Cotton wool is twisted into a "rat tail" or filament and touches the cornea 2 mm from the limbus at the 6 o'clock position after asking the patient to look up. The response to the touch was observed.

Tear break up time (BUT) is only a measure of the relative instability of the tear film. The tear BUT depends on the fact that given enough time, the tear film will thin and eventually rupture even in normal eyes. A sterile fluorescein strip is applied into the lower fornix. The patient is asked to blink two or three times to distribute the dye. The test is performed at the slit lamp by asking the patient to stare straight ahead and not to blink. Without touching the patient's eye lids the examiner scans the cornea with the cobalt blue light of the slit lamp, watching for an area of dark spot. The tear BUT is the time in seconds between the last blink and the appearance of the dry spot. A normal tear BUT is considered to be 10 secs or more. The test was repeated at least three times and only if it was consistently <10 secs was it taken as a reduced tear BUT.

RESULTS

Of the 75 patients, 41 were males and 34 females. There were 37 paucibacillary (PB) and 38 multibacillary (MB) cases. The

Schirmer's test results among cases and controls are shown in Table 1; 24.7% of the leprosy patients and 20% of the controls showed a Schirmer's value of <15 mm; a difference which was not statistically significant. There was also no significant difference in leprosy between MB and PB patients. The values of the tear BUT of patients and controls are given in Table 2. The differences were statistically significant between leprosy and nonleprosy as well as between MB and PB ($p < 0.01$)—30% of the leprosy patients showed a lower tear BUT of <10 secs; whereas only 16.7% of the controls showed a lower tear BUT. In MB patients, 31.6% showed a lower value of tear BUT of <10 secs; whereas only 11.8% of the controls showed a lower value of <10 secs. Patients with lagophthalmos and decreased corneal sensation also showed a lower tear BUT (Tables 3 and 4) which was statistically significant ($p < 0.01$).

The values of tear BUT in relation to lagophthalmos are given in Table 3. Among the eight patients with lagophthalmos, six (75%) had a tear BUT of <10 secs. Seventy percent of the patients with decreased corneal sensation showed a lower tear BUT, as shown in Table 4. Table 5 shows that the quantity of tears produced in cases with lagophthalmos and decreased corneal sen-

TABLE 3. Tear break up time (BUT) in relation to lagophthalmos.

| Tear BUT (secs) | Lagophthalmos | | | |
|-----------------|---------------|-------|--------|-------|
| | Present | | Absent | |
| | No. | % | No. | % |
| <10 | 6 | 75.0 | 39 | 27.5 |
| ≥10 | 2 | 25.0 | 103 | 72.5 |
| Total | 8 | 100.0 | 142 | 100.0 |
| Significance | p < 0.01 | | | |

TABLE 4. Tear break up time (BUT) in relation to corneal sensation.

| Tear BUT (secs) | Corneal sensation | | | |
|-----------------|-------------------|-------|--------|-------|
| | Decreased | | Normal | |
| | No. | % | No. | % |
| <10 | 7 | 70 | 38 | 27.1 |
| ≥10 | 3 | 30 | 102 | 72.9 |
| Total | 10 | 100.0 | 140 | 100.0 |
| Significance | p < 0.01 | | | |

TABLE 5. Schirmer's test results in relation to lagophthalmos and corneal sensation.

| Schirmer value (mm) | Lagophthalmos | | | | Corneal sensation | | | |
|---------------------|---------------|-------|--------|-------|-------------------|-------|--------|-------|
| | Present | | Absent | | Decreased | | Normal | |
| | No. | % | No. | % | No. | % | No. | % |
| <5 | 0 | 0 | 6 | 4.2 | 0 | 0 | 6 | 4.3 |
| 5-15 | 0 | 0 | 31 | 21.8 | 0 | 0 | 31 | 22.1 |
| >15 | 8 | 100.0 | 105 | 74.0 | 10 | 100.0 | 103 | 73.6 |
| Total | 8 | 100.0 | 142 | 100.0 | 10 | 100.0 | 140 | 100.0 |

sation is not decreased significantly as shown by the Schirmer test values.

DISCUSSION

The primary function of the corneal epithelium is with the tear film to provide a very smooth refracting surface at the front of the eye. Interference with this surface by drying can have severe visual consequences. Blinking is critically essential in spreading freshly secreted lacrimal gland fluid.

The tear film is a three-layered structure with an outer lipid layer that overspreads a larger aqueous layer. The third inner layer is composed of mucins that are adsorbed onto the corneal and conjunctival epithelial surface. Mucins play an important role in maintaining the wettability of the ocular surface and in stabilizing the tear film.

After a blink, the upper lid wipes the cornea and resurfaces it with a fresh, clean layer of mucus. But after a blink the lipid layer diffuses throughout the aqueous layer, eventually reaching the mucus. This lipid contamination may increase until the mucus becomes hydrophobic the tear film ruptures and a dry spot forms on the surface of the cornea. Enough mucus must be present to mask the lipid and maintain the tear film stability until the next blink occurs. When there is lagophthalmos, the eye lids do not spread tears evenly over the surface of the eye. Also there is increased evaporation of tears which leads to a drying up of the cornea (5). Hence, there is lower tear BUT in patients with lagophthalmos.

Although the main lacrimal gland secretes the major portion of the tear fluid volume, the contributions of the goblet cells in the conjunctiva and the meibomian glands in the lids are no less important in maintaining a functional tear layer. The findings of a normal Schirmer's test would

indicate that the aqueous component of the tear film is not significantly reduced. The lower tear BUT indicates that a significant number shows a deficiency of mucous component which is produced by the goblet cells of the conjunctiva. The mucous coat is important in the stability of the tear film. Although the quantity of tears produced are not affected in this study, the tear film seems to be unstable in many leprosy patients.

In leprosy, the eyes may be affected primarily by direct invasion or infiltration of the eyes by *Mycobacterium leprae* or abnormal exposure of the eyes secondary to involvement of the 5th and 7th cranial nerves (2). Earlier studies (5) have suggested an early autonomic denervation hypersensitivity response of the uveal tract in leprosy. Based on this study, Lamba *et al.* (9) have postulated that an autonomic denervation may play a similar role in producing an abnormality of the mucin layer, resulting in subclinical dry eyes. However, no nerve endings have been found in apposition to goblet cells in humans, and this argues against direct innervation of goblet cells and neural control of goblet cell secretions (1). Conversely, it has been demonstrated that in rats there is localization of nerve fibers adjacent to the goblet cells and that these goblet cells release their secretory granules in a reflex response mediated by the activation of either the parasympathetic or sympathetic nerves that surround them (3,8). Further studies that include conjunctival biopsies are needed to give credence to this hypothesis.

SUMMARY

Seventy-five leprosy patients and an equal number of age- and sex-matched controls were examined for tear functions, using Schirmer's test and tear break up time

(BUT). There was no statistically significant difference in the Schirmer's test, but the tear BUT showed a statistically significant lower value of <10 seconds in multibacillary patients compared to paucibacillary patients. Leprosy patients with lagophthalmos and decreased corneal sensation showed a lower value of tear BUT which was also statistically significant. This study shows that even though the quantity of tears is not affected, proper and prolonged wetting of the cornea is deficient in many leprosy patients.

RESUMEN

Se midió la función lagrimal en 77 pacientes con lepra y en 77 personas sanas de edad y sexo comparables, usando la prueba de Schirmer y el tiempo de lagrimación. No hubieron diferencias estadísticamente significativas en la prueba de Schirmer pero el tiempo de lagrimación fue significativamente más corto (<10 seg) en los pacientes multibacilares que en los paucibacilares. Los pacientes con lepra, con lagofthalmus y sensación corneal disminuida, mostraron un valor más bajo en el tiempo de lagrimación que los pacientes sin estas complicaciones y la diferencia fue estadísticamente significativa. El estudio muestra que aunque la cantidad de lágrima no parece estar afectada, la humectación apropiada de la córnea es deficiente en muchos pacientes con lepra.

RÉSUMÉ

Soixante cinq patients lépreux et un nombre correspondant d'individus témoins contrôlés pour l'âge et le sexe furent examinés pour la fonction lacrymale, en utilisant le test de Schirmer et le temps de rupture (BUT) lacrymal. Aucune différence significative du test de Schirmer ne fut observée; cependant, le BUT lacrymal était statistiquement inférieur de <10 secondes chez les patients multibacillaires par rapport aux patients paucibacillaires. Les patients hanséniens avec lagophthalmos et sensibilité cornéenne diminuée ont montré une valeur plus basse du BUT lacrymal, valeur qui était aussi statistiquement significative.

Cette étude montre que, malgré une quantité de larmes non modifiée, l'humidification adéquate et prolongée de la cornée est insuffisante chez de nombreux patients lépreux.

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