A COMPARITIVE STUDY OF CHANGES IN TEAR FILM FUNCTION IN NORMAL AND TYPE II DIABETIC SUBJECTS IN SOUTH INDIAN POPULATION

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Abstract

This study was performed to investigate, the changes of tear film and ocular surface in diabetic patients by assessing the corneal sensitivity test, tear secretion test and comparing the results with those in a normal control group. The present study was carried out in K.M.C. Mangalore in 100 eyes of fifty patients of Type 2 Diabetes Mellitus (Cases) and 100 eyes of fifty healthy individual (Controls). Corneal sensitivity, Tear film break up time, Rose bengal test and Schirmer test without topical anesthesia (total tear secretion test), and Schirmer test with topical anesthesia (basal tear secretion test) was measured. Results showed that corneal sensitivity was significantly lower (P < 0.001) in the diabetic group than in the control group. Tear film BUT was significantly shorter (P < 0.001) in the diabetic group than in the control group. Total and basal tear secretions were significantly lower (P < 0.001) in the diabetic group when compared to control group. The present study indicates that in patients with Type II diabetes, there is a decreased corneal sensitivity, decreased tear stability and secretion, suggesting an ocular surface disease. Early examination of the diabetic patients for the detection of the ocular surface disorders is indicated.

Keywords: Diabetes, Dry eye, Tear film, BUT, Corneal sensitivity

1. Introduction

Non-insulin Dependent Diabetes Mellitus (NIDDM) or Type 2 diabetes constitutes, nearly 95-97% of all diabetic patients in most population groups. The prevalence of NIDDM varies considerably from <1% in some countries to 50% in certain populations and developing countries like Pima Indians and Micronesians¹. The prevalence of diabetes in India is very rapidly rising and it is estimated that by the year 2010 A.D, 20% of all Type 2 patients in the world would be contributed from India. This form of diabetes till recently was considered as mild diabetes or "a touch of diabetes" and obviously the management strategies were less vigorous. Recently published studies²,³ have proved beyond doubt, that tight control of diabetes definitely prevents or slows down the progression of late complications of diabetes. Diabetes Mellitus is one of the most important causes of blindness in both developed & developing countries⁴.

The typical ocular complications are
diabetic retinopathy, cataract, glaucoma, keratopathy etc. Schultz reported that 47-67% of diabetic patients develop primary corneal lesions during their lifetime. The three important pathophysiological mechanisms for these complications are protein glycosylation, aldose reductase pathway and protein kinase pathway. Decreased tear production has been reported in very few studies in past but overall data is scanty. Changes of tear function parameters in diabetes have been studied, but the results remain controversial. Although several studies have documented tear secretion and tear film function in non insulin dependent diabetes mellitus, there have been few studies from south Indian population. In addition to this there has been a lack of research related to the changes of ocular surface in diabetic patients to clinical parameters of diabetes in South Indian population. In the present study, we investigated the changes of tear film and ocular surface in diabetic patients by assessing the corneal sensitivity test, tear secretion test and comparing the results with those in a normal control group.

2. Experimental

2.1. Materials and Methods

The study included 100 eyes of fifty patients of Type 2 Diabetes Mellitus (Cases) and 100 eyes of fifty healthy individual (Controls) attending the OPD of Department of Ophthalmology, KMC, Hospital Attavar, Mangalore. Both groups were age and sex matched the control group consists of healthy individuals attending eye OPD for the errors of refraction and senile cataract and all were non-diabetics. Informed consent was obtained from each of the participants and the study was approved by the Ethics Committee of our institution.

2.2. Inclusion criteria

- All diabetic patients had just been diagnosed with NIDDM and had not started on any medication.
- Non-diabetic controls had normal values of fasting blood glucose levels of 5.6 mmol/L and less, and negative personal and family histories of diabetes mellitus.

2.3. Exclusion criteria

Individuals who had a history of drug abuse, contact lens wear, topical medication, ocular surgery within the previous 3 months, abnormalities in the cornea, conjunctiva, or eyelid, and secondary ocular and systemic disease were excluded from this study. Dry eye symptoms were recorded in both the groups. Different symptoms included character of irritation whether it was burning, foreign body sensation or sand gritty feeling. The location of irritation whether on the lid margin, on the skin or involving the surface of the eye was also looked for any diurnal variation of symptoms at a particular time of day, like on awakening or in late evening and the onset of symptoms whether gradual or sudden was studied. The presence was noted of any aggravating factors or alleviating factor of the symptoms. All the individuals underwent routine general physical examination and thorough ophthalmological examination. The visual acuity of both eyes was done with Snellen's chart. Both eyes were examined first using the broad beam of the slit lamp to know the condition of the ocular surface and adnexa, observing the tear film meniscus, tear film, corneal changes, conjunctival changes and the eyelids. The diabetic patients were clinically evaluated with direct and indirect ophthalmoscopy to know the status of retina. Then following tests were performed in all of the subjects.

2.4. Corneal sensitivity

Corneal sensitivity was measured using an esthesiometer. The tip of the fully extended nylon filament was applied perpendicular to the surface of the central cornea and advanced steadily. When the subject felt its presence, the length of the filament was recorded in
millimeters. A measurement of less than 45 mm was considered as low corneal sensitivity.

2.5. Schirmer Test
It measures tear secretion over a specified time, Schirmer test without topical anesthesia (total tear secretion test), and Schirmer test with topical anesthesia (basal tear secretion test) was measure with the standardized strips. The strip was folded at the notch and placed at the junction of the middle and lateral thirds of the lower eyelids and allowed there to stay in place for 5 minutes. A value of more than 10 mm of wetting after 5 minutes was taken as normal and any value less than 10mm of wetting at the end of 5 minutes was considered abnormal.

2.6. Tear Break Up Time (TBUT)
The end of a fluorescein strip was moistened with one drop of distilled water and applied to the subject’s temporal bulbar conjunctiva. The subject was to blink several times to spread the dye over the corneal and conjunctival surfaces and then asked to keep the eyes open looking straight ahead. The slit lamp with the cobalt blue filter was used to scan the entire cornea looking for dry areas which appeared as dark spots or streaks. The time in seconds between the last blink and the first appearance of a dry spot was recorded with a stopwatch as the TBUT. The mean of three consecutive TBUT was taken. A TBUT of less than 10 seconds was indicative of an unstable tear firm.

2.7. Rose Bengal Test
Rose Bengal is a dye with an affinity for dead and devitalized epithelial cells and mucus. The typical staining pattern in dry eye consists of two triangles with their bases at the limbus nasally and temporally. Corneal filaments and plaques are also shown up more clearly after instillation of the dye. A drop of the RB dye was instilled in an unanaesthetised eye (to negate a false positive result) and the excess dye was rinsed out of the eye. The staining pattern was noted. Von Bijsterveld scoring was then done to describe 3 zones namely: a) Nasal bulbar conjunctiva(Mild) b)Cornea(Moderate) c)Temporal bulbar conjunctiva (Late).Grading is 0-3 cm in each zone, where 0 indicates no stain, 1 indicates < 1/3 area, 2 indicates 1/3 – 2/3 area and 3 is confluent stain for >2/3 area. If the total exceeds 3.5, it is positive for dry eye. Severity was scored by multiplying the area score by the density score. The product is an index of corneal surface damage.

3. Statistical Analysis
Data were expressed as mean ± SD. Parameters between groups were analyzed by the Student t-test and analysis of variance with SPSS software. P<0.05 was considered statistically significant.

4. Results
Corneal sensitivity was significantly lower (P < 0.001) in the diabetic group (26.08 ± 5.14 mm) than in the control group (53.58 ± 2.06 mm). Tear film BUT was significantly shorter (P < 0.001) in the diabetic group (6.8 ± 7.01 sec) than in the control group (12.8 ±5.71 sec). Total and basal tear secretions were 7.77 ± 3.9 mm and 3.82 ±2.22 mm in the diabetic group, and 13.4 ± 5.7mm and 6.42 ± 4.00 mm in the control group, respectively. The differences between the two groups were statistically significant (P < 0.001).

5. Discussion
In our study, we have assessed corneal sensitivity, tear film BUT, and Schirmer I test for tear secretion in Type II Diabetes Mellitus patients and compared the results with those in the normal subjects. This indicates that dry eye in diabetic patients is a significant feature of diabetic ocular surface disorder. The corneal sensitivity and tear film parameters were significantly reduced in the diabetic patients, whereas the Rose Bengal test did not show much difference when compared with non-
Several studies have reported decreased corneal sensitivity in diabetic patients, but the mechanism is unclear. Abnormal glucose metabolism may induce the functional disorder of corneal nerve fiber through activated polyol pathway. Another hypothesis is that loss of corneal sensation is a manifestation of diabetic polyneuropathy. Dogru et al. reported that corneal sensitivity was significantly lower in diabetes with poor metabolic control and peripheral neuropathy, but it was not related to the duration of diabetes or the stage of retinopathy. On the other hand, Rogell and Saito et al. insisted that the decrease in corneal sensitivity was correlated with the diabetic retinopathy stage. In our results, decreased corneal sensitivity in diabetic patients was related to poor metabolic control, advanced diabetic retinopathy stage. Changes of tear function parameters in diabetes have been studied, but the results remain controversial. In some studies, total and reflex tear secretions were significantly reduced, but basal tear secretion and tear film BUT did not change. However, other studies reported a decrease in basal tear secretion and BUT. Dogru et al. reported that BUT and basal tear secretion were decreased, especially in diabetes with poor metabolic control and peripheral neuropathy, but they were not related to the duration of diabetes or the stage of retinopathy, suggesting a neuropathy involving the innervation of the lacrimal gland. Ozemir et al. reported that abnormal tear function tests were associated with poorer metabolic glucose control, panretinal argon laser photoocoagulation, and PDR. In our results, all tear function parameters, including BUT, and total and basal tear secretions, were lower in the diabetic group. These results might be related to these abnormalities were related to poor metabolic control, presence of diabetic neuropathy, advanced diabetic retinopathy stage and ocular lesion.

Rose Bengal staining is an important diagnostic aid and is a very sensitive indicator for the level of protection of the ocular surface. Goblet cell densities may reflect the overall health of the ocular surface. Therefore, correlation between Rose Bengal Staining with goblet cell number reflects the problem of decreased protection of the ocular surface. However Nelson found no correlation between the two. This may be due to the different location of the conjunctival epithelium examined as goblet cells vary in number in different locations. However Rose Bengal staining is one of the most specific tests (95%) when testing in control subjects along with impression cytology (98.8%). Therefore increased Rose Bengal staining correlates with decreased goblet cell density mucosal epithelial deficiency. This result suggests that the decrease in total or reflex tear secretion may be the first change of tear film when diabetic retinopathy progresses. Decreased reflex tearing in diabetes may be the result of a diminished corneal sensitivity, and decreased tear production and abnormal tear composition may result in superficial ocular lesion.

6. Conclusion

Our study indicates that in patients with Type II diabetes, there is a decreased corneal sensitivity, decreased tear stability and secretion, suggesting an ocular surface disease. These results suggest that diabetic patients are more prone to suffering from dry eye symptoms than normal subjects and therefore eye care practitioners are advised to watch out for these symptoms. Hence, early examination of the diabetic patients for the detection of the ocular surface disorders is indicated.
Bibliography:

1. Zimmet P. Type II (non insulin dependent diabetes) – an epidemiological overview. Diabetologia. 1982; 22: 399-411


Table 1: Corneal sensitivity, tear film parameters in diabetes and normal control groups

<table>
<thead>
<tr>
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<th>Control group (Mean ± SD)</th>
<th>Diabetic group (Mean ± SD)</th>
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<tbody>
<tr>
<td><strong>Corneal sensitivity (mm)</strong></td>
<td>53.58±2.06</td>
<td>26.08±5.14**</td>
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<tr>
<td><strong>Break-up time (sec)</strong></td>
<td>12.8±5.71</td>
<td>9.8±7.01 **</td>
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<tr>
<td><strong>Total tear secretion (mm)</strong></td>
<td>13.4±5.7</td>
<td>7.77 ± 3.9**</td>
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<tr>
<td><strong>Basal tear secretion (mm)</strong></td>
<td>6.42 ± 4.00</td>
<td>3.82 ±2.22**</td>
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** P value <0.001; Compared between Diabetic group and Control group