



Tear Secretion and Tear Film Function in Diabetics

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Abstract

In the present study, the evaluation of the amount of the tear production, the stability of the tear film and the condition of the conjunctival surface by the use of impression cytology in the diabetics and the non diabetic individuals was done to detect the possible tear film anomalies in the Type 2 diabetic patients. We performed Schirmer 1 test, TFBUT (Tear film break up time) and CIC (Conjunctival Impression Cytology) on each subject in both groups. The mean values for Schirmer 1 test, TFBUT were significantly decreased in diabetes patient as compared to healthy controls. The CIC revealed pronounced degree of metaplasia with loss of goblet cells in diabetic patients. We found decreased tear production, unstable tear film and squamous metaplasia in diabetic patients

Key Words

Type 2 Diabetes Mellitus, Tear Secretion, TFBUT, CIC

Introduction

Diabetes Mellitus comprises of a group of common metabolic disorders that share the phenotype of hyperglycemia. Diabetes Mellitus is emerging as one of the most common chronic disease worldwide. In India the prevalence of Diabetes Mellitus in adults is 2.3% in rural and 4.0 - 11.6% in the urban population (1). Diabetes Mellitus is one of the most important causes of blindness in both developed & developing countries (2). 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 life time (3). 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 over all data is scanty. Hence, the present study was undertaken to evaluate the tear secretion, the tear film function and condition of ocular surface by the use of impression cytology.

Material & Methods

The study included 100 eyes of fifty patients of Type 2 Diabetes Mellitus (Cases) and 40 eyes of twenty healthy individual (Controls) attending the OPD of Department of Ophthalmology, GMC, Jammu. The control group consists of healthy individuals attending eye OPD for the errors of refraction and senile cataract and all were non-diabetics. 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. Any diurnal variation of symptoms at a particular time of day, like on awakening or in late evening. The onset of symptoms was gradual or sudden. If there was presence 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 adenexa, observing the tear film meniscus, tear film, corneal changes, conjunctival changes, 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.

Schirmer 1 Test: It measures tear secretion over a specified time without topical anaesthesia 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. **TEAR FILM BREAK UP TIME:** It measures the tear film stability. The TBUT was performed by applying a fluorescein strip after moistening

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it with a drop of sterile saline, to the lower tarsal conjunctiva without the use of topical anaesthesia. The tear film was examined using a broad beam of the slit lamp with the blue cobalt filtered light. The time lapse between the last blink to the appearance of the first random dry spot was taken as the tear film break up time. A value of between 10 to 30 seconds was taken as normal.

Conjunctival Impression Cytology: One drop of 4% xylocaine sterile solution was instilled into each eye of the patient. The sheets of nitro cellulose filter paper with pore size 0.2 microns were used as precut pieces of 5mm long and 5mm wide. The paper was aligned with the help of a blunt smooth forceps on the bulbar conjunctiva. After 3-5 seconds the paper was removed by grabbing the edge with a peeling motion. The filter paper with the detached epithelial cells was immediately placed in the fixative solution containing glacial acetic acid, 37% formaldehyde, 70% ethyl alcohol in a 1:1:20 volume ratios for at least 10 minutes. The staining procedure was facilitated by dipping the specimen into each solution for a specified time as used by Tseng SCG (4). After final step, the filter paper was transferred to the glass slide. The six different cytological stages were defined according to Tseng SCG4. The slides were labeled as having normal epithelium and mild, moderate or severe metaplasia.

Statistical Analysis : Data collected was compiled and then analyzed. We applied two tail't test. The p value of < 0.05, considered statistically significant.

Results

The mean age in the diabetic group was 61.1 years. The mean age was 58.9 years in the control group. There were twenty five (25) males and twenty five (25) females in the diabetic group. There were thirteen (13) males and seven (7) females in the control group. The mean duration of diabetes mellitus in the diabetic group was 9.58 ± 3.4 years. There were 64% of diabetic patients with ocular symptoms of dry eye as compared to 24% of the controls with dry eye symptoms. 45% of the diabetic patients had revealed abnormalities during the Slit lamp examination. These were reduced tear meniscus, presence of debris or particulate matter in the tear film, the conjunctival and the corneal changes. There were only 4% of control group with such abnormalities. The mean TFBUT was 8.87 seconds and 12.77 seconds in diabetic group and control group respectively, as shown in *Table 1*. The p value was < .001. The TFBUT was significantly lower in the diabetics as compared with the controls. The mean Schirmer 1 test value was 8.99 millimeters and 15.8 mm in diabetic group and control group respectively as shown in *Table 2*. The p value

was < .001. The Schirmer 1 test was significantly lower in the diabetic group as compared with the controls. The CIC analysis as shown in *fig 1 & 2* of the diabetic group revealed that there were twenty diabetic patients with normal conjunctiva, eighteen with mild metaplasia, seven with moderate metaplasia and five had severe metaplasia. In the control group only three had mild metaplasia, none were with moderate or severe metaplasia, and the rest had normal conjunctival cytology as shown in *Table 3*. The p value was < .001.

Discussion

Goebbels M (5), reported 33% of diabetics as compared to 26% of control group had dry eye symptoms. 78% of patients with Type 2 diabetes mellitus were reported with dry eye symptoms by Dogru *et al* (6). Goebbels M (5), Dogru *et al* (6), Kenji I *et al* (7), Ozdemir *et al* (8) observed significantly decreased TFBUT in the diabetics as compared to the non-diabetic group. Similar results were found in our study. Hosotani *et al* (9), observed decreased tear production in the patients with the diabetes mellitus. Goebbels M (5) reported decreased Schirmer 1 test values in the patients with diabetes. He suggested that amount of the reflex tearing is lowered in the diabetics which may be due to diminished corneal and conjunctival sensations or may be due to neuropathy involving the innervations of the Lacrimal gland Dogru *et al* (6) reported 22.7% of the diabetics had Schirmer test value < 5 millimeters. Saito *et al* (10) also reported both the corneal sensitivity and the basal or reflex tear secretion was decreased in the diabetic patients. In our study 9% of patients with diabetes mellitus had Schirmer 1 values < 5 millimeters Dogru *et al* (6) reported the average grade of squamous metaplasia in the diabetics was 1.12 ± 0.53 and in the controls it was 0.77 ± 0.18 which is highly significant. The average goblet cell densities were 736 ± 244 cell/ millimeters² and 1170 ± 180 cells / millimeters² in the diabetics and the control group respectively. The goblet cells density was significantly lower in the patients with poor metabolic control, peripheral neuropathy, but not affected by the duration of diabetes and status of retinopathy. The goblet cells loss is a well known sign of squamous metaplasia, along with the increase in cellular stratification and keratinization. In our study, the absence of goblet cells and increased cellular stratification with keratinization as observed in the diabetic patients was compared to the control group. Goebbels M (5), reported similar results and suggested that even though the basic unstimulated tear flow is normal in diabetics, the decrease in reflex tearing could be sufficient to induce chronic damage to the conjunctival surface. The trophic function of the tear

Table 1. The Tear Film Break Up Time (Sec) in the Cases (with Diabetes Mellitus) and the Controls

Tear film break-up time	Right Eye		Left Eye		Total (%)
	Case	Control	Case	Control	
	4.1 - 8.0	21 (15%)	-	19 (13.57%)	
8.1-12.0	27 (19.28%)	2 (1.42%)	29 (20.71%)	3 (2.14%)	61 (43.57%)
12.1-16	2 (1.42%)	18 (12.85%)	2 (1.42%)	17 (12.14%)	39 (27.85%)
Total	50 (35.7%)	20 (14.27%)	50 (35.7%)	20 (14.27%)	140 (100%)

Table 2. The Schirmer I Test Values in Cases & Controls

Schirmer I test	Right Eye		Left Eye		Total (%)
	Case	Control	Case	Control	
	0 - 9	21 (15%)	-	19 (13.57%)	
11 - 19	29 (20.71%)	18 (12.85%)	31 (22.14%)	18 (12.85%)	96 (68.57%)
20 - 30	-	2 (1.42%)	-	2 (1.42%)	4 (2.85%)
Total	50 (35.7%)	20 (14.27%)	50 (35.7%)	20 (14.27%)	140 (100%)

Table 3. Conjunctival Impression Cytology Results in the Cases (with Diabetes Mellitus) and the Controls

Condition of Conjunctiva	No. of cases (with diabetes)	No. of Control (without diabetes)	Total (%)
Normal Epithelium	20 (28.5%)	17 (24.2%)	37 (52.7%)
Mild metaplasia	18 (25.7%)	3 (4.2%)	21 (29.9%)
Moderate metaplasia	7 (10%)	-	7 (10%)
Severe metaplasia	5 (7.14%)	-	5 (7.1%)
Total	50 (71.4%)	20 (28.57%)	70 (100%)

film like vitamin A, vitamin A carrier, and epithelial growth factors could be disturbed in diabetic leading to chronic trophic damage to the conjunctival surface. The ocular surface changes found in the diabetics could partially be the result of a primary ocular surface disease or of metabolic alteration of conjunctival epithelial cells independent of the tear film abnormality. The concurrent involvement of the conjunctival and corneal epithelial surface may be viewed as a primary ocular surface disease. The mechanisms of these ocular surface changes during the course of the diabetic is not clear but tropic effects of trigeminal sensory nerves on the conjunctiva and cornea, may be responsible. The loss of neurotrophic effects as evidenced by the corneal hypoesthesia and alternating hyperglycaemia and euglycaemia may induce conjunctival squamous metaplasia in the diabetics. Alves *et al* (11) suggested that metabolic, neuropathic and vascular tissue damages lead to an inflammatory

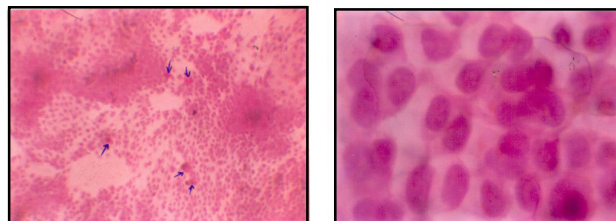


Fig 1& 2. The Conjunctival Epithelium Showing Mild & Moderate Metaplasia (X 1000)

process and functional degeneration. The physiopathological mechanisms include hyperglycemia, advanced glycated end product accumulation, oxidative stress and inflammation mediated by NF-kappaB signaling pathways. Potential treatments enlightened by those findings would include antioxidant, anti-inflammatory, secretagogues and/or anabolic agents that would mimic insulin effects.

Conclusion

The decreased mean Tear film break up time indicates increased instability of the tear film in the diabetic patients. The lower Schirmer I test value demonstrates decreased total (basal and reflex) tear secretion in the diabetic patients. The pronounced degree of metaplasia in the diabetics revealed compromised condition of the conjunctiva. Early examination of the diabetic patients for the detection of the ocular surface disorders is indicated.

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