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Effect of Long Term Glycemic Control on Precorneal Tear Film in Diabetic Patients

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Abstract :*Purpose of the study was to find out the relation between HbA_1c which is an useful indicator of long term glycemic control and the qualitative and quantitive activity of precorneal tear film with the help of Tear Film Break up Time(TBUT) and Schirmer's test respectively.40 type 2 diabetic patients and 20 age and sex matched healthy controls undergone HbA_1c level, TBUT estimation and Schirmer's test after proper consent and explanation. Statistically significant (p value <0.05) decrease in TBUT and Schirmer's test values were observed in diabetic patients when compared to control group which further deteriorates with increase in HbA_1c level. Our finding lead us to conclude that long term glycemic control can modify the qualitative and quantitative properties of tearfilm thus HbA_1c level can be considered as one of the important predictor of dry eye syndrome among the diabetic patients.*

Keywords: *HbA1C, TBUT, Schirmer's test, Dry eye*

I. Introduction

International Diabetic Federation estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025[(1)]. As a systemic disease diabetes mellitus affects the eyes in many ways—diabetic retinopathy which is the leading cause of vision loss in adults of working age (20-65 years) in industrialized country, neovascular glaucoma, cataract, refractory error, oculomotor nerve palsy, ptosis, lid infection are some of the typical ocular morbidity associated with diabetes. In addition often diabetic patients complain of typical dry eye symptoms such as burning/foreign body sensation[(2)],.Problems involving the ocular surface particularly dry eyes have been already reported and established in different studies among the diabetic patients[(3)].The pathophysiology of dry eyes is still uncertain but autonomic dysfunction[(4)], aldose reductase activity, the first enzyme of the sorbitol pathway, may be involved. Another study found that diabetic patients had decreased stability of tear film and lower value of tear secretion when compared with control group[(5)].Decreased stability of tear film can be estimated by TBUT which is a non invasive procedure described by Norm and revised by Lemp and Holly[(6)] about 30 years back. It is now accepted that tear film break up time (TBUT) is an easier and at the same time effective procedure in early diagnosis of tear film stability at same time tear secretion can be estimated by Schirmer's test which along with TBUT also helps in diagnosis of dry eye. HbA_1c also known as glucosylated hemoglobin is a minor proportion of hemoglobin to which glucose is bound nonenzymatically.[(7)] HbA_1c levels depend on the blood glucose concentration. That is, the higher the glucose concentration in blood, the higher the level of HbA_1c (normal level < 7%); and not influenced by daily fluctuations in the blood glucose concentration but reflect the average glucose levels over the period of six to eight weeks. Therefore, HbA_1c is a useful indicator of how well the blood glucose level has been controlled in the recent past. In our present study we have tried to evaluate the relation between HbA_1c, a useful indicator of long standing glycemic control and TBUT and Schirmer's Test which are the effective test for qualitative and quantitive activity of precorneal tear film and thus help in early diagnosis of dry eye.

II. Materials and Methods

The study was conducted from January 2014 to June 2014 in the Department of Ophthalmology, Medical College Kolkata.40 diagnosed cases of type 2 diabetes mellitus (ADA criteria) [(8)] of 30-60 years comprised the study group. 20 Controls were selected from patients (age and sex matched) who came for routine check up or some minor refractive error but no obvious ophthalmological or systemic disease. The ethical committee approval of the institutional review board and informed consent of all the subjects and were obtained.

Exclusion criteria included patient suffering from any painful ocular condition, one eyed person, contact lens, history of topical medication/ smoking within past 6 months, history of ocular surgery, LASER therapy,systemic disease as assessed by history and clinical evaluation (other than diabetes mellitus as for the diabetic group).

Fasting whole blood were collected in EDTA vials from the diabetics and the control for estimation of HbA1c level by 'Particle Enhananced Immunoturbidimetric Method'

TBUT was estimated with fluorescin strip and slitlamp biomicroscope under cobalt blue filter and Schirmer test by Whatman filterpaper No.41.Test were performed under relatively unvarying environmental condition for the entire subject to eliminate the variation of temperature. The tests were done in a semi dark room with no obvious ventilatory current. Between TBUT test and Schirmer's test a reasonable time gap was maintained so that no mutual interference occurred. The condition was confirmed by ocular surface dye staining pattern with fluorescein strip, tear film break up time (TBUT) (value 15s) and Schirmer test (value 15 mm in 5 min), according to American Academy of Ophthalmology by ophthalmologists[9]

Diabetic patients were further subdivided in three groups on the basis of HbA1c level.Group(1) (HbA1c between 7% - 8%), or Moderate glycemic control group, Group (2) or Poor glycemic control group (HbA1c between 8% - 10%), Group(3) or very poor glycemic control group (HbA1c above 10%) and Control Group- with HbA1c Less than or equal to 7%

The statistical analysis was done by SPSS software version 17. As the variables were continuous in nature, Numerical variables were presented as Mean ± SD. ANOVA test was done to check if the three groups differed statistically significantly. As p-value obtained by doing ANOVA test was < 0.05, three groups were taken to be different and pairwise student's t-test was done between every two groups and if the p-value obtained was<0.05 the difference between those two groups were considered statistically significant. P value less than 0.05 was taken as significant.

III. Results

Table 1: Comparative values TBUT (sec.) and Schirmer's test (mm/5min)

	Control (20) (Non diabetic with HbA_1c <7%)	Diabetic group (40) (with HbA_1c >7%)	
TBUT (sec.)	13.56±3.22	7.53±3.51	p<0.05
Schirmer test (mm/5min)	14.02±7.21	10.04±4.13	p<0.05

Table 2**:** TBUT in diabetic patients (Mean ± SE)

Group	HbA_1c	No.of patients	TBUT (sec.)	p-value (ANOVA)
1	7%-8%	21	9.14±2.13	0.05*
2	8%-10%	14	7.33±1.22	
3	>10%	5	6.14±1.05	

Table 3: Schirmer's test value in diabetic patients (Mean ± SE)

Group	HbA_1c	No.of patients	Schirmer's test (mm/5min)	p-value (ANOVA)
1	7%-8%	21	10.91±1.98	0.04*
2	8%-10%	14	9.01±1.66	
3	>10%	5	8.91±1.05	

Table:4 P-value for Pair wise student's t-test of TBUT values among Group1,Group2 & Group3

	Group1	Group2	Group3	P-value for Pair wise student's t-test values		
				Group 1 & 2	Group 2 & 3	Group 3 &1
Number of Patients	21	14	5	0.007*	0.07	0.005*
TBUT Test Value	9.14± 2.13	7.33±1.22	6.14±1.05			

Table:5 P-value for Pair wise student's t-test of Schirmer's test values among Group1,Group2 & Group3

	Group1	Group2	Group3	P-value for Pair wise student's t-test values		
				Group 1 & 2	Group 2 & 3	Group 3 &1
Number of Patients	21	14	5	0.007*	0.8	0.04*
Schirmer's Test Value	10.91± 1.98	9.07±1.66	8.91±1.05			

IV. Discussion

In this study the comparative values of TBUT and Schirmer test (mean ± SE)among 40 diabetic patients and 20 age and sex matched control group were 7.53±3.51sec,10.04±4.13mm and 13.56±3.22sec 14.02±7.21mm respectively. The decreased value of both the parameters among the diabetic subjects were statistically significant as the p value <0.05.This supports the fact that diabetics are more prone to Dry eye

which is already mentioned by different authors in there different studies[10,11] .Interestingly, it was observed that the mean values of TBUT and the Schirmer test in three different glycemic control group based on percentage (%)HbA1c level (above normal value) (Table 2&3) were decreased with an increase in HbA1c level (%).Once again this finding was statistically significant as the p value <0.05. This result of the study reflects that with rise in HbA1c level there is qualitative and quantitive decrease in tearfilm activity in diabetic patients.

As already mentioned the HbA_1c level is proportional to average blood glucose concentration over the previous four weeks to three months. Therefore, HbA_1c is a useful indicator of how well the blood glucose level has been controlled in the recent past and it also provides a much better indication of glycemic control than blood or urinary glucose determinations. Studies have already shown that poor long term glycemic control can contribute to complications like retinopathy [12], Our present study reflects that poor long term glycemic control can lead to both qualitative and quantitive decrease in tearfilm activity as estimated by TBUT and Schirmer test. This observation is in agreement with previous investigations by Seifart U, Strempel (1994)[13].In their study a correlation was found between the glycated hemoglobin (HbA1C) and the presence of dry eye syndrome. The higher the HbA1c values, the higher the rate of dry eye syndrome. Further studies with larger sample size need to be undertaken to establish an etiologic relationship.

V. Conclusion

Our present study lead us to conclude that there is qualitative and quantitive decrease in tearfilm activity among the diabetic patients with further deterioration with increase in HbA_1c level i.e. poor the glycemic control more the chances of dry eye. Thus HbA_1c level can be considered as one of the important predictor of dry eye syndrome among the diabetic patients and examination for dry eyes should be an integral part of poorly controlled diabetic patients.

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