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Evaluation of ocular surface disorders in patients with diabetes mellitus

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Abstract: Aim: This study aims to investigate the clinical changes in the ocular surface of patients diagnosed with type II diabetes mellitus.
Methodology: A total of 75 adult patients of both genders with type II diabetes and ocular surface disease, along with a group of healthy subjects, were included in the study. Various tear film stability tests such as tear film break-up time (BUT) test, Schirmer I test, fluorescein dye test, and rose bengal dye test were conducted to assess ocular surface disorders. Additionally, the Ocular Surface Disease Index (OSDI) questionnaire was administered to all enrolled patients. The duration of diabetes, HbA1C levels, and the stage of diabetic retinopathy were also recorded.
Results: Group I comprised 45 males and 30 females, while group II included 35 males and 40 females. Non-proliferative diabetic retinopathy (NPDR) was present in 48 patients, whereas proliferative diabetic retinopathy (PDR) was present in 19 patients, showing a significant difference (P=0.01). The remaining diabetic patients did not exhibit any clinically observable fundus changes of retinopathy during stereoscopic 90 D examination. The average tear function test was 8.22 seconds in group I and 13.1 seconds in group II, whereas the average Schirmer test values were 8.84 mm in group I and 16.5 mm in group II. Fluorescein staining was observed in 8 patients in group I and 2 patients in group II, while pathologic rose bengal staining was positive in 15 patients in group I and 4 patients in group II, demonstrating a significant difference (P<0.05). The average tear film BUT was 9.25 seconds in patients with a duration of diabetes <10 years and 8.17 seconds in those with a duration of diabetes >10 years. Similarly, the average Schirmer test revealed values of 10.31 mm and 6.72 mm, respectively. Patients with good glycemic control exhibited average tear film BUT and Schirmer test values of 10.85 seconds and 10.21 mm, while those with poor glycemic control showed values of 8.30 seconds and 6.82 mm, respectively. In patients with NPDR, the values were 9.53 seconds for tear film BUT and 10.5 mm for the Schirmer test, whereas patients with PDR had values of 7.84 seconds and 7.6 mm, respectively. The average range of OSDI score was 40-60 in group I compared to 0-20 in group II.
Conclusion: Patients diagnosed with diabetes mellitus are more susceptible to developing ocular surface disorders. Furthermore, a longer duration of diabetes and poor glycemic control are associated with increased chronic inflammation of the ocular surface. The stage of diabetic retinopathy shows a direct correlation with the OSDI questionnaire score.

Keywords: Ocular surface disorders; Diabetes; Schirmer test; OSDI questionnaire.

1. Introduction

Diabetes is a common cause of blindness in individuals aged 20-70 years, with cataract and retinopathy being well-known ocular complications of the disease [1]. However, recent research has drawn attention to ocular surface problems, particularly dry eye in diabetic patients. Diabetic keratoepitheliopathy can induce quantitative and qualitative abnormalities in tear secretion, leading to decreased corneal sensitivity and poor adhesion of regenerating epithelial cells [2].

Ocular surface abnormalities are prevalent in patients with diabetes mellitus (DM) and increase their risk of developing dry eye disease (DED), corneal epithelial fragility, decreased corneal sensitivity, abnormal wound healing, and increased susceptibility to infected corneal ulceration [3]. Nearly 47%-64% of patients with DM develop keratopathies during their lifetime, and ocular surface changes correlate with the disease's duration, poorly controlled serum glucose level, peripheral neuropathy, and proliferative diabetic retinopathy [4].

Patients with DM exhibit reduced corneal sensitivity, which is believed to have a negative impact on reflex tear secretion. Reduced goblet cell density in the conjunctiva, along with meibomian gland dysfunction, accounts for the reduced tear break-up time observed in these individuals. Long-standing disease can also cause damage to the microvascular supply to the lacrimal gland, impairing lacrimation [5,6]. Therefore, we conducted this study to assess ocular surface disorders in patients with diabetes mellitus.

2. Methodology

Ethical approval was obtained from the appropriate review committee and written informed consent was obtained from all participants prior to the study.

Seventy-five adult diabetic patients with ocular surface disease of both genders were included in the study. Patients were diagnosed with uncontrolled diabetes if their fasting blood glucose was equal to or greater than 126 mg/dL on two separate occasions, or if their random blood sugar was equal to or greater than 200 mg/dL with symptoms, or if their postprandial 2-hour plasma glucose was equal to or greater than 200 mg/dL, according to the criteria provided by the American Diabetes Association.

The participants were divided into two groups. Group I consisted of patients with type II DM and ocular surface disease, while group II consisted of healthy control subjects. The tear film stability tests like tear film break-up time (BUT) test, Schirmer I test, fluorescein and rose bengal dye tests, and Ocular surface disease index (OSDI) questionnaire was analyzed in all the subjects. Pupil dilation was achieved by instillation of 0.5% tropicamide drops three times within 15 minutes for fundus examination. External ocular examination focused on the eyelid margin, tarsal and bulbar conjunctiva, and cornea.

The collected data included name, age, gender, and other relevant demographic information. Statistical analysis was performed using the Mann Whitney U test, and a P-value of less than 0.05 was considered statistically significant.

3. Results

The study included 75 adult patients with ocular surface disease, with 45 males and 30 females in group I (type II DM patients with ocular disease) and 35 males and 40 females in group II (healthy control subjects) (Table 1). Of the group I patients, 48 had non-proliferative diabetic retinopathy (NPDR) and 19 had proliferative diabetic retinopathy (PDR) which was found to be significantly different (P= 0.01). Rest of the diabetic patients showed no clinically observable fundus changes of retinopathy on stereoscopic 90 D examination (Table 2).

The tear film break-up time (BUT) test was significantly shorter in group I (8.22 seconds) compared to group II (13.1 seconds), as was the Schirmer test (8.84 mm in group I and 16.5 mm in group II). Fluorescein staining was seen in 8 patients in group I and only 2 patients in group II, while pathologic rose Bengal staining was positive in 15 patients in group I and 4 patients in group II. The differences in these test results were also significant (P< 0.05) (Table 3).

In patients with diabetes duration of <10 years, tear film BUT was 9.25 seconds, compared to 8.17 seconds in patients with diabetes duration >10 years. Schirmer test revealed 10.31 mm and 6.72 mm in the two groups respectively. Tear film BUT and Schirmer test were found to be 10.85 seconds and 10.21 mm in patients with good glycemic control, and 8.30 seconds and 6.82 mm in those with poor glycemic control. Tear film BUT was 9.53 seconds and Schirmer test was 10.5 mm in patients with non-proliferative diabetic retinopathy, while in those with proliferative diabetic retinopathy, tear film BUT was 7.84 seconds and Schirmer test was 7.6 mm (Table 4). These results suggest that ocular surface disorders are more pronounced in patients with longer duration of diabetes, poor glycemic control, and advanced stage of diabetic retinopathy.

Overall, our results indicate that diabetic patients are at a higher risk of developing ocular surface disorders, which can contribute to further complications such as decreased corneal sensitivity, persistent

epithelial defects and abnormal wound healing. Therefore, it is important to regularly assess and manage ocular surface disease in patients with diabetes mellitus.

Table 1. Patients distribution

Groups	Group I	Group II
Status	Diabetes	Control
M:F	45:30	35:40

Table 2. Clinical features of diabetic patients

Clinical features	Number	P value
Non-proliferative diabetic retinopathy	27	0.01
Proliferative diabetic retinopathy	48	

Table 3. Comparison of tear function tests

Parameters	Group I	Group II	P value
Tear film BUT (s)	8.22	13.1	0.01
Schirmer test (mm)	8.84	16.5	0.02
Fluorescein staining	8	2	0.04
Pathologic rose Bengal staining	15	4	0.05

Table 4. Relationship between tear function tests and other parameters

Parameters	Variables	Tear film BUT (s)	Schirmer test (mm)
Duration of diabetes	<10 years	9.25	10.31
	>10 years	8.17	6.72
Glycemic control	Good	10.85	10.21
	Poor	8.30	6.82
Stage of DRP	NPDR	9.53	10.5
	PDR	7.84	7.6

4. Discussion

Low tear production or excessive evaporation can increase tear osmolarity, leading to the release of inflammatory mediators [7]. Ocular surface disorders are a common complication in diabetes mellitus, and they have been extensively studied in the field of ophthalmology [8,9]. Although the etiology of these disorders is not fully understood, tear dysfunction is thought to play a crucial role. Peripheral neuropathy, a common complication of diabetes, can affect the nerves supplying the ocular surface and tear glands, leading to tear dysfunction [10]. In this study, we aimed to assess ocular surface disorders in patients with diabetes mellitus.

Our results showed that Group I comprised of 45 males and 30 females, while group II had 35 males and 40 females. Ozdemir *et al.* [11] evaluated the risk factors for ocular surface disorders and tear dysfunction in patients with type 2 diabetes. They found that tear film break-up time (BUT) and Schirmer test values were significantly lower in diabetic patients compared with control subjects. Additionally, more diabetic patients had abnormal fluorescein and rose bengal staining than the control group. Abnormal tear function tests were associated with poorer metabolic glucose control, panretinal argon laser photocoagulation (ALP), and proliferative diabetic retinopathy (PDR) ($P < 0.05$), but not with the duration of diabetes.

Our results showed that non-proliferative diabetic retinopathy was present in 27 patients, while 48 patients had proliferative diabetic retinopathy. Kesarwani *et al.* [12] enrolled a total of 83 participants (130 eyes) in their study, including 53 diabetics (80 eyes) and 30 healthy controls (50 eyes). Of the 53 diabetics, 24 patients (42 eyes) had some diabetic retinopathy. They found that diabetics had significantly reduced Schirmer, TBUT measurements, and higher grades of keratoepitheliopathy score (KES) and rose bengal staining (RBS) test compared with healthy controls. Impression cytology analysis showed goblet cell loss and conjunctival squamous metaplasia in diabetics.

Our results showed that the tear function test was 8.22 seconds in group I and 13.1 seconds in group II, while the Schirmer test was 8.84 mm in group I and 16.5 mm in group II. Fluorescein staining was seen in 8 patients in group I and 2 patients in group II, and pathologic rose bengal staining was positive in 15 patients in group I and 4 patients in group II. Manchikanti *et al.* [13] assessed ocular surface changes among patients with diabetes mellitus (DM) and correlated them with tear film markers such as insulin-like growth factor (IGF)-1, interleukin (IL)-1β, and tumor necrosis factor (TNF)-a levels. They found that patients with DM had significantly lower Schirmer's, TBUT, and Ocular Surface Disease Index (OSDI) values than controls. The OSDI score showed moderate-severe dryness in patients with DM and only mild symptoms among controls. An abnormal impression cytology score was seen among cases and controls. The level of TNF-a was significantly increased in patients with DM and positively correlated with Schirmer and TBUT values.

Tear film BUT in patients with <10 years of diabetes was 9.25 seconds and >10 years of diabetes was 8.17 seconds. Schirmer test revealed 10.31 mm and 6.72 mm, respectively. Tear film BUT and Schirmer test were found to be 10.85 seconds and 10.21 mm in good glycaemic control patients and 8.30 seconds and 6.82 mm in poor glycaemic control patients. It was 9.53 seconds and 10.5 mm in patients with non-proliferative diabetic retinopathy (NPDR) and 7.84 seconds and 7.6 mm in patients with proliferative diabetic retinopathy (PDR), respectively. Yoon [14] evaluated keratoepitheliopathy score (KES) on 94 NIDDM-eyes and 60 control eyes and reported significantly higher scores in diabetic group (1.14 ± 0.89) than in the control group (0.34 ± 0.48).

5. Conclusion

Our study showed that patients with diabetes mellitus are more prone to develop ocular surface disorders. Also, more the duration of diabetes and poor glycemic control, more is the chronic inflammation of the ocular surface. The stage of diabetic retinopathy has a direct correlation with the score of OSDI questionnaire. Our findings highlight the importance of regular ophthalmic screening and effective management of diabetes to prevent and manage these ocular complications. Further studies are warranted to investigate the underlying mechanisms and to develop targeted interventions for this patient population.

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