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Original Article

Study on factors contributing to xerophthalmia among type-2 diabetes patients

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Abstract: Objective: Our aim was to discuss factors contributing to xerophthalmia among type-2 diabetes patients. Methods: A total of 32 type-2 diabetes patients treated at China-Japan Friendship Hospital from October 2015 to June 2017 were enrolled in the study group and 32 non-diabetic patients in the control group. Xerophthalmia morbidity, fasting blood glucose (FBG), glycated hemoglobin (HbA1c), tear break up time (TBUT), and results from Schirmer's test and fluorescein eye stain test of both groups were compared and multivariate logistic regression analysis was conducted to analyze contributing factors to xerophthalmia among type-2 diabetes patients. Results: The morbidity of the study group was 56.25% (36/64), significantly higher than that of the control group (12.50%, 8/64), with a statistically significant difference (P<0.001). TBUT of the study group was significantly shorter than the control group (6.31±2.27 s vs 13.26±2.65 s). The average filter paper wetting length in Schirmer's test of the study group was significantly shorter than that of the control group (8.68±3.79 mm vs 12.26±4.49 mm, P<0.001). Compared to the control group, the study group scored significantly higher than the control group in the fluorescein eye stain test (1.86±1.28 vs 0.52±0.18, P<0.001). Multivariate logistic analysis showed that age, progression of diabetes, TBUT, and HbA1c contributed to xerophthalmia among type-2 diabetes patients (all P<0.001). Conclusion: Type-2 diabetes is correlated with xerophthalmia. Therefore, better monitoring of blood glucose of diabetes patients and conducting ocular surface tests are conducive to preventing xerophthalmia.

Keywords: Type-2 diabetes, xerophthalmia, contributing factors, blood glucose

Introduction

Diabetes mellitus is a metabolic disorder caused by a number of different reasons. In patients with diabetes mellitus, their ability to utilize carbohydrates is hindered due to poor insulin sensitivity or insufficient and even absence of insulin secretion by pancreatic β-cells. Hence, the glucose in their body cannot be effectively used by peripheral tissues, resulting in high blood sugar concentrations as well as abnormal protein and fat metabolism [1]. If inadequate control of blood glucose is present long term, it will lead to a variety of chronic complications [2, 3]. It has been reported that incidence of dry eye syndrome and other ocular surface disorders is relatively high in diabetic patients since diabetes mellitus can affect the cornea, conjunctiva, and tears by changing the microenvironment of ocular surface in diabetic patients through a series of pathological processes [4]. With recent research and discussion on the causes and pathological mechanisms of dry eye syndrome, the International Dry Eye Workshop proposed a new definition of dry eye syndrome in 2007. As a disease of the tear film and ocular surface, dry eye syndrome is triggered by multiple factors and can lead to eye discomfort, visual impairment, and unstable tear films eventually resulting in damage to the ocular surface [5]. In addition, excessive dryness in the eyes may increase osmotic pressure and the presence of inflammatory mediators on ocular surface, inducing an inflammatory reaction to damage and impair the function of conjunctival epithelial cells which are responsible for the secretion and retention of tears on the ocular surface [6, 7]. A previous study has shown that the cause of dry eye syndrome is quite complex and is related to factors such as patient gender, age, and the presence of endocrine disorders or autoimmune diseases [8]. However, few reports have studied the factors related to dry eye syndrome in diabetic patients.

Table 1. Comparison of xerophthalmia morbidity between the two groups of patients (n, %)

Group	Case (eye)	Xerophthalmia morbidity
Study group (n=64)	36/64	56.25
Control group (n=64)	8/64	12.50
χ^2		25.17
P		<0.001

Table 2. Comparison of the level of fasting blood glucose and glycosylated hemoglobin between the two groups of patients

Group	Fasting blood glucose (mmol/L)	Glycosylated hemoglobin (%)
Study group (n=32)	8.76±3.82	9.57±2.71
Control group (n=32)	5.25±2.74	7.64±2.53
t	4.224	2.945
P	<0.001	0.004

In this study, we primarily investigated the relationship between dry eye syndrome and type-2 diabetes mellitus.

Clinical data and methods

General information

In this study, 32 cases (64 eyes) of type-2 diabetic patients (study group) and 32 cases (64 eyes) of non-diabetic patients (control group), treated in China-Japan Friendship Hospital from October 2015 to June 2017, were selected as study subjects. The study group consisted of 13 male patients and 19 female patients that were 24-75 years old. The average age of patients in the study group was 53.2±3.8 years and they had a diabetic history of 3 months to 20 years. The control group consisted of 14 male patients and 18 female patients that were 23-73 years old. The average age of patients in the control group was (54.7±3.4) years.

Inclusion criteria: No active inflammation in the eyes within the past 3 months; no history of eye surgery and trauma; the patients have not used drugs in the eyes.

Exclusion criteria: A history of hypertension, severe liver and kidney dysfunctions, autoimmune diseases, and malignant tumors.

Patients in the study group met the WHO diagnostic criteria for diabetes. The two groups of patients showed no significant difference in terms of general information, such as gender composition and age, so that their results were comparable. This study was approved by the Ethics Committee of China-Japan Friendship Hospital and informed consent was signed by both the patients and their family members.

Methods

All patients filled out a questionnaire for dry eye syndrome and underwent a routine eye examination to calculate the incidence of dry eye syndrome. In addition, the incidence of dry eye syndrome in the two groups was compared. Diagnostic criteria for dry eye syndrome included one or more of the following symptoms: dry eyes, a burning sensation in the eyes, a sensation of foreign matter in the eyes, debris on eyelashes, red eyes, and difficulty in opening the eyes after getting out of bed in the morning.

The differences in the level of fasting blood glucose and glycosylated hemoglobin (HbA1c) were compared between the two groups. In addition, tear break up time (TBUT), Schirmer's I test (SIt), and fluorescein vital staining (FL) in the two groups were also compared. The criteria for evaluating the values of above indices were: TBUT, a tear film with a TBUT value of <10 s was considered instable; SIt test, a moisture length of <10 mm in the SIt test was considered abnormal; FL, the result was considered positive if at least 8 vital stains were observed on the corneal epithelium or if the score was above 2, whereas a score of above 5 was considered strongly positive.

Statistical analysis

Statistical analysis of the observed results was conducted using the SPSS 23.0 statistical software kit. All measurement data were expressed as mean ± standard deviation while inter-group comparison of measurement data was performed using independent t-tests. Count data were expressed using the number of cases and percentages while inter-group comparison of count data was performed using χ^2 tests. Multivariate logistic regression analysis was used to analyze the relevant factors of dry eye syndrome in diabetic patients. A *P* value of <0.05 was considered statistically significant.

Table 3. Comparison of related symptoms between the two groups ($\bar{x}$±sd)

Group	Average tear film break-up time/s	Average moisture length of Schirmer I test (mm)	Score of fluorescein vital staining (points)
Study group (n=32)	6.31±2.27	8.68±3.79	1.86±1.28
Control group (n=32)	13.26±2.65	12.26±4.49	0.52±0.18
t	11.27	3.447	5.864
P	<0.001	<0.001	<0.001

Table 4. Multivariate logistic regression analysis of dry eye syndrome in type-2 diabetic patients

Index	Beta coefficient	Standard error	P	OR (95% CI)
Age	0.48	0.29	<0.001	1.76 (1.25-1.98)
The duration of diabetes	0.46	0.48	<0.001	1.68 (1.36-1.85)
TBUT	1.23	0.48	<0.001	4.57 (2.45-9.41)
HbA1c	1.76	0.18	<0.001	1.65 (1.33-1.95)

Note: TBUT, tear film break-up time; HbA1c, glycosylated hemoglobin; OR, odds ratio; CI, confidence interval.

Results

Incidence of dry eye syndrome in the two groups of patients

The incidence of dry eye syndrome in the study group was 56.25% (36/64), significantly higher than the value of (12.50%, 8/64) in the control group. The difference was statistically significant (P<0.001). See **Table 1**.

Level of fasting blood glucose and HbA1c in the two groups of patients

The level of fasting blood glucose and HbA1c in the two groups of patients was compared and analyzed using t-tests and the results showed that differences between the two groups were statistically significant (P<0.001, P=0.004). See **Table 2**.

Comparison of ocular surface indices between the two groups of patients

In the study group, the average TBUT was 6.31±2.27 s, significantly shorter than the value of 13.26±2.65 s in the control group. In addition, the average moisture length of SIt in the study group was 8.68±3.79 mm, also significantly lower than the value of 12.26±4.49 mm in the control group. The FL score of the study group was 1.86±1.28 points, significantly higher than the result of 0.52±0.18 points obtained from the control group. The differences between the two groups were statistically significant (all P<0.001). See **Table 3**.

Multivariate logistic regression analysis of dry eye syndrome in diabetic patients

The results from multivariate logistic regression analysis showed that risk factors for dry eye syndrome in type-2 diabetic patients included age, the duration of diabetes, TBUT, and HbA1c. See **Table 4**.

Discussion

Dry eye syndrome is a disease frequently seen in clinical settings. The main clinical features of dry eye syndrome include eye discomfort, visual impairment, unstable tear film, damage to the ocular surface, and may be associated with inflammatory reactions on the ocular surface as well as an increased osmotic pressure of the tear [9]. An epidemiological study has reported that incidence of dry eye syndrome in China is about 18.7%, of which 12% are males and 19% are females [10]. However, the pathological mechanisms underlying dry eye syndrome remain elusive. In recent years, change in the ocular surface of diabetic patients has attracted increased attention. Some scholars have studied the changes in the conjunctiva, corneal films, and tear films of diabetic patients and found that these patients often complained of foreign body sensations, burning sensations, and dry eyes also accompanied by alterations in the epithelial of cornea and tear films. Nevertheless, the relationship between type-2 diabetes mellitus and dry eye syndrome remains poorly understood. Therefore, the results of this study will provide an important basis for timely and effective treatment of dry eye syndrome in diabetic patients.

A foreign study has shown that 70% and 57% of patients with type-2 and type-1 diabetes mellitus suffer from dry eye syndrome, respectively.

In the general population, incidence of dry eye syndrome is 10.3-17% [11]. In this study, incidence of dry eye syndrome in the control group was 12.50%, consistent with the value shown in the above report. In addition, incidence of dry eye syndrome in the type-2 diabetic patients was about 56.25%, similar to the value reported by foreign studies.

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia. It is characterized by inadequate insulin secretion, poor insulin activity, or a combination of the two resulting in inappropriate hyperglycemia [12, 13]. The progression of diabetes mellitus can be explained by insulin resistance and the lack of insulin secretion. In the early stage of diabetes mellitus, the body will demonstrate a compensatory increase in insulin secretion as a result of insulin resistance leading to reduced utilization of glucose by peripheral tissues. At the same time, the ability of the body to inhibit glycogen release from the liver and muscles will also decrease, causing a continued increase in the level of blood glucose. With progression of the disease and the continuous presence of insulin resistance, pancreatic β cells will gradually degenerate and reduce their insulin secretion. The results of this study showed that, compared with the control group, patients in the study group were associated with a significantly elevated concentration of fasting blood glucose and HbA1c. This suggests that the presence of insulin resistance in diabetic patients seriously affects the level of blood glucose.

Instability of the tear film will further increase the hypertonic pressure of tears to form a vicious circle. In addition to hypertonic tear, instability of the tear film can also be induced by dry eyes, allergies, preservatives in ophthalmic formulations, or the use of contact lenses. Epidermal damage caused by dry eyes will stimulate the endings of corneal nerves to trigger eye discomfort and to increase the number of eye blinks. In addition, dry eyes can cause compensatory reflex lacrimal tear secretion. The reduction of mucin on the ocular surface will increase its friction with the medial side of the eyelid, thus aggravating and increasing discomfort in the eyes [14, 15]. Furthermore, diabetes mellitus can affect the quality and quantity of tear film. A previous study has shown that the function of tear film in diabetic patients could be affected by many factors including poor control of blood glucose and peripheral nervous diseases [16, 17]. It has also been shown that the quality of tear secretion in diabetic mice was significantly reduced, accompanied by atrophy of the lacrimal gland and weight loss of the tear gland [18]. The results of this study showed that the mean TBUT in patients with type-2 diabetes mellitus was 6.31±2.27 s, significantly shorter than the value of 13.26±2.65 s in non-diabetic patients. In addition, the average moisture length of SIt in the study group was 8.68±3.79 mm, also significantly lower than the value of 12.26±4.49 mm in the control group. The FL score of the study group was 1.86±1.28 points, significantly higher than the result of 0.52±0.18 points in the control group. These results are similar to those obtained by previous studies [19, 20]. In addition, the results from multivariate logistic regression analysis of this study show that risk factors for dry eye syndrome in type-2 diabetic patients include age, the duration of diabetes, TBUT, and HbA1c. The results also suggest the presence of significant lesions on the ocular surface of diabetic patients.

In summary, type-2 diabetes mellitus demonstrates a certain correlation with dry eye syndrome. Therefore, possible diseases of the ocular surface should be considered when ophthalmologists perform routine examinations in diabetic patients, ensuring that timely and effective treatment can be prescribed. However, this study has not discussed the specific mechanisms underlying dry eye syndrome in diabetic patients. These mechanisms require further study in future experiments.

Disclosure of conflict of interest

None.

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