Diagnostic value of tear films tests in type 2 diabetes

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Abstract

Objective: To compare the diagnostic value of Schirmer's tests, Rose Bengal test, and Tear Film Breakup Time test in patients with type 2 Diabetes.

Methods: Two hundred eyes of 100 patients were seen at the department of ophthalmology, Baqai Medical University Hospital who presented with complaints of redness and burning sensation and were aged between 45 to 75 years. Any history of systemic illness was recorded such as diabetes mellitus and hypertension. All subjects underwent routine ophthalmic examination and tear film tests such as Schirmer's test, Rose Bengal test and tear film break up time test.

Result: Total numbers of eyes subjected to Tear Film Tests were 200, of which 92 (46.0%) belonged to patients with type 2 Diabetes. Schirmer's test was positive in 56 (60.86%) eyes of Rose Bengal test was positive in 80 (86.95%) eyes and Tear film break up time test was positive in 50 (54.34%) eyes. Among non diabetics Schirmer's test was positive in 30 (68.18%) eyes, Rose Bengal test was positive in 10 (22.72%) eyes and tear film break up time test was positive in 24 (54.54%) eyes.

Conclusion: Keratoconjunctivitis sicca is another manifestation of Diabetes Mellitus. The ocular surface disease could be confirmed by performing multiple tear film tests. Among these tests Schirmer's test and Rose Bengal test have more diagnostic value in patients with type 2 diabetes as compared to Tear Film Break - up time test (JPMA 57:577;2007).

Introduction

The term dry eye and keratoconjunctivitis sicca (KCS) are synonymous.[1] Dry eye affects 10% to 15% of adults.[2] It refers to disorder of tear film caused by reduced tear production, poor tear quality or excessive tear evaporation.[3] A diagnostic classification scheme for dry eye disorders has been established which separates patients with dry eye into those who have aqueous tear deficiency and those with evaporative loss.[2]

The normal tear film on the surface of the eye is made up of three layers. The outer most the lipid layer secreted by meibomian glands, dysfunction of which results in evaporative dry eye. Middle aqueous layer secreted by the lacrimal gland, deficiency of this layer results in hyposecretive dry eye and inner most is the mucin layer secreted by the conjunctival goblet cell, crypts of Henle and glands of Manz. Deficiency of this layer is the feature of both hyposecretive and evaporative state.[1] Patients suffering from dry eye syndrome often complain of foreign body sensation, discomfort, redness and irritation. Many patients suffering from diabetes mellitus which is a systemic disease often complain of burning and foreign body sensation which are the symptoms of dry eye syndrome.[3] The tear film of diabetic patients has been reported to be unstable.[4] Diabetes mellitus affects eye in many ways such as diabetic retinopathy, neovascular glaucoma, cataract, refractive errors[5] and keratoconjunctivitis sicca.[3]

The aim of this study was to determine that from the three tear film tests, Schirmer's test, Rose Bengal test and Tear Film Break - up Time test, which had a greater diagnostic value for diagnosing keratoconjunctivitis sicca in patients with type 2 diabetes. Early diagnosis prevents corneal complications as persistent epithelial defects, recurrent corneal erosions and corneal ulceration.[4]

Patients and Methods

This cross sectional study included 100 patients (48 males, 52 females) selected from the out patient department of Baqai Medical University Hospital between January 2001 and December 2002, presenting with redness and burning sensation in the eyes. Out of these 100 patients 46 had type 2 diabetes and 54 patients were non - diabetics. To confirm the presence of diabetes among these 46 patients fasting blood glucose level was performed (normal limit $\leq$ 110 mg/dl).

These patients were not previously diagnosed of having dry eye syndrome. All patients aged below 45 years age and using topical medication within past three months were excluded from the study.

Routine ophthalmic examination was performed. Visual acuity was recorded by using Snellen's chart. Slit lamp (Nidek SL - 450) examination was performed with particular attention to lid margin, bulbar and tarsal conjunctiva and cornea. Binocular fundus examinations was carried out in each patient. Tear film tests, as Schirmer's test, Rose Bengal test and Tear film break - up time test were performed on these eyes.

Schirmer's test was performed by placing sterile Schirmer tear test strips 5mm x 35mm (Clement Clarke) after instillation of proparacaine hydrochloride 0.5 % (Alcaine - Alcone Couvreur Belgium),. The strips were placed in the lower fornix near the lateral canthus away from cornea and left in place for 5 minutes with eyes closed. The strip was removed after 5 minutes and length of wetting of filter paper was determined with a measuring scale. Both eyes were tested simultaneously. The test results were considered positive if length of wetting obtained was less than 5 mm or required more than 5 minutes.

Tear film breakup time test measurement was performed using fluorescein strips (Fluorets strips by Chauvin Pharmaceuticals Ltd), which were introduced in the conjunctival sac with minimal stimulation. The patient was asked to blink several times and then to keep the eyes open. Cornea was examined under cobalt blue filter on slit lamp. The dry area was indicated by the presence of a black spot. The time between the last blink and the appearance of a random dry spot was recorded in seconds as the tear film breakup time. The test was repeated three times and average was recorded. The test was considered positive if average tear film breakup time was less than 10 seconds.

Rose Bengal staining of the conjunctival was performed by using sterile Rose Bengal paper strip (Sno - strips by Chauvin Pharmaceutical Ltd) from which it was released by a drop of saline. After instilling topical anaesthetic drops (Alcaine), the strips were placed in the inferior fornix of each eye and then eyes were examined after removing the strips on the slit lamp to see any staining of conjunctiva and cornea. Staining of bulbar conjunctiva in nasal and temporal regions was taken into consideration. Any staining in inferior fornix was ignored. The Oxford grading scheme[6] was used for grading ocular surface damage. The grading chart is made up of five panels, each of which represents typical gradations of stain on either cornea or conjunctiva. Grading is done as 0, I, II, III, IV and V depending on number of dots per panel. Minimum being grade 0 and maximum score is V.

Statistical analysis was done by SPSS version 12. Sensitivity and specificity of Rose Bengal Test and Tear Film Break - Up Time Test was calculated taking Schirmer's test as gold standard.

Results

Out of hundred patients aged between 45 to 75 years, 52 were females and 48 were males. Type 2 diabetes was present in 46 patients (30 males and 16 females). Of the 54 non diabetics, 18 were males and 36 were females. Total number of eyes subjected to slit lamp examination and diagnostic tests were 200. Ninety-two eyes (46%) belonged to Diabetic patients, duration of Diabetes varied between 1 and 20 years. Thirty patients (65.21%) had good control of their diabetes. Eight eyes (8.69%) had non - proliferative diabetic retinopathy and four eyes (4.34 %) had proliferative diabetic retinopathy. Thirty four eyes (36.95%) did not show diabetic retinopathy. Slit lamp examination did not reveal any co-existent conjunctivitis or any other ocular surface disease. Among 92 eyes of diabetic patients, Schirmer's test was positive in fifty six (60.86%) eyes, Rose Bengal test was positive in eighty eyes (86.95%) and Tear film break up time test was positive in fifty eyes (54.34%). Among non diabetic patients, forty-four eyes (40.74%) had positive tests and in sixty-four eyes (59.25%) all tests were negative. Schirmer's test was positive in thirty eyes (68.18%), Rose Bengal test was positive in ten eyes (22.72%) and tear film break up time test was positive in twenty four eyes (54.54%) (Table 1). Among diabetic patients forty eight eyes had Schirmer's test and Rose Bengal test positive and twenty six eyes had Schirmer's and Tear Film Break - Up Time test positive (Table 2).

Taking Schirmer's test as gold standard, sensitivity of Rose Bengal test was 85.71% and specificity was 11.11%. Sensitivity of Tear Film Break - Up Time test was 46.42% and specificity was 33.33% (Table 3).

Table 1. Eyes with positive diagnostic tests

	Diabetic	Non - Diabetic
Schirmer's test	56 (60.86 %)	30 (68.18%)
Rose Bengal test	80 (86.95 %)	10 (22.72 %)
TBUT	50 (54.34 %)	24 (54.54 %)

TBUT = tear breakup time

Table 2. Validity of rose Bengal and tear break - up time test in type 2 diabetic patients

	Schirmer's +ve	Schirmer's -ve
Rose Bengal test +ve	48	32
Rose Bengal test -ve	08	04
TBUT test +ve	26	24
TBUT test -ve	30	12

TBUT = tear breakup time

Table 3. Sensitivity and specificity of rose Bengal and tear break - up time Test in Type 2 diabetic

Tests	Sensitivity	Specificity	PPV	NPV
Rose Bengal test	85.71%	11.11%	60.0%	33.33%
TBUT	46.42%	33.33%	52.0%	24.0%

TBUT = tear breakup time PPV= positive predictive value NPV= negative predictive value

Discussion

Dry eye is a disorder of tear film because of tear deficiency or excessive tear evaporation which causes damage to the inter palpaberal ocular surface and is associated with symptoms of ocular discomfort.[7] This ocular disorder is very common among general population with 28% of the adults having dry eye syndrome.[8] Early diagnosis and timely treatment, complications as secondary microbial infection and corneal ulceration could be avoided.[9]

Etiological factors for dry eye syndrome are: increasing age, when the secretion of tears from the lacrimal gland decreases and reaches a borderline at 60 years of age. Hormonal changes, commonly seen among menopausal women related to reduced level of androgens produced by the ovaries, autoimmune diseases as Sjogren's syndrome, cicatricial pemphigoid, and erythema multiforme. Pharmacological agents as antidepressants, anxiolytics, antihistamines, anticholinergics, antihypertensives, antipsychotics, antiparkinsonians, diuretics and vitamin A deficiency cause dry eyes.[10] Vitamin A has a specific effect on mucin production by the epithelium. Mucin is the agent responsible for wetting of the corneal surface and its deficient production affects tear film stability.[11] Dry eye can also be caused by inflammatory diseases or trauma to the lacrimal gland responsible for secretion of tear film constituents. Deficit afferent innervation due to trigeminal anaesthesia, contact lens wear and following laser in situ keratomileusis (LASIK) and deficit efferent innervation due to facial nerve paralysis often results in dry eye symptoms. Corneal defects as corneal epitheliopathy or corneal dystrophy and eyelid disorders as ectropion and lagophthalmos causes failure of tears to spread over the ocular surface resulting in dry eye syndrome. The term "dry eye" may be applied to three different conditions (i) The symptom is ocular dryness (ii) The syndrome is the group of associated clinical manifestations: itching, redness, foreign body sensation, photophobia, and blepharospasm (iii) A large variety of diseases are associated with dry eye and include blink disorders, trachoma and blepharitis.[10] Blepharitis causes dysfunction of meibomian glands and lipid component of the tear film as a result tear evaporation increases hence leading to dry eyes.[12]

Dry eye is a significant feature of diabetes mellitus[13], in which accumulation of sorbitol by the action of aldose reductase on excess glucose contributes to the alteration in epithelium and endothelium and corneal hypoasthaesia.[14] In Pakistan the prevalence of Type 2 Diabetes is 10% in age

group 25 and above.[15]

Patients with diabetes have dry eye syndrome more often than those without diabetes.[8] Diabetes mellitus is a systemic disease which is often accompanied by microvascular complications such as neuropathy, nephropathy and retinopathy.[13] The prevalence of diabetic microvascular complications is higher in patients with longer duration of diabetes.[16] These individuals are at an increased risk of developing dry eye syndrome. Seifart and associates demonstrated that diabetic patients had an increased rate of Keratoconjunctivitis sicca, which may be attributed to decreased corneal sensitivity, neuropathy involving innervation of lacrimal glands and loss of goblet cells.[13]

According to a Canadian dry eye epidemiology study, 37% of patients with diabetes have dry eye symptoms.[8] The ocular complications which occur in association with diabetes mellitus can lead to blindness. Schultz et al reported 47% to 64% of diabetic patients having corneal lesions as persistent epithelial defects, delayed epithelial healing, corneal ulceration and Keratoconjunctivitis sicca. Structural, metabolic and functional abnormalities are found in the conjunctiva and cornea of diabetic patients. These abnormalities may be responsible for clinical corneal manifestation of diabetes. The tear film has also been reported to be unstable.[4]

Diabetic patients often complain of dry eye symptoms as burning and foreign body sensation.[5] Most of our patients aged between 45 to 75 years presented with complaints of redness and burning sensation. Of these 100 patients, 52 were females and 48 were males. Moss and associates have also reported a high incidence of dry eye among females 16.7% compared to males 11.4%.[3] Nepp and associates have shown that severity of Keratoconjunctivitis sicca correlates with severity of diabetic retinopathy.[17] No such relation was found in our study, where of the 46 diabetic patients, 12 had diabetic retinopathy.

Most of our diabetic patients had fasting blood glucose level between 120 mg/dl to 180 mg/dl (normal limit = 110 mg/dl), showing that these patients did not have a good glycaemic control. Kaiserman and associates have reported that good blood sugar regulation is important for prevention and control of dry eye syndrome among diabetic patients.[3] Most of our diabetic patients had a fasting blood sugar level more than 110 mg/dl, depicting a poor glycaemic control.

We performed tear film tests such as Schirmer's test, Rose Bengal test and Tear Film Break up time test on 200 eyes of these 100 patients. In our diabetic patients, 60.86 % of the eyes had a positive Schirmer's test. This could be attributed to the damage of microvasculature of the lacrimal gland, with autonomic neuropathy leading to impaired function of the lacrimal gland. Goebbel has reported that the Schirmer's test reading is significantly reduced among diabetics.[5] Of the 108 non diabetic eyes 44 had positive tear film tests and Schirmer's test was positive among 68.18% eyes. This indicates that in people over 45 years, the tear secretion decreases. Kaiserman et al.[3] have also reported that the prevalence of dry eye increases with age.

Rose Bengal staining was positive among 86.95% eyes of diabetic patients as compared to 22.72% of eyes in non-diabetics. In diabetes goblet cell density is significantly reduced, especially patients with neuropathy. Goblet cell densities did not co-relate with the duration of diabetes, as reported by Dogru et al. Goblet cells are the major source of mucin in tear film. Loss of mucin layer results in involvement of conjunctival and corneal epithelial surface.[4] Rose Bengal stain has an affinity for dead and devitalized epithelial cells[1] so a higher percentage of diabetics had a positive test.

Tear Film Break - Up Time test was positive among 54.34 % of diabetic eyes and 54.54% non diabetic eyes, there is not much difference between the two groups. This is a very non-specific test for determination of tear film stability[5]; it indicates the integrity of the lipid layer of tear film which may also be affected in meibomian gland dysfunction.[12]

Conclusion

The study shows that Keratoconjunctivitis sicca (KCS) is another manifestation of type 2 Diabetes. The ocular surface disease in diabetes characterized by disorder of tear film could be confirmed by performing multiple tear film tests. Among these taking Schirmer's test as gold standard, the sensitivity of Rose Bengal tests was 85.71% indicating that it has more diagnostic value among patients with type 2 diabetes, as compared to Tear Film Break - up time test. Neither duration of diabetes nor stage of retinopathy correlates with tear film dysfunction. Good glycemic control is important for prevention and control of dry eye syndrome.

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