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The Relationship between Metabolic Syndrome, Its Components, and Dry Eye: A Cross-Sectional Study

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ABSTRACT

Purpose: The aim of this study was to evaluate tear osmolarity and tear film function and ocular surface changes in patients with metabolic syndrome.

Methods: 108 eyes of 64 patients with metabolic syndrome (group 1) and 110 eyes of 55 healthy individuals (group 2) were included in this cross-sectional study. All participants were evaluated using the Ocular Surface Disease Index (OSDI) questionnaire, Schirmer I test, tear film break-up time (TBUT), and tear osmolarity. Main outcome measures were Ocular Surface Disease Index (OSDI) questionnaire, Schirmer I test, tear film break-up time (TBUT), and tear osmolarity values.

Results: Tear osmolarity values and OSDI scores were significantly higher in group 1 (314.4 ± 19.1 mOsm and 38.9 ± 1.1, respectively) compared with group 2 (295 ± 14.3 mOsm and 18.69 ± 17.2, respectively) ($p = 0.01$ for both). The Schirmer test values and TBUT in group 1 (10 ± 3.7 mm and 14.8 ± 3.6 sec, respectively) were significantly lower compared with group 2 (16.8 ± 2.6 mm and 18.1 ± 0.5 sec, respectively) ($p < 0.001$ for both). There was significant correlation between tear osmolarity versus waist circumference and fasting blood glucose in the study group ($r = 0.364$, $p = 0.04$; and $r = 0.542$, $p \leq 0.001$, respectively).

Conclusions: This study showed that metabolic syndrome can influence tear osmolarity and tear film function. Patients with metabolic syndrome showed tear hyperosmolarity and tear film dysfunction.

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Dry eye; metabolic syndrome; Schirmer test; tear osmolarity; tear film

Introduction

Metabolic syndrome is becoming a worldwide medical and public health challenge as it has been seen increasing in prevalence over the years.[1] This is a syndrome which has components such as dyslipidemia, high blood pressure, and high fasting plasma glucose.[2] The etiology of metabolic syndrome mainly consists of two conditions: body fat accumulation which causes adult weight gain and dislocation of fat (central obesity) in intra-abdominal areas including liver, pancreas, and heart. The individuals who have metabolic syndrome are at great risk for diabetes, cardiovascular, and cerebrovascular disease.[3,4]

Some studies reported associations between components of the metabolic syndrome and eye diseases such as cataract, age-related macular diseases, and glaucoma.[5–8] Only one study investigated lacrimal function in patients with metabolic syndrome.[9] The authors stated impairment in lacrimal gland functions and tear volume in these patients.

Schirmer I test, tear break-up time (TBUT), and ocular surface fluorescein staining score are the most frequently used tests in diagnosis and follow-up of dry eye disease. Tear osmolarity is valuable method for detecting dry eye. At the present time, by understanding the importance of tear hyperosmolarity in dry eye pathogenesis, tear osmolarity measurement has started to be used in clinical application.[10]

In this study, we investigated the tear osmolarity and tear film function in patients with metabolic syndrome.

Materials and methods

A total of 128 eyes of 64 patients with metabolic syndrome (group 1) and 110 eyes of 55 healthy individuals (group 2) were included in this single-center, cross-sectional observational study. Right eye data for each patient were assessed.

Patients in group 1 were newly diagnosed with metabolic syndrome by an internal specialist (O.O.). The diagnosis of metabolic syndrome was established by the International Diabetes Federation.[4] According to the new IDF definition, for a person to be defined as having the metabolic syndrome, they must have: central obesity (waist circumference >80 cm for female and >94 cm for male) and any of the these two followings raised triglycerides; ≥150 mg/dl or specific treatment for this lipid abnormality, reduced HDL cholesterol; < 40 mg/dL in males, < 50 mg/dL in females or specific treatment for this lipid abnormality, raised blood pressure; systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg or treatment of previously diagnosed hypertension, raised fasting plasma glucose; ≥ 100 mg/dL, or previously diagnosed type 2 diabetes.

All subjects were excluded if they had a history of smoking, current or recent drug use that could affect the lacrimal

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Table 1. Comparison of metabolic syndrome components between two groups.

	Metabolic syndrome group mean ± SD	Control group mean ± SD	P* value
Waist circumference (cm)			<0.001
male	102.4 ± 4.7	89.4± 6.4	
female	89.3 ± 5.4	72.9 ± 7.5	
Systolic blood pressure (mmHg)	132 ± 27.3	103 ± 10.5	<0.001
Diastolic blood pressure (mmHg)	80 ± 15	69 ± 6	<0.001
HDL (mg/dl)	39.6 ± 13.8	54.3 ± 4.3	<0.001
Triglycerides (mg/dl)	176.8 ± 11.2	92 ± 6.8	<0.001
Fasting blood glucose (mg/dl)	108 ± 19	83 ± 3.6	<0.001

SD = Standard Deviation.
*Independent *t*-test.

Table 2. The comparisons of the mean tear film parameters and OSDI scores between two groups.

Parameter	Group 1	Group 2	P value*
Tear osmolarity (mOsm/L)			<0.001
Mean ± SD	314.4 ± 19.1	295 ± 14.3	
Schirmer test (mm)			<0.001
Mean ± SD	10 ± 3.7	16.8 ± 2.6	
TBUT (second)			<0.001
Mean ± SD			
Range	14.8 ± 3.6	18.1 ± 0.5	
OSDI			<0.001
Mean ± SD			
Range	38.9 ± 1.1	18.69 ± 17.2	

SD = standard deviation; TBUT = tear film break-up time; OSDI = ocular surface disease index.
*Independent samples t-test.

functional unit, active ocular infection or allergy, ocular surface scarring, previous eye surgery, or current contact lens or any eye drop use. Any systemic disease other than metabolic syndrome was the other exclusion criteria in the study group. Healthy control subjects were first examined by O.O. for routine check-up, after exclusion metabolic syndrome or any other systemic diseases, and were referred to ophthalmology department.

The study was reviewed and approved by the Istanbul Medipol University Ethics Committee, and written informed consent was obtained from each patient before enrollment. The study was conducted in accordance with the tenets of the Declaration of Helsinki.

Initially, patients completed the International Ocular Surface Disease Index (OSDI) survey. All subjects underwent a full ophthalmological examination in the same order, including visual acuity assessment, standardized slit-lamp examination, and fundus examination. Full ophthalmologic examination and evaluation of tear osmolarity were performed on the same day but at different sessions.

Tear osmolarity measurements were evaluated using a TearLab osmometer (TearLab Co, San Diego, CA, USA). Tears were collected from the inferior lateral tear meniscus. Three consecutive measurements were obtained, and their mean was used for statistical analysis.[11]

Tear film break-up time was assessed after instillation of 2% fluorescein staining under a cobalt blue filter. The time interval between the last complete blink and the appearance of the first dry spot was recorded. The mean of three consecutive measurements was obtained. The Schirmer I test was performed with topical anesthesia using a standardized filter strip (Bio-Tech Vision Care, Ahmedabad, Gujarat, India). The amount of wetting was measured after five minutes.

The normality of the distribution of each of the parameters was checked using the Kolmogorov–Smirnov normality test. The tear osmolarity, Schirmer I test, TBUT values, and OSDI scores between groups were compared using independent *t*-test. The correlations between each component of metabolic syndrome and tear osmolarity were evaluated using the Pearson's partial correlation controlled for gender. A p value less than 0.05 was considered statistically significant.

Results

The mean subject age was 47 ± 7years (range 32 to 58 years) in group 1 (32 females, 32 males) and 45 ± 7 years (range 31 to 59 years) in group 2 (28 females, 27 males). There were no significant differences between the groups with respect to age or sex ($p = 0.741$ and $p = 0.921$, respectively). Comparison of metabolic syndrome components between two groups was given in Table 1.

Summary statistics are shown in the Table 2. The mean tear osmolarity and OSDI scores were significantly higher in group 1 compared with group 2 ($p = 0.01$). The TBUT and Schirmer measurements for group 1 were significantly lower compared with those for group 2 ($p < 0.001$).

As regards the correlations between tear osmolarity and metabolic syndrome components, there was significant correlation between tear osmolarity versus waist circumference and fasting blood glucose ($r = 0.234$, $p = 0.04$; and $r = 0.542$, $p \leq 0.001$, respectively), whereas no significant correlation was found between tear osmolarity versus triglycerides, HDL and hypertension in the study group ($r = 0.231, 0.642, 0.356$, respectively, $p > 0.05$). No significant correlations were found among tear osmolarity versus waist circumference, fasting blood glucose, triglycerides, HDL, and hypertension in the control group ($r = 0.435, 0.347, 0.566, 0.678, 0.788$, respectively, $p > 0.05$)

Discussion

Metabolic syndrome is becoming a serious worldwide health problem. Its prevalence has been increasing year by year. The IDF estimates that approximately one-quarter of the world population has metabolic syndrome. Although there are different definitions of metabolic syndrome, all these definitions basically agree on the major components which are hyperglycemia, obesity, dyslipidemia, and hypertension.

The pathogenesis of metabolic syndrome is thought to result primarily from obesity. The IDF definition places obesity as the required criterion. Therefore, the IDF definition is the most accepted definition worldwide.[12] In our study, we also used the IDF definition.

There are numerous studies reported associations between the individual components of the metabolic syndrome and ocular diseases.[5–8] Several studies showed that metabolic syndrome was associated with diabetic retinopathy. An

association between metabolic syndrome and cataract has also been reported in large series.[5]

Previously only one study by Kawasaki et al mentioned tear film dysfunction in patients with metabolic syndrome.[9] They reported that patients with metabolic syndrome have dry eye risk approximately twofold than controls. In this valuable study, tear volume was measured using the Schirmer 1 method. Patients with metabolic syndrome had significantly lower Schirmer values.

In our study, we also found significantly lower Schirmer values in patients with metabolic syndrome compared to controls. Additionally, we assessed tear film functions in patients with metabolic syndrome using tear osmolarity, tear film break-up time, and ocular surface disease index. When comparing risk factors for dry eye, among the components of metabolic syndrome, we found that obesity and hyperglycemia were associated with tear osmolarity.

Dry eye has been shown to be associated with inflammatory changes in the entire ocular surface including the adnexa, conjunctiva, and cornea. It is known that metabolic syndrome may cause increased inflammation and oxidative stress.[13] This pathologic effect of metabolic syndrome may provide a potential explanation for tear film abnormalities in patients with metabolic syndrome. The other explanation is decreased tear production in these patients. Both insufficient tear production and excessive tear evaporation cause tear hyperosmolarity. Dry Eye Workshop Report reported tear osmolarity as the single best marker for dry eye disease.[14] New instruments such as the TearLab™ Osmolarity System offer quick and reliable measurements of tear osmolarity at clinical practice.

This study has some limitations such as small number of patients, the quantitative studies of conjunctival goblet cells, and meibography. Further studies with larger number of patients especially will be required to clarify this issue.

Overall, our study shows that metabolic syndrome components obesity and hyperglycemia are significant risk factors for tear film abnormalities. We conclude that routine eye examinations are necessary in patients with metabolic syndrome, for early detection of subclinical ocular surface diseases. Secondly, tear osmolarity, a noninvasive method for detection of dry eye, can be checked easily to rule out dry eye in patients with metabolic syndrome.

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