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Elevated monocyte to HDL ratio as a new inflammatory marker in patients with dry eye

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Abstract

Purpose: To assess the monocyte-to-high density lipoprotein (HDL) cholesterol ratio (MHR) as a marker of inflammation in patients with Sjögren syndrome dry eye (SSDE) and non-Sjögren syndrome dry eye (NSSDE), and in healthy controls.

Methods: The MHR and C-reactive protein (CRP) values were evaluated in 68 patients with SSDE, 72 patients with NSSDE, and 70 healthy controls. The MHR was calculated by dividing the monocyte count by the HDL.

Results: Demographic properties of the patients were similar among the groups. The mean MHR value was 15.8 ± 8.6 in SSDE, 12.4 ± 7.7 in NSSDE, and 7.7 ± 5.4 in control group ($p < 0.001$). The mean CRP value was 3.2 ± 1.4 in SSDE, 2.9 ± 1.1 in NSSDE, and 1.2 ± 0.6 in control groups ($p = 0.012$).

Conclusion: The MHR values were found to be higher in patients with SSDE and NSSDE. Also, a correlation was deteceted between MHR and CRP values. According to these results, both of dry eye groups may be associated with systemic inflammation.

Introduction

Dry eye disease (DED) is one of the most common ocular pathology in the world. Although, DED is a multifactorial disease, clinical and laboratory studies have shown that chronic immunological mechanisms have a very important role in pathogenesis [1]. DED is characterized not only local but also systemic inflammation [2-4].

Recently, the monocyte-to-high density lipoprotein (HDL) cholesterol ratio (MHR) is considered as a new marker of systemic inflammation due to proinflammatory effects of monocytes and the anti-inflammatory effect of HDL, and investigated in many well known diseases [5-8].

The aim of this study was to evaluate MHR as an indicator of systemic inflammation in patients with primary Sjögren syndrome dry eye (SSDE) and non-Sjögren syndrome dry eye (NSSDE).

Materials and methods

A cross-sectional study was conducted at the Ophthalmology Department of Ankara Ataturk Training and Research Hospital between June 2018 and November 2018. The study was performed in accordance with the Declaration of Helsinki and approved by the local ethics committee. Informed consent was obtained from all participants

Sixty-eight patients with SSDE, 72 patients with NSSDE, and 70 healthy controls were enrolled. Patients with primary Sjögren's syndrome who were diagnosed at least for one year according to the American-European Consensus Group criteria [9] were included in this study. NSSDE group consisted of patients who had dry eye and no rheumatologic disease.

Because primary Sjögren syndrome has a female-to-male predominance of 9:1, only women patients were enrolled in this study.

DED was evaluated according to 3 criteria: (1) DED symptoms were defined according to the ocular surface disease index (OSDI) questionnaire [10] (12 items of the OSDI quastionnaire which were translated to Turkish used to evaluate the symptoms of eye-related irritation and the effect on visual acuity. Each item was graded on a scale of 0 to 4. The total OSDI score of each patient was calculated as follows; OSDI score = Total score in all answered questions × 100/Total number of questions answered × 4. An OSDI score ≥ 13 was accepted as the cutoff value for DED; (2) abnormal tear function tests in terms of Schirmer I test (without anesthesia) was ≤ 5 mm/5 minutes and/or break up time < 10 seconds; and (3) abnormal ocular surface staining patterns according to Oxford grading scheme [11]. Tear break up time was repeated a total of three times and the average was considered the final result. All evaluations of the ocular surface were done by one ophthalmologist (NY).

Control group consisted of patients who were applied for preoperative evaluation for upper eyelid blepharoplasty surgery with no

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ocular and systemic disease. All of the healthy subjects had OSDI score < 13; Schirmer I test > 10 mm/min; tear break up time > 10 seconds and no fluorescein staining of the cornea.

Exclusion criteria were any previous ocular surgery, meibomian gland disease which may cause dry eye, blepharitis, allergic conjunctivitis, glaucoma, uveitis, or use of contact lens and topical drops other than artificial eye drops in the previous six months, a systemic disease such as diabetes mellitus, uncontrolled hypertension, hyperlipidemia, thyroid abnormalities, other rheumatologic disease, current treatment with any systemic medications which may affect blood parameters especially antihyperlipidemia therapy, smoking and alcohol comsumption.

After detailed ophthalmic examination, the blood biochemistry and hematology profile, and serum C-reactive protein (CRP) were measured.

Blood samples were obtained by venipuncture after a fasting period of at least 12 hours. Peripheral blood count parameters, HDL and CRP levels were recorded. The MHR was calculated for each individual by dividing their monocyte count with their HDL-C level.

Statistical analysis

Statistical analysis of the data obtained in this study was performed using the Statistical Package for Sciences (SPSS) software for Windows, version 20 (SPSS Inc.,Chicago, IL, USA). Normality of the data was assessed by the Kolmogorov-Smirnov test. Among the 3 groups, categorical variables were compared with Chi-square test and continuous variables were compared with Kruskal-Wallis analysis of variance. Pearson correlation test was used for correlation analysis. A *P*-values less than 0.05 were considered as statistically significant.

Results

The mean age of subjects was 57.2 ± 6.2 years (range: 42-74) in SSDE group, 54.7 ± 4.4 years (range: 40-76) in NSSDE group, and 56.6 ± 2.4 years (range: 42-76) in control group (p = 0.521). The mean OSDI scores, the Schirmer I test and tear break up time values, Oxford grading scores of the groups are summarized in Table 1.

The mean MHR value was 15.8 ± 8.6 in SSDE, 12.4 ± 7.7 in NSSDE, and 7.7 ± 5.4 in control group (p < 0.001). The mean MHR values were significantly higher in SSDE group than NSSDE group (p = 0.011). The mean MHR values of both SSDE and NSSDE groups were significantly higher than control group (p < 0.001, p < 0.001; respectively) (Table 2).

The mean CRP value was 3.2 ± 1.4 in SSDE, 2.9 ± 1.1 in NSSDE, and 1.2 ± 0.6 in control groups (p < 0.001). The mean CRP values were found significantly higher in SSDE group than NSSDE group (p = 0.041). The mean CRP values of both SSDE and NSSDE groups were significantly higher than control group (p = 0.002, p = 0.003; respectively) (Table 2).

In the correlation analysis, the MHR was positively correlated with CRP in SSDE and NSSDE groups (r = 0.321, p = 0.021; r = 0.298, p = 0.024; respectively).

Table 1. Dry eye examination parameters of study groups

	SSDE	NSSDE	Controls	p
OSDI Score	44.6 ± 6.9[a]	41.4 ± 4.6[a]	6.1 ± 1.8	< 0.001
Schirmer I	3.7 ± 0.9[a]	4.1 ± 1.1[a]	16.1 ± 1.2	< 0.001
TBUT	5.5 ± 1.7[a]	5.7 ± 1.5[a]	11.1 ± 0.9	< 0.001
Corneal Staining score	3.1 ± 0.3[a]	2.6 ± 0.4[a]	0.0 ± 0.0	< 0.001

Versus controls, [a]p < 0.05

Table 2. MHR and CRP values of study groups

	SSDE	NSSDE	Controls	p
MHR	15.8 ± 8.6[a]	12.4 ± 7.7[a, b]	7.7 ± 5.4	< 0.001
CRP	3.2 ± 1.4[a]	2.9 ± 1.1[a, b]	1.2 ± 0.6	< 0.001

Versus controls, [a]p < 0.05
Versus SSED group, [b]p < 0.05

Discussion

Today, DED is known as a complex disease that affects many people and causes a decrease in quality of life [12]. Although the etiology has not been fully elucidated; inflammation takes place in the center of complicated pathologic mechanisms. There are many studies showing the presence of increased inflammatory cytokines in the conjunctival epithelium and tear [13,14]. Although NSSDE is known as a localized inflammatory condition, systemic inflammation may have a role in the pathogenesis like some other eye pathologies such as pseudoexfoliation syndrome. Although there is no strong scientific evidence, there are studies suggesting that systemic nutritional support may be useful in controlling systemic inflammation in DED [15,16].

Monocytes play an important role in the release of pro-inflammatory and pro-oxidative cytokines in inflammatory conditions [17]. High-density lipoprotein (HDL) cholesterol molecule shows anti-inflammatory properties by inhibiting migration of monocytes in response to oxidized low-density lipoprotein (LDL), expression of endothelial adhesion proteins, and stimulating reverse transport of oxidized molecules [18]. In the light of these, MHR arose as a novel indicator of inflammation, which can be calculated by dividing the increased monocytes in inflammation by the anti-inflammatory HDL.

In this present study, MHR was evaluated as a different systemic inflammation marker in both SSDE and NSSDE patients and the MHR values were higher compared to controls. When these two different DED groups related to different etiologies were examined in their own, MHR values were higher in patients with Sjögren syndrome which has systemic manifestations. According to these results, it may be suggested that Sjögren syndrome is characterized by more systemic inflammation. In the SSDE group, the serum CRP level was higher than the NSSDE group, which supported the increased value of MHR. In addition, there was a positive correlation between MHR and CRP levels in both DED groups.

Accordingly, after the cut off values have been determined, MHR may find a place in clinical use like CRP which is one of the well known markers of systemic inflammation. Sekeryapan *et al.* [19] evaluated neutrophil-to-lymphocyte ratio as a marker of systemic inflammation in NSSDE patients and found higher results than control group.

The present study had several limitations. First, the number of patients was relatively small. Second, patients with secondary SS should be evaluated as the other important casue of DED. Third, different systemic inflammatory markers other than CRP should be evaluated and correlation analysis should be done between them and MHR values.

In conclusion, MHR is a practical, cheap, simple marker of systemic inflammation in dry eye patients. In clinical practice, MHR can be easily computable so it provides clinicians an easy assessment of systemic inflammation. Further studies are needed to use MHR in assessing the disease prognosis and treatment response.

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