

Serum Endocan Levels in Patients with Retinal Vein Occlusion

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ABSTRACT

Purpose: We aimed to evaluate the serum Endocan (endothelial cell-specific molecule-1, ESM-1) levels in patients with retinal vein occlusion (RVO) and compare them with those of the control group to determine the correlation with illness activity

Materials and Methods: Venous blood samples were obtained from 43 patients with RVO and 43 healthy subjects who attended Atatürk University Medical Faculty Eye Diseases Polyclinic between 1 June 2015 and 1 September 2015. Thirty-one of the 43 patients had branch RVO, and 12 of the patients had central RVO.

Results: The mean age of the patients was 62±10,19, and the mean age of the control group was 60,27±5,53. Twenty-four of the 43 patients (54,5%) suffered from RVO in their right eyes, and 19 of the patients (43,2%) suffered from RVO in their left eyes. No statically significant differences in age and sex were observed between the patients and the control group. All patients had hypertension, and 15 patients had diabetes mellitus. Thirty 30 patients (68,2%) had ischemic-type RVO, 13 patients (29,5%) had nonischemic-type RVO. Thirty-one patients (70,5%) had branch RVO, and 12 patients (27,3%) had central RVO. Statically significant differences in serum level of ESM-1 were observed between the patients and the control group (p<0.05). A comparison of the ischemic-type RVO and the non-ischemic-type RVO in the patients group revealed statically significant differences in the serum ESM-1 level (p=0,003).

Conclusion: The comparison of the serum ESM-1 levels in patients with RVO with the control group can be a guiding parameter for showing the severity of disease.

Key Words: Endocan, retinal vein occlusion, diabetes mellitus, hypertension.

INTRODUCTION

Retinal vein occlusion (RVO) is the second most common retinal vascular disease after diabetic retinopathy (DRP)¹. RVO is a retinal disease that can cause severe vision loss in a significant proportion of patients and is diagnosed in 0.7-1.6% of the population. Retinal cell damage is caused by hydrostatic, mechanical and pharmacotoxicological effects in retinal vascular occlusion. The most common pathophysiological problems are ischemia, inflammation and metabolic changes in RVO.

RVO is mainly separated into three sub-sections due to the location of the occlusion: branch retinal vein occlusion (bRVO), central retinal vein occlusion (cRVO) and hemisphere venous occlusion. Furthermore, cRVO can be

evaluated according to the following clinical features: non-ischemic RVO, ischemic RVO and papillophlebitis.

Endocan, which is also referred to as endothelial cell-specific molecule-1 (ESM-1), is a unique soluble endothelial dermatan sulfate², which was first described in endothelial cell cultures in 1996³. ESM-1 is considered to be an endothelial cell marker, which demonstrates endothelial injury on a large scale of endothelium dependent diseases, such as cardiovascular diseases, and cancers⁴. Serum ESM-1 levels are related to the severity of disease and their consequences^{5,6}. Studies indicate that ESM-1 levels are elevated in the plasma of patients with inflammatory and tumor progression. This finding suggests that ESM-1 may be a potential indicator of endothelial cell activation or dysfunction⁷. ESM-1 is considered to have a

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role in vascular diseases, organ-specific inflammation, and endothelium-dependent pathologic disorders.

RVO is an ophthalmological disease in which ischemia and inflammation play a role. Our idea in the study is that inflammation and retinal ischemia seen in RVO may increase serum ESM-1 level, so that ESM-1 can be a biomarker in determining the severity of the disease. As far as we know, there has been no previous study examining retinal branch and central occlusions together. The study aimed to evaluate the serum ESM-1 levels in patients with RVO and compare it with control group.

MATERIAL AND METHODS

Our study comprised 86 volunteers, who attended Atatürk University Research Hospital Department of Ophthalmology from June to September 2015. Forty-three patients who had cRVO or bRVO and 43 participants without retinal disease, as the control group, were prospectively included in this study. The study was carried out with the B.30.2.ATA.0.01.00/ numbered approval of the Medical Research Ethics Committee of Atatürk University Faculty of Medicine.

The best corrected visual acuity (BCVA) (Snellen chart), intraocular pressure measurement (pneumotonometer), biomicroscopic examination of anterior segment and panfundoscopic examinations were performed by the same physician (Yildirim, M). Optical coherence tomography (OCT-OPTUVOUE) was performed for all patients to identify macular edema in 5 micron details..

Fundus fluorescein angiography (FFA-KOVA WX-10 α) was performed for each patient to distinguish ischemia. Eyes with ocular neovascularization or wider retinal nonperfusion area than ten disk area were considered to be ischemic. At the beginning of the FFA, a 4 ml blood sample was taken via an intravenous catheter. Subsequently, fluorescein was injected and angiography was carried out. The blood samples were centrifuged in convenient conditions in Atatürk University Medical Faculty Biochemistry Laboratory, and serum samples were stored at -80 °C until they were analyzed. Serum ESM-1 samples were measured by CUSABIO, Cat no: CSB-E16530h, CHINA kits.

Statistical analyses were performed using the SPSS 20.0 (SPSS, Chicago, IL, United States) program. The normal distribution suitability of the parameters was assessed by the Kolmogorov-Smirnov test. The t-test (independent test, Student's t-test) and one-way analysis of variance (ANOVA) were employed with independent samples to compare the serum ESM-1 values of patients and controls. The results were expressed as the mean \pm Standard deviation (SD).

The level of statistical significance between the groups was accepted as $p < 0,05$.

RESULTS

In the control group, all participants have 20/20 best corrected visual acuity (BCVA) and corrected intraocular pressure (IOP) according to the corneal thickness in the normal range (10-20 mmHg). Additionally, 15 of the 43 volunteers have posterior chamber intraocular lenses (PCIOL) since they underwent cataract surgery. Normal findings were observed in the fundus examination in all participants of the control group.

The lowest and BCVA in the patient (RVO) group was hand motion (20/25,000) and 20/32, respectively. The IOP measurements were between 10 mmHg and 20 mmHg in all patients. PCIOL were determined in 15 participants of the RVO group.

All patients have RVO in a single eye, and any other retinal vascular disease findings included the eyes. All participants in the RVO group were diagnosed with hypertension, and 15 RVO patients had diabetes mellitus.

bRVO was detected in 31 of the patients (70,5%), while only 12 of the patients (27,3%) had cRVO. According to the FFA, 30 cases (68,2%) involved ischemic-type RVO, and 13 cases (29,5%) involved non-ischemic-type RVO. None of the patients in the groups received laser therapy in the case of ischemia or intravitreal injection therapy in the case of macular edema. Patients who had previously undergone any of these treatments have been excluded from the study.

No statistically significant difference in demographic characteristics was observed between the patient group and the control group ($p > 0,05$) (Table 1).

In the patient group, serum ESM-1 levels were statistically significantly higher than those of the control group (Table 2).

Serum levels of ESM-1 were compared in patients with ischemic and nonischemic RVO. ESM-1 levels were significantly higher for the ischemic type (Table 3).

A comparison of serum ESM-1 levels between cRVO patients and bRVO patients showed that the difference between these groups was not statistically significant ($p > 0,05$) (Table 4)

CONCLUSION

Severe vision loss is not an unusual consequence in RVO cases. Macular edema, due to retinal hypoxia, mainly causes a decrease in vision.

Table 1. Demographic features of patient and control groups.			
Parameter	Patient	Control	P
Age	62.23±10.19	60.27±5.53	0.267
Gender (M/F)	25 / 18	24 / 19	0.977
Systemic Disease	43 HT/ 15 DM	Null	

HT: Hypertension, DM: Diabetes Mellitus.

Table 2. ESM-1 levels of patient and control groups.			
Parameter	Patient	Control	P
ESM-1 (ng/ml)	10.54 ±2.99	7.36±1.62	0.001

ESM-1: Endothelial cell- specific molecule- 1.

Table 3. Comparison of ESM-1 serum levels in ischemic and non ischemic RVO patients.			
Parameter	Ischemic RVO	Non-ischemic RVO	P
ESM-1 (ng/ml)	11.22±2.72	8.67±2.79	0.003

ESM-1: Endothelial cell- specific molecule- 1.

Table 3 4. Comparison of serum ESM-1 levels in CRVO and BRVO patients.			
Parameter	BRVO	CRVO	P
ESM-1 (ng/ml)	9.93±3.04	11.78±2.31	0.054

ESM-1: Endothelial cell- specific molecule- 1.

ESM-1, which can be detected in vascular circulation, is a biomarker that indicates endothelial cell activation and angiogenesis². ESM-1 allows adhesion and migration of leukocytes to activated vascular endothelium by facilitating the effect of VEGF-A on endothelial cell receptors and increasing the endothelial permeability⁸.

Kose et al. conducted a study of patients with acute coronary syndrome (ACS). According to this study, blood ESM-1 levels are higher in ACS patients who had DM than the non-diabetic ACS group. In this context, researchers asserted that vascular damage was intensified in DM⁹.

ESM-1 is assumed to be an angiogenic marker that is released in response to pro-angiogenic signals and causes endothelium activation. Therefore, Abu El- Asrar researched the relationship between ESM-1 and VEGF in proliferative DRP (pDRP). Vitreous samples, which were obtained from patients with pDRP and non-diabetic patients, were evaluated by ELISA. The results indicated not only higher levels of ESM-1 in patients with active pDRP than patients with inactive pDRP and non-diabetics but also positive correlation between ESM-1 levels and

VEGF levels. These findings suggested that an increment of ESM-1 can be an indicator of angiogenesis-related endothelium activation in proliferative pDRP.¹⁰

Behçet's disease is a chronic inflammatory vasculitic disease with multisystemic, recurrent oral aphthae, genital ulcers, uveitis and skin lesions. In a study¹¹, serum ESM-1 levels in Behçet's disease were assessed. According to the results, ESM-1 levels were related to Behçet's disease activity, which is similar to other vascular diseases.

We investigated the serum ESM-1 levels in patients who either have central or branch retinal vascular vein occlusion and a control group. ESM-1 levels were higher in RVO patients with a statistically significant difference. No statistically significant difference in the ESM-1 levels between patients with central RVO and patients with retinal RVO. However, patients with ischemic RVO have obviously higher levels of ESM-1 than non-ischemic RVO patients (p=0,003).

ESM-1 is a molecule that is functional in endothelial-dependent pathological diseases, and therefore, can aid the determination of endothelial dysfunction. Serum ESM-1

levels may be helpful in determining the severity of disease in RVO patients and can be a new marker for cardiovascular diseases. This noninvasive method might help to predict the severity of RVT and the effectiveness of the treatment. Assessment of ESM-1 level seems easy since it can be evaluated from the blood taken intravenously from the patient. However, the cost of biochemical kit of ESM-1 needs to be evaluated economically. We think that further studies are essential for defining ESM-1 levels as a marker of RVO and might be useful for reaching the target during treatment.

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