Increased Serum Levels of Leptin in Retinal Vein Occlusion

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Retinal vein occlusion is an important cause of visual loss. Several ocular and systemic conditions have been reported for retinal vein occlusion. The pathogenesis of thrombus formation in the retinal vein, which results in retinal vein occlusion, is unclear. The aim of this study was to investigate the correlation between increased serum leptin levels and the occurrence of retinal vein occlusion (RVO). The study group consisted of 40 patients with RVO (58.1 ± 6 years old; 17 males and 23 females): 15 patients with central RVO, 23 with branch RVO, and 2 with hemispheric RVO. The patients who had any ocular or systemic pathology were not included in the study. The control group consisted of 40 healthy individuals of similar gender, age, date and type of health survey, and geographic region. The blood samples of the RVO patients (n = 40) and controls (n = 40) were obtained antecubitaly. Leptin levels were measured by an enzyme-linked immunosorbent assay (ELISA) method, and Student’s t-test was used to determine differences between the groups. The mean serum leptin levels were 12.5 ± 1.64 ng/ml in patients with RVO and 8.4 ± 1.22 ng/ml in the control subjects; namely, the mean serum leptin levels were significantly higher in the patients with RVO (p < 0.001). These results suggest that leptin may be involved in the pathogenesis of venous thrombosis in the retina probably through its effects on homeostasis of the vessel wall.

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The presence of following conditions was investigated, including hypertension, abnormalities of homeostatic factors and blood viscosity, hyperhomocysteinemia, renal impairment (creatinine of > 1.2 mg/dl and/or proteinuria of > 30 μg/day), diabetes mellitus (fasting glucose of > 126 mg/dl), cardiac failure (ejection fraction of < 55%), hyperlipidemia (LDL cholesterol > 160 mg/dl), high serum fibrinogen concentrations, Protein C, Protein S and Antithrombin deficiencies, and factor V Leiden mutation, findings of depression, smoking habit, glaucoma, ocular trauma or surgery, existing ocular pathology, gestation and use of sex hormone therapy, acute infections, or any significant changes in weight within the last three months (more than 25% of total weight). Patients with any one of these conditions were not included in the study. A thorough ophthalmologic examination was done and ocular pathologies were recorded. The control group consisted of 40 healthy volunteers (19 males and 21 females) whose age, gender, geographic region, and BMI were similar to those in the patient group.

A thrombophilia routine investigation was performed at least 3 months after the most likely time of the RVO attack. The blood samples, which were obtained from the antecubital area, were collected between the hours of 08:00-09:00 following a 12-hour fasting period, to ensure that the leptin level was not affected by diurnal rhythms. The samples were drawn into vacutainer tubes containing 0.105 ml sodium citrate and the plasma was separated by centrifugation at 3,600 g for 15 min and stored at −80°C until assayed. The samples stored in the deep freezer were thawed for 12 hours in a fridge of +4 to +8°C, and the serum leptin levels were then measured by enzyme-linked immunosorbent assay (ELISA, Biosource leptin ELISA kit, Nivelles Belgium). The coefficient of variation (CV) of for this method was 3.6%. One-way ANOVA statistical analyses were performed and P-values of < 0.05 were considered to be statistically significant.

Ethics

The study was approved by the Research Ethics Committee of Medical Faculty, Erzurum Ataturk University. Each patient signed a purpose-made informed consent form.

RESULTS

The changes in all parameters are shown in Table 1. Of the 40 RVO patients, 23 (57%) had BRVO; 15 (38%) had CRVO, and 2 had HRVO (5%). The patients had higher levels of total cho-
lesterol, LDL cholesterol, triglyceride (TG), and fasting glucose, as well as higher BMI at the time of investigation than the control group. However, these differences between the two groups were not statistically significant. In contrast, the mean serum leptin level of the patients was 12.5 ± 1.6 ng/ml, which was significantly higher than the mean serum leptin level of the control subjects (8.4 ± 1.22 ng/ml; $p < 0.001$).

We did not find statistically significant differences in the mean serum leptin levels between the patients with CRVO and the patients with BRVO (12.90 ± 2.01 vs 12.10 ± 1.36 ng/ml, $p > 0.05$). There was no statistically significant difference in the serum leptin level between male and female patients (12.07 ± 1.22 vs 12.73 ± 1.85 ng/ml, $p > 0.05$) and between male and female control subjects (8.33 ± 1.28 vs 8.63 ± 1.15 ng/ml, $p > 0.05$).

**DISCUSSION**

The effects of the changes in leptin level on metabolism have been reported in earlier studies. Wallaschofski et al. (2004) have reported that leptin is a potent platelet aggregation coactivator as well as being an additional risk factor for both arterial and venous thrombosis. Gariano et al. (2000) detected leptin in human vitreous humor and showed that leptin concentrations in vitreous humor correlated with those in serum. They also found that leptin levels were elevated in eyes with vascular and fibrotic proliferation, and that leptin receptors were located within diabetic epiretinal proliferative tissue. Their results indicated a range of diseases associated with leptin, including microvascular and proliferative complications of retinal vascular disease, including diabetes mellitus. They described the mechanism by which leptin contributes to neovascular ocular disease.

According to researchers, leptin induces endothelial cell migration and promotes assembly of endothelial cells into tubes and capillary-like structures. Thus, intraocular leptin receptors and leptin, which is produced locally or arises from systemic circulation, may participate directly in neovascular ocular disease (Maberley et al. 2006).

Although RVO is caused by thrombosis and is closely related to the above-mentioned systemic diseases, our patients had no systemic disease, such as hypertension, diabetes, and/or hyperlipidemia. The number of patients ($n = 40$) comprising the study group of this study was small, which is one limitation of our study. Therefore, to generalize our findings, a larger series of RVO patients should be evaluated in univariate analyses, and the systemic factors that could help predict an occurrence of RVO may be identified. Further studies may also adopt a multivariate model and determine which of the univariate factors are excluded.
CONCLUSION

Our results support the hypothesis that leptin may play a role in the development of retinal vein occlusion. However, it is more likely a marker of atherosclerosis and the consequence of other well-established risk factors. Further studies are required to confirm the role of leptin and its contribution to the risk of RVO.

References


