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Influence of rheological factors on the development of primary open angle glaucoma

Wpływ czynników reologicznych na rozwój jaskry pierwotnej otwartego kąta

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Streszczenie: Cel: jaskra pierwotna otwartego kąta (JPOK) to przewlekła choroba oczu, która charakteryzuje się wolno postępującą neuropatią nerwu wzrokowego z typowymi uszkodzeniami anatomicznymi oraz czynnościowymi i towarzyszącymi im charakterystycznymi ubytkami w polu widzenia. Celem pracy jest przedstawienie wpływu czynników reologicznych na rozwój jaskry i jej progresję – na podstawie piśmiennictwa i naszych wstępnych badań, których wyniki nie zostały jeszcze opublikowane.
Słowa kluczowe: jaskra pierwotna otwartego kąta, ciśnienie wewnątrzgałkowe, czynniki reologiczne.
Summary: The aim of this study was to compare our non published investigation on the effect of rheological factors on the development of primary open angle glaucoma (POAG) – to literature data. POAG is a chronic eye disease characterised by a slowly progressive neuropathy of the optic nerve with typical anatomical and functional lesions and is associated with specific visual field defects.
Key words: primary open angle glaucoma, intraocular pressure, rheological factors.

1. Introduction

Primary open angle glaucoma (POAG) is a chronic and slowly progressive optic neuropathy with typical anatomical and functional defects. The cause of this condition remains unknown. For many years, elevated intraocular pressure (IOP) was believed to be the most significant risk factor for glaucoma progression. Now it is known that pathogenesis of glaucomatous neuropathy is multifactorial (1). There are several theories of POAG pathogenesis, including those concerning vascular autoregulation disorders.

Several POAG risk factors have been postulated, including systemic hypertension, systemic hypotension, nocturnal drops of arterial blood pressure, vasoconstriction syndromes, diabetes mellitus, hyperlipidaemia and elevated pressure in the ophthalmic artery. The up-to-date review of these factors might be found elsewhere (2-6). However, it could not be specified whether these risk factors are of causal or casual association (7). Nevertheless, it has been shown in different studies that ocular blood flow is deteriorated in POAG patients (8-9).

It has also been proposed that at least in a group of POAG patients there is a local or systemic vascular endothelium dysfunction (10), vascular dysregulation syndrome (11-12), choroidal ischemia (13), activation of the coagulation cascade (14), abnormal blood fatty acid composition (15), increased red cell aggregability (16) and their loss of flexibility (17).

The different mechanisms of intracellular and extracellular interactions in the pathogenesis of glaucomatous neuropathy was postulated, including the role of free radical species (18), endothelin (19) and circulating autoantibodies (20).

The role of increased blood viscosity, which impairs tissue perfusion in various diseases (e.g. myocardial infarction, cerebral infarction, diabetic retinopathy, central retinal vein occlusion), is of note. Similarly, an increase in blood viscosity was included in the pathogenesis of glaucomatous neuropathy and the associated visual field defects. An increase in blood viscosity in glaucomatous patients has been confirmed in several studies (21-23), although the different techniques used and small sample size limited much of the impact of these studies. Recently, it was shown that there are no differences between haemorheological parameters of glaucomatous and non-glaucomatous patients (24).

The aim of the study was to compare rheological parameters, blood viscosity, haematocrit values and the values of biochemical and morphological parameters of blood in patients with POAG and in a population of healthy individuals. The analysis was done between our group of patients (54 persons – non published data) and ophthalmological literature in this subject.

2. Comparative discussion

POAG occurs in 2–3% of the entire population over 40 years of age, and its prevalence increases with age (22). There are numerous reports in the literature on the role of both vascular and haemorheological factors in POAG pathogenesis (25). The influence of vascular factors on the progression of glaucoma neuropathies has been demonstrated by Kaiser et. al. (26), James (27), and others (8,21,28-30) and the role of reduced ocular perfusion in glaucoma patients was extensively discussed (8).

A questionnaire survey conducted in Poland in over 14.000 patients revealed an important role of vascular factors (31). Fifty-nine per cent of the respondents reported arterial hypertension, 15% reported arterial hypotension, and 19% were diagnosed with migraine headaches. Among individuals with arterial hypertension, 42% had hypercholesterolemia, which is known to have a significant effect on the rheological properties of blood. Similarly, in our study, 67% of the patients were being treated for hypertension, 17% had migraine headaches and 33% experienced symptoms of cold hands, while 57% had high total cholesterol levels. However, our statistical analysis showed a negative correlation between blood viscosity and total cholesterol level. Further statistical analysis revealed that in many patients the results were affected by anticoagulant therapy. According to Garcia-Salinas et al. (23), lowered blood viscosity has a protective influence on the optic nerve in patients with high IOP. Other studies draw attention to the fact of circadian fluctuations in arterial blood pressure, especially in patients with low tension glaucoma (23,27,29).

Haemorheological disorders have already been reported in cardiovascular conditions, such as diabetes mellitus, atherosclerosis, ischaemic heart disease and hypertension. Blood viscosity is the basic rheological parameter of blood. It is known to be affected by multiple factors, such as haematocrit level, plasma viscosity and erythrocyte aggregation, as well as plasma protein and fibrinogen concentration. Erythrocyte aggregation has the most notable effect on blood viscosity at low speeds of clot formation. The greatest effect of erythrocyte aggregation is in the areas of the circulatory system where blood flow velocity gradients are reduced, resulting in an increase in blood viscosity (27). Some studies show that primary open angle glaucoma is associated with changed erythrocyte aggregation. The pathogenic role of changing erythrocytes aggregation is not entirely clear. Theoretically, it is assumed that the increased erythrocytes aggregation has a negative effect on blood flow in the short ciliary arteries supplying the optic disk (32). Dutch researchers found in their study a significantly higher extent of erythrocyte aggregation in patients with primary open-angle glaucoma in patients over 70 years (33). The seven-year follow-up study of the same group showed that the percentage of patients with erythrocyte aggregation was higher in patients with visual field deterioration than in patients with primary open angle glaucoma without progression of visual field loss and in patients with suspected glaucoma (32).

Altered rheological factors, such as increased blood viscosity, red blood cell deformability or increased aggregation cause increased resistance to blood flow in blood vessels (34), which is also a risk factor for the development of glaucoma (25). Additionally, erythrocyte deformability plays a significant role in capillary blood flow. In order to flow through capillaries, blood cells have to be deformed and adjusted to the diameter of the vessel. Mary et al. compared the deformation of erythrocytes and plasma fibrinogen levels in groups of 21 patients with open-angle glaucoma and in control group (n = 18). They noted reduced erythrocyte deformability and an increase in fibrinogen level in patients with glaucoma, although there was no difference in erythrocyte aggregation between these groups (16). It was confirmed that blood viscosity was increased in glaucomatous patients in several studies (21-23), although different techniques were used and small sample size limited much of the impact of these studies. Trope et al. measured the blood viscosity for three shear rates of 27 patients with primary open-angle glaucoma and in 18 in a healthy control group, matched by gender, mean arterial pressure and smoking habits and found that the average viscosity is significantly higher in patients with primary open angle glaucoma than in controls (22). In similar studies, Wolf et al. reported increased viscosity in patients with primary open angle glaucoma (n = 51) but found no differences in erythrocyte aggregation between patients and control subjects (35). In contrast, Hamard and colleagues found increased erythrocyte aggregation in patients with open angle glaucoma, although no differences were found for hematocrit, fibrinogen and plasma proteins (36). Sekeroglu et al. in their study presented that there were no differences between haemorheological parameters of glaucomatous and non-glaucomatous patients (24).

Our – non published study did not show elevated blood viscosity values in patients with POAG (54 persons) as compared to the control group (40 persons), and the fibrinogen level was found to be elevated in 37% of the subjects. However, some limitations of the study should be noted. They include selection of patient and control groups which are not truly homogeneous – the study group presented the increased female representation (what probably is related to the greater risk of POAG in females) and represented the older age of patients than the control group. It is therefore difficult to draw unequivocal conclusions from the above-mentioned studies about whether increased blood viscosity affects the development and progression of glaucoma-related changes. The relation of glaucoma progression to both vascular and haemorheological disorders requires further study.

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ISSN 0023-2157 Index 362646

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The study was originally received 08.08.2011 (1317)/
Praca wpłynęła do Redakcji 08.08.2011 r. (1317)/
Accepted for publication 31.03.2012
Zakwalifikowano do druku 31.03.2012 r.

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