Circulating Platelet Aggregates and Progression of Visual Field Loss in Glaucoma

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ABSTRACT

The aim of the study was to assess a relationship between circulating platelet aggregates (CPA) and progression of visual field loss in primary open-angle glaucoma patients. CPA was determined in 27 patients with open-angle glaucoma with nonprogressive visual field loss and 15 patients with open-angle glaucoma and progression of visual field loss. Intraocular pressure (IOP) under topical therapy was <18 mmHg in all patients. CPA in glaucoma patients with progression of visual field loss was not significantly higher than those without visual field progression (p=0.59). In conclusion, our study shows that increased platelet aggregability is not solely responsible for progression of visual field loss in glaucoma patients, and indicates the role of IOP in the pathogenesis of visual field loss.

Introduction

Glaucoma is multifactorial syndrome of progressive optic neuropathy characterized by an unphysiological large cup/disc ratio with reduced retinal sensitivity, visual field defects and additional psychophysical alterations. In addition to intraocular pressure (IOP) which is an established risk factor, many other risk factors have been described. Both IOP and vascular factors appear to play an important role in the pathogenesis of glaucomatous optic neuropathy. Rheological factors remain controversial. An increase in platelet adhesiveness has been found in some studies, while others have found differences in fibrinolysis. Hoyng et al found an age dependent association between spontaneous platelet aggregation (SPA) and visual field deterioration in glaucoma patients. Platelet activation in circulation can be followed by measurement of circulating platelet...
aggregates (CPA) in venous blood. It was shown that the level of CPA was higher in glaucoma patients than in normal control.

In this study we tried to evaluate a hypothesis that a higher level of CPA in some glaucoma patients with progression of visual field defects and IOP in statistically normal range could be responsible for progression of visual field loss.

Patients and Methods

In controlled clinical study the patients were divided into two groups: experimental and control group. The experimental group consisted of 27 primary (high-pressure) open angle glaucoma patients. Patients were required to have a diagnosis of open-angle glaucoma, including IOP under topical therapy <18 mmHg, papillary excavation (C/D>0.5), non progressive visual field loss demonstrated by Goldmann perimetry and no other ocular abnormality that would affect the visual field. A control group consisted of 15 primary (high-pressure) open-angle glaucoma patients with papillary excavation (C/D>0.5), IOP under topical therapy <18 mmHg and progressive visual field loss. A progressive visual field loss was considered progressive if the following changes developed within a period of less than six months: enlargement of the paracentral and nasal scotoma by >5° or >10° in diameter, occurrence of new scotomatous defects and progression of relative into absolute scotoma.

Patients were excluded if they had any disease or were taking medications known to modify the aggregability of the blood, or had arterial hypertension or hypotension, diabetes mellitus, and cardiovascular disease or smoking.

The ratio of CPA was investigated according to the platelet function system described by Wu and Hoak and modified by Kiesewetter et al.

Briefly, the test for circulating aggregates was based on the effect of ethylenediaminetetraacetic acid (EDTA) and formalin (a 40% solution of gaseous formaldehyde) on platelet aggregates occurring in vivo or resulting from blood sampling. These aggregates were broken up by EDTA, but immediately fixed with EDTA + formalin. Blood samples were obtained using a two-syringe technique. Each 0.5 ml blood sample was added to 2 ml buffered EDTA or to 2 ml buffered EDTA + formalin. The blood picture was determined in each sample. The platelets were counted in an electronic particle counter (Technicon instruments, New York, USA). Blood samples were taken at 9 a.m. to avoid diurnal variations.

The results were expressed as a ratio of the platelet count in the buffered EDTA solution divided by the platelet count in the buffered EDTA + formalin solution. The calculated ratio is the inverse of that described by Wu and Hoak.

The quotient becomes larger with increased CPA. CPA values greater than 1.05 should arouse suspicion, while values over 1.2 are pathologic.

Statistical analysis was performed using Statistica for Windows (Stat Soft Inc, USA, Version 6.0). All data were analyzed by a descriptive analysis. Comparisons between the platelet aggregate ratio of the two groups and comparisons in platelet aggregability according to sex were made using the non-parametric Mann-Whitney U test. A Chi-square test and Student’s t-test were used to compare patients’ data such as sex and age. Findings with an error probability value of <0.05 were considered to be statistically significant.

Results

The demographic data of all patients are shown in Table 1. The results of platelet aggregates studies in glaucoma patients are given in Table 2.
Using the Mann-Whitney U-test we did not find a significant difference between the groups (z=0.52; p=0.59).

No significant gender-based differences in platelet aggregability were found in glaucoma patients with non progressive visual field loss (z=0.73; p=0.46) or those with progressive visual field loss (z=0.81; p=0.41).

Discussion

Despite the achieved IOP <18 mmHg in primary (high pressure) open-angle glaucoma, progression of visual field loss and optic nerve cupping continues in many subjects12,13. Vascular factors have been implicated in the development of glaucomatous damage1. The mechanism of their involvement, either as part of a generalized vascular disorder or as a purely localized disturbance are still unclear. Rheological factors remain controversial4,5,7,8,13,14. Hoyng et al. found that glaucoma patients over 70 years old have a high incidence of SPA. It was speculated that an intravascular condition such as SPA plays a pathogenic role in some glaucoma patients7. A relationship between SPA, visual field damage and disc hemorrhages was observed by Hoyng et al4,8. To what extent platelet hyperactivity is involved in the pathogenesis of glaucoma is not well understood. Recent studies point to activation of the coagulation cascade and fibrinolysis in glaucoma15. The measurement of CPA is a simple method for clinical evaluation of platelet hyperfunction16. According to Iwase et al. SPA is more sensitive than agonist induced platelet aggregation in diabetes16. We did not find a difference in platelet aggregability according to sex, that is, in accordance with observations of Abbate et al17. Hoyng et al. found that in glaucoma patients with progression of visual field loss has higher prevalence of SPA than in glaucoma patients without deterioration of visual field decay4,8. The result of our study showed that the level of CPA are not significantly increased in glaucoma patients with progression of visual field loss compared in those without progression of visual field loss. Our results could not be compared with the studies of Hyong et al. because the mean age of glaucoma patients in their studies was higher than in our study and the platelet aggregation in vitro (according to Born) was performed4,8).

Although there was no statistical difference in CPA values between the two groups, the CPA values are pathologic and the CPA value of the glaucoma patients with progression of visual field was

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**TABLE 1**

DEMOGRAPHIC DATA OF ALL PATIENTS

<table>
<thead>
<tr>
<th></th>
<th>Experimental</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>27</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>12/15</td>
<td>8/7</td>
<td>0.58b</td>
</tr>
<tr>
<td>Mean age (X SD)</td>
<td>58.1 4.4</td>
<td>60.6 4.2</td>
<td>0.08a</td>
</tr>
<tr>
<td>IOP (X SD)</td>
<td>16.0 2.1</td>
<td>16.9 1.1</td>
<td>0.02a</td>
</tr>
</tbody>
</table>

a Student’s t-test; b ² test

**TABLE 2**

PLATELET AGGREGATES IN EXPERIMENTAL AND CONTROL GROUP

<table>
<thead>
<tr>
<th>Groups</th>
<th>Platelets aggregate ratio (X SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental (N=27)</td>
<td>1.27 0.47*</td>
</tr>
<tr>
<td>Control (N=15)</td>
<td>1.41 0.65</td>
</tr>
</tbody>
</table>

*Mann-Whitney U-test; z = 0.52, p = 0.59

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higher than those without progression. Further controlled studies may be required to clarify this. Recently, Matsumoto et al. found that increased platelet aggregation as defined by adenosine diphosphate or collagen induced abnormal secondary aggregation in vitro is frequently associated with glaucoma.

Our study showed that visual fields continued to progression although the level of IOP was <17 mmHg. A recent study by the Advanced Glaucoma Intervention Study group showed that visual progression loss can be practically halted if the IOP is lowered below 12 mmHg.

In conclusion, our study shows that increased platelet aggregability is not solely responsible for the progression of visual field loss in glaucoma patients and indicates the role of IOP in the pathogenesis of the visual field loss.

It might be necessary to conduct more clinical trials in order to provide more information about the role of platelet aggregability in glaucoma, and identify those risk factors, which are potentially treatable in order to prevent the progression of glaucomatous damage.

REFERENCES


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CIRKULIRAJUĆI AGREGATNI KOMPLEKSI I PROGRESIJA GUBITKA VIDNOG POLJA KOD GLAUKOMA

SAŽETAK

Cilj rada je utvrditi vezu između cirkulirajućih trombocitnih agregata (CTA) i progresije gubitka vidnog polja kod primarnog glaukoma otvorenog kuta. CTA su ispitivani kod 27 glaukomskih bolesnika otvorenog kuta sa stabilnim vidnim poljem, kao i kod 15 bolesnika sa glaukomom otvorenog kuta sa progresijom gubitka vidnog polja. Intraokularni tlak (IOT) kod svih bolesnika bio je manji od 18 mmHg, uz lokalnu terapiju. CTA kod bolesnika sa progresijom gubitka vidnog polja nisu bili značajno veći od onih sa stabilnim vidnim poljem (p = 0,59). U zaključku, naša studija pokazuje da agregabilnost trombocita nije isključivo odgovorna za progresiju gubitka vidnog polja kod glaukomskih bolesnika i ukazuje na ulogu IOT-a u patogenezi gubitka vidnog polja.