Haemorheological parameters in patients with retinal artery occlusion and anterior ischaemic optic neuropathy

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Abstract
The haemorheological parameters haematocrit (Hct), plasma viscosity (PV), red cell aggregation (RCA), red cell filterability (RCF), apparent whole blood viscosity (WBV), and fibrinogen were measured in 31 patients with retinal artery occlusion (RAO), 25 patients with anterior ischaemic optic neuropathy (AION), and 19 patients with giant cell arteritis (GCA). The patient groups were compared with controls of same age and similar prevalence of cardiovascular risk factors. Patients with RAO and AION have a significantly decreased RCF in comparison with controls. All other parameters showed no differences. Patients with GCA had significantly decreased Hct and RCF and increased PV and fibrinogen. After 2 weeks of systemic treatment with high dose steroids in patients with GCA the plasma viscosity had returned to normal and was even lower than in controls, and the Hct and fibrinogen had reached normal levels.

Arterial occlusions of the eye are usually acute events followed by an alarming diminution of visual acuity with only few or no possibilities of a therapeutic reversal. This specially applies to the severe reduction of retinal function caused by acute retinal artery occlusion (RAO).

The limited survival time of the retinal tissue in relation to visual acuity requires an immediate initiation of therapy, but there is still no treatment scheme that has gained wide acceptance. Non-arteritic anterior ischaemic optic neuropathy (AION) characteristically causes precipitous visual loss accompanied by partial visual field loss in about 50% of eyes, probably due to occlusion of posterior ciliary arteries. The arteriosclerotic origin of both diseases is probable, but further investigations into the pathophysiology of this disease are necessary to develop new therapeutic concepts.

Giant cell arteritis (GCA) often leads to severe visual loss caused by inflammatory occlusion of the central retinal artery or posterior ciliary arteries. The accepted therapy in this disease is systemic treatment with high dose steroids. However sometimes visual loss or striking of the second eye cannot be prevented despite immediate therapy. This may depend on a changed haemorheological situation as increased fibrinogen concentrations and decreased haematocrit (Hct) are constant features of this disease.

The possible role of haemorheological factors in the development of arterial occlusions of the eye has been pointed out by Wiederholt, but so far only Kiesewetter et al and Wolf et al have presented data on rheological findings in patients with RAO, detecting slight haemorheological abnormalities in these patients. To our knowledge no measurements of blood fluidity have been obtained from patients with non-arteritic AION and GCA. Improvement of blood fluidity by isovolaemic haemodilution in RAO produced conflicting results in pilot studies, but preliminary data of a randomised study on this treatment modality in non-arteritic AION seem quite promising.

The aim of the study was to elucidate a possible role of systemic haemorheological factors in different arterial occlusions of the eye. We investigated patients with atherosclerotic and arteritic occlusions of retinal and ciliary arteries and measured four basic haemorheological parameters (haematocrit (Hct), plasma viscosity (PV), red cell aggregation (RCA), red cell filterability (RCF)) and additionally the apparent whole blood viscosity (WBV).

Materials and methods
All patients with recent RAO, AION, and GCA referred to the Augenklinik, Klinikum Steglitz, Free University Berlin, from 1985 to 1989, were considered for a prospective inquiry.

Every patient underwent a physical examination, ECG, chest x-ray and a laboratory routine check-up. In addition patients were submitted to a detailed ophthalmological examination and funduscopy.

We performed the following rheological measurements: Hct with micromethod, PV with a capillary viscosimeter, RCA with a Myrenne aggregometer, RCF with a Myrenne MF4 (nucleopore filters of 5 μm pore diameter), apparent whole blood viscosity with a Wells-Brookfield cone plate microviscometer. The rheological measurements are described in detail elsewhere. The results of RCA are given after the blood sample was disaggregated with 600/s for 5 s and then aggregation was measured at a stop to 0/s. Values are without dimension. WBV was measured at six different shear rates. In our results we only give the value at 23/s, measurements at lower shear rates were discarded because they are less reliable. Fibrinogen concentration was measured in the routine laboratory of the clinic (method: Clauss, fibrinogen standard curves by Merz and Dade) and compared with the normal values of the laboratory.

The systemic treatment of patients with GCA with prednisolone was begun with an oral dose of 200–400 mg/day and reduced within 14 days to
75–50 mg/day. In these patients the rheological measurements were repeated after 14 days' treatment.

The rheological data were compared with controls of same age and with similar prevalence of cardiovascular risk factors. The controls were recruited from patients without vascular diseases of the eye, but who were to undergo surgery for cataract or retinal detachment; they are described elsewhere.16

STATISTICAL ANALYSIS
Statistical variations of the results are expressed as standard deviation of the mean (SD). The Student's t test was used for comparison of two means. RCF has additionally been tested by the U test of Mann, Whitney and Wilcoxon, which is not dependent on a normal distribution of the variables. Significant differences were considered to be present with p<0.05.

Results
We measured basic rheological data in 31 patients with RAO (14 women, 27 central and four branch artery occlusions) aged 70.4 (12.9) years (40–95 years), 25 patients with AION (12 women) aged 65.5 (9.0) years (51–83 years) and 19 patients with GCA (15 women) aged 76.1 (5.3) years (62–84 years). We compared the measurements with the data of 20 control subjects (10 women) aged 68.1 (10.9) years.16 There were no significant differences between the patient groups and the controls in age and risk factors (Table 1) except in patients with GCA, who had a significantly higher age than controls (p<0.05) and a larger proportion of women.

Table 2 shows the results of haemorheological measurements in patients with RAO and AION in comparison with control subjects. We found no significant differences in Hct, PV, RCA, WBV, and fibrinogen concentration. Measurements of WBV with shear rates of 230, 115, and 46/s show a significant decrease (p<0.05) in the two patient groups (not given in the table), probably due to a somewhat lower Hct. The values of RCF in both patient groups were significantly decreased compared with controls (p<0.01).

Table 3 and Fig 1 present the results of measurements in patients with GCA before and after 2 weeks of treatment with systemic steroids in comparison with controls. Hct was significantly decreased in all patients, which is a well known feature of GCA, due to an infection anaemia. The difference from controls might be increased by the larger portion of women in the patient group (15 of 19) as women have a lower Hct (about 4%) than men. Along with a significant increase in fibrinogen concentration the PV was elevated in comparison with controls, RCF was decreased, but despite these changes in Hct, PV, and RCF the WBV was not significantly different compared with controls. As a typical sign of GCA the ESR was significantly elevated.

After steroid treatment ESR has normalised, as had the Hct. PV decreased significantly (p<0.001), to even lower levels than in controls (p<0.05), RCF remained unchanged after therapy although Hct had normalised. WBV diminished significantly with steroid therapy in comparison with controls (p<0.01), probably because of reduced PV, thus resulting in an overall better haemorheological situation for the patients.

Discussion
The role of systemic haemorheological factors has only partly been investigated in patients with acute arterial occlusions of the eye.8–11 Hence, the aim of the study was to check the importance of such factors in different arterial occlusions of the eye. We investigated patients with atherosclerotic and arteritic occlusions of retinal and ciliary arteries and measured four basic haemorheological parameters (Hct, PV, RCA, RCF) and additionally the apparent WBV. These are the first determinations of haemorheological parameters in patients with AION and in GCA. As it is known that cardiovascular risk factors may influence blood rheology17 it was compared the data of the patients and control subjects with similar prevalence of cardiovascular risk factors.

In patients with RAO we only found a lower RCF; all other parameters did not show differences from control subjects. This contrasts with results of Kiesewetter et al18 and Wolf et al.19 These authors reported a normal erythrocyte deformability but an elevated PV (due to higher fibrinogen levels) and increased RCA in six patients with central RAO. The very low number of patients investigated make these results preliminary and different rheological methods (single erythrocyte passage time vs RCF, yield stress vs WBV) do not allow a proper comparison. Furthermore Kiesewetter et al18 did not define their 'healthy' controls or give the occurrence of cardiovascular risk factors in patients and controls. This is also a likely explanation for the different results obtained.

Wolf et al19 measured rheological parameters
in 40 patients with retinal artery occlusion. In comparison with our results they found elevated PV in the patient group. But the values of their patients were compared with the data of controls without any cardiovascular risk factors.\(^5\) Comparing the absolute values of PV in Wolf’s and our patient group there is no significant difference. Wolf et al did not find decreased RCF as we did. This may also be due to different methods (single erythrocyte passage time vs RCF). Measurements of the filterability of erythrocytes are still a matter of much controversy\(^6,\)\(^7\) and technical problems have still not been solved, so these different results may be caused by methodological problems. The meaning of our finding of a decreased RCF is not quite clear, especially as it does not influence the WBV in medium shear rates. It might support the use of pentoxyphylline, which is known to improve blood filterability,\(^8,\)\(^9\) but up to now has not been shown to be an effective treatment in arterial occlusions of the eye.

The pathogenesis of the non-arteritic AION has not been firmly established, but a posterior ciliary vascular-occlusive process is postulated as the initial event.\(^1\) This is supported by the finding that AION tends to occur in the age group most susceptible to the manifestations of atherosclerotic vascular disease.\(^10,\)\(^11\) and fluorescein angiography has shown delayed perfusion of the peripapillary choroid in this disease.\(^12,\)\(^13\) To our knowledge no rheological measurements have been carried out in patients with non-arteritic AION. In comparison with age and risk factor matched control subjects we only found decreased RCF in the patient group; all other rheological parameters showed no significant differences.

In patients with GCA in comparison with control subjects with similar risk factors we found unchanged WBV along with elevated PV (which should increase WBV) and diminished Hct (which should decrease WBV). The limitations of the method we applied for measurements of WBV, however, do not exclude rheological abnormalities in low flow states with shear rates below 1175/s.\(^14\) After systemic treatment with steroids WBV was significantly decreased due to normalised PV. This occurred despite an increased Hct. These results show that treatment with steroids not only lowers the inflammation of the vessel walls, but may have a beneficial effect on microcirculation also by improving blood fluidity. In some cases even an immediate vigorous treatment with steroids cannot avoid visual loss. The reduction of an elevated fibrin-
Haemorheological in Forschungsgemeinschaft Heidelberg. Changes does factors have however, that patients with cardiovascular risk factors have an abnormal blood rheology. Furthermore lack of measurable systematic rheological changes does not exclude local changes that participate in the disturbance of microcirculation found in non-arteritic RAO and AION. Hence improving the blood fluidity by different treatment modalities (for example isovolamica hemodilution, pentoxyfylline) may well have a beneficial effect on the visual outcome of these diseases and should be tested by randomised prospective studies.

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21 Leonhardt H, Gregoriﬁt HG. Effects of pentoxyfylline on red cell deformability and blood viscosity under hypoxemal conditions. Naunyn Schmiedebergs Arch Pharmacol 1977; 299: 197–205.