

AGE AND HEMORHEOLOGIC CHANGES IN STROKE

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SUMMARY – Stroke is known to be most common in the elderly. Rheologic factors play an important role in the cerebral flow regulation and distinctly correlate with the atherosclerotic process. The aim of this study was to assess the degree to which rheologic changes were related to the age of patients with acute cerebral ischemia. The study included 26 patients and 12 control subjects. Patients were divided into two age groups: ≥ 70 ($n=11$, mean age 77.8) and ≤ 60 ($n=15$, mean age 52.3) years. The following hemorheologic parameters were observed: blood viscosity (BV), plasma viscosity (PV), hematocrit (Htc), red cell deformability (RCD), internal erythrocyte viscosity (IEV), red cell aggregation (RCA), and fibrinogen concentration. Hemorheologic factors were estimated during the first 48 hours and after 3 weeks of disease onset. BV, PV, RCA, IEV and fibrinogen were significantly elevated, whereas Htc and RCD were significantly decreased in the ≥ 70 -year group as compared with control subjects. Relative to the ≤ 60 -year group, patients from the ≥ 70 -year group showed significantly higher values of BV, PV, IEV and RCA, and significantly lower values of RCD and Htc. The hemorheologic profile at 3 weeks from stroke onset was similar to that recorded in the acute phase. Results of the study indicated that hemorheologic changes in patients with cerebral ischemia were clearly dependent on the patient age.

Key words: *Cerebrovascular disorders, blood; Cerebrovascular accident, blood; Hemorheology; Age factors; Aged*

Introduction

Stroke is known to most commonly occur in the elderly. Factors such as quantitative and qualitative changes of red and white blood cells and platelets, as well as changes in the composition of plasma have been identified as being responsible for the increase in blood viscosity. Hemorheologic abnormalities occurring in patients with cerebrovascular disease should be considered as part of a multifactorial mechanism leading to cerebral infarction¹.

Abnormal hemorheologic conditions can be favorably influenced upon by various substances, however, there is no simple relation between the hemorheologic profile and clinical status of stroke patients.

The aim of the study was to assess the degree to which rheologic changes were related to the age of patients with acute cerebral ischemia.

Subjects and Methods

The study included 26 patients with acute cerebral ischemia and 12 control subjects. Patients were divided into two age groups: ≥ 70 ($n=11$, mean age 77.8) and ≤ 60 ($n=15$, mean age 52.3) years. Venous blood was sampled into EDTA tubes (1 mg/ml). In acute cerebral ischemia patients, blood sampling was performed during the first 48 hours and at 3 weeks of disease onset. The following hemorheologic parameters were observed:

- whole blood viscosity (WBV) by use of rotational viscosimeter at a shear rate of 216.513 s^{-1} ;
- plasma viscosity (PV) by use of capillary viscosimeter;
- relative blood viscosity (RBV) was calculated as a quotient of WBV and PV;

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- internal erythrocyte viscosity (IEV) was calculated according to the equation:

$$IEV = \frac{/RBV /^{0.4} - 1}{/RBV /^{0.4} \times Htc}$$

- red cell deformability (RCD) by use of the filtration method; filtration index was estimated for whole blood and 42% of RBC suspension in separate; and
- red cell aggregation (RCA) was estimated on the basis of erythrocyte sedimentation rate (ESR) and plasma viscosity value (the result was adjusted to 30% of Htc).

The following biochemical parameters were determined in all study patients and control subjects: albumin, IgG, IgA, IgM, apolipoprotein A1 and B by use of

nephelometer (Behring), cholesterol, triglycerides, LDL (Cobas Mira) and HDL (Abbott). The level of fibrinogen was determined by the method of Claus.

Hemorheologic data are presented as mean and standard error of mean. Student's t-test was used on statistical analysis.

Results

During the first 48 hours of the disease, significantly higher values of the following hemorheologic parameters: WBV ($p < 0.05$), RBV ($p < 0.05$), IEV ($p < 0.005$), RCA ($p < 0.005$) and lower values of whole blood RCD and Htc ($p < 0.05$ both) were recorded in the ≥ 70 -year group as compared with the ≤ 60 -year group patients (Table 1). Comparison with the control group of subjects showed no significant differences for the ≤ 60 -year group, however, in

Table 1. Hemorheologic profile characteristics in two patient age groups (≥ 70 and ≤ 60 years of age) at 48 hours from disease onset

Parameter	Controls	≥ 70 yrs	p	≤ 60 yrs
WBV (cP)	3.74±0.11	5.45±0.56****	<0.05	4.19±0.20
PV (cP)	1.42±0.01	1.54±0.05**	n.s.	1.47±0.02
RBV	2.62±0.07	3.49±0.30***	<0.05	2.84±0.12
Fibrinogen (g/l)	2.85±0.12	3.72±0.27***	n.s.	3.60±0.49
Whole blood RCD (ml/min)	0.99±0.03	0.75±0.07***	<0.05	0.96±0.06
42% suspension RCD (ml/min)	1.15±0.04	0.99±0.03*	n.s.	1.11±0.06
IEV	0.70±0.03	0.89±0.05*****	<0.005	0.74±0.02
RCA (mm/h)	11.19±2.0	42.05±9.43****	<0.005	15.47±1.91
Htc	0.45±0.006	0.43±0.01*	<0.05	0.46±0.01

Significance vs controls: * $p < 0.05$; ** $p < 0.02$; *** $p < 0.01$; **** $p < 0.005$; ***** $p < 0.001$

Table 2. Hemorheologic profile characteristics in two patient age groups (≥ 70 and ≤ 60 years of age) at 3 weeks from disease onset

Parameter	Controls	≥ 70 yrs	p	≤ 60 yrs
WBV (cP)	3.74±0.11	4.52±0.37*	n.s.	4.21±0.24
PV (cP)	1.42±0.01	1.55±0.03****	n.s.	1.51±0.03
RBV	2.62±0.07	2.90±0.21	n.s.	2.78±0.15
Fibrinogen (g/l)	2.85±0.12	4.00±0.47**	n.s.	3.19±0.18
Whole blood RCD (ml/min)	0.99±0.03	0.87±0.03*	n.s.	0.85±0.09
42% suspension RCD (ml/min)	1.15±0.04	1.04±0.03	n.s.	1.06±0.03
IEV	0.70±0.03	0.84±0.04***	<0.02	0.72±0.02
RCA (mm/h)	11.19±2.0	61.28±9.93****	<0.01	24.72±7.63
Htc	0.45±0.006	0.40±0.01***	<0.001	0.46±0.01

Significance vs controls: * $p < 0.05$; ** $p < 0.02$; *** $p < 0.005$; **** $p < 0.001$

the ≥ 70 -year group the following parameters were found to be significantly different: WBV ($p < 0.005$), PV ($p < 0.02$), RBV ($p < 0.01$), level of fibrinogen ($p < 0.01$), whole blood RCD ($p < 0.01$), RCD for 42% RBC suspension ($p < 0.05$), IEV ($p < 0.001$), RCA ($p < 0.005$), and Htc ($p < 0.05$).

At 3 weeks from the onset of disease, higher values of IEV ($p < 0.01$) and RCA ($p < 0.01$) were found in the ≥ 70 -year group as compared with the ≤ 60 -year group patients, whereas Htc was significantly lower ($p < 0.001$) in the former group (Table 2). In comparison with control subjects, a significantly higher value of PV was observed in the ≤ 60 -year group patients ($p < 0.05$), whereas in the ≥ 70 -year group patients significant differences were recorded for the following parameters: WBV ($p < 0.005$), PV ($p < 0.001$), level of fibrinogen ($p < 0.02$), whole blood RCD ($p < 0.05$), IEV ($p < 0.005$), RCA ($p < 0.001$), and Htc ($p < 0.005$). There were no statistically significant differences in the hemorheologic profile between the acute and late phase of stroke in the study groups of patients.

Comparative analysis of biochemical parameters other than fibrinogen (Tables 3 and 4) revealed a higher level of IgM ($p < 0.01$) in the ≥ 70 -year group as compared with either ≤ 60 -year group patients or control subjects ($p < 0.01$); the level of IgA was significantly higher ($p < 0.01$), while albumin, apolipoprotein A1 and HDL

were significantly lower in the ≥ 70 -year group patients as compared with controls ($p < 0.02$, $p < 0.05$ and $p < 0.05$, respectively).

Discussion

A strong relationship was demonstrated between the hemorheologic changes and age of stroke patients. It is no surprise, because hemorheologic disturbances increase with arteriosclerotic lesions of the cerebral vessels. The frequency of whole blood viscosity parameters has been found to increase with the degree of arteriosclerotic lesion². It has also been observed that some hemorheologic changes seem to have a specific character in relation to a certain vascular pathology³.

Monitoring of the hemorheologic properties after acute cerebral ischemia reveals a persistent profile of factors such as blood and plasma viscosity, red cell aggregation, and erythrocyte deformability. Red cell aggregation increased in the ≥ 70 -year group of stroke patients during 3 weeks from the onset of disease, predominantly due to the role of biochemical factors other than fibrinogen and properties immanently associated with red cells.

The possible effect of hemorheologic changes in elderly stroke patients should be expected to involve a more

Table 3. Protein factors in two stroke patient age groups (≥ 70 and ≤ 60 years of age)

Parameter	Controls	≥ 70 yrs	p	≤ 60 yrs
Albumin (mg%)	4273.33 \pm 94.10	3896.25 \pm 95.72*	n.s.	4220.0 \pm 219.64
γ Globulin (mg%)	1758.08 \pm 120.79	1834.81 \pm 93.81	n.s.	1757.62(100.53
IgG (mg%)	1299.25 \pm 87.74	1275.93 \pm 51.25	n.s.	1178.50 \pm 79.98
IgA (mg%)	235.83 \pm 28.96	440.0 \pm 55.16**	n.s.	360.87 \pm 33.98*
IgM (mg%)	223.0 \pm 31.79	118.87 \pm 8.99**	<0.01	218.25 \pm 28.33
Albumin/ γ globulin	2.55 \pm 0.18	2.21 \pm 0.13	n.s.	2.47 \pm 0.23

Significance vs controls: * $p < 0.02$; ** $p < 0.01$

Table 4. Lipid factors in two stroke patient age groups (≥ 70 and ≥ 60 years of age)

Parameter	Controls	≥ 70 yrs	p	≤ 60 yrs
Apolipoprotein A ₁ (mg%)	168.0 \pm 6.64	145.86 \pm 6.42*	n.s.	144.72 \pm 9.99
Apolipoprotein B (mg%)	145.33 \pm 11.44	128.50 \pm 7.97	n.s.	130.37 \pm 11.15
Cholesterol (mg%)	227.25 \pm 11.08	199.94 \pm 11.09	n.s.	215.37 \pm 17.01
Triglycerides (mg%)	169.66 \pm 33.49	169.47 \pm 19.37	n.s.	137.0 \pm 16.24
HDL (mg%)	58.33 \pm 5.30	46.0 \pm 2.64*	n.s.	46.50 \pm 3.86
LDL (mg%)	134.91 \pm 12.29	120.52 \pm 10.27	n.s.	142.62 \pm 12.73

Significance vs controls: * $p < 0.05$

severe impairment of cerebral microcirculation than in younger patients. The lower level of Htc observed in the ≥ 70 -year group patients suggests the existence of a certain mechanism of feedback, initiated by the high value of blood viscosity.

Conclusion

Hemorheologic changes observed in patients with brain ischemia are clearly dependent on the patient age, and their role in the cerebral blood flow regulation should be considered in relation to a certain vascular pathology.

References

1. OTT E. Rheological therapy of vascular dementia: a rational basis? In: HARTMANN A, KUSCHINSKY W, HOYER S, eds. Cerebral ischemia and dementia. Berlin, Heidelberg: Springer-Verlag, 1991:424-31.
2. LECHNER H, OTT E, FAZEKAS F. Cerebrovascular disease: were are we now? In: GOTOH E, LECHNER H. Clinical haemorheology: a new approach to cerebrovascular disease. London: Royal Society of Medicine Services Ltd., 1986:11-8.
3. KOWAL P. Arterial hypertension decreases fibrinogen molecule contribution to the inter-red cell connections in stroke patients. Clin Hemorheol Microcirc 1999;21:321-4.

Sažetak

STAROSNA DOB I HEMOREOLOŠKE PROMJENE KOD MOŽDANOG UDARA

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Poznato je da su starije osobe najčešće žrtve moždanog udara. Reološki čimbenici imaju važnu ulogu u regulaciji moždanoga krvotoka i jasno koreliraju s aterosklerotskim procesom. Cilj ovoga ispitivanja bio je utvrditi do kojeg su stupnja reološke promjene povezane s dobi bolesnika s akutnom moždanog ishemijskom. Ispitivanje je provedeno u 26 bolesnika i 12 kontrolnih osoba. Bolesnici su bili podijeljeni u dvije dobne skupine: ≥ 70 godina ($n=11$, srednja dob 77,8) i ≤ 60 godina ($n=15$, srednja dob 52,3) godina. Ispitivani su sljedeći hemoreološki parametri: viskoznost krvi (VK), viskoznost plazme (VP), hematokrit (Htc), deformabilnost crvenih stanica (DCS), unutarnja viskoznost eritrocita (UVE), agregacija crvenih stanica (ACS) i koncentracija fibrinogena. Hemoreološki čimbenici određeni su u prvih 48 sati te 3 tjedna nakon nastupa bolesti. VK, VP, UVE, ACS i razina fibrinogena bili su značajno povišeni, a Htc i DCS značajno niži u skupini bolesnika u dobi od ≥ 70 godina u usporedbi s kontrolnim osobama. U odnosu na skupinu bolesnika u dobi od ≤ 60 godina, stariji su bolesnici (≥ 70 godina) imali značajno više vrijednosti VK, VP, UVE i ACS, dok su Htc i DCS bili značajno niži. Tri tjedna nakon nastupa bolesti hemoreološki je profil bio sličan onomu u akutnom stadiju. Rezultati ispitivanja pokazali su kako hemoreološke promjene u bolesnika s moždanom ishemijskom jasno ovise o dobi bolesnika.

Ključne riječi: *Cerebrovaskularne bolesti, krv; Cerebrovaskularni inzulit, krv; Hemoreologija; Dobni čimbenici; Osobe starije dobi*