Rat Model of Blood Hyperviscosity Syndrome: Informativity of Blood Rheological Parameters in Cerebral Ischemia

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Blood rheological status is studied in Wistar rats with cerebral ischemia induced by ligation of the left coronary artery and reduced blood flow via the right coronary artery. Substantial changes in blood rheology and manifestations of the sludge syndrome are noted. The results obtained are compared with clinical observations, and the informativeness of each parameter is evaluated.

Key Words: *cerebral ischemia; blood rheology*

Numerous clinical trials show that the sludge syndrome aggravates myocardial infarction [1,6], ischemic stroke [10,13], essential hypertension [11], etc. Therefore, it is necessary to investigate the mechanisms of this syndrome and develop pharmacological means of correcting blood rheological disorders. The aim of the present study was to create an adequate animal model of the sludge syndrome in cerebral ischemia to analyze the interplay and informativeness of rheological parameters.

MATERIALS AND METHODS

Experiments were carried out on 20 male rats weighing 200-250 g. Ischemia was modeled as described previously [8]. The following parameters were measured 5, 7, and 10 days after ischemia: relative viscosity of the blood and plasma (on a VK-4 capillary viscosimeter), erythrocyte aggregation (half-time of aggregate formation, $T_{1/2}$, i.e., the time during which the signal amplitude decreased 2-fold), hematocrit (in an MGC-8 microcentrifuge), and plasma content of fibrinogen [2]. The results were processed using Student's t test, nonparametric Wilcoxon test, correlation analysis, and a geometrical approach to evaluation of informativeness of the parameters [7].

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RESULTS

On day 5 after cerebral ischemia, blood viscosity in rats with cerebral ischemia was significantly higher than in intact controls and remained at this level up to the 10th day; the tendency towards normalization (on day 7) was statistically insignificant (Table 1). The increase in blood viscosity is consistent with that occurring in patients with cerebral ischemia [5,12]. In our experiments, blood viscosity was increased due to enhanced aggregation of erythrocytes and hyperfibrinogenemia persisting throughout the experiment. This conclusion is based on the results of correlation analysis showing that blood viscosity positively correlates with both spontaneous erythrocyte aggregation (r=0.96, p=0.04) and fibrinogen content (r=0.97, p=0.03). The presence of the mechanisms responsible for the increase in blood viscosity upon enhanced erythrocyte aggregation is confirmed by the finding that erythrocyte aggregation correlates with plasma fibrinogen content (r=0.95, p=0.048). Despite sustained hyperfibrinogenemia, plasma viscosity in rats with cerebral ischemia did not differ from that in the controls. Plasma viscosity tended to decrease on days

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TABLE 1. Blood Rheological Parameters in Rats with Cerebral Ischemia ($M \pm m$)

Parameter	Control	Day 5	Day 7	Day 10
Blood viscosity, rel.units	4.01±0.06	5.32±0.29*	4.82±0.19*	4.85±0.13*
Plasma viscosity, rel.units	1.42±0.07	1.32±0.04	1.26±0.02	1.54±0.06
Half-time of erythrocyte aggregation, sec	9.25±0.56	5.70±0.09*	6.30±0.60*	6.19±0.50*
Fibrinogen content, mg/100 ml	192.5±8.5	265.0±10.0*	225.0±11.2*	243.8±21.3*
Hematocrit, %	45.5±0.5	46.4±0.5	41.6±0.6*	46.4±1.2

Note. *$p<0.05$ compared with the control.

TABLE 2. Informativeness of Blood Rheological Parameters in Cerebral Ischemia

Rank	Day 5	Day 7	Day 10
1	Erythrocyte aggregation	Erythrocyte aggregation	Erythrocyte aggregation
2	Blood viscosity	Blood viscosity	Blood viscosity
3	Fibrinogen	Hematocrit	Fibrinogen
4	Plasma viscosity	Plasma viscosity	Plasma viscosity
5	Hematocrit	Fibrinogen	Hematocrit

5 and 7 postischemia (Table 1). On days 5 and 10, hematocrit in experimental rats was not higher than in intact controls, showing a slight decrease on day 7. It was reported [10] that such a decrease may result from hemolysis caused by metabolic disorders in the brain against the background of necrosis. There was no significant correlation between plasma viscosity, fibrinogen concentration, and blood viscosity.

The geometrical approach made it possible to arrange the parameters of rheological state in cerebral ischemia according to decreasing informativeness (Table 2). Spontaneous erythrocyte aggregation is the most valuable parameter. It is noteworthy that this parameter ranks first throughout the experiment in accordance with its maximal informativeness. These data suggest that erythrocyte aggregation plays an important role in the pathogenesis of sludge syndrome in cerebral ischemia. Blood viscosity ranks second, which attests to the importance of both parameters in the study of disturbances of blood rheological properties.

Thus, changes in blood rheological properties occurring in rats with cerebral ischemia manifest themselves as the development of a sustained sludge syndrome involving both plasma and cell factors. This model of cerebral ischemia can be used for the search and investigation of new preparations correcting blood rheological disorders and for further studies of the mechanisms underlying the alterations of blood rheological properties in cerebral ischemia.

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