Blood Hyperviscosity Syndrome: Adequacy of Experimental Model in SHR Rats

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In comparison with Wistar rats, SHR rats demonstrated significantly higher viscosity of the whole blood and plasma, fibrinogen content, and erythrocyte aggregation, but a lower erythrocyte deformability. The differences in hemorheological indices in SHR and Wistar rats correspond to the deviation of these indices in the blood hyperviscosity syndrome observed in hypertensive patients.

Key Words: *arterial hypertension; blood hyperviscosity syndrome; SHR rats*

Both essential and arterial hypertension are characterized by significant deviation of some rheological indices and their combinations [3,6,8,9, 11-17], which are the manifestations of the blood hyperviscosity syndrome (BHVS) in these patients.

In order to develop adequate experimental models of BHVS for the search of new hemorheological drugs, we carried out a comparative study of the hemorheological indices in Wistar and SHR rats.

MATERIALS AND METHODS

Experiments were carried out on 15 male Wistar and SHR rats bred from the strain of the Institute of Cytology and Genetics, Siberian Division of the Russian Academy of Sciences. Blood was collected from carotid artery under ether narcosis. The following parameters were measured: relative viscosity of the whole blood and plasma (in a VK-4 capillary viscosimeter), hematocrit (in an MGC-8 microcentrifuge), plasma fibrinogen [1], erythrocyte aggregation [4], and deformability [2] at a shear rate of 890 sec^{-1}. Arterial pressure was measured before blood collection. The results were statistically analyzed using Student's *t* test and Wilcoxon's nonparametric test.

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RESULTS

The mean arterial pressure was 143±5 mm Hg in SHR rats and 95±3 mm Hg in Wistar rats.

Basic hemorheological parameters were significantly different in these rats (Table 1). In SHR rats, the viscosity of the whole blood and plasma was increased by 29 and 27%, respectively. Plasma fibrinogen was increased 1.5-fold. The half-time of erythrocyte aggregation ($T_{1/2}$) and erythrocyte deformability index were decreased to 68% and by 12%, respectively. A significant correlation between whole blood viscosity and erythrocyte aggregability (r=0.71), blood viscosity and plasma fibrinogen (r=0.72), erythrocyte aggregability and plasma fibrinogen (r= 0.85) was revealed in SHR rats. Direct relation of reversible erythrocyte aggregation to fibrinogen content in patients with arterial hypertension was also shown by other researchers [14].

Taking the hemorheological indices in Wistar rats as the control values, the hemorheological status of SHR rats can be determined as a variant of BHVS (Type VII according to [5]). Comparison of our data with clinical evidence corroborates this hypothesis.

The patients with essential hypertension (EH) have increased viscosity of the whole blood, which is an integral index characterizing BHVS [3,6,10, 13,17]. By its relative value this increase is similar

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TABLE 1. Basic Hemorheological Parameters in Wistar and SHR Rats (*M±m*)

Index	Wistar	SHR
Whole blood viscosity, rel. units	3.96±0.05	5.12±0.13*
Plasma viscosity, rel. units	1.43±0.04	1.81±0.03*
Hematocrit, %	45.1±0.3	45.3±0.5
Plasma fibrinogen, mg/100 ml	186.6±5.1	280.6±7.8*
Half-time of erythrocyte aggregation, sec	10.11±0.52	6.89±0.28*
Erythrocyte deformability index	2.390±0.085	2.754±0.095*

Note. *$p<0.05$ compared with Wistar rats.

to the difference between blood viscosity in Wistar and SHR rats [6,8]. Similar difference was revealed in the indices of plasma viscosity [3].

The decrease in erythrocyte deformability may be the most sensitive index characterizing rheological status in patients with EH [6,9,17], which correlates with the stage of the disease [6]. In comparison with Wistar rats, SHR rats were characterized by a marked deterioration of erythrocyte deformability, since the shear rate in our model of capillary viscometer was about 300 sec^{-1}, which is in the range of so called "asymptotic viscosity". In this range of shear rates blood viscosity is determined mainly by deforability of erythrocytes [7].

Taking into account that regular enhancement of erythrocyte aggregation takes place only at the stage III of EH [6], one can assume that the SHR model reflects this stage of the disease. Moreover, in patients with the 3rd stage of EH the relative deviation of $T_{1/2}$ (index of spontaneous aggregation of erythrocytes [6]) from the normal value corresponds to the difference in $T_{1/2}$ revealed in our experiments on rats of both strains.

As in clinical studies [6,13], which revealed no pronounced hematocrit deviation from the normal value in patients with various degree of EH, no significant difference of this index was observed in Wistar and SHR rats. Other researchers did not reveal any regular increase in hematocrit in EH patients [3,16].

Thus, comparison of absolute values and relative difference of basic rheological parameters in Wistar and SHR rats, on the one hand, and in virtually healthy subjects and hypertensive patients, on the other, attests to the possibility of using the rheological status of SHR rats as a model of BHVS during EH.

REFERENCES

1. V. P. Baluda, Z. S. Barkagan, E. D. Gol'dberg, *et al.*, *Laboratory Tests of the Hemostasis System* [in Russian], Tomsk (1980).
2. A. V. Belkin, S. A. Storozhok, and L. N. Katyukhin, *Fiziol. Zh. SSSR*, No. 1, 133-138 (1991).
3. V. A. Lyusov and V. A. Dudaev, Kardiologiya, No. 8, 70-73 (1986).
4. M. B. Plotnikov, O. I. Aliev, and F. V. Popel', Klin. Lab. Diagn., No. 3, 457-458 (1995).
5. S. A. Seleznev, G. I. Nazarenko, and V. S. Zaitsev, *Clinical Aspects of Microhemocirculation* [in Russian], Leningrad (1985).
6. V. A. Shabanov, N. D. Kitaeva, G. Ya. Levin, *et al.*, *Ter. Arkh.*, No. 5, 89-94 (1990).
7. S. Chien, *Science*, **168**, 977-979 (1970).
8. I. Freitas, I. Braz-Nogueira, I. Nogueira De Costa, *et al.*, *Clin. Hemorheol. Microcirc.*, **3**, No. 4, 367-373 (1983).
9. V. Hossmann, G. Bonner, G. Wambach, *et al.*, *Clin. Exp. Hypertens.*, **8**, No. 4-5, 673-680 (1986).
10. R. L. Letcher and S. Chien, *Am. J. Med.*, **10**, No. 6, 1195-1202 (1981).
11. T. Linde, B. Sandhagen, A. Hagg, *et al.*, *J. Hypertens.*, **11**, No. 7, 731-736 (1993).
12. G. C. Maggi, R. Zacco, and M. Ornaghi, *Ric. Clin. Lab.*, **15**, No. 1, Suppl., 243-250 (1985).
13. R. R. Puniyani, R. Ajmani, and P. A. Kale, *J. Biomed. Eng.*, **13**, No. 5, 441-443 (1991).
14. S. M. Razavian, M. Del Pino, A. Simon, and J. Levenson, *Hypertension*, **20**, No. 2, 247-252 (1992).
15. B. Sandhagen, G. Frithz, U. Waern, and G. Ronquist, *J. Intern. Med.*, **228**, No. 6, 623-626 (1990).
16. A. Vaya, M. Martinez, J. Garcia, *et al.*, *Thromb. Res.*, **66**, No. 2-3, 223-229 (1992).
17. F. Zannad, P. Voisin, F. Brunnotte, *et al.*, *J. Hypertens.*, **6**, No. 4, 293-297 (1988).