Plasma and Lymph Electrolyte and Endocrine Parameters in Rats with Genetically-Determined Arterial Hypertension

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Hemolymphatic interactions of electrolytes and plasma contents of aldosterone and insulin are studied in rats with genetically-determined stress-induced arterial hypertension (NISAG) and in normotensive rats (Wistar). Correlation analysis shows that alterations in electrolyte metabolism in NISAG are strongly determined by endocrine influences. These alterations are regarded, on the one hand, as a mechanism responsible for generically-determined arterial hypertension, and, on the other hand, as a variant of "adaptation disease" accompanied by transformation of primarily adaptive reactions into a pathogenic factor of arterial hypertension.

Key Words: *hypertension; electrolytes; hormones; blood; lymph*

Arterial hypertension (AH) is a polymorphic pathology involving numerous endo- and exogenous factors. The exchange of electrolytes (Na and K) largely determines both vascular tone and fluid homeostasis in the organism [3]. Although lymph vessels play substantial role in the regulation of fluid homeostasis [8], the contribution of the lymph flow impairments to the genesis of AH has not been evaluated. Moreover, the compensatory potential of lymphatic system under pathological conditions (including cardiovascular disorders) is poorly investigated [1,2], and the information regarding hemolymphatic interactions is scarce. There is little evidence on modifications of hormonal systems and generally it does not provide any information on qualitative interhormonal interactions in AH. Although aldosterone and insulin belong to different hormonal systems, they have common targets, and Na-K exchange may be one of them. In this study we investigated hemolymphatic interactions between electrolytes (Na and K), aldosterone and insulin, and their correlations in normo- and hypertensive rats.

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MATERIALS AND METHODS

Male normotensive rats (Wistar) and rats with genetically-determined stress-induced AH (NISAG) were used. The rats weighed 180-200 g. NISAG rats were bred at the Laboratory of Evolutionary Genetics, Institute of Cytology and Genetics (Siberian Division of the Russian Academy of Sciences). Arterial pressure in stress was 205±2 mm Hg, basal level being 172±2 mm Hg. Lymph was collected from the thoracic duct under intraperitoneal Nembutal anesthesia. Blood was collected after decapitation. The contents of Na and K were determined by flame photometry in a Hitachi-180-80 spectrophotometer. Plasma concentrations of aldosterone and insulin were determined by radioimmune assay. The results were analyzed using standard statistical methods, Student's *t* test, and correlation analysis.

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RESULTS

In hypertensive rats, plasma Na content was significantly increased (Table 1), while that of K was slightly decreased. An increased Na concentration is associated with high sensitivity of blood to the pressor influences [4,6], thus forming premorbid background for realization of hypertensive reactions [5,14]. Impaired function of Na,K-ATPase, and Na-H antiport, which are typical of AH [3], may promote Na increase in the plasma. At the same time, elevated plasma Na is initiated or maintained by high basal level of aldosterone in hypertensive rats (Table 1), which is reflected by positive correlation between plasma aldosterone concentration (PAC) and plasma Na content (r=0.58) in hypertensive but not in normotensive rats.

A similar increase in Na and K contents was observed in the lymph of NISAG rats. For integrated estimation of hemolymphatic relationships between electrolytes, we analyzed the Na/K ratio in plasma and lymph. It was found that Na concentration in plasma and K concentration in lymph are increased. Changes in lymph composition are determined predominantly by changes in blood composition and specific features of tissue exchange [10]. Since AH is accompanied by a number of metabolic disorders (the concept of metabolic syndrome [14]), it is reasonable to suggest that lymphatic system participates both in the development and compensation of this syndrome. Elevation of lymph K content stimulates tonic contractions of lymph vessels. A synergism between this elevation and a decrease in lymph Na content should be noted (Na is known to increase the frequency of contractions of lymph vessels [10]). Presumably, the specific relationship between Na and K in the lymph are determined by the fact that K more readily "leaves" the blood than Na via arterioles and venules. A strong positive correlation (r=0.7) has been established between PAC and K content of central lymph, which may account for a parallel increase in the studied parameters as a manifestation of autoregulation in the maintenance of systemic arterial pressure. Increased contractility of lymph vessels may reflect the compensatory nature of the observed hemolymphatic changes in electrolyte exchange in NISAG rats: under the conditions of hemodynamic overload increased outflow of lymph reduces the load on the cardiovascular system. These changes are consistent with the concept of cellular resetting [7] which maintains that "the development of cellular resetting simultaneously initiates changes of hormonal-neurocellular relationships" originating from the pathology of plasma membrane in AH. According to this concept, calcium plays the primary

TABLE 1. Plasma and Lymph Contents of Electrolytes, Aldosterone, and Insulin in Wistar and NISAG Rats

Group		Wistar	NISAG
Aldosterone, nmol/liter		1.0±0.1*	1.5±0.02
Insulin, μU/liter		29.1±3.0*	14.5±3.4
Plasma, mmol/liter	Na	140.2±1.2*	190.0±1.3
	K	5.9±0.2	5.1±0.2
Lymph, mmol/liter	Na	153.9±1.3*	183.2±1.2
	K	5.6±0.1*	9.5±0.1

Note. *$p \le 0.05$ compared with NISAG rats.

role in the pathogenesis of AH. However, we believe that modifications of Na-K-turnover are more important, which was confirmed by recent investigations [12,15].

We think that immanent hyperinsulinemia in AH is not very frequent and is not present in all variants of this pathology. We have established a strong negative correlation between PAC and insulin level in NISAG rats, which may result from the stimulating effect of low insulin concentration in steroidogenesis in the adrenals, including the synthesis and secretion of aldosterone [11]. This was confirmed morphologically: the width of zona glomerulosa and the volume of adrenocorticocytes in NISAG rats are greater than in Wistar rats [9]. Hyperplasia of steroid-producing organelles of cells located in zona glomerulosa has been revealed by electron microscopy. The possibility that the decrease in insulin content potentiates the effects of angiotensin II [13] cannot be ruled out. A decrease in plasma content of potassium may account for hypoinsulinemia in hypertensive rats. Hypoinsulinemia and high arterial pressure fulfill the same function, namely, prevent sodium retain in the plasma. In some respect the lymphatic system acts synergistically in this reaction.

The revealed changes in electrolyte turnover and endocrine parameters can be interpreted as initially adaptive reactions specific for NISAG rats. These reactions reflect changes in the adaptation norm in ontogeny, when systemic reactions of the organism are aimed at maintaining the elevated blood pressure. Bearing in mind the high sensitivity of NISAG rats to stress, it can be suggested that the studied hormonal-electrolyte changes are transformed into a pathogenetic factor ("adaptation disease") in stress or myocardial ischemia. It can be concluded that the "price of adaptation," which is determined by the number of structures involved in the adaptation process, is essentially high in hypertensive animals, which excludes the possibility of readaptation.

REFERENCES

1. V. M. Buyanov and A. A. Alekseev, *Lymphology of Endotoxicosis* [in Russian], Moscow (1990).
2. G. M. Garaev, Ya. D. Mamedov, and F. I. Mirzabekova, *Azerbaidzh. Med. Zh.*, No. 2, 3-8 (1985).
3. M. S. Kushakovskii, *Hypertensive Disease* [in Russian], St. Petersburg (1995).
4. T. M. Lyakhova, I. N. Gribkova, and S. F. Datsenko, in: *Arterial Hypertension* [in Russian], Moscow (1989), pp. 28-31.
5. M. N. Maslova, L. E. Ogorodnikova, and Yu. S. Titkov, in: *Pathophysiological Analysis of Risk Factors of Arterial Hypertension and Atherosclerosis* [in Russian], Novosibirsk (1992), pp. 74-75.
6. V. M. Merzhievskaya and I. Sh. Shterental', *Kardiologiya*, **28**, No. 12, 30-33 (1988).
7. Yu. V. Postnov, *Ibid.*, **33**, No. 8, 7-15 (1993).
8. V. K. Khugaeva and A. V. Ardasenov, *Ibid.*, **35**, No. 8, 63-70 (1995).
9. G. S. Yakobson, A. R. Antonov, G. V. Petrova, *et al.*, in: *Modern Problems of Cardiology* [in Russian], Tomsk (1995), p. 98.
10. I. V. Yarema and B. M. Urtaev, *Transfusion of Lymph and Its Components* [in Russian], Moscow (1995).
11. E. Ferrannini, G. Seghieri, and E. Muscelli, *J. Cardiovasc. Pharmacol.*, **24**, Suppl. 3, S61-S69 (1994).
12. G. G. Krishna and S. C. Kapoor, *Ann. Intern. Med.*, **115**, 77-83 (1991).
13. R. Natarajan, S. Kathuria, L. Lanting, *et al.*, *Am. J. Physiol.*, **31**, No. 1, E100-E106 (1995).
14. J. M. Neutel, D. H. G. Smith, W. F. Graettinger, *et al.*, *Am. Heart J.*, **126**, No. 4, 924-929 (1994).
15. J. P. Reeves and A. Aviv, *Hypertension*, **25**, No. 5, 978-980 (1995).