Slow Cooling Improved Blood Lipoprotein Composition in Hypertensive Rats

T. V. Kozyreva, S. V. Lomakina, F. V. Tuzikov, and N. A. Tuzikova

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Under normal thermal conditions, hypertensive NISAG rats are characterized by lower plasma levels of high-density lipoproteins and increased coefficient of atherogenicity compared to normotensive Wistar rats. Slow cooling significantly modified fractional composition of plasma lipoproteins in hypertensive rats: decreased the content of low-density lipoproteins, markedly increased the content of high-density lipoproteins, and normalized coefficient of atherogenicity. Our results demonstrated the possibility of correcting disturbances in lipoprotein spectrum in essential hypertension by using thermal exposures.

Key Words: *arterial hypertension; cold*; *blood lipoproteins*

Patients with arterial hypertension often exhibit specific changes in plasma lipid spectrum, in particular, increased levels of triglycerides and very-low-density lipoproteins (VLDL) and decreased content of high-density lipoprotein cholesterol (HDL CH) [4,13]. These changes are typical of atherosclerosis and cardiovascular diseases, the most prevalent cause of death in Russia and other countries [2,14]. Correction of plasma lipoprotein spectrum is an important component in prevention of cardiovascular disease and atherosclerosis in hypertensive patients.

Thermal stimulation strongly affects lipid metabolism. Sympathetic nervous system and its neurotransmitter norepinephrine play an important role in the regulation of a series of events induced by cold, including changes in lipoprotein composition and, in particular, HDL fraction [1,6,7]. The study of the effects of external thermal stimuli on the regulation of lipid metabolism is interesting not only from the viewpoint of human and animal survival at low temperatures, but also as a feasible way for correction of disturbances in lipid metabolism.

Laboratory of Thermophysiology, Institute of Physiology, Siberian Division of Russian Academy of Medical Sciences, Novosibirsk. ***Address for correspondence:*** Kozyreva@iph.ma.nsc.ru. Kozyreva T.V.

Here we studied possible difference between plasma lipoprotein compositions in normotensive Wistar rats and rats with hereditary stress-induced arterial hypertension (NISAG rats), and to study the changes in plasma lipoprotein fractions induced by slow-rate cooling in hypertensive rats.

MATERIALS AND METHODS

Experiments were performed on normotensive Wistar rats and hypertensive NISAG rats. NISAG rats were bred at the Institute of Cytology and Genetics, Novosibirsk. Basal blood pressure was 109.0±15.6 mm Hg in Wistar rats and 172.0±12.2 mm Hg in NISAG rats [11].

Cooling was performed under Nembutal anesthesia (40 mg/kg) in order to exclude emotional component of stress. Cutaneous temperature at the site of application of cooling element decreased by by 3.5°C at a rate of 0.005°C/sec (slow cooling), than the animals were warmed to initial temperature. Cutaneous temperature of cooled abdominal area and rectal temperature were continuously measured with thermocouples.

On day 5 after cold exposure the rats were decapitated and the blood was collected for analysis of lipoprotein fractions.

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Plasma lipoprotein fractions and subfractions were analyzed using small-angle X-ray scattering on a Siemens diffractometer [8].

The results were statistically analyzed using Student's t test ($p<0.05$).

RESULTS

Under normal conditions NISAG and Wistar rats significantly differed in HDL content. In hypertensive rats HDL content decreased predominantly due to a decrease in HDL_3 subfraction (by 48%; Fig. 1). The decrease in HDL content in hypertensive NISAG rats was similar to that in hypertensive patients [4]. According to published data, HDL fraction is very similar in humans and rats [1]. The decreased HDL content in hypertensive rats is probably associated with disturbed reverse CH transport from tissues [4,15]. Of particular interest is the decrease in HDL_3 fraction exhibiting antioxidant properties and protecting LDL from atherogenic modifications [3,4,9].

According to clinical and experimental data [2], the ratio of atherogenic to antiatherogenic lipoprotein cholesterol fractions referred to as "cholesterol atherogenicity coefficient" is an important predictor of coronary heart disease. This coefficient was calculated by the formula:

$$C_{CH}=(\text{LDL CH}+\text{AVLDL CH})/(\text{HDL CH}).$$

The greater is atherogenic coefficient, the higher is the risk of atherogenic changes, ischemic disease, and athrosclerosis [4].

Under normal conditions C_{CH} in hypertensive rats was higher than in normotensive rats (1.5±0.2 and 0.6±0.1, respectively), which resulted from lower levels of HDL in hypertensive rats.

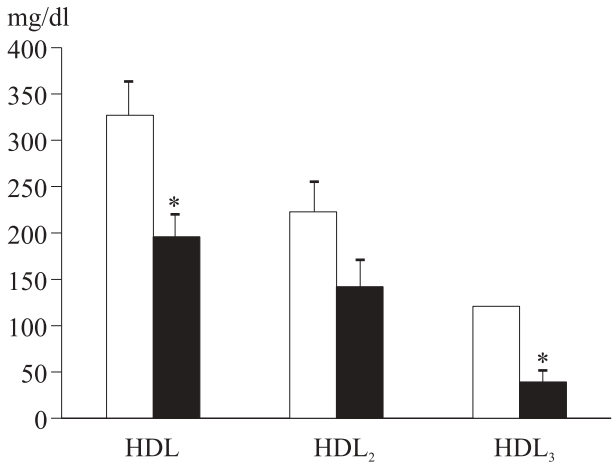

Fig. 1. Content of HDL and their subfractions (HDL_2 and HDL_3) in normotensive (light columns) and hypertensive (dark columns) rats under normal thermal conditions. *$p<0.05$ compared to normotensive rats.

Slow cooling (rectal temperature decrease by 3.5°C) caused pronounced changes in plasma fractions of HDL, LDL, and VLDL in hypertensive rats (Fig 2).

The content of triglyceride-rich VLDL increased by more than 2-fold (primarily at the expense $VLDL_2$ subfraction). This could result from accumulation of unesterified fatty acids utilized as high-energy substrate during cooling, which was previously reported for early periods after cooling [5,10,12]. Slow cooling 2.5-fold decreased plasma content of LDL. It should be noted that these particles after modification play the major role in atherosclerotic process. The decrease in LDL CH is the primary goal in the treatment of patients with coronary heart disease [4,13].

Changes in HDL fraction after slow cooling in hypertensive rats appeared as accumulation of HDL_2 particles (by 1.6-fold). This probably results from enhanced VLDL catabolism after their accumulation induced by slow cooling (Fig. 2).

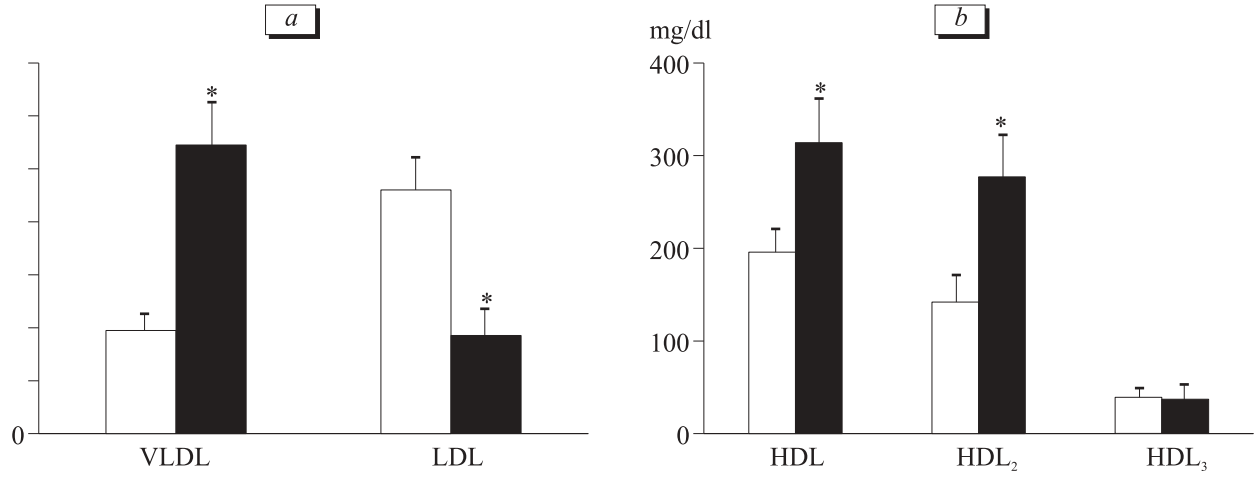

Fig. 2. Changes in blood lipoprotein fractions in hypertensive rats induced by slow cooling. VLDL (*a*) and HDL (*b*) fractions before (light columns) and after slow cooling (dark columns). *$p<0.05$ compared to initial level.

Slow cooling significantly decreased cholesterol atherogenicity coefficient in hypertensive rats (C_{CH}= 0.56±0.07) compared to the initial value (C_{CH}=1.50± 0.21). This results from both the decrease in LDL and increase in HDL content in these rats after cold exposure (Fig. 2).

Thus, under normal conditions, hypertensive NISAG rats are characterized by lower plasma level of HDL fraction and high cholesterol atherogenicity coefficient compared to normotensive Wistar rats. Cold exposure considerably modified plasma lipoprotein spectrum in hypertensive rats. Considerable increase in HDL fraction observed after slow cooling improves both HDL plasma levels and coefficient of atherogenicity in hypertensive rats. This suggests the possibility of correcting disturbances in lipoprotein spectrum typical of essential arterial hypertension using a new strategy based on thermal stimulation.

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