PHYSIOLOGY

Role of Serum Renin and Aldosterone in Animal Adaptation to High-Altitude Conditions

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Adaptation to high-altitude conditions in rats with experimental renal failure is associated with shifts in the rennin–angiotensin–aldosterone system, which manifested in different serum levels of renin and aldosterone in response to water and salt loads depending on the stage of the compensation processes.

Key Words: *renin; aldosterone; hypoxia; high-altitude*

Human capacities to adapt to high-altitude conditions (low atmospheric pressure, hypoxia, high UV radiation, air ionization and humidity, great differences between day and night temperatures) are an important trend of researches [1-4]. Homeostasis of physicochemical constants of extracellular fluid ensured by mechanisms of autoregulation of the water-salt metabolism is very important for adaptation to high-altitude conditions [5,8,9]. Due to the functions of the renin–angiotensin–aldosterone system (RAAS), a decrease in the volume of extracellular fluid under conditions of sodium deficiency, decrease in blood circulation volume, or blood pressure drop lead to intensification of renin secretion in the kidneys and activation of the whole system stimulating sodium reabsorption, which is essential for adaptation [5,9]. However, exact mechanisms of RAAS involvement in these processes, particularly in concomitant renal failure, are poorly studied.

Here we studied the dynamics of RAAS changes during adaptation to the high-altitude conditions on the model of experimental renal failure.

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MATERIALS AND METHODS

Experiments were performed on 300 mongrel male rats (100-120 g) kept under high-altitude conditions (Anzob pass, 3372 m above sea level). Three experimental series were performed: in series I, adapted and non-adapted control rats were used; in series II – non-adapted animals; in series III – adapted animals. Under high-altitude conditions, the rats were exposed unilateral nephrectomy through lumbar incision parallel to the spine. Urine and blood samples were taken on days 1, 2, 5, 10, 15, 30, and 60 after nephrectomy. Diuresis for each sample obtained per unit time (in hours) per 100 g body weight, glomerular filtration rate, and water reabsorption values (by excreted fraction) were determined. For evaluation of the renal function, volume and isosmotic loads were used; to this end, water or 1% NaCl was administered into the stomach in a volume of 5% body weight. Urine was sampled over 4 h after salt or water load and volume of excreted fluid was measured. Serum renin and aldosterone concentrations were measured by radioimmune method using Sea Sorin kits.

The data were processed routinely using ANOVA and the Student–Fisher test (p=0.05).

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RESULTS

Blood renin levels in nephrectomized non-adapted rats after water loads on days 5, 15, and 30 after surgery were significantly higher ($p<0.01$) than in adapted animals (Fig. 1). Renin level after salt load was higher only on day 5 after nephrectomy, while on days 15 and 30 it was significantly lower ($p<0.05$) in non-adapted animals than in adapted animals (Fig. 2).

A correlation was found between blood levels of aldosterone after water loads in nephrectomized rats and time after surgery. Thus, on day 5 after nephrectomy aldosterone level in non-adapted rats was significantly ($p<0.05$) lower, on day 15 did not differ, and on day 30 significantly ($p<0.05$) surpassed the corresponding parameter in adapted animals. After salt loads, differences in plasma levels of aldosterone were noted only on day 5 after nephrectomy and were more pronounced in non-adapted rats.

Thus, adaptation to high-altitude conditions in nephrectomized animals is associated with certain shifts in aldosterone and renin plasma levels. Changes in their concentrations depend on the stage of compensatory processes. According to our data, water and salt loads demonstrating reserve capacities of the water-salt balance regulation system, suggest that adaptation to high-altitude conditions primarily involves activation of the mechanisms of neurohumoral compensation of reabsorption and secretion in the kidneys. In addition, days 5 and 15 after unilateral nephrectomy can be considered to be critical for filtration, and day 30 – for reabsorption.

Function of the remaining kidney at first stage (day 5 after nephrectomy) reflects recovery of filtration capacities in adapted animals due to autoregulation of renal blood flow and due to the renni–angiotensin mechanism [5,8]. However, our data show that under high-altitude conditions (in non-adapted rats), this compensation stage takes more time, *i.e.* subsystem of autoregulation of filtration processes can restore this function, but with participation of CNS (at a different hierarchy level). Thus, our findings show that non-adapted animals have impaired hormonal regulation of blood osmotic pressure up to day 15 after nephrectomy. There was no adequate reduction of renin secretion or increase in aldosterone release after volume load, and no reverse shifts after isosmotic load.

The role of angiotensin-converting enzyme genetically determining the resistance and the rate of high-altitude adaptation for normalization of water-salt metabolism is now actively discussed [6,8,10]. Therefore, the observed staging in adaptation to high-altitude conditions with involvement of central mechanisms suggests that these processes successively involve nervous system, genetic factors, and hormonal substrates.

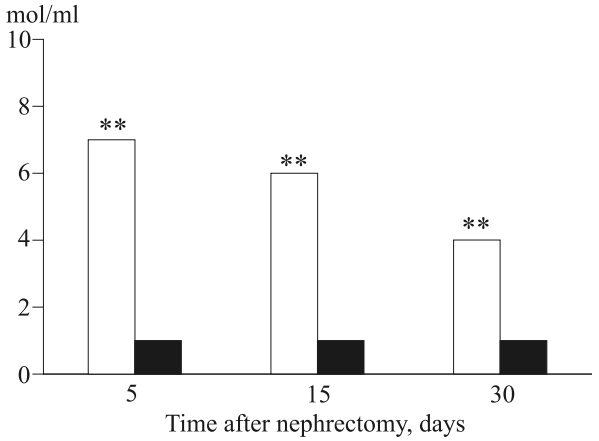

Fig. 1. Dynamics of renin plasma levels after water load in nephrectomized animals adapted (dark bars; control) and non-adapted (light bars) to high-altitude conditions. Here and in Fig. 2: $^{**}p<0.01$ in comparison with the control.

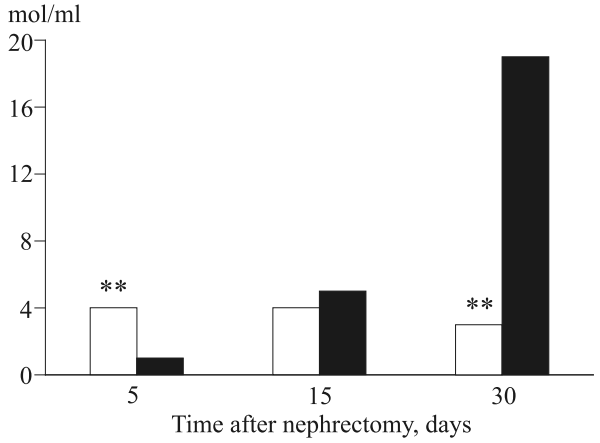

Fig. 2. Dynamics of renin plasma levels after salt load in nephrectomized animals adapted (dark bars; control) and non-adapted (light bars) to high-altitude conditions.

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