PHYSIOLOGY

Effect of Age and Sex on Blood Pressure, Development of Renal Hypertension, and Concentration of Nitric Oxide in the Blood of Albino Rats

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The mean blood pressure did not depend on the sex of animals and was characterized by the same ontogenetic changes in males and females. The mean blood pressure in infantile and, particularly, in old rats was higher than in adult animals. The increase in blood pressure in old rats was accompanied by a decrease in NO production. Infantile rats were least resistant to the development of renal hypertension. The degree of hypertension in infantile and adult females was lower than in males. However, the concentration of NO in these females was higher than in male rats. Aging was accompanied by inversion of sex differences in the resistance to renal hypertension. The severity of hypertension in old females was greater than in males. It was accompanied by a significant age-related decrease in NO concentration in female animals. Our results indicate that NO plays an important role in sex differences in the resistance of infantile, adult, and old rats to hypertension, while the decrease in NO concentration during aging leads to blood pressure elevation in females and males.

Key Words: *sex; age; blood pressure; renal hypertension; nitric oxide*

Arterial hypertension is a most prevalent pathology of the cardiovascular system (CVS). Increased blood pressure (BP) preceding hypertension is observed in the childhood period [2], and the number of patients with hypertension sharply increases in elderly and old people. Hypertension is more typical of men than of premenopausal women. Opposite differences are revealed in the old age group. It contributes to higher mortality rate from strokes and infarctions among women [9,10]. Age- and sex-specific features of hypertension reflect the existence of sex differences in the ontogenetic development, properties [12], and regulatory mechanisms of CVS [5]. Age-related changes in endothelial function are of particular importance in this respect [7]. Little is known about the effect of age and sex factors on BP, development of hypertension, and NO production. Here we evaluated the level of BP, resistance to renal hypertension, and NO concentration in the blood of infantile, adult, and old female and male albino rats.

MATERIALS AND METHODS

Experiments were performed on albino rats of the following three groups: 6-week-old animals (20 infantile female and 20 male rats; mean body weight

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52 and 66 g, respectively); 7-month-old animals (18 adult female and 18 male rats; mean body weight 220 and 260 g, respectively); and 25-month-old animals (16 old female and 16 male rats; mean body weight 310 and 360 g, respectively). Renal hypertension in 50% animals was induced by the method of Goldblatt with modifications [3]. A clip was applied to the left renal artery under nembutal anesthesia (40 mg/kg). The remaining animals were subjected to laparotomy (control). After 6 weeks (period of arterial hypertension development), BP in hypertensive and control rats was measured using a catheter. The measurements were performed on a PowerLab/400 ML401 measuring and computing complex. The concentration of NO in control rats was evaluated from the amount of nitrites in the blood (Griess reagent) [1]. The results were analyzed by means of Statistica 5.0 software (Wilcoxon test, Mann–Whitney test) and ANOVA (Duncan's test). The differences were significant at $p<0.05$.

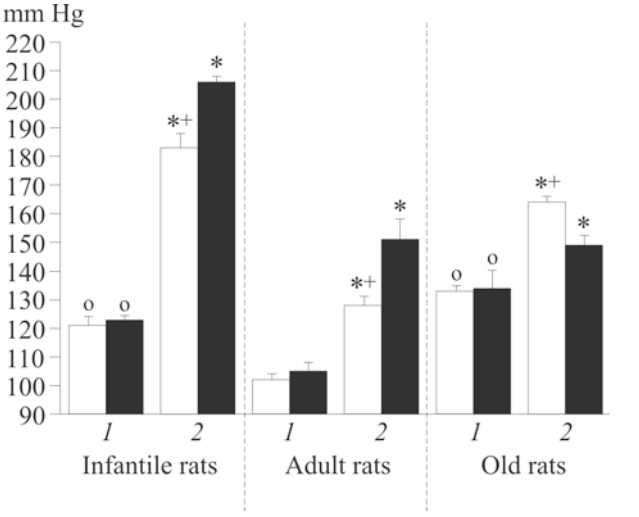

Fig. 1. MBP in females and males of various age groups. Control (*1*); hypertension (*2*). Here and in Fig. 2: light bars, females; dark bars, males. $p<0.05$: *compared to the control; +compared to males; °compared to adult animals.

RESULTS

The mean BP (MBP) depended on the age, but not on the sex of experimental animals (Fig. 1). MBP in infantile, and particularly, in old rats was much higher than in adult animals. No differences in MBP were found between females and males. It was observed not only in the group of adult rats [10], but also in infantile and old animals. Ontogenetic changes in chronotropic function of the heart were shown to be insignificant ($p>0.05$). Therefore, age-related variations in BP are mainly mediated by vascular mechanisms. Evaluation of age-related changes in BP in male specimens revealed the existence of interstrain differences [8,11].

The resistance of animals from various groups to hypertension and age-related changes in this parameter depended on the sex of experimental rats (Fig. 1). Young animals were least resistant to disturbances in blood supply to the kidneys. These data are consistent with the result of previous studies on other models of hypertension [12]. The degree of hypertension in infantile rats was higher than in adult and old animals (Fig. 1). MBP in infantile specimens was higher than in animals of older age groups. Moreover, the elevation of MBP in infantile males and females (by 51 and 67%, respectively; $p<0.05$) was more pronounced than in other rats. The absolute and relative values of MBP in infantile females were lower than in males. Therefore, infantile females are more resistant to renal ischemia than males.

In adult rats, baseline MBP was reduced. These animals were more resistant to hypertension than infantile rats. The severity of hypertension in adult and infantile females was lower than in males by absolute MBP value (Fig. 1) and by the degree MBP increase (by 25 and 44% in females and males, respectively; $p<0.05$). Higher resistance of adult females to renal ischemia (compared to males) was observed in our previous experiments [4]. Similar results were obtained on other models of hypertension [10].

In adult rats, baseline MBP was elevated. These rats were characterized by inversion of sex differences in the resistance to hypertension (compared to infantile and adult specimens): the degree of hypertension in old females was higher than in males by absolute MBP values (Fig. 1) and degree of MBP increase (by 23 and 11% in females and males, respectively; $p<0.05$). These data indicate that the advantage of female rats over males in terms of their resistance to hypertension disappears during aging.

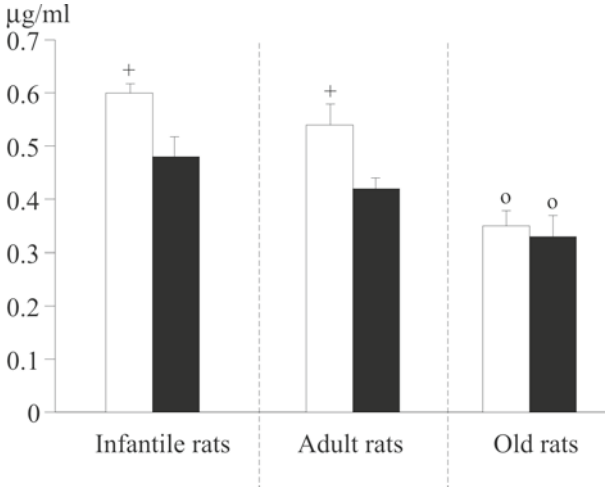

Fig. 2. NO concentration in the blood from control females and males of various age groups.

Figure 2 illustrates NO concentration in blood samples from females and males of various age groups. Blood NO concentration tended to increase in infantile rats (as compared to adult animals). Previous studies showed that baseline MBP increases under these conditions [12]. These data confirm the hypothesis that BP during the prepubertal period is mainly determined by the structure and sympathetic innervations of vessels, but not by vascular sensitivity to vasoactive substances. Similarly to humans, the decrease in NO production in old animals [6] was accompanied by an increase in baseline BP (as compared to adult rats; Fig. 2).

We compared the resistance to hypertension and concentration of NO in specimens of various age groups. Blood NO concentration in infantile and adult females was higher than in males. Renal hypertension in these females was less pronounced than in males. The age-related decrease in the production of NO in old females was more significant than in males. No sex differences were found in the concentration of NO. These changes were accompanied by the development of severe hypertension in females. Therefore, the advantages of females over males in relation to the resistance to hypertension are observed until certain age and depend mainly on increased production of NO in infantile and adult females. The increased concentration of NO is provided by strong cholinergic influences on CVS in females [4], including the endothelium-dependent effect of acetylcholine. These features are also determined by the effect of estrogens, which stimulate NO production via various mechanisms [6]. The age-related decrease in the content of estrogens is accompanied by the reduction of NO production and development of severe hypertension. Hence, the degree of hypertension in old females is higher than in males.

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