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RAPID COMMUNICATION

The Influence of Age on the Development of Two-kidney, One-clip Hypertension in the Rat

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Summary

The role of age in the development of two-kidney, one-clip (2K1C) renal hypertension was evaluated. Blood pressure response to aortic constriction was more pronounced in young rats although the alterations of renal renin activity and body fluid volumes were greater in adult ones. Obtained results suggested that 2K1C renal hypertension is maintained by reciprocal interaction of renin-angiotensin system and body fluid volume alterations only in adult rats. In young rats other factors might be more important.

Key words

Renal hypertension – Renin-angiotensin system – Plasma volume – Extracellular fluid volume – Rats

The initial work of Harry Goldblatt (Goldblatt *et al.* 1934, Hass and Goldblatt 1959) stimulated the search for a better understanding of the relationship between the renin-angiotensin system and renovascular hypertension. Two distinct models of renal hypertension (one-kidney, one-clip and two-kidney, one-clip) differ in their pathophysiology. Body fluid volumes are expanded and plasma renin activity remains normal or suppressed in one-kidney, one-clip model (Liard *et al.* 1974). On the other hand, in two-kidney, one-clip model, plasma renin activity and renin content are increased in stenotic kidney but decreased in the contralateral one (Möhring *et al.* 1975).

Immature rats are more prone to develop hypertension due to chronic excess salt feeding than adult ones (Dahl *et al.* 1968) and they are also more susceptible to various forms of experimental hypertension (for review see Zicha *et al.* 1986). Moreover, we have observed higher blood pressure response to high salt intake in young subtotally nephrectomized rats (Kuneš and Jelínek. 1984) as well as in the rats influenced by a transient renal ischemia (Kuneš *et al.* 1986).

The influence of age on the development of two-kidney, one-clip (2K1C) hypertension in young and adult Wistar rats is described in this paper. The role of renin-angiotensin system and body fluid volume alterations in the development of this type of renal hypertension were also studied.

Experiments were performed on male Wistar rats fed a standard diet and tap water *ad libitum*. In animals aged 10 days (young) and 60 days (adult) the abdominal aorta was constricted between both renal arteries (the internal diameter 0.4 mm). Sham-operated age-matched animals served as a controls. Arterial pressure, body fluid volumes and renal renin activity were measured 50 days after the aortic constriction. Blood pressure was measured by direct puncture of the carotid artery under light ether anaesthesia by using a Statham P23Db transducer. Plasma volume (PV) was determined by the Evans blue dilution and extracelullar fluid volume (ECFV) by means of sodium ferrocyanide distribution (Kuneš and Jelínek 1984). Renal renin activity (RRA) was determined in renal homogenates by method of Gross *et al.* (1965) as adapted in our laboratory (Pohlová *et al.* 1974).

Results are expressed as mean±SEM. Student's t-test was used for statistical evaluation of the data. $P<0.05$ was considered as a level of statistical significance.

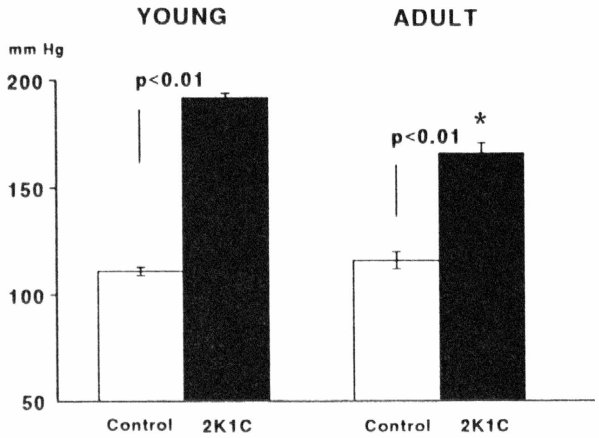

Fig.1
Mean arterial pressure of young and adult rats with two-kidney, one-clip (2K1C) renal hypertension. * - $p<0.01$ vs corresponding young group.

Table 1
Body fluid volumes in rats with two-kidney, one-clip (2K1C) renal hypertension.

	YOUNG		ADULT	
	Control (8)	2K1C (10)	Control (8)	2K1C (9)
PV (ml/100 g)	3.8±0.1	3.9±0.1	3.3±0.1 $^{+}$	3.7±0.04*
ECFV (ml/100 g)	17.3±0.5	18.3±0.8	15.9±0.5	18.3±0.4*
IFV (ml/100 g)	13.5±0.4	14.4±0.7	12.6±0.5	14.6±0.4*

Data are means±SEM, number of animals are in parenthesis, PV - plasma volume, ECFV - extracelullar fluid volume, IFV - interstitial fluid volume, * - $p<0.01$ vs corresponding controls, $^{+}$ - $p<0.05$ vs corresponding young group.

Table 2
Renal renin activity (ng Ang II/ mg protein/ 10 min) in rats with two-kidney,one-clip (2K1C) renal hypertension.

	YOUNG		ADULT	
	Control	2K1C	Control	2K1C
Left kidney	25.3±1.1	39.1±3.0*	18.2±1.2	69.6±10.6* $^{+}$
Right kidney	20.3±3.1	3.6±0.6*	14.5±1.3	3.7±0.8*

* - $p<0.01$ vs corresponding controls, $^{+}$ - $p<0.05$ vs corresponding young group.

Blood pressure was significantly increased after aortic constriction in both young and adult rats (Fig. 1). In spite of relatively milder constriction in young animals, the increment of their blood pressure was significantly ($p<0.01$) higher in comparison with adult ones. On the other hand, body fluid volumes were increased only in adult rats (Table 1). Nevertheless, plasma volume to interstitial fluid volume ratio was not

changed indicating no redistribution of extracellular fluid between intravascular and interstitial space. There was negative correlation between blood pressure and extracellular fluid volume ($r = -0.74$, $p<0.05$) in adult rats. Age-dependent changes of renal renin activity (RRA) were seen in kidneys of experimental groups compared to controls (Table 2). RRA was decreased in the right kidney of both age groups to the same extent. Nevertheless, the increase of RRA in the left kidney was bigger in adult rats in comparison with younger ones. Only in adult rats there was a negative correlation between weight of the left kidneys and their RRA ($r = -0.69$, $p<0.05$).

The development and maintenance of two-kidney, one-clip renal hypertension has been suggested to occur as a result of the impairment in renal pressure-volume regulation (Guyton *et al.* 1974). The clipped kidney alters the balance between pressure and volume regulation by several different mechanisms, e.g. increase of renal nerve activity (Katholi *et al.* 1982), change in renal hemodynamics (DeForrest *et al.* 1978) and the alteration in renal hormone production (Anderson *et al.* 1985).

The results of our study are in a good agreement with a suggestion that renin-angiotensin system plays a significant role in this model of renal hypertension, particularly during the first 6–12 weeks (Carretero *et al.* 1978).

We did not measure plasma renin activity but we can speculate that it was higher in adult rats because renal renin activity in stenotic kidney was greater in this age group when compared with the younger one. Body fluid volumes were expanded only in adult rats suggesting that the impairment of volume regulation was also present in these animals. The different response of young and adult animals to the aortic constriction could be explain by the fact that the severity of stenosis at the beginning of the experiment was not same in both aged group. In 10-day-old rats the constriction on the diameter 0.4 mm was relatively milder but became progressively more critical with aging. This is in contrast to the situation of adult animals in which the narrowing of renal artery was more severe from the beginning. Nevertheless, the mechanism by which blood pressure of young rats was increased even more than that in adult ones remains to be elucidated. It seems that some other factors (Anderson *et al.* 1991) might be more important in development of 2K1C renal hypertension in young animals.

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