MINERVA UROLOGICA E NEFROLOGICA

Minerva Urologica e Nefrologica 2010 September;62(3):225-9

ORIGINAL ARTICLES

Sodium sensitivity and its role in the maintenance of high blood pressure in two-kidney, one-clip renovascular hypertension after remova of the clipped kidney in rats

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AIM: The aim of the present study was to define the role of sodium balance and sodium sensitivity in the maintenance of two-kidney, one-clip renovascular hypertension in rats.
METHODS: Six months after induction of hypertension, systolic blood pressure, sodium balance, water intake and urine excretion were measured under normal conditions, after nephrectomy of the clipped kidney, and under conditions of sodium load.
RESULTS: No difference between control rats and rats with or without post-Goldblatt hypertension emerged during the development of renovascular hypertension and after nephrectomy of the clipped kidney. Under conditions of high sodium intake, the contalateral kidney of the post-Goldblatt hypertensive rats was unable to excrete surplus sodium. Sodium retention was not correlated with water retention. In contrast to the controls, systolic blood pressure increased in the animals with post-Goldblatt hypertension and those with post-Goldblatt normotension during the sodium load period. No correlation was found between blood pressure increase and sodium retention. The animals were considered sodium sensitive in relation to blood pressure.
CONCLUSION: In the chronic phase of two kidney-one clip renovascular hypertension, the post-Goldblatt hypertensive and the post-Goldblatt normotensive animals showed sodium sensitivity of blood pressure. The contralateral kidney of the post-Goldblatt hypertensive animals was unable to excrete surplus sodium under conditions of high sodium intake. But this inability and the sodium sensitivity of blood pressure cannot be thought responsible for the maintenance of renovascular hypertension in this model.

language: English

INTRODUCTION

High blood pressure does not always normalize completely after an operative correction of renal arterial stenosis or nephrectomy of the stenotic kidney in the chronic two-kidney renovascular hypertension (1, 2). The mechanisms that contribute to the maintenance of hypertension are still unclear. Several clinical and experimental studies suggested that the contralateral kidney is involved in maintaining hypertension (1, 3, 4, 5, 6, 7, 8), because in individual cases, only the removal of the contralateral kidney led to a complete normalization of blood pressure (1). Activation of central pressure mechanisms by renal afferences from this kidney is one explanation of the failure of the normalization of blood pressure during the chronic phase of hypertension after correction of the arterial stenosis (1).
However some investigators postulated, that in the chronic phase of the two-kidney, one clip renovascular hypertension (2K,1C-RVH) "volume factors" are responsible for the maintenance of high blood pressure (9). In this phase of 2K, 1C-RVH a positive correlation between sodium retention and hypertension has been found. Increase of sodium and water excretion by chronic treatment with Angiotensin-Converting Enzyme blockers led to a significant blood pressure reduction (9). These findings could not be confirmed by other authors (10). They found an increase of sodium excretion and even a negative sodium balance in the chronic phase of renovascular hypertension (10).
The purpose of this study was to examine, whether the contralateral kidney is able to eliminate surplus sodium after nephrectomy of the stenotic kidney and if not, whether possible sodium retention is responsible for the maintenance of hypertension.

METHODS

Male Spanque-Dawley rats, weighing at the operations day 115-130 g, were used
The right renal artery was constricted by a silver clip (I.D. 0.23-0.25 mm) in 63 rats, while sham operation was carried out in 17 rats. The operated animals were kept in groups of 2-3 rats in Makrolon cages (temperature 22-24°, light-dark periods of 12 h). Rats had free access to water and food.
Six months after constriction or sham operation, blood pressure was measured in conscious rats using tail plethismography, 3-4 times at different days. For tail artery occlusion an external pressure cuff was used (I.D. 8 mm, length 30 mm).
For the experiments, only rats with documented hypertensive systolic blood pressure (SBP) were used (SBP>150 mm Hg). Animals with malignant hypertension and growth retardation (SBP > 220 mm Hg) were excluded.
The first 8 days of the test series were considered as control period. At the 9th experimental day, nephrectomy of the clipped kidney was performed. On the basis of blood pressure behaviour after nephrectomy two animal groups were formed. The group of "Post Goldblatt" normotension (SBP < 140 mm Hg), (group II) and the group of "Post Goldblatt" hypertension (SBP > 150 mm Hg), (group III). Animals with sham operation and also nephrectomy of the shame operated kidney were considered as controls (group I).
After nephrectomy and animals convalesce a period of sodium load followed (food composition Tab. 1), (Co. ATROMIN).
For all operations the animals were anaesthetized with Ketamin/Xylacin in dose of 100/12 mg/kg body weight i.m. During operation body temperature was maintained at 37°-37.5° with the aid of heated board.
All animals stayed during experiments in individual metabolic cages. Faeces und urine were collected separated. The urine and faeces drainage system of the cages and the collecting container were every day cleaned and silicon sprayed to avoid collecting losses. Into the collecting container a known amount Paraffin-Oil was daily added to avoid evaporation of urine.
Sodium in urine was measured by flame photometer. Faeces were pulverized at first and extracted in acid 15 minutes. Afterwards sodium was determined by flame photometer also.
Statistical analyses were performed by the t-test and Wilcoxon test for paired and unpaired groups and X^2-

test for values distribution. Results are referred to as no significant when their P value was > 0.05.

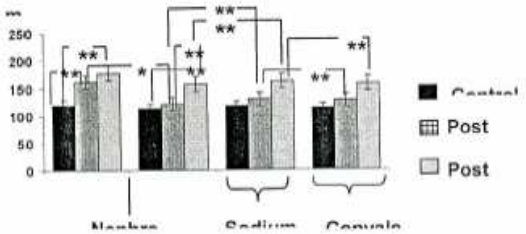
TABLE I (FOOD COMPOSITION)

	normal food	sodium load food
Sodium	2500 mg	16000 mg
Potassium	7000 mg	7000 mg
Row protein	172650 mg	172650 mg
Row fat	53530 mg	53530 mg
Disaccharide	110364 mg	110364 mg
Polysaccharide	455800 mg	455800 mg
Calcium	2500 mg	2500 mg
Phosphor	7500 mg	7500 mg
Magnesium	750 mg	750 mg

RESULTS

Six months after clipping or sham operation, clipped animals developed arterial hypertension. The mean systolic blood pressure of animals with "Post Goldblatt" normotension (group II) was 162±15 mm Hg and of animals with "Post Goldblatt" hypertension (group III) 178±20 mm Hg. The blood pressure of sham operated rats (group I) was normal (120 ±10 mm Hg). Nephrectomy of clipped kidney caused normalization of blood pressure in animals of group II (127 ±11 mm Hg). These animals were termed as "Post Goldblatt" normotensive rats. Animals of group III continued to have high systolic blood pressure despite a mild decrease (157 ±13 mm Hg). These rats were termed as "Post Goldblatt" hypertensive. In control animals nephrectomy of the sham clipped kidney didn't have any effect on blood pressure (Figure 1).

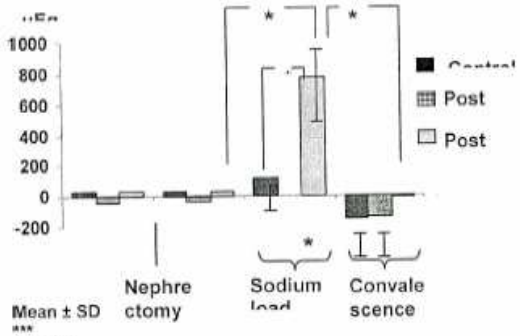
During the first period of adaptation no differences appeared between the three groups in the sodium balance (Figure 2). Sodium balance for control animals was 33±12 µEq/24h, for "Post Goldblatt" normotensive animals (group II) -39±16 µEq/24h and for Post Goldblatt" hypertensive animals (group III) -35±16 µEq/24h. Nephrectomy of the clipped kidney didn't affect sodium balance in all rats. Under condition of high sodium intake sodium balance only of the controls and the rats with "Post Goldblatt" normotension has not changed. Sodium balance for control animals was in this period 102±32 µEq/24h and for "Post Goldblatt" normotensive animals -2±9 µEq/24h. The sodium balance of the rats of the group III ("Post Goldblatt" hypertensive rats) became much more positive (774±96 µEq/24h) and differed significantly from the group II as well as from the controls. In this period water intake (Figure 3) and urine excretion (Figure 4) were higher in all animals. No any water retention was noted, particularly in animals with "Post Goldblatt" hypertension. During next period of convalescence animals of the group III eliminated surplus sodium and the sodium balance become negative. The sodium balance was again not different between three groups.



Mean ± SD
*** P<0.001

DISCUSSION

According to other authors appeared in our experiments, that for the maintenance of the chronic two-kidney, one clip renovascular hypertension (2K,1C-RVH) sodium retention does not play an important role (10,11,12,13). In our study didn't come obviously during development of hypertension to any sodium retention. Because it would be to be expected, that one in the course of the hypertension development retained sodium amount would have excreted after nephrectomy of clipped kidney. However, we have not proved in our experiments an at least passing negative sodium balance after removal of the stenotic kidney. We also found under normal condition no sodium retention after nephrectomy of the clipped kidney. But under condition of high sodium intake the contralateral kidney of the rats with "Post Goldblatt" hypertension (group III) is not able to excrete surplus sodium.



Mean ± SD
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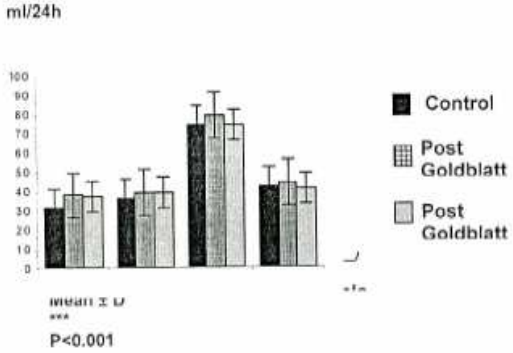
P<0.001
* P<0.05

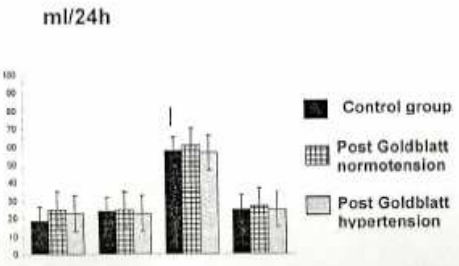
The result was sodium retention. A inability of the contralateral kidney to excrete surplus sodium under condition of sodium load has not been mentioned before. However, during the following period and under condition of normal sodium intake excreted the contralateral kidney of the animals with "Post Goldblatt" hypertension the accumulated sodium. Observed sodium retention was not correlated with water retention. In contrast to controls come during period of sodium load to an increase of systolic blood pressure in animals with "Post Goldblatt" hypertension (group III) and also with "Post Goldblatt" normotension (group II). We found no any correlation between blood pressure increase and sodium retention

in this rats. Obviously it concerned in our experiments a volume independent increase of the systolic blood pressure. Animals with as well as without "Post Goldblatt" hypertension are in relation on the blood pressure salt sensitive. The existence of a sodium sensitivity of the blood pressure has been shown in animals as well as in people (10, 11, 12, 13). The mechanisms of the salt sensitivity are still unclear. It is supposed that the sodium sensitivity is associated with a dysregulation of the sympathetic nerve system (10, 11, 12, 13, 14, 15). Under sodium load following changes can appear:

a) Noradrenalin concentration in plasma increases in salt-sensitive animals (16)
b) Sensitivity of the resistance vessels against noradrenalin increases (16)
c) During noradrenalin infusion stronger blood pressure increase is found in salt sensitive animals as in salt resistant animals (16, 17)
d) The neural resumption of noradrenalin is decreased (16)
e) Adrenalin and noradrenalin concentration increase stronger after cold stress under sodium load as under normal sodium intake (16).



The aspect of sodium sensitivity for the maintenance of renovascular hypertension has not been examined experimental or clinical before. In our study come in the chronic phase of 2K,1C-renovascular hypertension to a salt sensitivity of blood pressure. However, sodium sensitivity alone can not explain maintenance of hypertension. Because both groups, rats with as well as without "Post Goldblatt" hypertension showed salt sensitivity of systolic blood pressure.



CONCLUSION

Contralateral kidney of "Post Goldblatt" hypertensive rats is unable to excrete surplus sodium under condition of high sodium intake. Increase of systolic blood pressure under sodium load in this model of Two Kidney, One Clip renovascular hypertension is volume independent. Systolic blood pressure is salt sensitive. Sodium sensitivity is associated with an increase of the activity of sympathetic nerve system. However, sodium sensitivity alone is not enough for the maintenance of hypertension in Two Kidney, One Clip renovascular hypertensive rats.

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