

Role of Sodium Balance on Maintenance of Blood Pressure in the Chronic Phase of Two-Kidney, One-Clip Hypertension*

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Blood pressure and sodium balance have been studied after unclipping, nephrectomy and sham operation of ischemic kidney in the chronic phase (16 weeks) of two-kidney, one clip hypertension. In hypertensive rats the fractional excretion of sodium was $85.5 \pm 2.3\%$ and blood pressure (BP) was significantly increased (187.1 ± 4.5 mmHg, $p < 0.001$). Removal of either the constricting clip or ischemic kidney induced a decrease of BP to normal level whereas sham operation did not produce any change. However, rats submitted to these three experimental manipulations showed, at 1, 2, 3 and 4 days, and at 3 weeks, similar changes in sodium excretion. In the groups with unclipping or nephrectomy of ischemic kidney, water intake was less and urine volume smaller than in the sham operated group. These results suggest that a positive sodium balance is not important to maintain hypertension at this stage and that changes in sodium balance, after both unclipping and nephrectomy of ischemic kidney, have no influence in BP normalization.

Key words: Sodium balance, Nephrectomy, Unclipping, Two-kidney, One-clip hypertension.

The role of sodium balance on maintenance of high blood pressure in the chronic phase of two-kidney, one-clip hypertensive rats has been discussed for a long time. During this phase, hypertension could be volume-dependent, due to an increase of sodium retention (3, 10).

However, this hypothesis has not been recently confirmed by other authors (11, 17). Moreover, MOHRING *et al.* (10) noticed that, when blood pressure is higher than 180 mmHg, a depletion of sodium occurs and hypertension is then maintained by an increase of renin secretion.

Since both nephrectomy and unclipping of ischemic kidney normalise blood pressure in these animals (16), changes of

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blood pressure and sodium balance have been studied after reversal of hypertension by either of these two corrective manoeuvres. If the sodium balance is responsible for the hypertension, these surgical manipulations will produce a great excretion of sodium. On the other hand, if there is a negative sodium balance in hypertensive animals, both nephrectomy and unclipping of ischemic kidney will produce sodium retention.

Materials and Methods

Male Wistar rats weighing 195-220 g were lightly anaesthetised with ether and a silver clip (internal diameter 0.20 mm) was placed around the left renal artery. The contralateral kidney was left untouched. Unclipping ($n=8$), nephrectomy ($n=8$) or sham operation ($n=9$) of ischemic kidney was carried out in animals through the same incision at 16 weeks from clipping. Blood pressure and sodium balance were determined 16 weeks after clipping and 1, 2, 3, 4 days and 3 weeks after each surgical manipulation. In all groups systolic blood pressure (BP) was measured without anaesthesia by the tail-cuff method (LE 5000, Letica), as has been previously described (16) and only those rats having a BP of 150 mmHg, or above, were used.

Rats were housed in individual metabolic cages for 4 days, in order to allow their adaptation, before the start of data collecting to evaluate sodium balance. They were given distilled water and a purified diet (0.34 % sodium and 0.71 % potassium) ad libitum. Water and food intake was measured daily. Uneaten food was weighed at the end of each balance period. Every 24 h urine was analysed for Na^+ and K^+ determination by flame photometry (Corning 435). Feces were not analysed. Furthermore, at the end of every 24-hour collection period, the collection funnel of each cage was rinsed

with 50 ml of distilled water and the rinse saved for analysis of Na^+ and K^+ content. Daily sodium excretion was calculated as the product of urine volume and urine sodium concentration plus the product of wash volume and wash sodium concentration. Daily sodium output was calculated as the fractional excretion of sodium (24-hour urinary sodium excretion divided by 24-hour sodium intake $\times 100$). The data obtained at 16 weeks from clipping and 3 weeks after unclipping, nephrectomy and sham operation of ischemic kidney are the mean of three determinations, each of 24 hours.

The data are expressed as means \pm SE. In the statistics, double-way analysis of variance (ANOVA) has been used, with a later comparison by means of a statistics distributed as a t-Student.

Results

In rats with chronic hypertension blood pressure significantly increased (from 124.2 ± 1.2 mmHg to 187.1 ± 4.5 mmHg, $p < 0.001$). One day after both nephrectomy and unclipping of ischemic kidney BP decreased significantly ($p < 0.001$) and was normal in these groups after 3 weeks. Nevertheless, sham operation did not produce any change (fig. 1). In the groups of chronic hypertensive animals the mean fractional excretion of sodium was 85.4 ± 2.3 %. One day after both nephrectomy and unclipping there was a significant decrease in sodium excretion compared to preoperative levels ($p < 0.001$). However, a similar effect was also achieved in the sham operated group (table I). After one day and from then on there was an increase of sodium excretion; at the end of study the fractional excretion of sodium in the sham operated animals was not different from that observed in the two other experimental groups (table I). These surgical manipulations also produced a significant

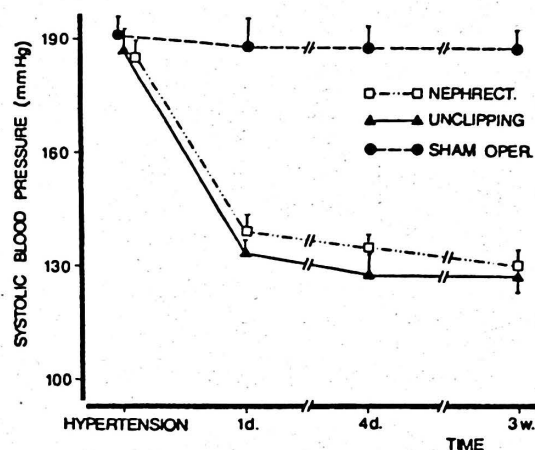


Fig. 1. Variations of systolic blood pressure in rats with chronic hypertension at 1 and 4 days and at 3 weeks of nephrectomy, unclipping or sham operation of ischemic kidney.

decrease ($p < 0.001$) in both urine volume (fig. 2) and water intake (fig. 3), during the first twenty-four hours. In the groups with either removal of clip or ischemic kidney, urine volume (fig. 2) and water intake (fig. 3) remained unchanged throughout, whereas in the sham operated group it increased to the pre-surgical level.

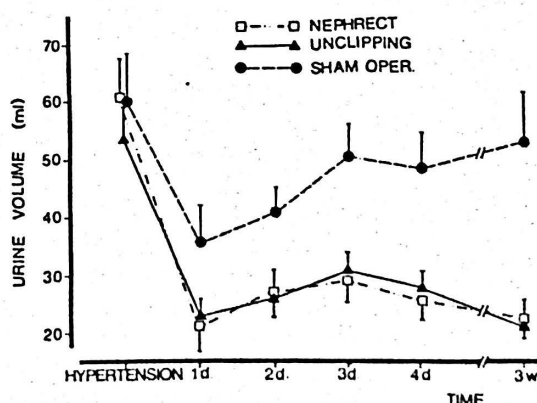


Fig. 2. Variations of urine volume in rats with chronic hypertension at 1, 2, 3 and 4 days and at 3 weeks of nephrectomy, unclipping or sham operation of ischemic kidney.

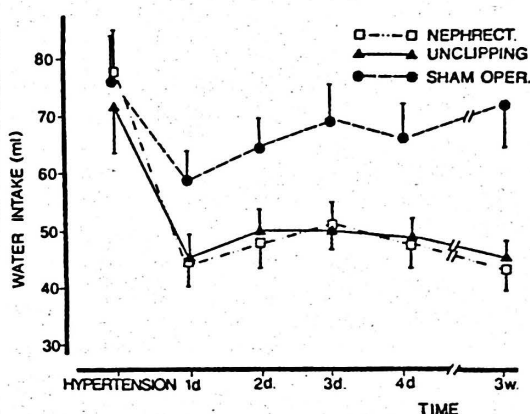


Fig. 3. Variations of water intake in rats with chronic hypertension at 1, 2, 3 and 4 days and at 3 weeks of nephrectomy, unclipping or sham operation of ischemic kidney.

Compared to that of a group of similar weight and normal arterial pressure, the urinary sodium concentration in the hypertensive animals was significantly decreased (from 143.7 ± 12.9 to 58.0 ± 16.8 mEq Na⁺), all surgical manipulations producing a slight decrease at one day which, in the sham operated group, returned to preoperative levels (fig. 4). However, in the groups with unclipping or nephrecto-

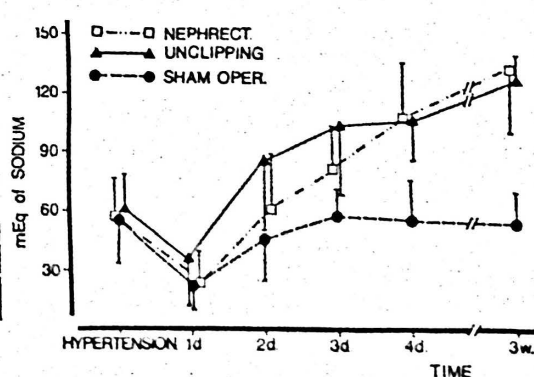


Fig. 4. Variations of urinary sodium concentration in rats with chronic hypertension at 1, 2, 3 and 4 days and at 3 weeks of nephrectomy, unclipping or sham operation of ischemic kidney.

Table I. Fractional excretion of sodium in hypertensive rats (16 weeks) and after 1, 2, 3 and 4 days and 3 weeks of nephrectomy, unclipping or sham operation of ischemic kidney.
Significance with respect to hypertensive animals. * $p < 0.001$. Significance with respect to the first day after each surgical manipulation ** $p < 0.001$.

	Fractional excretion of sodium					
	16 W.	1 D.	2 D.	3 D.	4 D.	3 W.
Nephrectomy	85.9 ± 4.9	30.5 ± 14.6 *	59.6 ± 13.8	70.0 ± 13.6	72.0 ± 6.4	75.8 ± 4.7 **
Unclipping	82.0 ± 3.7	32.4 ± 8.1 *	64.9 ± 16.4	76.4 ± 10.5	74.0 ± 3.5	73.6 ± 5.3 **
Sham operation	88.4 ± 3.6	37.4 ± 9.0 *	58.7 ± 8.5	75.6 ± 9.2	75.7 ± 5.9	77.6 ± 3.5 **

my of ischemic kidney, urinary sodium concentration increased and was significantly different ($p < 0.001$) from that of the sham operated group (fig. 4).

Discussion

The influence of sodium balance in the maintenance of two-kidney, one-clip hypertension has been studied during the chronic phase (16 weeks). Some authors (3, 10) affirm that the hypertensive process is sodium-volume dependent at this stage. However, it has also been postulated that the increase of renin secretion, and therefore of hypertension, is secondary to a depletion of sodium when the BP is higher than 180 mmHg (10). The results of this work seem to suggest that the increase of plasma renin activity in these hypertensive animals (16, 17) is not induced by a loss of sodium, because the fractional excretion of sodium was $85.5 \pm 2.3\%$. These observations disagree with those of MOHRING *et al.* (10), since there was a retention of sodium in spite of BP being 187.1 ± 4.5 mmHg. In disagreement with KRAMER and OCHWADT (8), we found that the renal excretory function had increased in these animals. This, and the low urinary sodium concentration, were probably due to a greater renal blood flow in the nonclipped kidney (14).

Both nephrectomy and unclipping of ischemic kidney produced an immediate and significant decrease of BP and, after three weeks, BP was similar to that found in the control group. This response of BP agrees with some previous reports (6, 16-18), though not with others (7, 9, 11, 12). The increase of sodium retention after the surgical manoeuvres suggests that sodium balance is not important for the maintenance of high blood pressure in this experimental model since the decrease of blood pressure is not

accompanied by a greater excretion of sodium. On the other hand, as there are no significant differences in sodium excretion between the experimental groups and the sham operated group, it is unlikely that the decrease of renin secretion after unclipping and nephrectomy of ischemic kidney (16, 18) is produced by an increase of sodium retention. It seems that the decrease of sodium excretion found in the postoperative periods is not produced by a lack of food intake, as noted by GULATY *et al.* (4), since there is a greater sodium retention. Thus, as other authors have already noted (2, 6), there is no relation between BP and sodium excretion changes. The difference in water intake between groups could be secondary to changes in angiotensin II (15), because a decrease of plasma renin activity occurs after these surgical procedures (16, 18). As has been supported by other authors (5, 12), the greater urine volume is probably produced by an increase of renal perfusion pressure since there is a significant decrease of urine volume when the BP is normalised by nephrectomy and unclipping of ischemic kidney. These results support the hypothesis that the capability of these kidneys to autoregulate renal blood flow is impaired (1, 13). The greater celerity in the increase of urinary sodium concentration in the group with unclipping of ischemic kidney compared to the group with nephrectomy could be just due to the latter having the contralateral kidney.

The results of the present work, therefore, seem to suggest that the variation of sodium balance during the chronic phase of two-kidney, one-clip hypertension, does not influence either the increase in blood pressure or alterations of renin secretion which have been observed in previous reports (16, 17, 18) after the experimental manipulations have been undertaken.

Resumen

Se estudian las variaciones de la presión arterial y del balance de sodio después del desclipado, nefrectomía y operación simulada del riñón isquémico durante la fase crónica (16 semanas) de la hipertensión (2 riñones-1 clip). En esta fase, la excreción fraccional de sodio es del $85,5 \pm 2,3\%$, a pesar de que la presión arterial está significativamente aumentada ($187,1 \pm 4,5$ mmHg). Tanto la extracción del clip como la nefrectomía del riñón isquémico producen la normalización de la presión arterial, y la operación simulada no provoca ningún cambio de presión. Los animales sometidos a estas 3 manipulaciones quirúrgicas experimentan cambios similares en la excreción de sodio a los 1, 2, 3, 4 días y 3 semanas de cada operación. La ingesta de agua y la eliminación de orina son significativamente inferiores en los grupos con desclipado o nefrectomía del riñón isquémico que en el grupo con operación simulada. Estos resultados sugieren que el balance de sodio no es importante para el mantenimiento de la presión arterial elevada durante esta fase de la hipertensión y que los cambios en el balance de sodio, después de la nefrectomía y desclipado del riñón isquémico, no influyen en la normalización de la presión arterial.

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