Effect of Removing the Clipped Kidney on Renovascular Hypertension in Rabbits

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SUMMARY

Constriction of one renal artery in the presence of the opposite kidney can produce persistent hypertension which is often associated with increase in plasma renin activity, decrease in serum potassium and increase in water intake. In the present study the clipped kidney was removed in 15 hypertensive rabbits 12 to 54 weeks after the constriction. Blood pressure showed a prompt and transient fall which was followed by a slight rebound and subsequently a gradual decline. However, it still remained above the normal 5 weeks after the removal. Removal of the clipped kidney resulted in return to normal of increased plasma renin activity, decreased serum potassium and increased water intake at the end of the postoperative first week.

Additional Indexing Words:

Renin   Serum potassium   Water intake

CONSTRICION of one renal artery can produce persistent hypertension in rats,^{1),2)} rabbits,^{3),4)} and dogs⁵⁾ even if the opposite kidney is left intact. The effect of removing the clipped kidney on hypertension of this type has been studied in rats,^{1),6),7)} rabbits,⁴⁾ and dogs.⁵⁾ Removal of the clipped kidney is generally followed by a fall in blood pressure, but whether or not the blood pressure can return to normal remains a subject of controversy.

The hypertension produced by clipping one renal artery in the presence of an intact contralateral kidney is often associated with increase in plasma renin activity, decrease in serum potassium and increase in water intake.⁸⁾⁻¹⁰⁾ However, there is little information about the effect of removing the clipped kidney on these metabolic derangements. The present study was attempted to observe the effect of removing the clipped kidney not only on blood pressure but also on plasma renin activity, serum potassium and water intake in hypertensive rabbits. A part of the present study was previously reported in a preliminary form.¹¹⁾

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METHOD

The present study was carried out on 15 hypertensive rabbits. Male rabbits weighing 2.0 to 2.5 Kg were fed standard pellets for the rabbit (CR 1, Japan Clea Ltd) which contain 14 mEq of sodium and 28 mEq of potassium per 100 Gm. Each animal was given 100 Gm of the pellets and water ad libitum. Hypertension was produced by applying a silver clip of 0.9 mm id on the left renal artery. The right kidney was left intact. After establishment of persistent hypertension the clipped kidney was removed. Persistent hypertension was defined in the present study as blood pressure that had been elevated above 120 mmHg over the past 5 weeks or more. The interval between clipping of the renal artery and removal of the clipped kidney ranged from 12 to 54 weeks. Operative procedures were performed through a small flank incision under sodium pentobarbital anesthesia (30 mg/Kg, iv). Blood pressure was measured by an indirect method¹²⁾ on the central ear artery of unanesthetized animals usually at a weekly interval.

Plasma renin activity (PRA), serum sodium and serum potassium were measured just before, 1 and 4 weeks after removing the clipped kidney. About 10 ml of blood were taken by a heparinized syringe from the ear vein of resting animals without anesthesia for the measurement of PRA, and thereafter about 3 ml of blood by a dry syringe for the measurement of serum electrolytes. PRA was determined by the method of Pickens et al¹³⁾ with a minor modification.⁴⁾ Values for renin

Table I. Blood Pressure, Serum Potassium, Water Intake, and Plasma Renin Activity before and after Removal of the Clipped Kidney

No.	Interval after Clipping (Weeks)	B. P. (mmHg)			Serum K (mEq/L)			Water Intake (ml/day)			PRA (ng/ml)		
		0	1	4	0	1	4	0	1	3	0	1	4
		(Weeks)			(Weeks)			(Weeks)			(Weeks)		
1	40	184	143	117	4.0	3.5	3.5	413	302	300	1.6	1.2	3.2
2	26	130	100	97	2.7	3.3	3.7	706	378	337	25.9	0.9	0.4
3	22	143	137	98	3.6	4.5	3.4	306	272	298	2.5	1.0	3.8
4	48	141	128	120	3.7	4.1	3.9	737	442	546	1.6	2.0	1.6
5	51	170	143	105	4.1	4.8	4.1	729	607	664	1.5	1.6	3.2
6	43	174	144	122	2.9	3.5	4.0	836	719	669	6.1	0.8	4.0
7	12	171	152	141	3.0	4.6	4.0	659	506	396	1.8	0.4	1.2
8	17	169	160	130	2.3	3.2	4.1	782	514	569	21.6	0.5	2.2
9	17	155	98	83	2.3	2.9	4.2	846	615	659	41.2	0.2	0.5
10	42	171	115	129	3.5	4.0	3.8	407	317	236	52.6	0.8	6.3
11	54	151	136	112	3.3	3.4	3.5	603	416	340	14.0	2.4	5.0
12	25	183	160	138	2.8	3.5	3.9	691	493	330	28.2	2.2	4.4
13	50	157	142	122	3.5	4.0	3.5	617	355	334	16.6	1.6	1.0
14	52	160	103	110	3.2	4.0	4.0	353	323	304	1.6	1.8	1.2
15	18	174	135	99	2.1	4.1	4.6	651	363	350	20.0	2.6	8.2
Means		162	133	115	3.13	3.87	3.88	622	441	422	15.8	1.3	2.9
SE		4	5	4	0.14	0.15	0.08	45	34	40	4.1	0.2	0.6

activity were expressed as nanograms (ng) angiotensin II amide (Hypertensin, Ciba) equivalents generated per ml of plasma after incubation of 4 hours. Serum sodium and potassium were determined by flame photometry. Water intake was measured every day by weighing the water bottles in the period from 2 weeks before to 3 weeks after removal of the clipped kidney. Values for the water intake were expressed as an average of values for the past 7 days.

Average values obtained from 20 normal animals were 85.5 ± 6.7 (SD) mmHg ranging from 76 mmHg to 104 mmHg for blood pressure, 3.1 ± 2.0 ng/ml ranging from 1.0 ng/ml to 9.7 ng/ml for PRA, 140.9 ± 2.2 mEq/L ranging from 136 mEq/L to 146 mEq/L for serum sodium, and 3.90 ± 0.26 mEq/L ranging from 3.4 mEq/L to 4.5 mEq/L for serum potassium. An average for water intake obtained from 18 normal animals was 436 ± 120 ml/day ranging from 271 ml/day to 659 ml/day.

RESULTS

The data on individual animals are presented in Table I and the changes in average values are illustrated in Figs. 1 and 2. Changes in PRA are individually illustrated in Fig. 3.

Blood pressure was measured every day during the first 7 days. As shown in Fig. 1, removal of the clipped kidney induced an abrupt and transient fall in blood pressure which was followed by a slight rebound. In the subsequent

Fig. 1. Effect of removing the clipped kidney on blood pressure and body weight. Values are means $\pm$ SE (N=15).

Fig. 2. Changes in serum sodium (Na), serum potassium (K) and water intake before and after removing the clipped kidney. Values are means $\pm$ SE (N=15). Removal of the clipped kidney at time zero.

course to the 5th week blood pressure gradually fell to a lower level which still remained higher than normal. Any significant relationship did not exist between the fall in blood pressure and the interval from clipping of the renal artery to removal of the clipped kidney. For example, animal No. 7 was operated upon for removing the clipped kidney 12 weeks after clipping. The interval from clipping to removing was the shortest among the animals, but blood pressure only slightly fell from 171 mmHg to 141 mmHg after 4 weeks. Animal No. 14 showed a prompt and marked fall in blood pressure from 160 mmHg to 103 mmHg at the end of the first week although the clipped kidney was removed as long as 52 weeks after clipping.

As shown in Table I, serum potassium was below the normal range in 9 of 15 hypertensive animals. Removal of the clipped kidney was followed by return to normal of serum potassium at the end of the first week in 8 of the 9

Fig. 3. Changes in plasma renin activity of individual animals before and after removing the clipped kidney. Values of plasma renin activity are plotted on a logarithmic scale. Removal of the clipped kidney at time zero.

animals. After removing the clipped kidney serum potassium was also increased in 5 of 6 animals that had showed normal serum potassium values. An average of serum potassium in all 15 animals was 3.13 ± 0.14 (SE) mEq/L before, 3.87 ± 0.15 mEq/L 1 week and 3.88 ± 0.08 mEq/L 4 weeks after removing. The increments of serum potassium were highly significant ($p < 0.001$, respectively). Serum sodium was within normal range in 14 of 15 hypertensive animals. After removal of the clipped kidney an average of serum sodium showed a transient and slight increase from 140.4 ± 0.8 mEq/L to 142.4 ± 0.6 mEq/L at the end of the first week. The increment was statistically significant ($p < 0.05$).

Water intake was increased above the normal range in 7 of 15 hypertensive animals. After removal of the clipped kidney it returned to normal in 6 of the 7 animals at the end of the first week. An average of water intake in all

15 animals was decreased from 622 ± 45 ml/day to 441 ± 34 ml/day after 1 week and to 442 ± 40 ml/day after 3 weeks. The decrements of water intake was significant both at the end of the first and at the end of the third week ($p < 0.01$, respectively).

PRA was elevated above the normal range in 8 of 15 hypertensive animals. Removal of the clipped kidney resulted in a prompt fall in PRA to normal or subnormal level at the end of the first week in all of the 8 animals (Fig. 3). At the end of the 4th week PRA showed a slight rebound in most animals. There was not sufficient evidence to indicate any relationship between pre-operative values of PRA and responses of blood pressure to removing the clipped kidney. Considerable fall in blood pressure was observed also in animals with normal values of PRA.

DISCUSSION

Previous studies from our laboratory^{3),4)} have revealed that in the presence of the opposite kidney constriction of one renal artery can produce persistent hypertension in rabbits. The hypertension sharply differs from hypertension produced by clipping of one renal artery with contralateral nephrectomy.^{8),10)} Metabolic derangements including increase in PRA, decrease in serum potassium and increase in water intake were observed only in the former type of hypertension. The difference in PRA and sodium metabolism between the 2 types of hypertension was observed in rats by Gross¹⁴⁾ and Swales et al.^{15),16)} The present study demonstrated that removal of the clipped kidney was followed by a fall in blood pressure and return to normal of the metabolic derangements. The results suggest that the presence of both clipped and intact kidney is essential to the development of the metabolic derangements. In the present study a slight but significant increase in serum sodium was transiently observed at the end of the first week. However, the changes in serum sodium were really slight in comparison with those in serum potassium.

Lupu et al⁵⁾ reported that removal of the clipped kidney uniformly resulted in return of blood pressure to normal in dogs even as long as 16 months after clipping of the renal artery. The present study showed that removal of the clipped kidney could reduce blood pressure but not to the normal level. Kolestky and Rivera-Velez⁷⁾ demonstrated that the fall in blood pressure by removing the clipped kidney was closely related to the duration of hypertension in rats. Removal of the clipped kidney resulted in a complete return of blood pressure to normal in animals which were hypertensive for 3 days or 1 week. The fall in blood pressure was smaller and less prompt with hypertension of 2 or 3 weeks' duration and often slight or insignificant at 4 weeks. The present

study did not reveal any relationship between the duration of hypertension and the responses of blood pressure to removing the clipped kidney.

In the present study an abrupt and transient fall in blood pressure was observed during a few days just after removal of the clipped kidney. This observation suggests that 2 different mechanisms are involved in maintenance of hypertension. One may rapidly and the other may slowly disappear after removal of the clipped kidney. The abrupt and transient fall in blood pressure may be attributed to a rapid loss of one hypertensive mechanism and the gradual fall in blood pressure during the several weeks may be attributed to a slow loss of the other hypertensive mechanism.

The present study showed that the fall in blood pressure was not necessarily parallel to that in PRA. At the end of the first week blood pressure still remained high in some animals in spite of return to normal of PRA and metabolic derangements.

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