Increase of Hematocrit in Experimental Renal Hypertension and Its Reversal

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SUMMARY

Hematocrit can be increased in experimental animals with renal hypertension of two-kidney type. The present study showed that the increased hematocrit was returned to normal by removal of the clipped kidney.

The left renal artery was clipped in 13 rabbits with an intact contralateral kidney, and a sham operation was performed in 10 rabbits as a control. After an interval of 10 weeks the left kidney was removed in all animals. Blood pressure, hematocrit, hemoglobin content, and erythrocyte count were rapidly increased and remained raised after clipping of the renal artery but they did not show any significant changes after sham operation. A transient but significant increase of reticulocyte count was found at the end of the first week after clipping of the renal artery. Removal of the clipped kidney was followed by a rapid return of hematocrit, hemoglobin content, and erythrocyte count to normal within 2 weeks. Blood pressure was also decreased but not returned to normal by removal of the clipped kidney.

Additional Indexing Words:
Clipping of the renal artery Erythrocytosis Removal of the clipped kidney Renovascular hypertension Two-kidney hypertension

An association between renovascular hypertension and increase of hematocrit was suggested in a patient by Luke et al¹) and was supported by Tarazi et al²) who had found an increase of hematocrit in 18% of patients with renovascular hypertension. Recently Schramek et al³) reported a patient with hypertensive crisis, erythrocytosis, and uremia due to renal artery stenosis of a transplanted kidney. In this patient the hypertension and erythrocytosis disappeared after surgical repair of the renal artery stenosis. An increase of hematocrit has also been observed in animals with renovascular hypertension of two-kidney type by Gross et al,⁴) Fujii et al,⁵) and Kurihara et al.⁶) Re-
moval of the clipped kidney is not always followed by return to normal of blood pressure in this type of experimental hypertension. The present experiments were designed to study effect of removal of the clipped kidney on hematocrit and other blood counts in rabbits with chronic two-kidney hypertension.

**Method**

Male rabbits weighing 2.0 to 2.5 Kg were fed a standard diet for the rabbit (Japan Clea Ltd). Each animal was given 100 Gm of the diet per day and water ad libitum. A silver clip of 0.9 mm id was applied on the left renal artery in 13 animals with an intact contralateral kidney (clip group) and a sham operation was performed in 10 animals (sham-operation group). After an interval of 10 weeks the left kidney was removed in animals of both groups. The operative procedures were performed through a small flank incision under pentobarbital anesthesia (30 mg/Kg, iv). Special care was taken to minimize loss of blood during the surgery. Blood pressure was measured at weekly intervals on the central ear artery by an indirect method. One ml of blood was taken from the ear vein for blood counts before, and 2 days, 1 week, 2 weeks, 6 weeks, 10 weeks, 11 weeks, 12 weeks, and 16 weeks after clipping or sham-operation. Reticulocytes were counted on blood film stained with brilliant cresyl blue.

**Results**

Effects of clipping of the renal artery and removal of the clipped kidney on blood pressure and blood counts were illustrated in Fig. 1. Preoperative values were 90.2±1.4 mmHg (mean±SE) for blood pressure, 39.1±0.8% for hematocrit, 12.6±0.2 Gm/100 ml for hemoglobin content, 5.91±0.13 million/mm³ for erythrocyte count, and 20.7±2.1% for reticulocyte count in the clip group. They were about the same in the sham-operation group. After clipping of the renal artery blood pressure, hematocrit, hemoglobin content, and erythrocyte count rapidly increased and remained raised until the end of 10th week when the clipped kidney was removed. At that time blood pressure was 130.9±4.8 mmHg which ranged from 105 to 157 mmHg, hematocrit was 46.4±1.8% which ranged from 38.0 to 56.5%, hemoglobin content was 15.5±0.6 Gm/100 ml which ranged 12.8 to 18.8 Gm/100 ml, and erythrocyte count was 7.00±0.31 million/mm³ which ranged from 5.53 to 9.06 million/mm³. These variables did not show any significant increase after sham operation. There were significant differences in these variables between the 2 groups during the first to the 10th week. Reticulocyte count showed a transient increase at the end of the first week in the clip group. At that time a significant difference was found between the clip and the
Fig. 1. Effects of clipping of the renal artery and removal of the clipped kidney on blood pressure (BP), hematocrit (Ht), hemoglobin content (Hb), erythrocyte count (RBC), and reticulocyte count (Ret). Solid circles represent clip group (N=13) and open circles represent sham-operation group (N=10). Clipping of the renal artery or sham operation at time zero and removal of the clipped or sham-operated kidney at the 10th week. Values are means ± SE. * p<0.05 between the 2 groups. ** p<0.01 between the 2 groups.

Table 1. Correlation Coefficients between Hematocrit and Blood Pressure

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<tr>
<td>Clip Group (N=13)</td>
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<td>Sham-Operation Group</td>
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* At the end of 10th week the clipped or the sham-operated kidney was removed.

sham-operation group.

Correlation coefficients were calculated between hematocrit and blood pressure in each group at every point of the observation period (Table I). Any of them were statistically not significant, but the values were greater in the clip group than in the sham-operation group during the period from the first to the 10th week. This tendency disappeared after removal of the clipped
or the sham-operated kidney. Fig. 2 shows another relationship between hematocrit and blood pressure. Values of hematocrit were those measured at the 6th week and those of blood pressure were averages during the period from the 5th to 7th week. In this figure a significant correlation was found on the clip group (r=+0.61, p<0.05) but not on the sham-operation group (r=+0.22, n.s.).

At the end of 10th week the clipped or the sham-operated kidney was removed. Blood pressure was decreased to 108.7±4.4 mmHg in the clip group and was increased to 102.5±3.5 mmHg in the sham-operation group at the end of 12th week. There was not a significant difference in blood pressure between the 2 groups at that time, but blood pressure was not returned to the normal level in the clip group. After removal of the clipped kidney hematocrit, hemoglobin content, and erythrocyte count were also decreased to 40.0±1.2%, 13.3±0.4 Gm/100 ml, and 6.24±0.23 million/mm³ respectively at the end of the 12th week. These values did not significantly differ from those obtained before clipping of the renal artery. These 3 variables did not show any significant changes in the sham-operation group after removal of the sham-operated kidney. There were not significant differences in these variables between the 2 groups at the end of 12th week.

Discussion

Clipping of the renal artery can induce hypertension in experimental
animals. This procedure can be accompanied by metabolic or fluidal changes such as increase of plasma renin activity, decrease of serum potassium, increase of hematocrit, and increase of water intake if the opposite kidney is left intact.\textsuperscript{4-6} A recent study of our laboratory\textsuperscript{7} showed that after removal of the clipped kidney plasma renin activity, serum potassium, and water intake were returned to normal in a week and blood pressure was decreased but not to the normal level. The present study was attempted to make up the previous one and provided an additional observation that the increased hematocrit was also returned to normal by removal of the clipped kidney.

It remains unsettled whether the increase of hematocrit is caused by true erythrocytosis or reduction of plasma volume, because neither erythropoietin nor plasma volume was measured in the present study. Takaku et al\textsuperscript{9} reported that the serum erythropoietic activity was rapidly increased in rats by clipping of the renal artery. The present study also showed a transient increase of reticulocyte count at the end of the first week after clipping of the renal artery. These results suggest that a true erythrocytosis develops during the initial stage. On the other hand, reduction of plasma volume can be one of factors responsible for the increase of hematocrit in this type of hypertension. Gross et al\textsuperscript{4} indicated that the increase of hematocrit was associated with reduction of plasma volume in rats with a severe form of two-kidney hypertension. Kurihara et al\textsuperscript{6} also showed that plasma volume was reduced during the first 4 weeks and was returned to normal at the 12th week in rabbits with two-kidney hypertension. Whatever mechanisms are involved, the present study indicates that they are closely related with the presence of the clipped kidney.

**Acknowledgements**

The authors gratefully acknowledge the technical assistance of Mr. S. Ushiama and Mr. H. Irie.

**References**