Increased Plasma Renin Activity after Peritoneal Dialysis

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SUMMARY

An examination was made of the effects of changes in plasma sodium concentration and water balance during peritoneal dialysis on renin secretion. Plasma renin activity, plasma sodium concentration, plasma volume, and arterial blood pressure were measured in 14 patients with chronic renal failure (chronic glomerulonephritis) before and after peritoneal dialysis. The amount of water removed by peritoneal dialysis was also measured.

The results were as follows: 1) Plasma renin activity was increased significantly after peritoneal dialysis. The average increase was 58.1 ± 15.8 (S.E.)% of the initial value. 2) There was no significant correlation between the amount of water removed and plasma renin activity. 3) Mean arterial pressure rose slightly after peritoneal dialysis but not to a statistically significant degree. 4) Plasma sodium concentration was increased significantly after peritoneal dialysis. There was no significant inverse correlation between plasma sodium concentration and renin activity. There was also no significant inverse correlation between the increased plasma renin activity and changes in plasma sodium concentration. 5) The decrease in plasma volume after peritoneal dialysis was significant. There was a significant correlation between the increased renin activity and the decreased plasma volume.

From the present study, we conclude that the dominant stimulus to renin secretion in peritoneal dialysis is a decrease in plasma volume.

Additional Indexing Worlds:
Renin secretion Plasma volume Plasma sodium concentration

The mechanisms that control renin secretion have not been fully established, although many investigators have proposed various factors, such as blood pressure, circulating blood volume, sodium balance, or activity of the sympathetic nervous system. Some investigators have proposed a relationship between plasma sodium concentration and renin secretion.

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Brown et al. report an inverse relationship between plasma sodium concentration and renin concentration in hypertensive patients. However, the experiments of other investigators clearly demonstrate an increase in renin secretion in response to a reduction of blood volume, or blood pressure without a decrease in plasma sodium concentration.

The present study was undertaken to clarify the effects of changes of plasma sodium concentration and water balance during peritoneal dialysis on renin secretion.

**Materials and Methods**

Plasma renin activity, plasma sodium concentration, and arterial blood pressure were measured in 14 patients with chronic renal failure (chronic glomerulonephritis) on 18 occasions before and after peritoneal dialysis. The amount of water removed by peritoneal dialysis was also measured and was expressed in terms of ml. per Kg. of body weight in post-dialysis. Measurement of plasma volume was made in 8 of the patients on 12 occasions at the night before peritoneal dialysis and immediately after dialysis.

The procedure used for determination of renin activity of peripheral venous plasma was based on the improved assay method described by Skinner in 1967. The venous blood for determination of renin activity was delivered immediately before and after peritoneal dialysis. The samples were assayed for pressor activity in 150 to 200 Gm. female rats treated at least 1 hour before with intraperitoneal sodium pentobarbital (5 mg. per 100 Gm. as an initial dose and 1 to 0.5 mg. per 100 Gm. as supplemental doses) and pentolinium tartrate (2 mg. per 100 Gm. initially and 0.4 mg. per 100 Gm. supplementally). Mean arterial pressure was measured from a cannulated carotid artery and recorded on a smoked-drum kymograph. Pressor activity generated in plasma as a result of 24-hour incubation was determined by bracketing the unknown response between standard angiotensin II (Hypertensin, Ciba) at 2 similar levels and was designated as plasma renin activity. Plasma renin activity was expressed as rate of angiotensin formation in ng. per ml. per hour. Plasma sodium concentration was measured by routine laboratory method. Plasma volume was determined with the dilution method, using serum albumin-¹³¹I (RISA) before and after peritoneal dialysis. Thirty to forty microcuries of RISA was diluted to 1,000 ml. of physiological saline of which 2 ml. was used as the standard. Plasma volume was determined in patients at bed rest. Another 30 to 40 μc. of RISA was injected with calibrated syringe into the antecubital vein. Ten min. after the injection of the isotope, approximately 6 ml. of the blood was delivered into a heparinized test tube and centrifuged immediately and then 2 ml. of plasma was counted for 2 min. in a well type scintillation counter. The calculation was made as follows:

\[
\text{Plasma Volume (ml.)} = \frac{\text{Counts per ml. per min. (Standard)}}{\text{Counts per ml. per min.}} \times 1,000
\]

Plasma volume was expressed in terms of ml. per Kg. of body weight. The arterial pressure was recorded by the auscultatory method at supine position immediately
before and after dialysis and mean arterial pressure (diastolic plus one-third of pulse pressure) was calculated. Dietary sodium intakes of the patients were restricted to 85 mEq./day. Peritoneal dialysis consisted of 15 exchanges over 2 days with 2 L. of dialysate per exchange. The chemical composition of dialysate was as follows: sodium, 140.0 mEq./L.; calcium, 4.5 mEq./L.; magnesium, 1.5 mEq./L.; chloride 101.0 mEq./L.; lactate, 45.0 mEq./L.; glucose, 13.0–33.0 Gm./L.; and osmolality, 361–472 mOsm/L. The amount of glucose added to it was determined according to the degree of edema of each patient.

Results

Plasma renin activity, plasma sodium concentration and mean arterial pressure before and after peritoneal dialysis and the amount of water removed by peritoneal dialysis are summarized in Table I.

Plasma renin activity: Plasma renin activity was increased in 17 out of 18 determinations. The increase in plasma renin activity after peritoneal dialysis was significant (p<0.05) and the average increase was 58.1±15.8 (S.E.) % of the initial value. The extent of the increase in the individual patient, however, varied considerably, the minimal increase being 3.4% of the initial value, which is a barely detectable change by the present method, and the maximal increase being 278.8% of the initial value. Renin activity of peripheral venous plasma of 14 patients on 18 occasions before peritoneal dialysis ranged from 0.7 to 3.3 ng. per ml. per hour, with the mean of 2.0±0.2 ng. per ml. per hour. The average value of renin activity of peripheral venous plasma of normal controls calculated by the present method was considered to be 1.4±0.1 ng. per ml. per hour. The difference in average renin activity between patients with chronic renal failure and normal controls was significant (p<0.05).

Plasma sodium concentration: Plasma sodium concentration was increased significantly after peritoneal dialysis (p<0.05) and the average increase was 3±1 mEq./L. There was no significant correlation between plasma sodium concentration and plasma renin activity (p>0.05; Fig. 1). There was also no significant correlation, when the increased rate of plasma renin activity was plotted against increments in plasma sodium concentration (p>0.05; Fig.2).

Arterial blood pressure: Mean arterial pressure was not changed significantly after peritoneal dialysis (p>0.05).

The amount of water removed: The amount of water removed by peritoneal dialysis ranged from 25 to 336 ml./Kg., with the mean of 167±17 ml./Kg. There was no significant correlation between plasma renin activity and the amount of water removed (p>0.05; Fig. 3).

Plasma volume: Estimation of plasma volume was made in 8 of the
Fig. 1. Relationship between renin activity of peripheral venous plasma and plasma sodium concentration measured before and after peritoneal dialysis. Both renin activity and plasma sodium concentration are plotted on the arithmetic scale.

Fig. 2. Relationship between the increased rate of plasma renin activity and increments in plasma sodium concentration after peritoneal dialysis.
Fig. 3. Relationship between the increased rate of plasma renin activity after peritoneal dialysis and the amount of water removed by peritoneal dialysis.

Fig. 4. Relationship between the increased rate of plasma renin activity and the decrements in plasma volume after peritoneal dialysis.
patients on 12 occasions before and after peritoneal dialysis and was decreased in all determinations after peritoneal dialysis. The decrease in plasma volume was significant ($p<0.01$) and the average decrease was $6.2 \pm 1.5$ ml./Kg. Significant correlation was observed when the increased rate of plasma renin activity was plotted against the decrements in plasma volume ($p<0.05$; Fig. 4).

**DISCUSSION**

The present study suggests that peritoneal dialysis can stimulate renin release in patients with chronic renal failure (chronic glomerulonephritis).
Tu\textsuperscript{11} and Blaufox et al.\textsuperscript{12} reported that plasma renin activity was not increased in chronic renal failure. In contrast, Brown et al.\textsuperscript{13} observed that in chronic renal failure renin activity varied from abnormally low to abnormally high levels. DEL Greco et al.\textsuperscript{14} also found high levels of renin activity in patients maintained on dialysis who had grade II to IV retinopathy and severe hypertension. In our study the pre-dialysis levels of renin activity were found over a wide range of values with an increase following peritoneal dialysis. The present findings as well as those reported by others,\textsuperscript{13–15} therefore, show that renin release by the kidney may occur despite advanced anatomic and functional derangements.

<table>
<thead>
<tr>
<th>Plasma Sodium mEq./L.</th>
<th>Mean Pressure mm.Hg</th>
<th>Removed Water ml./Kg.</th>
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<td>Before</td>
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The factors which control renin secretion are not yet fully understood. Brown et al. emphasized that plasma sodium concentration was the principal and sole determinant of renin release. According to their concept, an increase in plasma sodium concentration would be expected to suppress renin release. On the other hand, Maebashi et al. showed that plasma renin activity was increased in the face of elevated plasma sodium concentration during water deprivation. In our study there was no significant inverse correlation between plasma renin activity and plasma sodium concentration. We suggest that changes in plasma sodium concentration does not play a principal role in the control of renin secretion during peritoneal dialysis.

The experiments of Skinner, McCubbin and Page suggested that renin is released in response to a decrease in mean renal arterial pressure. Acute systemic hypotension, due to nitroprusside infusion, also increased renin release in humans. Several other experiments, however, showed that reduction in arterial blood pressure is not essential for renin secretion. In our study there was no consistent change in arterial blood pressure after peritoneal dialysis in spite of an increase in renin activity.

Increased plasma renin activity after peritoneal dialysis in our study could be on the basis of a reduction in plasma volume. It is noteworthy that plasma volume is often reduced in certain conditions in which plasma renin activity is increased such as experimental sodium deprivation, untreated Addison's disease, and hepatic cirrhosis with ascites. The well known experiment in which acute hemorrhage in dogs elicits an increased secretion of renin from the kidneys without consistent alteration in arterial pressure supports this interpretation. Therefore a primary cause of the increase in plasma renin activity in our study seemed to be hypovolemia induced by peritoneal dialysis rather than hyponatremia and hypotension.

There is a possibility that a small increase in plasma renin activity, in proportion to the fall in plasma volume, might occur in this study if the rate of secretion of the enzyme remained unchanged. However, the increase in renin activity in plasma exceeded the observed change in plasma volume. An increased release of renin from the kidney is considered the most likely factor in the present study. It must be noted that we did not measure renal blood flow and the arterial and renal venous activity of renin.

From the results discussed above, we conclude that plasma sodium concentration is not a major stimulus to renin secretion. The increased secretion of renin seen in peritoneal dialysis seems to be due to the decrease in plasma volume induced by the dialysis.
REFERENCES