Change in Plasma Renin Substrate Level after the Intravenous Furosemide Administration

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SUMMARY

Plasma renin substrate (PRS) was determined immediately before and 30 min after the intravenous administration of 40 mg of furosemide in 26 hypertensive subjects. PRS level after the administration of furosemide was found elevated by $30.5 \pm 4.7\%$ which was statistically significant.

Additional Indexing Words:

Angiotensin Hematocrit Plasma renin activity Sodium
depletion

IT has been assumed that plasma renin substrate level is regulated by angiotensin II,¹⁾ glucocorticoid,²⁾ and estrogen^{3),4)} based upon static experiments. What may happen to the PRS level when it is rapidly consumed by an acute increase of renin secretion has not been investigated. By the use of furosemide, which is well known stimulator of renin secretion,⁵⁾⁻⁷⁾ acute change of PRS level is studied in the present report.

MATERIALS AND METHODS

Twenty-six hypertensive subjects, 19 men and 7 women, with an average age of 41, ranging from 13 to 70, were studied either before starting any antihypertensive therapy or after discontinuing all medications for at least 1 week. They were kept on an ordinary hospital diet of 10–15 Gm of salt a day for 7 days. An initial blood sample for assay of plasma renin activity (PRA) and PRS was obtained in early morning without breakfast in recumbent position, being followed by the intravenous administration of 40 mg of furosemide. The subjects were then kept standing for the next 60 min, during which the second and third blood samples were taken at 30th and 60th min. PRA was measured by the method described

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by Arakawa et al,⁸⁾ and PRS by its modification with an addition of excess human kidney renin which was prepared according to the procedure described by Arakawa et al.⁹⁾

Statistical analysis was performed using Student's t test. Data are presented as the mean $\pm$ the standard error of the mean (SEM), and p value of less than 0.05 was considered significant.

RESULTS

The PRS levels before and after the administration of furosemide are compared in Fig. 1. The mean value of PRS level before the administration of furosemide was 999.6 ± 69.2 ng/ml, and, after furosemide, 1340 ± 116.5 ng/ml. The change was significant ($p < 0.001$). Because of diuresis caused by furosemide, hematocrit increased from $43.5 \pm 3.0\%$ to $46.3 \pm 3.0\%$, which was also statistically significant ($p < 0.02$). However, as the rate of increased hematocrit value ($2.9 \pm 0.86\%$) was considerably less than that of increased PRS level ($30.5 \pm 4.7\%$), it is apparent that the elevation of PRS level was not merely due to the hemo-concentration.

The levels of PRA before and after the administration of furosemide are

Fig. 1. Changes in the levels of plasma renin substrate before and after 40 mg of furosemide.

Fig. 2. Changes in the levels of plasma renin activity before and after 40 mg of furosemide.

shown in Fig. 2. The mean value of PRA before the administration of furosemide was 13.8 ± 1.9 ng/ml and increased to 27.3 ± 4.4 ng/ml at 30th min. The change was significant ($p < 0.001$). PRA value 60 min after furosemide was 35.2 ± 5.8 ng/ml ($n=7$) and this was also a significant change ($p < 0.01$).

DISCUSSION

An increased renin after the administration of furosemide should consume PRS, and consequently PRS should decrease. In contrast to the expectation, however, the present study disclosed that the PRS level did not decrease, but rather significantly increased after the administration of furosemide, along with the increase of PRA. In fact the increase of PRS level after furosemide far exceeded even the amount of what might be expected from hemoconcentration. Thus, present experiment has clearly shown that furosemide administration definitely resulted in a rapid increase of PRS, as well as that of PRA.

The mechanism of this rapid elevation of PRS level after furosemide is not investigated here. Several possibilities, like the followings, remain to be elucidated; a) either increased PRA itself or thereby increased angiotensin II, b) depletion of serum sodium, c) sympathicotonic reflex, both indirectly, or, d) furosemide itself, directly, may stimulate renin substrate secretion.

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