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Short Report

Active and Inactive Renin after SQ 14225 (Captopril) Administration

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Goto, T., Abe, K., Otsuka, Y., Itoh, T., Imai, Y., Satoh, M., Omata, K. and Yoshinaga, K. *Active and Inactive Renin after SQ 14225 (Captopril) Administration.* Tohoku J. exp. Med., 1980, **132** (3), 363-364 —— The changes of active and inactive renin in plasma after the oral administration of 25 mg or 50 mg of SQ 14225 (Captopril) were studied in 29 hypertensive patients. Inactive renin was calculated as plasma renin activity (PRA) after cold storage minus PRA before cold storage. The patients were divided into 2 groups, responders and non-responders, according to the response of active renin to Captopril. In 9 responders, the active renin increased markedly while the inactive renin decreased. On the other hand, in 20 non-responders, both renin activities increased only slightly. These results suggest that inactive renin may be converted in vivo to active renin by Captopril. ———— SQ 14225; active renin; inactive renin; cold storage

It is well known that angiotensin I converting enzyme inhibitor (SQ 14225, Captopril) induces an increase in plasma renin activity by the inhibition of negative short feedback mechanism of renin release (Case et al. 1978). There are different types of renin in circulating plasma, active and inactive, and the latter can be activated by acidification or low temperature. In relation to the mechanism of an augmented renin release by Captopril, there are two possibilities; one is an increment of conversion of inactive renin to active renin and the other is an increase in both, active and inactive renin. The present study was done to investigate these possibilities.

Materials and Methods

Twenty-nine hypertensive patients (15 men and 14 women aged from 14 to 63) were studied. They consisted of 19 cases of essential hypertension (EH), 7 of renovascular hypertension (RVH), and 3 of renal parenchymal hypertension (RPH). Blood samples were taken after 1 hr of recumbent position (control), and at 1 hr (SQ1) and 2 hr (SQ2) after the oral administration of 25 mg or 50 mg of Captopril. PRA was determined by a modification of Haber's method. Inactive renin was calculated as the PRA after 10 days of cold (-5°C) storage (total renin activity) minus PRA before cold storage (active renin, Saito et al. 1979). Statistical analysis was performed with paired t-tests. Values were given as mean±S.E.M.

Results

As a whole, active renin increased significantly by Captopril (control: 15.9±3.0 ng/ml, SQ1:41.7±6.9 ng/ml, $p<0.001$, SQ2:43.4±7.6 ng/ml, $p<0.001$). Inactive renin decreased at SQ1 and returned to the control level at SQ2 (control: 19.8±3.4 ng/ml, SQ1:11.9±2.7 ng/ml, $p<0.05$, SQ2:18.1±3.3 ng/ml).

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The patients were divided into 2 groups, responders and non-responders, according to the response of active renin. Patients with active renin values at SQ2 of 60 ng/ml or above, and those who showed a response of greater than twice over the control values were classified as responders. Nine patients, including 5 with RVH and 4 with EH, were responders. In these responders, active renin increased markedly (control: 24.0±5.0 ng/ml, SQ1:79.6±7.2 ng/ml, $p<0.001$, SQ2:93.7±9.5 ng/ml, $p<0.001$), while inactive renin decreased significantly (control: 29.1±8.9 ng/ml, SQ1:7.6±3.8 ng/ml, $p<0.05$, SQ2:4.3±3.0 ng/ml, $p<0.01$). The remaining 20 patients including 15 EH, 3 PRH and 2 RVH were non-responders. In these patients, active renin increased slightly as a whole (control: 12.3±3.5 ng/ml, SQ1:24.7±6.6 ng/ml, $p<0.05$, SQ2:20.8±4.6 ng/ml, $p<0.01$), and inactive renin was not changed at SQ1 but increased a little at SQ2 (control: 15.5±2.7 ng/ml, SQ1:13.9±3.4 ng/ml, SQ2:24.2±3.9 ng/ml, $p<0.05$).

Discussion

In the present study, the different responses of active renin to Captopril were found. One third of patients showed a hyperresponse, while the remaining two thirds showed a hyporesponse. Between responders and non-responders there is no significant difference in control values in either active or inactive renin. However, in responders who exhibited marked increase in active renin by Captopril, inactive renin decreased significantly. These data suggest that Captopril augments the conversion of inactive to active renin. But it is still unknown in what manner the renin is stored (active, inactive, or mixed) in the juxtaglomerular cell. It is to be determined whether Captopril converts inactive renin to active intracellularly or it stimulates the release of active renin selectively without affecting inactive renin secretion.

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References

1) Case, D.B., Atlas, S.A., Laragh, J.H., Sealey, J.E., Sullivan, P.A. & McKinstry, D.N. (1978) Clinical experience with blockade of the renin-angiotensin-aldosterone system by an oral converting-enzyme inhibitor (SQ 14,225, Captopril) in hypertensive patients. *Prog. Cardiovasc. Dis.*, **21**, 195–206.
2) Saito, K., Abe, K., Ito, T., Irokawa, N., Otsuka, Y., Kusaka, T., Yasujima, M., Imai, Y., Sakurai, Y., Chiba, S., Ritsu, K., Sato, M., Haruyama, T., Omata, K. & Yoshinaga, K. (1979) Changes in plasma renin activity by cold storage of plasma with essential hypertension and primary aldosteronism. *Tohoku J. exp. Med.*, **129**, 13–18.