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Tissue Plasminogen Activator in Essential Hypertension

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Tissue plasminogen activator (t-PA) is regarded as the major activator of fibrinolysis. It is synthesised and stored in endothelial cells, from where it is released into the blood stream. Although several stimuli for t-PA release have been described such as exercise [1], venous occlusion [2] and cardiopulmonary bypass [3], the effect of blood pressure alterations on endothelial t-PA secretion remains to be clarified. It has been attempted to correlate blood fibrinolytic activity with arterial blood pressure in a number of studies [4–8], but no clear-cut conclusions could be attained. Based on these considerations, the present study was designed in order to compare the basal plasma t-PA levels in hypertensive and normotensive subjects and to determine the effect of acute blood pressure reduction by sublingual nifedipine on plasma t-PA levels in essential hypertension.

The study group included 18 previously untreated patients with diastolic blood pressure 105 mm Hg or higher, mean age 46 ± 2 years and 13 healthy age- and sex-matched normotensive patients. Blood samples were drawn without stasis, by means of an indwelling catheter placed in the antecubital fossa 30 min prior to test. The patency of the needle was maintained by slow saline infusion. Upon the completion of a 30-min period of recumbent rest, the baseline samples were drawn at 9:00 a.m. in both groups. Immediately after the baseline sampling, the hypertensive patients were given 10 mg nifedipine sub-lingually. Additional samples were drawn 15, 30 and 60 min after nifedipine. All subjects remained in the supine position during the study. Blood pressure measurements were performed at 0, 15, 30 and 60 min just after sampling. T-PA antigen levels were measured by the sandwich ELISA technique [9].

The significance of the difference was analysed by the Mann-Whitney U and Wilcoxon rank tests for intergroup and intragroup measurements, respectively. The values were expressed as mean $\pm$ standard error of mean.

Fig. 1. The effect of sublingual nifedipine on blood pressure and plasma t-PA antigen level in hypertensive patients (n = 18).

Figure 1 shows the changes in mean systolic and diastolic blood pressure and t-PA antigen levels after the administration of sublingual nifedipine. The mean systolic and diastolic blood pressure in the hypertensive group at 0 min were 174.2 ± 6.0 mm Hg and 118.1 ± 2.8 mm Hg, respectively. Gradual lowering of systolic and diastolic blood pressure was observed during the study period; minimal blood pressure values (systolic 155.0 ± 6.3 mm Hg, diastolic 103.6 ± 3.2 mm Hg) were reached at 60 min ($p < 0.001$). The mean baseline (0 min) t-PA antigen level of hypertensive patients was 7.9 ± 1.6 ng/ml, which was not found to be significantly different from the mean t-PA antigen level

of the control group, which was 6.7 ± 1.4 ng/ml. Mean t-PA antigen levels at 15, 30 and 60 min were 7.1 ± 1.1 , 7.8 ± 1.0 and 7.0 ± 1.0 ng/ml, respectively. These values were not found to be significantly different from the baseline value ($p > 0.05$).

In this study, no difference in t-PA antigen levels between hypertensive and normotensive subjects was observed. Furthermore, acute lowering of blood pressure by sublingually administered nifedipine, in hypertensive patients, also did not cause any change in t-PA antigen levels. However, it cannot be excluded that more abrupt lowering of blood pressure via intravenous administration of anti-hypertensive agents with different modes of action might cause alterations on plasma t-PA levels. The effect of chronic maintenance of normal blood pressure in essential hypertension on t-PA antigen levels, as well, remains to be determined.

Based on the findings drawn from this preliminary study, it is suggested that chronic elevation and acute lowering of blood pressure might not directly mediate the release of t-PA from endothelial cells.

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