ORIGINAL ARTICLE

Annals of Nuclear Medicine Vol. 8, No. 3, 193–199, 1994

In vivo kinetics of ^{99m}Tc labeled recombinant tissue plasminogen activator in rabbits

Kazuo ITOH,* Masahiro IEKO,** Etsuro HIRAGUCHI,*** Hide KITAYAMA** and Eriko TSUKAMOTO*

*Departments of *Nuclear Medicine, **Second Internal Medicine and ***Second Surgery, Hokkaido University School of Medicine*

Our previous studies demonstrated that ^{99m}Tc labeled recombinant tissue plasminogen activator (rt-PA) retained high affinity with fibrin *in vitro* but showed unexpectedly low uptake in fresh thrombi *in vivo*. The present study was performed to determine the *in vivo* kinetics of radiolabeled t-PA in the rabbit.

Sequential images and blood samples after the intravenous administration of ^{99m}Tc labeled rt-PA in thrombus-bearing rabbits were taken. The radioactivity and immunological level of t-PA and PAI-l in the solution eluted to each fraction by gel permeation chromatography were measured by means of a well scintillation counter and enzyme-linked immunosorbent assay (ELISA). Most of the radioactivity was eluted in the fraction (Fr. 7) of larger molecular weight than that (Fr. 9) of intact t-PA. The level of intact rt-PA was increased with a regimen involving the preadministration of cold rt-PA which was followed by the administration of hot rt-PA. The level of PAI-1 in plasma showed an increased rebound 15 minutes after the intravenous injection. These results suggest two possible reasons why rt-PA retains high affinity with fibrin *in vitro*, once radiolabeled, but was ineffective in delineating fresh thrombi with a gamma camera: 1) some plasma components such as PAI-1 combine with circulating radiolabeled rt-PA and form a larger molecule immediately and/or 2) radiolabeled rt-PA is modulated as a consequence of the radiolabeling and forms a larger molecule than intact rt-PA.

Key words: recombinant tissue plasminogen activator, radiolabeling, pharmacokinetics, animal study