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

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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-1 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