rt-PA causes a dose-dependent increase in the extravasation of cellular and non-cellular blood elements after focal cerebral ischemia.

Abstract:
While recombinant tissue plasminogen activator (rt-PA) is successfully used for thrombolysis in human stroke, it may increase the risk of hemorrhagic complications. We describe the effects of different doses of rt-PA (saline, 0.9, 9, or 18 mg rt-PA/kg body weight) on the extravasation of blood components following experimental cerebral ischemia (3 h, 24 h reperfusion, suture model) in rats. The damage to the blood-brain barrier and the hemoglobin extravasation were quantified by Western blotting and immunohistochemistry. Both were significantly elevated in the ischemic cortex and basal ganglia. As rt-PA doses rose, the hemoglobin content as well as the damage to the blood-brain barrier in the ischemic side also rose significantly (p<0.001). This correlated significantly with the rising MMP-9 (matrix metalloproteinase) after increasing doses of rt-PA. Despite various benefits, rt-PA is responsible for a dose-dependent increase of edema and hemorrhage after cerebral ischemia. Clinicians should consider using the lowest effective dose of rt-PA in stroke patients.

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