Recombinant human tissue plasminogen activator

(tPA, alteplase)

General information

A fibrin specific thrombolytic protease that converts plasminogen to plasmin.

Recombinant human tissue plasminogen activator for acute ischemic stroke

Recombinant human tissue plasminogen activator for acute ischemic stroke

Recombinant human tissue plasminogen activator for chronic subdural hematoma

Recombinant human tissue plasminogen activator for chronic subdural hematoma

Intraventricular tissue plasminogen activator

Intraventricular tissue plasminogen activator

Intravenous Recombinant human tissue plasminogen activator

Intravenous Recombinant human tissue plasminogen activator

Case series

2017

Medical records were collected from patients suffered from AIS between 2010 and 2013 and allocated into either the intravenous recombinant tissue plasminogen activator (as rt-PA group) treatment, or non-rt-PA treatment group (as control group). The primary outcomes included a proportion of patients

with favorable outcome [as defined with a modified Rankin Scale (mRS) of 0-1], functional independence (mRS of 0-2) or with bad outcome (mRS of 5-6) at 3, 6 and 12 months and the overall mortality. The secondary outcome included the events of intracranial hemorrhage. A total of 357 patients from Xinhua Hospital were selected. At 3-month follow-up, 86 patients in rt-PA vs. 99 in control group had favorable outcome, 105 vs. 122 were independent and 23 vs. 27 had bad outcome. At 6-month follow-up, 101 patients in rt-PA vs. 104 in control group had favorable outcome, 114 vs. 124 were independent and 20 vs. 34 had bad outcome. At 12 months, 104 patients in rt-PA vs. 105 in control group had favorable outcome, 117 vs. 125 were independent and 12 vs. 32 had bad outcome. At the end of 12 months, more deaths occurred in control group (20) than in the rt-PA group (11), but it was not statistically significant. Alteplase treatment in AIS patients showed the superior primary outcomes compared with control group, especially during the middle/long follow-up [1].

Recombinant human tissue plasminogen activator (tPA) is the effective drug for the treatment of acute ischemic stroke. In addition to thrombolysis, tPA is also involved in neuroplasticity.However, tPA has potential adverse side effects when administered intravenously including brain edema and hemorrhage.

Administered by intranasal delivery during the subacute phase after traumatic brain injury (TBI), provides therapeutic benefit. Animals with TBI were treated intranasally with saline or tPA initiated 7 days after TBI. Compared with saline treatment, subacute intranasal tPA treatment significantly 1) improved cognitive (Morris water maze test) and sensorimotor (footfault and modified neurological severity score) functional recovery in rats after TBI, 2) reduced the cortical stimulation threshold evoking ipsilateral forelimb movement, 3) enhanced neurogenesis in the dentate gyrus and axonal sprouting of the corticospinal tract originating from the contralesional cortex into the denervated side of the cervical gray matter, and 4) increased the level of mature brain-derived neurotrophic factor. These data suggest that subacute intranasal tPA treatment improves functional recovery and promotes brain neurogenesis and spinal cord axonal sprouting after TBI, which may be mediated, at least in part, by tPA/plasmin-dependent maturation of brain-derived neurotrophic factor [2].

rtPA amplified microglia recruitment early after stroke in association with a rapid CCL3 production. This early response may take part in the higher susceptibility of rtPA-treated animals to reperfusion injury [3].

1)
Li H, Wu Y. Prognosis comparisons in acute ischemic stroke patients with thrombolysis and nonthrombolysis therapy: a retrospective study with larger sample size. Blood Coagul Fibrinolysis. 2017 Dec 11. doi: 10.1097/MBC.0000000000000685. [Epub ahead of print] PubMed PMID: 29232256.
2)
Meng Y, Chopp M, Zhang Y, Liu Z, An A, Mahmood A, Xiong Y. Subacute Intranasal Administration of Tissue Plasminogen Activator Promotes Neuroplasticity and Improves Functional Recovery following Traumatic Brain Injury in Rats. PLoS One. 2014 Sep 3;9(9):e106238. doi: 10.1371/journal.pone.0106238. eCollection 2014. PubMed PMID: 25184365; PubMed Central PMCID: PMC4153585.
3)
Lenglet S, Montecucco F, Denes A, Coutts G, Pinteaux E, Mach F, Schaller K, Gasche Y, Copin JC. Recombinant tissue plasminogen activator enhances microglial cell recruitment after stroke in mice. J Cereb Blood Flow Metab. 2014 Jan 29. doi: 10.1038/jcbfm.2014.9. [Epub ahead of print] PubMed PMID: 24473480.