J Neurol Neurosci 2018, Volume 9
DOI: 10.21767/2171-6625-C2-012

Short-term local hypothermia prevents ischemia-reperfusion injury following delayed tissue plasminogen activator treatment in an embolic stroke model

Mohammadreza Zarisfi
Rafsanjan University of Medical Sciences, Iran

Background: Limiting reperfusion injury immediately after delayed tissue plasminogen activator (tPA) therapy in cases of acute ischemic stroke seems to be beneficial for extending the time window of this drug. The present study sought to determine whether short-term, mild local brain cooling can prevent hyperemia and/or adverse effects of delayed tPA in a rat embolic stroke model.

Materials & Methods: Male wistar rats were subjected to embolic stroke using homologous clots and randomly assigned to one of the following conditions: control, tPA (10 mg/kg; i.v.), local hypothermia (LH), and tPA + LH (10 mg/kg; i.v.). The tPA was injected at 6 h following embolic stroke. LH was conducted at 6.5 h after ischemia and maintained thereafter for approximately 30 min. Cerebral blood flow was evaluated for 60 min, starting from the time of tPA injection. Infarct volume, blood–brain barrier (BBB) disruption, brain edema, neurological deficits, and the serum level of matrix metalloproteinase-9 (MMP-9) were measured 48 h later.

Results: Compared to the tPA and control groups, the combination of tPA + LH significantly reduced infarct volume ($P<0.001$ and $P<0.05$, respectively). tPA significantly increased rCBF at approximately 30mins after administration ($P<0.001$) but applying LH at 30 min after tPA injection not only prevented the increase of rCBF but caused a 20% decrease in reperfusion compared to the control and tPA groups ($P<0.001$). The combination of LH + tPA reduced BBB leakage ($P<0.001$), MMP-9 level, and brain edema ($P<0.01$). LH alone also decreased BBB disruption ($P<0.01$) and brain edema ($P<0.05$). Moreover, the combination of LH + tPA decreased neurological deficits at 48 h following stroke ($P<0.01$) and increased grasping ability and sensory-motor function ($P<0.001$).

Conclusion: The application of short-term local hypothermia is a promising strategy to mitigate reperfusion injuries following delayed tPA therapy and to extend its time window up to 6 hrs.

zarisfi_mr@yahoo.com