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The effectiveness of mild general hypothermia in reducing the side effects of delayed r-tPA treatment after embolic stroke in rats

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Objective: Late alteplase (tPA)-associated complications cause narrow treatment time window of only Food and Drug Administration (FDA) approved drugs. In addition, induced hypothermia has neuroprotective properties in acute ischemic stroke, so in this study, we investigate whether general hypothermia can prevent side effects of late tPA treatment in the embolic model of stroke.

Materials & Methods: 40 male wistar rats were randomly assigned into five groups 1: Sham, 2: Control, 3: Hypothermia, 4: r-tPA and 5: Hypothermia/r-tPA). General hypothermia (GH) was induced at 5.5 hours after induction of embolic stroke. 30 mins after initiation of cooling treatment, tPA was administrated. The infarction volume, brain edema, blood-brain barrier (BBB), matrix metalloproteinase 9 (MMP9) and neurological deficits were assessed after 2 days.

Results: In comparison with control group, the general inducing of hypothermia decreased the infarct volume, BBB, MMP9, neurological deficit and brain edema at 5.5 hours after stroke. GH at 5.5 h after stroke decreased infarction volume, BBB, MMP9, neurological deficit and brain edema. In brain edema, no significant difference was observed between hypothermia and control group. In group number 5, hypothermia and r-tPA led to decrease in infarction volume, brain edema, BBB, MMP9 and neurological deficit of 6 h after stroke.

Conclusion: The findings of the present study suggest that general hypothermia can prevent the side effects of delay tPA treatment in an embolic model of stroke.

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