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Tissue Plasminogen Activator-Induced Reperfusion Injury After Stroke Revisited
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A limitation of the study by Strbian and colleagues with respect to future clinical applications is that the MC stabilizer cromoglycate had to be administered directly into the cerebrospinal fluid via the intraventricular route because this substance does not cross the blood-brain barrier. This approach is not applicable under clinical conditions in which the systemic (preferably intravenous) delivery of pharmacological compounds is desirable. Furthermore, Strbian et al investigated a model of mechanically induced ischemia-reperfusion injury, not of cerebral thromboembolism/thrombolysis, which would be clinically more relevant. Thus, proof-of-concept studies are required to determine whether the benefits of MC stabilization can be applied to thromboembolic stroke.

We propose that the bench-to-bedside translation of findings from experimental animals to human patients is a priority issue for the future, given that reperfusion therapies have not achieved implementation in acute ischemic stroke similar to that in acute myocardial infarction. Even in large university hospitals with excellent infrastructures, thrombolysis rates hardly exceed 5% to 10% of patients with stroke admitted to stroke units. These low thrombolysis rates in stroke can be attributed to local bleeding complications, which may result at least in part from secondary reperfusion injury triggered by tPA.

On the pathophysiological level, the striking parallels between the role of MCs in inflammatory responses in the brain and atherosclerotic plaque rupture deserve our attention. Along this line, the role of allergen-induced or IgE- or MC-mediated immune responses in atherogenesis, thrombosis, or reperfusion injury would be a promising research avenue. The data by Strbian and colleagues suggest that IgE receptor blockade might mimic the beneficial effects of pharmacological MC stabilizers in the stroke brain. A better understanding of the mechanisms underlying tPA-induced reperfusion injury may provide valuable tools to decrease the detrimental effects of tPA, thereby increasing its therapeutic potential in stroke patients. Such insights will cross-fertilize research concepts in the cardiovascular field.

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Disclosures

None.

References


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