Topically applied adipose-derived mesenchymal stem cell treatment in experimental focal cerebral ischaemia

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KEY MESSAGES

1. Topically applied mesenchymal stem cells plus fibrin sealant can home to ischaemic penumbra, reduce cerebral infarction volume, and improve the neurological function from cerebral ischaemia in a rodent middle carotid artery occlusion model mimicking severe stroke secondary to a major cerebral artery occlusion.
2. Topical mesenchymal stem cell plus fibrin sealant treatment is promising and should be optimised for safety and efficacy.

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Introduction

Stroke is the third most common cause of death in developed countries after ischaemic heart disease and malignancy, and the fourth most common cause of death in Hong Kong. Despite prophylactic decompressive craniectomy after hemispheric infarction (typically middle cerebral artery infarction), the rates of death and disability remain high. In the micro-environment, mesenchymal stem cells (MSCs) suppress inflammation and apoptosis, enhance angiogenesis, and stimulate proliferation and cellular differentiation. Experimental and pilot clinical studies have reported the board therapeutic effects of MSCs in various neurological disorders including cerebral ischaemic injury.[1-3]

Topical application is an efficient delivery of MSCs to the brain. Theoretically billions of MSCs in a single topical transplantation can be readily applied to the surface of human cerebral cortex without causing additional injury to the brain or related complications. This study aimed to investigate the engraftment and underlying mechanism of topically applied adipose-derived MSCs in experimental cerebral ischaemia, and to assess the neuroprotective effects.

Methods

A rat focal cerebral ischaemia model was used. At 24 hours after experimental focal cerebral ischaemia, 120 rats were randomised to three groups: topical application of MSCs plus fibrin (n=40), topical application of MSCs alone (n=40), and no treatment (n=40). Radiological and histological assessment of cerebral infarction, neurological assessments, microscopic assessments, and expression of inflammatory cytokines were performed.

Results

Topically applied MSCs plus fibrin sealant homed to the ischaemic penumbra, reduced cerebral infarction volume, and improved the neurological function from cerebral ischaemia. However, these effects could not be explained by suppression of inflammation and apoptosis in the ischaemic penumbra.

Conclusion

Topical MSC plus fibrin sealant treatment is promising and should be optimised for safety and efficacy in severe stroke secondary to major cerebral artery occlusion.

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