Effect of Microglia Activation by Idebenone on Cerebral Ischemia-Reperfusion and Mechanism Study

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Abstract

Objective: Microglia-mediated neuroinflammation is crucial in ischemic stroke and a target for research. Idebenone treats ischemic stroke but its effects and mechanism on microglia are unclear. This paper investigates idebenone's neuroprotective effects on cerebral ischemia/reperfusion injury via microglial cells and NF-κB pathway. We established MCAO/R and OGD/R models to observe idebenone's impacts on cerebral cortex pathology, microglial cell polarization, and NF-κB pathway activation. Findings provide a new basis for ischemic stroke treatment. *Methods*: (1) Set up mouse MCAO/R model, divide into the sham operation group, the MCAO/R model group, and the MCAO/R+IDE treatment group. Assess neuromotor functions, count deaths and weight changes. Detect infarct volume by TTC staining. Observe Nissl substance. Assess apoptosis. Analyze microglia polarisation. Detect inflammatory factors and M1/M2 markers by Western blot.(2) Set up BV2 cell OGD/R model, divide into the control group, OGD/R model group and OGD/R+IDE treatment group. Detect cell viability by CCK8. Detect M1/M2 markers and NF-κB pathway proteins by Western blot. *Results*: (1) Idebenone treatment improves motor nerve function of MCAO/R mice. (2) Idebenone treatment significantly increased the survival rate of MCAO/R mice ($P<0.05$). (3) Mice after MCAO/R exhibited obvious infarcted areas in the brain, which were reduced with idebenone treatment ($P<0.01$). (4) Idebenone treatment reduced the number of apoptotic cells in the brains of mice after MCAO/R ($P<0.05$). (5) Idebenone treatment reduced the number of microglia, resulting in an decrease in M1-type microglia and an increase in M2-type microglia ($P<0.05$). Idebenone treatment reduces the width of microglia accumulation zones in the cerebral cortex 7 days after MCAO/R ($P<0.001$). (6) BV2 cell viability significantly decreased after OGD/R, but increased after the addition of Idebenone ($P<0.05$). (7) Idebenone inhibited the M1-type pro-inflammatory state and promoted the M2-type anti-inflammatory state of BV2 cells at 24 hours after OGD/R ($P<0.05$). (8) Idebenone treatment reduced NF-κB p65 and IκB-α phosphorylation levels at 24 hours after OGD/R ($P<0.05$). *Conclusion*: Idebenone treatment reduced mortality, cerebral infarct volume, apoptosis, and attenuated the inflammatory response in ischemia-reperfusion mice. The mechanism may involve the inhibition of the NF-κB pathway, thereby reducing microglial over-activation and, reducing microglia M1-type polarization and promoting their M2-type polarization, ultimately providing neuroprotective effects.

Keywords

Cerebral Ischemia Reperfusion, Mircoglia, Neuroinflammation, Idebenone, NF-κB Pathway