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Human Mesenchymal Stem Cells and Endothelial Progenitor Cells exert a neuroprotective effect on rat cortical neurons injured by oxygen and glucose deprivation

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Oxygen and glucose deprivation (OGD) due to ischemic events or trauma in the brain result in neuronal loss. The therapeutic approaches available inadequate and often the outcome is unfavorable for the patient or at least unpredictable.

Stem cells could be useful for the treatment of OGD injured-neurons. Mesenchymal Stem Cells (MSCs), isolated from bone marrow as well as from various tissues, have poor immunogenicity and neuroprotective properties being able to alleviate ischemic brain injuries in animal models. The Endothelial Progenitor Cells (EPCs) are present at low frequencies both in the bone marrow and in the peripheral blood. They are thought to play a role in the recovery of cerebrovasculature integrity after stroke.

In the present study we evaluated the potential neuroprotective effect of human MSCs and human EPCs on rat embryonic cortical neurons injured by OGD.

OGD was induced by incubating the cortical neurons in a hypoxia chamber in a 95% N_2 + 5% CO_2 atmosphere at 37°C without glucose. To set up the experimental protocol, OGD was maintained for 1, 2 and 3 hours. The neurons were returned in normoxic atmosphere and after 2 and 5 days neuronal survival was evaluated by MTT assay, LDH assay and viable cellular counting. The 2 hours OGD was able to reduce neuronal viability by 50% and was chosen for the subsequent experiments.

To assess MSCs and EPCs neuroprotective action, after 2 hours-long OGD the neurons were 1) co-cultured with either MSCs or EPCs seeded on a cell culture insert avoiding direct contact while sharing the same medium, or 2) cultured in a medium previously conditioned by either MSCs or EPCs. Neuronal survival was evaluated by MTT assay after 2 and 5 days. Both MSCs and EPCs increased neuronal survival after ODG. The effect was observed in absence of a direct contact between MSCs or EPCs and the injured neurons, suggesting that the release of soluble factors may be involved in their neuroprotective action.

In conclusion both MSCs and EPCs could represent a potential therapeutic approach for the treatment of brain ischemic injury. Further studies are needed to identify the specific molecules and pathways that play a role in the neuroprotective effect of MSCs and EPCs.

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Keywords

Mesenchymal stem cells; endothelial progenitor cells: oxygen and glucose deprivation; embryonic cortical neurons.

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