INTRANASAL ADMINISTRATION OF DEXAMETHASONE REDUCES MORBI-MORTALITY AND INFLAMMATORY INFILTRATING CELLS IN A MURINE MODEL OF STROKE

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Ischemic stroke is the second main cause of death worldwide, leading to severe, long-time disability in adults. Thrombolytic drugs provide some benefits to stroke patients, but only when employed within the first few hours after stroke. While early neuroinflammatory reaction helps to restore ischemia-induced damage, late neuroinflammation plays a key role in brain damage by increasing the extension of the ischemic focus.

Glucocorticoids (GCs) are effective to treat inflammation but their benefit in stroke treatment remains controversial. Notwithstanding their effectiveness, their use to control neuroinflammation (NI) is limited by the severe side-effects observed when administered in doses required to reach therapeutic central levels. In contrast, the intranasal route allows us to directly reach the central nervous system with lower doses, decreasing systemic concentrations and the ensuing side-effects.

Thus, the effectiveness of intranasally administered dexamethasone (DX) to control sub-acute NI was tested in a 60-min middle cerebral artery occlusion (MCAO) model of ischemic stroke in male C57BL/6 mice. Twelve hours after reperfusion, mice were intranasally treated with a single DX dose (0.25 mg/kg). DX administration significantly reduced the number of mice that died within 7 days post-MCAO (8/15 vs 1/10, $P = 0.04$) and the stroke-associated neurological severity score. A decrease in inflammatory infiltrate and focal ischemic necrosis was observed at 24 and 48 hours, as well as a decrease in cerebral edema-associated tissue damage, with less marked revascularization zones, until 7 days post-surgery.

This study demonstrates the neuroprotective therapeutic effects of a unique dose of IN DX in a transient middle cerebral artery occlusion murine model.