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Role of T-lymphocyte depletion using fingolimod in ischemia reperfusion injury related to heart transplantation

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Background & Aim: Heart failure followed by ischemiareperfusion injury is a major issue in heart transplantation. During last decade, multiple strategies have been used to control this important problem. It is well-known that fingolimod, a sphingosine 1 Phosphate receptor modulator may cause anti-inflammatory, antioxidant and Tlymphocyte depletion leading to lymphopenia. Thus, it leads to a reduction in ischemiareperfusion injury and ultimately, prevention of heart failure. The aim is to investigate the preoperative effect of fingolimod was to evaluate cardioprotective role in heterotopic heart transplantation experimental model in comparison of placebo administration.

Method: Male Sprague-Dawley (SD) rats (300-350 g) (n=30) treated with either fingolimod (1 mg/kg total body weight) or normal saline solution. Ischemia was applied for 60 minutes and reperfusion was followed for 24 hours and 1 week. Post heterotopic heart transplantation at 24 hours and 2 weeks all surviving rats were sacrificed. Blood and myocardial tissue were collected for analysis of myocardial biomarkers, inflammatory markers, oxidative stress and signaling pathways. Myocardial fibrosis was investigated using Masson's trichrome staining, Fluorescein Activated Cell Sorting (FACS) to measure Tlymphocyte and TUNAL assay for level of apoptosis.

Result: Following 60 minutes of ischemia, both saline treated and vehicle group showed significant myocardial injury following heterotopic heart transplantation. In fingolimod treated group, reduction of inflammation and oxidative stress have been observed significant as compared to salinetreated or vehicle group. FACS analysis showed a significant Tlymphocyte depletion in peripheral blood after fingolimod treatment, which was not observed after saline or vehicle treatment, on TUNAL assay significant reduction in apoptosis has been observed.

Conclusion: The longterm survival improved in this study might be due to a cardioprotective role of fingolimod to prevent ischemia reperfusion injury in heterotopic heart transplantation model, which may be mediated by decreased inflammation, reactive oxygen species and the lymphocyte depletion shown in the FACS analysis leading to reduced apoptosis.

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Hippocampal biochemical, morphological and behavioral changes following short-term adrenalectomy in albino wistar rats

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Bilateral Adrenalectomy (ADX) has been shown to damage the hippocampal neurons. However, the effects of short-term ADX are not studied. Therefore, we aimed to investigate the effects of short-term ADX on the levels of pro-inflammatory cytokines, response of microglia, astrocytes, neuronal cell death and oxidative stress markers (4 h, 24 h, 3 days, 1 week and 2 weeks) in the hippocampus. Our results showed a transient significant elevation of pro-inflammatory cytokines IL-1 β and IL-6 from 4 h to 3 days in the ADX compared to sham. TNF- α levels were significantly elevated at 4 h only in ADX compared to sham. Time dependent increased in degenerated neurons in the dorsal blade of the dentate gyrus from 3 days to 2 weeks after ADX. Quantitative analysis showed significant increase in the number of microglia (3, 7 and 14 days) and astrocytes (7 and 14 days) of ADX compared to sham. A progression of microglia and astroglia activation all over the dentate gyrus and their appearance for the first time in CA3 of adrenalectomized rats hippocampi compared to sham was seen after 2 weeks. A significant decrease of GSH levels and SOD activity and increase in MDA levels were found after 2 weeks of ADX compared to sham. In order to investigate the effect of adrenalectomy on the behavior of the animals we used a passive avoidance test at 3, 7 and 14 days after adrenalectomy. Our results showed a significant reduction in the latency time in the adrenalectomized rats compared to the sham operated rats 3, 7 and 14 days after adrenalectomy. Our study showed an early increase in the pro-inflammatory cytokines followed by neurodegeneration and activation of glial cells as well as oxidative stress. Hence, early inflammatory components might contribute to the initiation of the biological cascade responsible for subsequent neuronal death.

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