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Preclinical studies of apilimod for neuroprotective effect in brain ischemic injury model in rats

Dinesh Tripathi, Sunita Tiwari and Chetna Mishra
King George's Medical University, India

Introduction: Blood brain barrier disruption is one of the most important phenomenon during ischemia stroke. Cell death following ischemia reperfusion injury leads to life threatening problem to patients. Inflammation and cascades play a detrimental role on brain tissue during reperfusion which contributes to brain infarct progression as well as to the disease severity and outcome. Interleukin -12 (IL-12) involved in the pathophysiology of acute cerebral ischemia and responsible for progression of neuroinflammation. An elevated level of Interleukin -23 (IL-23) contributes to many neurological disorders. Apilimod is a potential regulator of certain autoimmune and inflammatory diseases. The aim of this study was to investigate the neuroprotective effects of Apilimod on blood brain barrier disruption and Interleukin12 receptor IL12Rβ2 and Interleukin 23 protein expression following brain ischemic injury.

Methods: Rat underwent middle cerebral artery occlusion for 2 hour followed by 24 hour reperfusion. Rats were post treated with Apilimod at 3 hour post reperfusion. Apoptosis ratio in brain was determined by performing flow cytometry. Blood brain barrier disruption was determined by Evans blue method and the expression levels of different molecules were assessed by using Western blot, and enzyme-linked immunosorbent assay (ELISA).

Results: The results showed that Apilimod prevents the blood brain barrier damage after the ischemic injury as well as significantly decreased the apoptotic cells at 24 hr after the ischemic stroke. Western blot showed that the expression levels of Interleukin 12 receptor IL12Rβ2 and Interleukin 23 were significantly down regulated in rats with Apilimod treatment. Moreover, ELISA assay revealed that the level of Interleukin 12 and Interleukin 23 were also significantly decreased after 3 hour post treatment with Apilimod.

Conclusions: These results suggested that the treatment of Apilimod protects against cerebral ischemia/reperfusion injury in rats. These data also suggest that Interleukin 12 and Interleukin 23 pathways are the potential target for therapeutic intervention in stroke therapy and Apilimod may be better drug in the treatment of stroke.

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