Dual Inhibition Of Cyclooxygenase And 5-Lipoxygenase By Flavocoxid Protects Against Kainic Acid-Induced Brain Excitotoxicity

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Systemic administration of kainic acid causes inflammation and apoptosis in the brain resulting in neuronal loss. Dual inhibitors of cyclooxygenase (COX) and 5-lipoxygenase (5-LOX) could represent a possible neuroprotective approach in preventing acute glutamate excitotoxicity. Consequently, we investigated the effects of flavocoxid, a dual inhibitor of COX/5-LOX following intraperitoneal administration of kainic acid (KA, 10 mg/kg) in rats.

Animals were randomized to receive either flavocoxid (20 mg/kg i.p.) or its vehicle (1 ml/kg i.p.) 30 minutes after KA administration. A first set of animals was sacrificed after KA administration to evaluate the protein expression of extracellular signal-regulated kinase (ERK 1/2) and tumor necrosis factor-alpha (TNF-α) in hippocampus and serum levels of prostaglandin E2 (PGE2) and leukotriene B4 (LTB4). A second set of animals was sacrificed for histological analysis and brain edema evaluation, respectively. All animals were observed for monitoring the behavioral changes according to Racine Scale. Sham brain injury rats were used as controls.

Treatment with flavocoxid significantly reduced PGE2 and LTB4 serum levels, decreased the protein expression of ERK1/2 and TNF-α in hippocampus, and also ameliorated brain edema. Histological analysis showed a reduction of a cell damage in flavocoxid-treated samples, particularly in hippocampal subregion CA3c. Finally, flavocoxid reduced the behavioral scores after 120 and 240 minutes following KA administration in treated animals.

Our results suggest that flavocoxid displays neuroprotective effects against excitotoxicity induced by kainic acid.