ASSESSMENT OF CELECOXIB, A SELECTIVE COX-2 INHIBITOR, AS A NEUROPROTECTIVE AGENT IN ALZHEIMER’S MODEL OF RATS.

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INTRODUCTION

- Reduced cerebral blood flow (CBF) has been associated with neurodegenerative disorders including Alzheimer’s disease.
- Experimentally, a condition of chronic cerebral hypoperfusion due to reduced CBF can be induced by permanent bilateral occlusion of common carotid arteries (2-vessel occlusion, 2VO) in rats.
- Neuroinflammation has been suggested to play a crucial role in the development and progression of many neurodegenerative diseases.
- The neuroinflammatory response induces activation of microglia and release of inflammatory mediators such as prostaglandins, leukotrienes, and cytokines. The sustained release of inflammatory mediators works to perpetuate the inflammatory cycle and leads to apoptosis and neuronal cell death.

Aim of the study

- Since neuroinflammation, leading to neuronal apoptosis and death, is one of the mechanisms which is thought to play a significant role in chronic degenerative neurological disorders like Alzheimer’s disease, the present study was planned to assess the neuroprotective role of celecoxib, a selective COX-2 inhibitor, in Alzheimer’s model of rats (2VO).

MATERIALS AND METHODS

- After acclimatization, fifteen Sprague Dawley rats weighing 200-250 g were equally divided into A, B, and C groups. Group A served as – sham control, Group B – 2VO, and Group C – 2VO-C (treated daily with celecoxib 50 mg/kg, orally following 2VO).

2VO method: Under ketamine (90 mg/kg) and xylazine (10 mg/kg) anesthesia, a mid cervical incision was made and both the common carotid arteries were separated and permanently ligated.

RESULTS

Histopathological studies

- Light microscopic images of hippocampal CA-1 region for SHAM, 2VO and 2VO-C groups

Hippocampal CA-1 Neuronal Cell Count

Number of hippocampal CA-1 neuronal cells in SHAM, 2VO and 2VO-C groups

COX-2 mRNA Expression

Expression level of hippocampal COX-2 mRNA in SHAM, 2VO, and 2VO-C groups

PGE-2 Level Measurement

Hippocampal PGE-2 levels in SHAM, 2VO, and 2VO-C groups

DISCUSSION

The present study was conducted to understand the impact of chronic cerebral hypoperfusion-induced neurodegeneration in rats as it occurs in Alzheimer’s disease and to assess the role of celecoxib as a neuroprotective agent in this model.

There was a significant difference in neuronal cell death, increase in COX-2 mRNA expression and PGE-2 levels in 2VO group as compared to sham control group.

In celecoxib-treated 2VO (2VO-C) rats, the viable neuronal cell count of the hippocampal CA-1 region was significantly higher as compared to the untreated 2VO group.

The hippocampal COX-2 mRNA expression and hippocampal PGE-2 levels were found to be significantly lower in the celecoxib-treated 2VO rats as compared to untreated 2VO rats.

Impact of the study: The results clearly point out that celecoxib is an effective neuroprotective agent in Alzheimer’s model in rats and can be successfully used in the management of Alzheimer’s disease.

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