Pharmacological Reports
2008, 60, 692–698
ISSN 1734-1140

Cyclooxygenase inhibitors: a novel direction for Alzheimer's management

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Abstract:
Research in Alzheimer's disease (AD) currently includes various cellular, molecular, genetic, clinical and therapeutic approaches. The cytopathological significance of oxidative damage has been studied in neurons of AD patients. Many epidemiological studies suggest that use of non-steroidal anti-inflammatory drugs (NSAIDs) delay or slow the clinical expression of AD, and anti-oxidant properties of NSAIDs have also been previously described. Therefore, in this study we examined the role of various cyclooxygenase (COX)-1 and COX-2 inhibitors (NSAIDs) in a rat model of aluminum-induced oxidative stress to mimic AD-like conditions. We found that the animals receiving aluminum treatment for one month (4.2 mg/kg, *ip*) had highly elevated levels of reactive oxygen species (expressed as malondialdehyde – MDA). Moreover, treatment with the COX-2 inhibitor, rofecoxib (0.83 mg/kg, *po*), was able to significantly reduce this oxidative stress ($p < 0.05$ when compared to aluminum treatment alone on MDA levels). But, non-specific COX inhibitors (flurbiprofen, 0.83 mg/kg twice a day *po* and ibuprofen, 100 mg/kg, *po*), did not protect again oxidative stress. Thus, in agreement with earlier epidemiological studies, we propose that COX-2 specific NSAIDs may be beneficial in AD management. Further experimental work towards identifying the most efficacious COX-2 inhibitors, as well as the mechanism of action and the optimal dosage regimen should be executed.

Key words:
cyclooxygenase inhibitors, rofecoxib, flurbiprofen, ibuprofen, Alzheimer's disease, NSAIDs