EFFECT OF CYCLOOXYGENASE AND NO SYNTHASE INHIBITORS ON ANTINOCICEPTIVE ACTION OF ACETAMINOPHEN

Magdalena Bujalska, Witold S. Gumulk

Department of Pharmacodynamics, Medical University of Warsaw, Krakowskie Przedmieście 26/28, PL-00-927 Warszawa, Poland


The influence of cyclooxygenase (COX) and NO synthase inhibitors on antinociceptive action of acetaminophen (ACETA) was studied in rats. ACETA increased the nociceptive threshold for both mechanical (Randall-Selitto test) and chemical stimuli (writhing test). In both models the existence of ceiling dose of ACETA was observed. Indomethacin (IND), an inhibitor preferentially acting on COX-1, as well as nimesulide (NIM) and celecoxib (CECOX), i.e. respectively preferential and selective inhibitors of COX-2, markedly decreased the antinociceptive activity of ACETA in Randall-Selitto test. In contrast, IND increased, whereas both NIM and CECOX did not have any effect on ACETA action in writhing test. Pretreatment with L\textsuperscript{\textgamma}-nitro-L-arginine (L-NO-ARG), an unspecific inhibitor of NO synthase, 7-nitroindazole (7-NI), relatively specific inhibitor of neuronal NO synthase, and L-N6(1-iminoethyl)lysine (L-NIL), relatively selective inhibitor of inducible NO synthase, significantly increased the action of the lower doses of ACETA (50 and 100 mg/kg) in writhing test, whereas it did not modify the effects of the higher doses. Similar effect of L-NO-ARG and 7-NI was observed in Randall-Selitto test, whereas L-NIL did not influence the action of ACETA. The possible involvement of COX and NO synthase systems in antinociceptive activity of ACETA is discussed.

Key words: acetaminophen, NO synthase, cyclooxygenase, antinociception

\textsuperscript{\textcircled{\textasteriskcentered}} correspondence; e-mail: mbujalski@proplsp.com.pl