EFFECT OF CYCLOOXYGENASE AND NO SYNTHASE INHIBITORS ADMINISTERED CENTRALLY ON ANTINOCICEPTIVE ACTION OF ACETAMINOPHEN (PART II)

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As it has been demonstrated in a previous study, both cyclooxygenases (COXs) and nitric oxide synthases (NOSs) participate in the mechanism of acetaminophen (ACETA) action. Results obtained in this study indicate that intrathecal (it) or intracerebroventricular (icv) pretreatment with L-G-nitro-L-arginine (L-NO-Arg), a non-selective inhibitor of NOS activity, as well as with 7-nitroindazole (7-NI), a selective nNOS inhibitor, potentiated the antinociceptive activity of subceiling doses of ACETA, but were without effect on the action of supramaximal doses in Randall-Selitto test. Similar effect of L-NO-Arg and 7-NI it was observed in writhing test, whereas L-NO-Arg icv or L-NIL it did not influence the action of ACETA in this model. Indomethacin (IND), an inhibitor preferentially acting on COX-1, as well as nimesulide (NIM) and celecoxib (CECOX), i.e. preferential and selective inhibitor of COX-2, respectively, administered icv almost completely blocked the antinociceptive effect of ACETA in Randall-Selitto method. On the other hand, pretreatment with NSAIDs it initially increased and then attenuated the ACETA antinociception. Yohimbine (YOH), an α2-adrenergic receptor antagonist, did not modify the antinociceptive action of ACETA administered alone. However, YOH decreased the nociceptive threshold increased by simultaneously administered IND and ACETA, NIM and ACETA, as well as CECOX and ACETA in Randall-Selitto model. In contrast to the peripheral (sc) application, IND administered centrally (icv or it) did not modify the ACETA antinociception in writhing test. Neither NIM nor CECOX administered sc, it or icv changed the ACETA antinociception in this model. Possible mechanisms and sites of antinociceptive effects of ACETA are discussed.

Key words: acetaminophen, nitric oxide synthase, cyclooxygenase, antinociception

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