



Lack of effect of naltrexone on the spinal synergism between morphine and non steroidal anti-inflammatory drugs

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Abstract:

To enhance analgesia, the combinatorial use of analgesic drugs with proven efficacies is a widely-used strategy to reduce adverse side effects. The present study characterizes the antinociceptive interaction of intrathecal morphine co-administered with different NSAIDs using isobolographic analysis. Antinociceptive activity was evaluated using a model for acute visceral pain, the writhing test of mice. The possible involvement of opioid receptors in the mechanism of action of the intrathecal co-administration of morphine and NSAIDs was investigated using the non-selective receptor antagonist naltrexone. The study demonstrated a synergistic antinociception of intrathecal administered combinations of morphine with the following NSAIDs: diclofenac, ketoprofen, meloxicam, metamizol, naproxen, nimesulide, parecoxib and piroxicam. The supra additive effect was obtained with very low doses of each drug and it appeared to be independent of the COX-1 or COX-2 inhibition selectivity of each NSAID and was not significantly modified by intrathecal naltrexone. The findings of the present work suggest that the combination of opioids and NSAIDs has a direct action on spinal nociceptive processing, which may be achieved *via* mechanisms that are independent of the activation of opioid receptors. The ineffectiveness of naltrexone to reverse the analgesic activity of opioids + NSAIDs combinations indicates that other complex pain regulatory systems are involved in this effect.

Key words:

antinociception, COXs inhibitors, morphine, NSAIDs, isobolographic analysis, writhing test
