Antinociception by metoclopramide, ketamine and their combinations in mice

Fouad K. Mohammad, Banan Kh. Al-Baggou, Ahmed S. Naser

Department of Physiology, Biochemistry and Pharmacology, College of Veterinary Medicine, University of Mosul, PO box 11136, Mosul, Iraq

Correspondence: Fouad K. Mohammad, e-mail: fouad.mohammad@yahoo.com

Abstract:
Background: Metoclopramide is a centrally acting antiemetic and ketamine is a general anesthetic used with sedatives, tranquilizers and analgesics. Metoclopramide has analgesic effects and its combination with ketamine causes sedation and hypnosis. The contribution of metoclopramide to the analgesic effect of ketamine is not known. The purpose of the present study was to explore the analgesic effects of metoclopramide and ketamine alone or in combination in mice.

Methods: The up-and-down method was used to determine the median effective analgesic dosages (ED$_{50}$s) of metoclopramide and ketamine administered intraperitoneally (ip) either alone or concomitantly in male albino Swiss mice. Analgesia was measured by using a hot plate. The ED$_{50}$s of both drugs were analyzed isobolographically to determine the type of interaction between them. The analgesic effect of metoclopramide-ketamine combination (62.3 and 4.3 mg/kg, ip) was also monitored by the hot plate and acetic acid writhing methods.

Results: The analgesic ED$_{50}$s for metoclopramide and ketamine in mice were 30.15 and 2.15 mg/kg, ip, respectively. Concomitant administration of the drugs reduced their ED$_{50}$s to 10.17 and 0.68 mg/kg, ip, respectively. Isobolographic analysis of these ED$_{50}$s for both drugs revealed synergistic analgesic effect. Further, the combination of the drugs was effective analgesic as seen by the hot plate test and by another analgesic test paradigm, the acetic acid-induced writhings in mice.

Conclusions: The data suggest that the combination of metoclopramide and ketamine synergistically controls acute pain in mice. This combination could be used clinically for restraint and minor surgical interventions in mice.

Key words:
analgesia, hot plate, isobolographic analysis, ketamine, metoclopramide, writhing