

Antinociceptive effects of morphine, fentanyl, tramadol and their combination, in morphine-tolerant mice

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The development of morphine-tolerance after chronic administration, reduces analgesic efficacy and is a significant clinical problem in some patients; may be managed clinically by increasing the doses of morphine and/or the administration of a second mu-opioid agonist. In morphine-tolerant mice, we investigated the presence of an interaction when two opioids are administered simultaneously. We determined the antinociceptive effects of morphine (M), fentanyl (FEN), and tramadol (TRM) individually and combined in a 1:1 proportion, based on their potency. Nociceptive thresholds were evaluated in CD1 mice using the hot plate test. Morphine tolerance was induced by the subcutaneous implantation of a 75mg morphine pellet, whereas control animals received a placebo pellet; the experiments were performed three days later. In both (placebo and morphine pellets), dose-response curves for M, FEN and TRM, individually and combined were obtained, and the doses that produced 50% inhibition (ED50) we