

Analysis of the opioid-opioid combinations according to the nociceptive stimulus in mice

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The purpose of the present study was to characterize the antinociceptive effects of tramadol, fentanyl and morphine, when two of them were systemically combined in a 1:1 potency ratio, in the hot plate, the acetic acid writhing, and the formalin tests in mice. Interaction indexes and isobolographic analysis were used to assess the type of interaction. Fentanyl was the most potent drug, followed by morphine and tramadol, with the exception in the phase I of formalin test. Synergistic interactions were obtained when tramadol was combined with fentanyl or with morphine in the writhing and formalin tests. But, in the hot plate only additive interactions were obtained. Changes were induced on the type of interaction depending on the level of effect of opioid-opioid combinations. Moreover, co-administration of fentanyl with morphine showed additivity, regardless of the type of stimulus. Standard rotarod test analysis confirmed intact motor coordination. The present findings suggest that the