Fluoxetine uses in nociceptive pain management: a promising adjuvant to opioid analgesics

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Abstract:

Fluoxetine, a commonly prescribed antidepressant, use in nociceptive pain management represents one of the unsettled issues of fluoxetine therapeutics. By reviewing the literature about fluoxetine's possible roles in this setting, those could be solitary antinociceptive effect, enhancement of acute morphine analgesia, blocking morphine tolerance development, and blocking dependence development and associated abstinence syndrome. In this study, we examined those four alleged roles of fluoxetine. Moreover, as effective alleviation of morphine tolerance, dependence, and abstinence syndrome represents one of the most challenging medical needs, we biochemically analyzed fluoxetine effect on these phenomena. Fluoxetine (10 mg/kg, IP) was examined in hot plate test for assessment of possible analgesic activity and enhancement of morphine acute analgesia (1 and 5 mg/kg, SC). Repeated morphine (5 mg/kg, SC) administration for 9 days developed tolerance and dependence; fluoxetine was co-administered to evaluate its potential to modulate these processes. We also determined concomitant changes in neurotransmitters (glutamate and noradrenaline), inflammatory status, and prooxidant–antioxidant balance. Our results indicated that fluoxetine did not possess significant analgesia solely and did not enhance acute morphine analgesia. However, fluoxetine administration with morphine significantly attenuated tolerance and dependence development and abstinence syndrome with corresponding suppression of morphine-induced changes in neurotransmitters (glutamate and noradrenaline), inflammatory status, and prooxidant–antioxidant balance. These biochemical results may reflect both direct and indirect effects of fluoxetine. Our conclusion is that despite fluoxetine possesses low – if any – analgesic activity, it significantly adds to opioids not via enhancing analgesic activity but through modulation of tolerance and dependence development.

Keywords:

analgesia, fluoxetine, inflammation, morphine tolerance and dependence, neurotransmitters, oxidative stress

Published In:

Fundamental & Clinical Pharmacology, NULL, NULL