Bupropion attenuates morphine tolerance and dependence: possible role of glutamate, norepinephrine, inflammation, and oxidative stress

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Abstract:

Morphine - the main pillar of nociceptive pain management - systemic use is associated with development of tolerance and dependence. Tolerance and dependence lay a heavy burden in clinical pain management settings. An added weight to this dilemma is that effective, safe, and tolerable solution to this problem is still beyond reach. Antidepressants were reported as possible alleviators of opioid tolerance and dependence. One of the increasingly used antidepressant in clinical practice is bupropion given its high safety and tolerability profile. Methods The study was performed on male Balb-c mice weighing 20-30 grams. Hot plate test was used for assessment of bupropion (5 mg/kg, ip) 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, bupropion (5 mg/kg, ip) was concurrently administered to evaluate its potential to modulate these processes. We also biochemically analyzed bupropion effect on these phenomena through modulation of neurotransmitters (glutamate and norepinephrine), inflammatory status (nitric oxide), and pro-antioxidant balance (malondialdehyde and reduced glutathione). Results Bupropion was devoid of intrinsic analgesic activity and did not enhance morphine acute analgesia. However, bupropion significantly attenuated morphine tolerance and dependence development and abstinence syndrome with corresponding suppression of morphine induced changes in glutamate, norepinephrine, inflammatory status, and prooxidant-antioxidant balance. ACCEPTED MANUSCRIPT 3 Conclusion Bupropion efficacy in attenuation of morphine tolerance and dependence with its high safety and tolerability profile provide an alternative option to conventional agents e.g., ketamine and clonidine to modulate these phenomena.

Keywords:

Bupropion; Analgesia; Morphine tolerance and dependence

Published In:

Pharmacological Reports, NULL, NULL