Antinociceptive effect of clavulanic acid and its preventive activity against development of morphine tolerance and dependence in animal models

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Abstract:
Glutamate has a key role in pain perception and also development of tolerance and dependence to morphine. It has been reported that clavulanic acid affects glutamatergic transmission via activation of glutamate transporter. Therefore the present study was aimed to evaluate possible antinociceptive effect of clavulanic acid and also its preventive activity against development of morphine tolerance and dependence in animal models. Male Swiss mice (25-30 g) were used in this study. Acetic acid-induced writhing, formalin test and hot plate method were used to assess the antinociceptive effect of clavulanic acid. Morphine tolerance and dependence were induced by repeated injections of morphine according to standard protocols. Naloxone (5mg/kg, i.p.) was used to induce morphine withdrawal syndrome and the number of jumpings and presence of ptosis, piloerection, tremor, sniffing and diarrhea were recorded and compared with control group. Clavulanic acid at doses of 10, 20 or 40 mg/kg inhibited abdominal constriction and licking behavior of acetic acid and formalin tests respectively. Clavulanic acid could not show any antinociception in hot plate model and could not prevent development of tolerance and dependence to morphine. Clavulanic acid has considerable antinociceptive activity and further studies are needed to clarify its exact mechanism.

Keyword: Clavulanic acid; Antinociceptive; Tolerance; Dependence; Morphine