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Effects of ethosuximide on morphine tolerance and dependence in mice

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Abstract

In the present study, the effects of ethosuximide (an anticonvulsant with T-type calcium channel blocking activity) on the expression and development of morphine antinociceptive tolerance, and naloxone-precipitated abstinence syndrome in morphine dependent mice were investigated. Mice were rendered tolerant and dependent on morphine by repeated administration of morphine. The tail-flick test was used to assess the nociceptive threshold, naloxone-induced jumping to assess the morphine dependence and open field to evaluate the locomotion. Repeated administration of ethosuximide (100, 200 and 400 mg/kg, 2 time/day for 4 day) and also single administration of ethosuximide (100 mg/kg, simultaneously with last dose of morphine) reduced the development and expression of tolerance to the antinociceptive effect of morphine. Repeated administration of ethosuximide (100, 200 and 400 mg/kg, 3 time / day for 3 day) and also single administration of ethosuximide (100, 200 and 400 mg/kg, 30 min before the last dose of morphine) reduced the development and expression of naloxone-induced jumping in dependent mice that was comparable with clonidine (0.1 mg/kg) as positive control. Single (200 and 400 mg/kg) and repeated (only in 400 mg/ kg) administration of ethosuximide reduced the activity of animals in open field test. Ethosuximide in 200 and 400 mg/kg had direct antinociceptive effect that wasn't blocked by naloxone. These results showed that ethoseximide, a relatively selective T-type calcium channel blocker has direct antinociceptive effect, prevents the development and expression of antinoceptive tolerance to morphine and suppress morphine withdrawal syndrome.

Reaxys Database Information

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Author keywords

Antinociception; Dependence; Ethosuximide; Morphine tolerance; T-type voltage dependent calcium channels; Withdrawal

Indexed Keywords

EMTREE drug terms: calcium channel T type; clonidine; ethosuximide; morphine; naloxone

EMTREE medical terms: animal experiment; animal model; antinociception; article; controlled study; dose response; drug dose comparison; drug selectivity; jumping; locomotion; male; morphine addiction; morphine tolerance; mouse; nonhuman; open field test; repeated drug dose; single drug dose; tail flick test; withdrawal syndrome

Chemicals and CAS Registry Numbers: clonidine, 4205-90-7, 4205-91-8, 57066-25-8; ethosuximide, 77-67-8; morphine, 52-26-6, 57-27-2; naloxone, 357-08-4, 465-65-6

Manufacturers:Drug manufacturer: Sigma, Germany;Darou Pakhsh, Iran;Tolid Daru, Iran.

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