

Role of 5-HT_{1A} receptors in nicotine withdrawal syndrome in mice

M. Hoseinzade*, A. Naebi

Department of Pharmacology, School of Pharmacy, Tabriz University of Medical Sciences, Tbriz, Iran

Background and Aims: Nicotine is the most important psychoactive alkaloid in tobacco products. It causes significant pharmacological effects in the nervous system such as increasing levels of dopamine and Ach. Acute and chronic administration of nicotine increases and decreases serotonin release from hippocampus respectively. 8-OH-DPAT is an agonist and NAN190 is an antagonist of 5-HT_{1A} receptor that could be used potentially in treatment of nicotine withdrawal syndrome. Purpose: In this study we tried to investigate the effect of 8-OH-DPAT and NAN190 on nicotine withdrawal syndrome in mice. The recorded nicotine withdrawal syndrome symptoms i.e. somatic and locomotion behaviours.

Methods: Ten groups of mice (8 mice in each group) were considered in this study as follows: intact, nicotine, 8-OH-DPAT (1, 0.5, 0.25 mg/kg), NAN190 (1, 0.5, 0.1 mg/kg) and/or 8-OH-DPAT with NAN190. The weight of mice was approximately 25±2 gr. In order to induce dependency, nicotine (4 mg/kg) was injected subcutaneously twice daily for 14 days. Drugs were injected intraperitoneally (i.p.) from day 15 for a 10 days period and then somatic and locomotor behaviours were assessed at days 15 and 25.

Results: The effective doses of both the 8-OH-DPAT and NAN190 were 1 mg/kg. The signs of withdrawal syndrome were increased in the case of 8-OH-DPAT (1 mg/kg) and NAN190 (1 mg/kg) but this cotreatment was also effective in diminishing the withdrawal symptoms.

Conclusions: 8-OH-DPAT attenuates nicotine withdrawal syndrome by affecting on 5-HT_{1A} receptors and increasing effect of serotonin, however NAN190 almost causes the same result by blocking 5-HT_{1A} autoreceptors and subsequent increases of serotonin level. NAN190 decreases the effects 8-OH-DPAT by blocking 5-HT_{1A} receptors, but because synchronic blocked 5-HT_{1A} autoreceptors causes increasing level of serotonin in synapses.

Keywords: 8-OH-DPAT; NAN190; 5-HT_{1A}; Withdrawal syndrome; Nicotine