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Evaluation the effect of Chronic administration of Pregabalinon Morphine withdrawal syndrome in rats

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Abstract

Introduction:
Opioids as one of the most important groups of drugs to reduce severe acute and chronic pains that are still widely used. But the major problem of long-term use of opioid is development of tolerance followed by the onset of dependence on them. Several studies have been performed inmedications and the agents that can reduce opioid tolerance and dependence which all suggest that understanding the mechanisms involved in tolerance and dependence is essential to reduce this phenomenon. One of the most important branches of study in neuropharmacology is tostudy the mechanism of opiate dependence and find ways to prevent or postpone it. In case of reaching the ability to prevent this phenomenon, clinical application of these drugs will increase. Obviously, among all mechanisms involved in opioid dependence, theneurotransmitter system of glutamate and receptors of excitatory amino acids especially NMDA receptors play important roles.

Pregabalin is a member of Antiepileptic group of drugs and also an analogue of GABA, which is very similar to gabapentin.Pregabalin is used to treat neuropathic pain,the painscaused by nerve damage. This drug binds with high affinity to the alpha-2-delta subunit (the accessory subunit) of voltage-gated calcium channels in the central nervous system and causes voltage dependent calcium channels are closed .So that it decreases the release of calcium-dependent neurotransmitters such as glutamate, substance p and norepinephrine.

Opioid addiction is a disease that is increasing in our country, Turkey, and around the world, which it is difficult to treat in medical, social, and economic terms. Pregabalin is a preparation used for the treatment of epilepsy, neuropathic pain, and anxiety disorders. In opioid users, pregabalin is increasingly being self-administered off-label due to its euphoria effect at high doses. We investigated the effects of pregabalin on addiction profile and opioid withdrawal severity by comparing patients with opioid addiction who were and were not using off-label pregabalin.

According to the above, since the chronic use of morphine leads to the increased release ofglutamate, substance p and norepinephrine neurotransmitters, therefore, it is likely to reduce theses neurotransmitters with the same mechanism and beeffective in morphine withdrawal syndrome.

Objectives: To evaluate the effect of chronic administration of pregabalin on morphine withdrawal symptoms in rats.

Results: Chronic treatment with pregabalin not only reduced withdrawalsymptoms individually and dose-dependently, but also could significantly reduce the total symptoms of the withdrawal syndrome. Conclusion: chronic injection of pregabalin, is capable of reducing most of the symptoms ofmorphine withdrawal syndrome.

Conclusion: According to the results of this study, it can be concluded that pregabalin can reduce most symptoms of morphine withdrawal in rats and this reduction is dose dependent. This means by increasing the dose, its impact in reducing withdrawal symptoms increases. The drug can be used as a component of pharmacological therapies in the treatment of addiction.