Original Paper

Effect of methadone and valproate combination on morphine withdrawal-induced anxiety and depression in male mice

Vahidi S (M.Sc)*[1], Khalili M (Ph.D)[2], Kiasalari Z (Ph.D)[3], Yaghoutpoor E (M.Sc)[1]

[1]M.Sc in Animal Physiology, Department of Biology, Faculty of Sciences, Shahed University, Tehran, Iran. [2]Professor, Neurophysiology Research Center, Shahed University & Iranian Traditional Medicine Clinical Trial Research Center, Tehran, Iran. [3]Associate Professor, Neurophysiology Research Center, Shahed University & Iranian Traditional Medicine Clinical Trial Research Center, Tehran, Iran.

Abstract

Background and Objective: Anxiety and depression are experienced following addicted patients durg withdrawal. This study was done to determine the effect of methadone and valproate combination on morphine withdrawal-induced anxiety and depression in male mice.

Methods: In this experimental study, ninety-eight male mice were allocated into acute and chronic categories. Animals in acute chronic categories allocated into seven groups including: saline, morphine, methadone (10 mg/kg/bw), valproate (150 mg/kg/bw), three groups of valproate+methadone, in of ratio 1:1, 2:1 and 1:2. Animals were received escalating dose of morphine for 8 consecutive days except saline group. In chronic group, drugs were injected for 30 minutes before morphine administration, while in acute group; the drugs were used only at day 8. Anxiety and depression due to naloxone injection (5 mg/kg/bw) was investigated by elevated plus-maze, tail-suspension and open field tests.

Results: In the chronic group, valproate + methadone (2:1) combination therapy showed a significant increase in the percentage of open arm entries (53.86±1.9) and percentage of time spent in the open arm (58.58±4.15) compared to the morphine group, with a percentage of entering (28.12±2.03) and percentage of time (17.88±1.77) ($P<0.05$). In open field test, the ratio of the number to the duration of time spent in the central square, in the combination therapy groups of methadone+valproate (27±2), valproate+methadone (1:2) and valproate+methadone (2:1) were significantly increased in compare to the morphine group ($P<0.05$). In tail-suspension test, duration of immobility as an indicator of depression, in the treatment group of valproate+methadone (2:1) was significantly reduced ($P<0.05$).

Conclusion: Valproate and methadone combination therapy particularly in ratio of 2:1 can reduce morphine withdrawal-induced anxiety and depression in animal model.

Keywords: Anxiety, Depression, Methadone, Valproate, Mice

*** Corresponding Author: Vahidi S (M.Sc), E-mail: samiravahidi@yahoo.com**

Received 7 May 2013 **Revised** 23 Apr 2014 **Accepted** 30 Apr 2014

This paper should be cited as: Vahidi S, Khalili M, Kiasalari Z, Yaghoutpoor E. [Effect of methadone and valproate combination on morphine withdrawal-induced anxiety and depression in male mice]. J Gorgan Uni Med Sci. 2015; 16(4): 21-27. [Article in Persian]