THE RELATIONSHIP BETWEEN HEROIN WITHDRAWAL SIGNS AND SYMPTOMS AND EXISTENCE OF DEPRESSION

Alireza Ghaffari-Nejad MD•, Kambiz Shahabi MD

Background: The opioid withdrawal syndrome can vary greatly in intensity. Depression is proposed to be one of the contributing factors in withdrawal intensity of opioid dependents.

Methods: Fifty-one male heroin dependents were enrolled in this study. All of them were admitted to Beheshti Psychiatric Hospital in Kerman, Iran for detoxification of heroin dependence. Existence of depression was evaluated by means of Beck Depression Inventory (BDI), and DSM IV criteria for major depressive disorders before the start of withdrawal complaints. The opiate withdrawal questionnaire was used for evaluating withdrawal signs and symptoms, 24 and 72 hours after the start of withdrawal.

Results: The mean age of subjects was 33.67 ± 8.36 years. By means of BDI, 28 (54.9%) and by means of DSM IV criteria 11 (21.57%) subjects were ranked as depressed. Scores of withdrawal signs and symptoms were higher in the depressed patients, 24 hours after beginning of withdrawal, but were only higher in patients with major depressive disorder 72 hours after the start of withdrawal.

Conclusion: Existence of depression, especially in the form of major depressive disorder, could intensify withdrawal signs and symptoms. This should be taken into account by the treating physicians, during the detoxification period and further treatment plans.

Keywords: Depression • heroin • opioid withdrawal

Introduction

The opioid withdrawal syndrome including craving for substance and other complaints such as dysphoric mood, nausea, vomiting, muscle aches, yawning, etc, can vary greatly in intensity. Some known contributing factors in determining the intensity of this syndrome include dose of the opioid used, the degree to which the opioid effects on the CNS are being continuously exerted, the duration of use, and the rate at which the opioid is removed from the receptors.1 There might be other contributing factors, such as the coexistence of depression.

Most psychoactive substances abuse or dependence disorders are associated with other psychiatric disorders. Depression, anxiety, and psychoactive disorders are the more frequent co-morbid disorders. The occurrence of depression among opioid dependents is frequent and withdrawal from them provokes depression.2 Opioid-dependent subjects experience severe depression as one of the subjective symptoms during withdrawal.3

Based on our clinical experience, we propose that one of the contributing factors of the opioid withdrawal syndrome is comorbidity of depression in dependent patients and opioid dependents with and without a depressive disorder may differentially experience the opioid abstinence syndrome. Hence, we studied depression in a sample of heroin-dependent patients before the start of withdrawal signs and symptoms. The results of withdrawal scores in two depressed and
nondepressed groups were compared with each other.

**Patients and Methods**

In this descriptive study, 51 male heroin-dependent patients who wanted to undergo withdrawal for dependence were enrolled. They were consecutively admitted over a 2-month period to Beheshti Psychiatric Hospital in Kerman, Iran. Diagnosis of heroin dependence was confirmed by two psychiatrists, based on DSM IV criteria via the structured clinical interview. Sample size was determined, using a previous pilot study. To be included in the study, subjects had to cooperate and complete an interview. Patients were excluded if they were psychotic and if their main reason for referral was not undergoing withdrawal for dependence. Patients were initially questioned about their demographic factors and then in order to assess depression, two separate methods were used. First of all, patients were evaluated by the Beck Depression Inventory (BDI), which was standardized in Iran. Cut-off point was considered as 16. Then after, patients were evaluated for the probability of presence of major depressive disorders based on DSM IV criteria, via a structured clinical interview. Evaluation of depression was carried out before the start of withdrawal complaints. All the depressed and nondepressed patients were detoxified with clonidine, which is suggested for treatment by the Ministry of Health, Treatment, and Medical Education. Subjects had no somatic problem or history of heart disease and had a blood pressure of at least 90 mmHg. All patients received oral clonidine (0.2 mg, three doses daily), ibuprofen (400 mg every 4 hours) for pain relief, oral hyoscine (20 mg every 4 hours) for vomiting and abdominal problems, and chlorpromazine (100 mg at the time of sleep) for sleep regulation. Although tricyclic antidepressive drugs have been suggested during detoxification with clonidine, in order to avoid drug interference, they were not used. Patient’s withdrawal complaints were assessed by means of an opiate withdrawal questionnaire, 24 and 72 hours after the start of withdrawal symptoms. In this questionnaire, 18 symptoms and 13 signs were evaluated. The symptoms evaluated were yawning, muscle cramp, pounding heart, runny nose, sneezing, experienced pins and needles, hot/cold flushes, diarrhea, gooseflesh, sick feeling, somatic cramps, difficulty in falling asleep, aches in the bones and muscles, twitching and shaking, irritability, sweating, runny eyes, and craving. The observed signs included yawning, lacrimation, rhinorrhea, perspiration, tremor, piloerection, restlessness, pupil size, anorexia, vomiting, diarrhea, insomnia, and drug seeking. These signs and symptoms were evaluated by a trained nurse, 24 and 72 hours after the onset of withdrawal. The score of each item was ranged from 0 to 3, leading to a total score of 0 – 93.

In assigning rating, if the item was absent it was scored zero. A rating of 1 to 3 corresponded to incremental levels of severity of signs and symptoms. Based on the clinical interview and the score of Beck Depression Inventory, patients were divided into the depressed and nondepressed groups, and the results obtained compared with each other. The results were statistically analyzed with \( \chi^2 \) and \( t \)-test, using the SPSS-10 software.

**Results**

The age of the patients ranged from 19 to 52 years, with a mean of 33.67 ± 8.36 (SD) years. The mean amount of heroin consumed per day was 2.35 ± 1.48 (SD).

According to Beck depression inventory, 28 (54.9%) of the subjects were depressed and 23 (45.1%) were nondepressed. Based on the DSM IV criteria for major depressive disorder, 11 (21.57%) were depressed. There were no statistical differences between the age, state of marriage, level of education, and route of heroin consumption between the groups.

Withdrawal signs and symptoms were assessed in two study groups within 24 and 72 hours after the start of withdrawal. Mean scores of withdrawal symptoms, 24 and 72 hours after the start of heroin withdrawal, in the depressed patients were 12.71 ± 8.23 and 11.96 ± 6.91, respectively. These scores were 7.91 ± 5.75 and 7.87 ± 4.54 in the nondepressed patients. Differences between the groups were significant 24 hours after the beginning of withdrawal syndrome but was not significant 72 hours after the start of withdrawal syndrome.
Results are shown in Table 1.

Based on the DSM IV criteria, patients were divided into two groups, those with and without major depressive disorders. Scores of the withdrawal signs and symptoms were significantly higher in patients with major depressive disorder than those without this diagnosis, 24 and 72 hours after the start of withdrawal syndrome. Results are shown in Table 2.

**Discussion**

Depression and addiction have some similarities. Methodological precedents for biobehavioral correlations in depressive illness have suggested an important association between changes in the mood and biogenic amine excretion pattern in the urine of patients during depression and recovery. In a separate study, authors showed that subjective changes in mood were associated with heroin users and mental status effects were associated only with the individuals whose methoxyhydroxyphenylglycol (MHPG) excretion increased during the period of opiate administration.6 Other findings implied that the degree of inhibitory endogenous opioid tone is reduced in depression. Hence, a reduced endogenous opioid tone may explain why some depressed individuals self-medicate with opiates, and depression is associated with opiate withdrawal.7 Observations over animals and humans, experiencing withdrawal from chronic opiate administration, suggest that the development of supersensitive alpha 2 adrenoceptors may lead to affective illness in vulnerable individuals.8

As mentioned earlier, we observed that depressed patients with opioid dependence had more intense withdrawal complaints. In this article we showed that this hypothesis could be justified. All depressed individuals, whether based on the Beck Depression Inventory or DSM IV criteria, had more intense withdrawal signs and symptoms than the nondepressed patients with heroin dependence. Only patients who had DSM IV criteria for major depressive disorder had more intense withdrawal scores 72 hours after the start of withdrawal complaints. So, heroin-dependent patients with more severe depressive symptoms, experienced more withdrawal signs and symptoms in later days after the beginning of detoxification period. Hence, they are in need of more attention to be paid and intense psychiatric caring to remain within therapeutic program. In a study, it has been shown that drug-dependent depression is a more

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<table>
<thead>
<tr>
<th>Group/Score</th>
<th>Depressed group Mean ± SD</th>
<th>Nondepressed group Mean ± SD</th>
<th>Analysis T</th>
<th>P</th>
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<td>Score of withdrawal symptoms 24 hours after the beginning of heroin withdrawal</td>
<td>12.71 ± 8.23</td>
<td>7.91 ± 5.75</td>
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<td>Score of withdrawal symptoms 72 hours after the beginning of heroin withdrawal</td>
<td>11.96 ± 6.91</td>
<td>7.87 ± 4.54</td>
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<td>Score of withdrawal signs 24 hours after the beginning of heroin withdrawal</td>
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<td>Score of withdrawal signs 72 hours after the beginning of heroin withdrawal</td>
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<td>3.56 ± 2.97</td>
<td>−1.70</td>
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<td>Score of withdrawal symptoms 24 hours after the beginning of heroin withdrawal</td>
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<td>Score of withdrawal symptoms 72 hours after the beginning of heroin withdrawal</td>
<td>13.63 ± 9.25</td>
<td>9.15 ± 4.86</td>
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<td>Score of withdrawal signs 24 hours after the beginning of heroin withdrawal</td>
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<td>3.3 ± 2.85</td>
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<td>Score of withdrawal signs 72 hours after the beginning of heroin withdrawal</td>
<td>6.54 ± 4.30</td>
<td>3.87 ± 2.95</td>
<td>−2.40</td>
<td>0.02</td>
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Table 1. Comparison between the mean scores of withdrawal signs and symptoms 24 and 72 hours after the beginning of withdrawal in depressed and nondepressed groups according to the Beck Depression Inventory.

Table 2. Comparison between the scores of withdrawal signs and symptoms 24 and 72 hours after the beginning of withdrawal in depressed and nondepressed groups based on the DSM IV criteria for major depressive disorder.
important factor for the continuation of treatment in comparison to the intensity of dependency.9

In another study, hypnotically-induced depression produced significant increases in drug craving for opiates. Depression also tends to increase global self-rating of opiate withdrawal. The results suggested that negative mood states, perhaps in the context of repeated attempts at self-medication, may become conditioned stimuli capable of triggering craving and other drug-related responses.10

In a similar study on individuals with a history of regular cocaine use, it was demonstrated that those meeting the criteria for the cocaine withdrawal syndrome, according to DSM IV, in comparison to those who did not, were significantly more likely to have a life time history of depression. Results suggested that a life time history of depression is strongly related to whether or not a cocaine abuser self-reported withdrawal symptoms.11 In a recent study, using spect with 99 mtc-HMPAO as tracer, 27 detoxified opiate addicts were compared with nine healthy controls. Significant hypoperfusion in the right frontal and left temporal lobes was found in addicts with a co-morbid depression. The asymmetrical findings in cerebral blood flow (CBF) that characterized the addicts relative to normal control subjects may be more closely related to mood than substance abuse, per se.12

Prescribing antidepressants is an important part of treating addiction in long-term. Clonidine as one of the main drugs during the detoxification period, has an antidepressant property.13 Identifying major depressive disorders in opioid-dependent patients is difficult. Dexamethazone Suppression Test (DST) and thyroid releasing hormone (TRH) test have held some promise for making the diagnosis14 and clinical evaluation before the beginning of withdrawal complaints could help clinicians in making this comorbid diagnosis. Physicians are recommended to consider such diagnosis in their detoxification planning and further therapeutic efforts.

Acknowledgement

We want to offer our special thanks to Dr. Hassan Ziaadini who gave us opiate withdrawal questionnaires.

References