A new taper off treatment of opium dependents can lead to cure the addiction as well as improvement of cognitive functions

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Research Article

Keywords: taper off treatment, opium, congress 60, cognitive functions

Posted Date: January 4th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2410457/v1

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Abstract

Opium is the dried latex obtained from the opium poppy. Opium addiction is the most prevalent addiction in Iranian society. During the last two decades "congress 60" a nongovernmental organization, has been performed a taper off treatment of opium associated with a package of psychological treatment group classes. Present study aimed to evaluate the effectiveness of taper off method in opium addiction in Iran, during more than 20 years as well as the effects of the treatment method on addiction associated cognitive dysfunctions.

In present study the taper off treatment method of opium addiction called Dezhakam step time (DST) were assessed. We used data collected via the congress 60 non-governmental organization in Iran dedicated to addiction treatment with DST method, since Jan 2018 until December 2020. In addition, executive functions including memory and decision making were analyzed in a large sample size from addicted subjects which were successfully treated with DST method in Congress 60.

Results showed high number of successful treatment of opium addiction and very low number of substance abuse relapse. Also, significant improvements in memory and decision making were determined in addicts after therapy and these improvements were correlated with duration of individuals’ membership in congress 60.

Findings revealed the effectiveness of taper off method in treatment of opium addiction as well as improvement in cognitive functions in opium dependent persons. Findings of the study may help to a better understanding from a novel method of opium addiction treatment called DST and its effects on neuropsychological mechanisms and brain functions of opium dependents.

Introduction

Addiction is a major chronic and severe psychiatric disease which is responsible for a several major health, social and economic problems and causing about 13% of deaths worldwide. Opioids are the most prevalent class of addictive substances that affect the nervous system and use to produce as euphoric drugs and pain killer as well. (1) Dependence to Opioid is characterized with powerful and compulsive urge to use opioid drugs. It is common in Opium dependents to prioritize drug abuse over all other activities in their lives that in turn may impact badly to their career, social activities and significantly reduce their quality of life (2).

Addiction is a multifactorial complex behavioral characteristic with psychological, social and neurobiological issues. Heritability rate of addiction in different drugs are ranged from 39 to 72 percent (3). Number of physiological and psychological mechanisms were found associated to opioids addiction that most of these pathways are related to dopamine signaling(4).

Genetic association studies discovered the role of endogenous genes of opioid and monoaminergic systems, which encode the receptor target of some endogenous opioids, heroin, or morphine including μ opioid receptor, in genetic tendency on opiate addiction (5). On the other hands, it has been reported that dopamine β-hydroxylase and serotonin transporters are also involved in the neurobiology of addiction that make the pattern of addiction cause, more complicated (6, 7). The neurobiological pathways which play role in modulation of reward, stress resiliency and behavior inhibition are among those addiction related pathways(8).

Currently, only three opioid addiction medication were approved by United States Food and Drug Administration that including methadone, buprenorphine, and naltrexone (9). Methadone is a long-acting opioid agonist which may be used as detoxification drug to suppress withdrawal and cravings as well as maintenance medication to decrease nonmedical opioid use (10). Methadone maintenance treatment (MMT) is a well-known method for opiate addiction worldwide which is designed to normalization of many physiological abnormalities caused by chronic use of short-acting opiates (11) but the MMT side effects including methadone dependence, low bone density, and even hepatotoxicity had been raised serious concerns (12). Buprenorphine, is another opioid agonist that use during detoxification and maintenance stages of treatment for opioid dependent individuals (13). Naltrexone is a long-acting opioid antagonist like Methadone that binds to opioid receptors for up
to 30 days (14). Naltrexone blocks opioid receptors, which lead to significant reduction of subjective effects of ingested opioids. Opioid dependent should completely detoxified of all opioids before taking naltrexone that may cause potential side effects for dependents especially for individuals that taking the detoxification period (15).

Focusing on the acute phase of illness and ignorance of psychological and genetic bases of addiction are the most important dilemma of all FDA approved treatment methods for opium addictions. On the other hands, the quality of life for opium dependents who get treated is highly associated with reduction of psychological craving to opium that is the missing part of all of these treatments (16). The aim of addiction treatments is not limited to cutting the substance abuse but is related to cutting or significantly reduction of substance craving and the increase of quality of life. Improvement of cognitive disabilities that caused by opium abuse especially improvement of executive functions such as memory and decision making have the key role to increase the quality of life for treated persons.

**What is Dezhakam step time (DST) method?**

During the last two decades "congress 60" a nongovernmental organization in the Islamic Republic of Iran, has been performed a taper off treatment of opium associated with a package of comprehensive psychological treatments, group classes, social caring, and harm reduction methods for patients and their family members. Opium addicts who became members of "congress 60" called passengers do not take any medication besides opium tincture (OT). During the 12 months, passengers will reduce the dosage of OT use step by step and each step takes 21 days. while they are participating in the classes and group training of congress 60 which is including sports training, passing the courses about the reason of human tendency to addiction, and some cognitive-behavioral therapies. It is supposed that passengers finish the process and leave opium abuse completely after twelve months. During last 24 years, more than 50000 Iranians were successfully finished the 12 months of treatments of DST method in congress 60 and cut the opium abuse until now. A regular five years follow-up in the individuals who treated with DST method and became congress60 members, was shown less than ten percent relapse which is one of the lowest rates of relapse worldwide compared with other opioid addiction treatment methods (17). The present study aimed to examine the effectiveness of the DST method by evaluating of two clinical parameters successfulness of treatment and relapse rate as well as neuropsychological assessment to evaluate the cognitive functions improvement of treated subjects.

**Material And Methods**

**Subjects recruitments for cohort study:**

The present study is the report of a two years follow-up of 21034 opium dependents who registered for DST taper off treatments in 66 out of 100 branches of congress 60 around Iran. Subjects with any sever psychological or somatic disorders have been excluded from the study. None of the subjects had a current or history of any severe medical condition, neurological disorder, history of head trauma with loss of consciousness, and any psycho-stimulant drug abuse and alcohol dependence. All subjects have explained about the aim of the study and next, written informed consent has been provided based on declaration of Helsinki obligations and guidelines. Demographic data of subjects were presented in Table 1.
Table 1
Demographic data of subjects

<table>
<thead>
<tr>
<th>GROUPs</th>
<th>Age (year)</th>
<th>Gender</th>
<th>Marital status</th>
<th>Duration of addiction before registration to Congress60 (year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort group</td>
<td>33.2 ± 3.5</td>
<td>Male: 17037</td>
<td>Married: 15437</td>
<td>10.4 ± 1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female: 3997</td>
<td>Single: 5597</td>
<td></td>
</tr>
<tr>
<td>Cognitive analysis group</td>
<td>31.4 ± 4.1</td>
<td>Male: 1484</td>
<td>Married: 1422</td>
<td>11.1 ± 3.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female: 606</td>
<td>Single: 668</td>
<td></td>
</tr>
</tbody>
</table>

Cohort group: all 21034 participants of study
Cognitive analysis group: all 2090 subject who participated in cognitive testing

Urine drug monitoring:

All participants were analyzed with urine drug monitoring in two separate periods. First period of testing was after the termination of treatment period and second period was 12 months after the treatment as follow-up approach to measure the rate of relapse. In each period both immunoassay and chromatography (GC-MS, gas chromatography–mass spectrometry) of the opiate panel for opium alkaloids and/or their metabolites, including morphine and codeine were assessed. Participants gave a minimum of 30 mL of urine collected in a private restroom. Validity testing of urine specimens including temperature (33–36 Celsius), specific gravity (1.002–1.03), pH (4.5-7), urine creatinine (20–400 mg/dL), and presence of adulterants were conducted. Any specimen outside of the physiological range were excluded from study. The opiate test cut off line has set for 2000 ng/ml and any subject with higher opiate rate in first testing period in any of immunoassay or chromatography considered as untreated; and in second testing period considered as relapsed subjects. Urine drug monitoring conducted based on the standard protocols and previous studies (18).

Subjects selection for cognitive study:

The cognitive functions' situation in subject were evaluated in 2090 subjects registered in congress 52 out of 100 branches of congress 60 around Iran. These subjects recruited from the main 21034 opium dependents who registered for DST taper off treatments in 66 out of 100 branches of congress 60 around Iran. Three period of cognitive testing were conducted in this study. First period conducted in the first day of opium addict's registration to congress 60 and before the start of DST method, second period was after the participant's treatment, and third period was 12 months after the termination of DST method. Participation in cognitive testing wasn't a part of registration to congress60 or DST method and was completely voluntary, after the signing of written consent form.

Cognitive assessments:

Subjects with IQ total score (Wechsler Abbreviated Intelligence Scale, 1999) lower than < 80 were excluded from the study. None of the subjects had a current or history of any severe medical condition, neurological disorder, history of head trauma with loss of consciousness, and any psycho-stimulant drug abuse. For better presentation of data test groups showed by this order: C (addicts before admission in congress 60), and PC (participants from group C after treatment in congress 60) and F (participants from group PC, 12 month after the termination of treatment in congress 60). Cognitive functions including working memory and decision making were measured by neuropsychological tests listed below:

N-Back and spatial N-Back tests:

Working memory and spatial working memory were assessed by n-back and spatial n-Back tasks respectively. All subjects had been presented with a sequence of stimuli, and the task consisted of indicating when the current stimulus was matched the
one from n steps earlier in the sequence (19, 20).

**Digit span test:**

The digit-span task is one of the subsets of the Wechsler Adult Intelligence Scale (WAIS). It is a well-known tool to evaluate the working memory's number storage capacity (23, 24). Participants in present study were sitting in an isolated room and after 20 minutes of inhabitations, they should listen to examiner that read a sequence of numerical digits and asked to recall the sequence correctly, with increasingly longer sequences being tested in each trial. Digit-span tasks were performed forwards and backward, to evaluate the verbal and spatial working memory respectively (21, 22).

**GO no GO test:**

Go/no Go testing is a worldwide accepted pass/fail test which measure the sustained attention and decision-making abilities (23). We used a computational form of the test and participants were using binary classification. The test is passed only when the Go condition is met and also the No go condition fails.

**Statistical analysis:**

Normal distribution for continuous variables was examined by the Kolmogorov-Smirnov test. One-way ANOVA and Pearson correlation analysis was conducted to determine the relationship between the 2 independent variables. Descriptive data are expressed as mean ± SD (range) and the level of statistical significance was set at P < 0.05. Bonferroni correction test was used for multiple comparison examinations. SPSS version 23 software used for statistical analysis.

**Results**

**Treatment successfulness and relapse rate:**

Results of both immunoassay and chromatography (GC-MS, gas chromatography–mass spectrometry) of the opiate panel for opium alkaloids and/or their metabolites in all period of analysis presented in Table 2. Significant successfulness of treatment and also significant rate of prevention of relapse were detected.

**Neuropsychological examinations:**

Significant improvement of memory deficiencies and abnormalities in sustained attention and decision-making were determined during the follow up from first day of treatment to last day of treatment and after the treatment until twelve month after the treatment termination. Also, significant improvement in verbal and spatial memory and decision making were detected in participants after the DST treatment period and 12 months later than last day of treatment period. Neuropsychological test results were presented in Table 3.

<table>
<thead>
<tr>
<th>Testing period</th>
<th>immunoassay subject with negative result Vs. subject with positive results</th>
<th>Chromatography subject with negative result Vs. subject with positive results</th>
</tr>
</thead>
<tbody>
<tr>
<td>First time</td>
<td>P : 0.002</td>
<td>P : 0.003</td>
</tr>
<tr>
<td>(day after treatment)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second time</td>
<td>P : 0.008</td>
<td>P : 0.008</td>
</tr>
<tr>
<td>(12 months after treatment)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3
Comparison of neuropsychological results in subjects during three period of testing

<table>
<thead>
<tr>
<th>GROUP COMPARISONS</th>
<th>spatial N back result</th>
<th>Spatial N back time</th>
<th>N back result</th>
<th>N back time</th>
<th>Go/no Go FA M</th>
<th>Go/no Go I</th>
<th>Go/no Go time</th>
<th>Digit span forward</th>
<th>Digit span backward</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC vs. C</td>
<td>P value= 0.002</td>
<td>P value= 0.003</td>
<td>P value= 0.001</td>
<td>P value= 0.0003</td>
<td>P value= 0.0004</td>
<td>P value= 0.0002</td>
<td>P value= 0.0005</td>
<td>P value= 0.0006</td>
<td>P value= 0.0003</td>
</tr>
<tr>
<td>F vs. PC</td>
<td>P value= 0.004</td>
<td>P value= 0.01</td>
<td>P value= 0.04</td>
<td>P value= 0.005</td>
<td>P value= 0.07</td>
<td>P value= 0.06</td>
<td>P value= 0.12</td>
<td>P value= 0.1</td>
<td>P value= 0.002</td>
</tr>
</tbody>
</table>

C: addicts before admission in congress 60, PC: participants from group C after treatment in congress 60, F: participants from group PC, 12 month after the termination of treatment in congress 60

Discussion

Twelve months of DST treatment which is standard treatment periods in congress 60, opiate were significantly reduced in addicts. Follow up of the treated subjects after 12 months showed the relapse rate is very low. Regarding to the quality of life after the treatment, the cognitive situation of subjects were examined. Improvement of memory and decision-making abilities and sustained attention indicates that the DST method can provide a significant improvement in the social life of treated subjects and help them to get back to the normal life. Opium addiction may cause a lack of cognitive and executive functions and lack of decision-making functions respectively. On the other hand, neuropsychological examinations have been detected memory and decision-making disabilities in addicts before starting the DST treatment method.

Findings suggest that DST as a package of psychological caring, group educations similar to cognitive behavioral therapy along with the opium taper-off method instead of using synthetic materials including methadone, buprenorphine or naltrexone could be a reliable treatment for opioid addiction. In addition, DST is not just a treatment method to reduce or cut the dependency of addicts on opioids but it can improve the cognitive problems as well. Improvement of cognitive abilities in addiction could be considered as a harm reduction tool that also helps the addict to back to normal life.

Conclusion

The present study was a follow-up of a new alternative method for the treatment of opioid addiction. Present study aimed to assess the rate of the change of neuropsychological and treatment-relapse rate of same subjects during and after the treatment to a better understanding of the nature of DST effectiveness. It seems that the DST method with providing an effective 21 days period has successfully led opium dependents to taper off and leave the opioid abuse without any second dependence or craving behavior on opium or other substances or somatic or psychological side effects of a sudden leave of opioid abuse. In addition, psychological caring and educational programs for under treatment addicts that call "passengers" in congress 60, have helped them to improve their cognitive abilities that are confirmed in a large sample size in a 24 month of follow up.

Declarations

Ethical statement: The studies' proposal and all processes of study have been approved by the central ethical committee of Islamic Azad University.

Conflict of interest: The authors declare no competing interests.
References
