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

Abstract

Aim: Opium addiction is the most prevalent addiction in all Middle East countries including Iran. Since 1998, a nongovernmental organization called "congress 60", has developed an opium addiction treatment method based on taper-off dosage of opium using Opium tincture. The present study aimed to assessment of the effectiveness of the taper-off method in opium addiction in Iran, for more than 20 years as well as the effects of the treatment method on addiction-associated cognitive dysfunctions.

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

Results: Results showed a high number of successful treatments for opium addiction and a very low number of substance abuse relapses. In addition, major improvements in cognitive functions such as decision-making and memory were determined in opium dependents after therapy. Cognitive improvements were significantly correlated with the duration of individuals' membership in congress 60.

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

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

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Abbreviations: DST, Dezhakam step time; MMT, Methadone maintenance treatment; OT, opium tincture; GC-MS, gas chromatography–mass spectrometry

Introduction

Addiction is a major chronic and severe psychiatric disease which is responsible for several major health, social, and economic problems and causes 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. The heritability 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 globally approved method for treatment of different kind of dependence to opium and other opioid-based compounds. MMT aimed to improve physiological and psychological problems induced by chronic use of short-acting opiates.[11] Although the side effects of MMT method such as methadone dependence, low bone density, and even hepatotoxicity in some cases may raise 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?

For more than 20 years a non-governmental organization called "congress 60" headquartered in Tehran, Iran, developed a new taper off treatment method for opium named Dezhakam step time (DST). The protocol is associated with a package of psychological consultations, group classes, social caring, and harm reduction methods. Opium dependents who register for taper off treatment program of congress 60 or DST, called passengers, take no medication besides opium tincture (OT). In taper off treatment program of congress 60 each step takes twenty one days and passengers will reduce the OT dosage in each step and dosage reduction will continue step by step during the next 12 months. Congress 60 treatment program is also including group training, sports training, passing the courses about the reason of human tendency to addiction, along with cognitive-behavioral therapies. Twelve months is the normal time for the whole process of DST, which is supposed to lead to completely leaving opium abuse. During last 24 years, more than 50000 Iranians were successfully finished the 12 months period of DST method in congress 60 and cut the opium abuse until now. A regular five-year follow-up in the individuals who treated with DST method and became congress 60 members, was shown less than ten percent relapse which is very low relapse rate in comparison with other treatment protocols for opioid dependence.[17] We aimed to evaluate the effectiveness of the DST method using two clinical parameters success 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-year 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 severe psychological or somatic disorders have been excluded from the study. Subjects with high depression or anxiety disorder were excluded from study. No history of serious somatic or psychological medical problems, any psycho-stimulant drug abuse or alcohol dependence were found in participants' medical reports. A comprehensive explanation about the aim of the study was given to all volunteers of participation in the study. After the briefing, written informed consent has been obtained from the participants. The consent form was designed based on declaration of Helsinki obligations and guidelines. Demographic data of subjects were presented in Table 1.

Table 1 Demographic data of subjects

GROUPs	Age (year)	Gender	Marital status	Duration of addiction before registration to Congress 60 (year)
Cohort group	33.2±3.5	Male: 17037 Female: 3997	Married: 15437 Single: 5597	10.4±1.5
Cognitive analysis group	31.4±4.1	Male: 1484 Female: 606	Married: 1422 Single: 668	11.1±3.7

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 un-treated; 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 periods 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 was not a part of registration to congress 60 or DST method and was completely voluntary, after the signing of written consent form. Groups revealed by this order: group C (addicts before admission in congress 60), group PC (participants from group C after treatment in congress 60) and group F (participants from group PC, 12 months after the termination of treatment in congress 60).

Cognitive assessments: Any participants with IQ total score (Wechsler Abbreviated Intelligence Scale, 1999) lower than < 80 have been excluded from the study. Any severe medical situation, neurological disorder, head trauma, or psycho-stimulant drug abuse were exclusion criteria. 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. Memory testing performed based on protocols used in previous studies.[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.[21] Participants in present study were sitting in an isolated room and

after 20 minutes of inhabitations, they should listen to examiner that read a series of numerical digits and try recall the sequence quick and correctly. After each two series, the number of numerical digits in sequence will increase. Digit-span task is included forwards and backward numerical digits sequence. Forward digit span is to examine the verbal working memory while backward digit span is to test the spatial working memory.[22,23]

GO no GO test: Go/no Go examination analyzes the sustained attention and decision-making capacities.[21] A computational form of the Go/no Go test was used in the present study.

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. Population study among the subjects in present study showed DST method were successful in different populations of Iran such as Azeri, Kurds and Fars ethnicities.

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. Clinical data and statistical results of Neuropsychological tests results were presented in Table 3 and Table 4.

Table 2 Urine drug monitoring data of subjects

Testing period	Immunoassay subject with negative result Vs. subject with positive results	Chromatography subject with negative result Vs. subject with positive results
First time (day after treatment)	P : 0.002	P : 0.003
Second time (12 months after treatment)	P : 0.008	P : 0.008

Table 3 Neuropsychological examinations results for Cognitive analysis group

GROUPs	Spatial N back result	Spatial N back time	N back result	N back time	Go/no Go FA	Go/no Go M	Go/no Go I	Go/no Go time	Digit span forward	Digit span backward
C	26.7±4.1	776.5±30.4	86.2±15.3	683.2±34.2	0.91±0.25	4.8±1.6	35.7±3.6	441.2±12.5	5.3±1.1	3.32±2.5
PC	24.2±3.3	742.9±28.7	83.6±11.2	626.1±32.1	0.84±0.38	3.6±1.2	36.9±2.9	418.7±32.5	7.6±2.1	5.6±1.4
F	23.31±2.6	723.7±38.3	101.2±16.7	621.2±23.6	0.81±0.22	3.2±1.3	37.64±1.5	411.5±12.1	8.2±2.6	5.9±3.8

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

Table 4 Comparison of neuropsychological results in subjects during three period of testing for cognitive analysis group

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

C: addicts before admission in congress 60, PC: participants from group C after treatment in congress 60, **F:** participants from group PC, 12 months 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 the quality of life after the treatment, the cognitive situations 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 could cause a great and constant cognitive and executive function deficiencies and lack of decision-making functions. Also, neuropsychological testing revealed memory and decision-making disabilities in opium dependents before starting the DST protocol in congress 60.

Findings of our study provide evidence that DST as a total package of psychological caring, group educations and opium taper-off method is more effective and reliable for opium dependence reduction besides using synthetic materials including methadone, buprenorphine or naltrexone. The DST method is not just a treatment method to decrease or cut the opium abuse but also a good solution for cognitive problems for opium addicts as well. Gain of function in cognitive abilities could be considered as a harm reduction tool that may help opium addicts to return to normal life.

Conclusion

The present study was the report of the follow-up of a novel alternative method for the treatment of opioid addiction. On the other hand results of neuropsychological situation and treatment-relapse rate of subjects were analyzed to increase our knowledge about the

effectiveness of DST method. The DST method could provide an effective 12 months period which has been successfully led opium dependents to taper off and leave the opioid abuse. It should be noticed that opium abstain with DST method has very low relapse rate or craving behavior on opium or tendency to other substance abuse. In addition, unlike sudden leave of opioid abuse there is no somatic or psychological side effects in DST treated individuals. Passengers in congress 60, take a comprehensive psychological care and educational programs which aimed to improve the cognitive capabilities.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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