A Randomized Effectiveness Trial of Methadone, TENS and Methadone plus TENS in Management of Opiate Withdrawal Symptoms

Nour Mohammad Bakhshani, Kobra Lashkaripour, Seyed Alireza Sadjadi
Psychiatric and Clinical Psychology Department, School of Medicine, Zahedan, University of Medical Sciences, Zahedan, Iran.

Abstract

Objective: To compare effectiveness of methadone, TENS (Transcutaneous Electrical Nerve Stimulation) and methadone+ TENS in management of opiate withdrawal symptoms.

Methods: The study was conducted in Zahedan Psychiatric center in 2005. Forty five opiate addicted men meeting DSM-IV criteria for substance dependency disorder participated in the study after informed consent. The subjects were randomly assigned to 3 treatment groups. Patients of first group were given 20-60 mg methadone daily, tapered over a period of 2 weeks. Patients of second group received daily 10-30mg methadone, tapered similar to first group in combination with TENS treatment. The other 15 patients (third group) experienced low frequency (2 Hz) TENS for two weeks.

Results: There was no statistically significant difference in severity and number of withdrawal symptoms between the 3 groups prior to the start of treatments. But, severity and number of symptoms were significantly higher in TENS group (third group) in third day. In addition, 10 patients of TENS-group left the treatment programme after 5 days. The results showed that methadone only and Methadone plus TENS for the management of opioid detoxification were effective treatments. The comparison of number and severity of withdrawal symptoms in the methadone group and methadone+TENS group by seventh day didn't show significant differences. But, number and severity of withdrawal symptoms in methadone+TENS group were significantly lower than methadone group during tenth and fourteenth days.

Conclusion: The results provide support for the use of methadone alone and methadone plus TENS for managing opiate withdrawal, but TENS by itself has no significant effect on withdrawal symptoms. However, TENS in combination with a moderate dose of methadone could reduce severity of withdrawal symptoms effectively (JPMA 58:667; 2008).

Introduction

Drug dependency is a complex, chronic and multi-dimensional disorder which is considered a compulsory and unresisting desire of using drugs, with negative side effects and even frequent relapses after long periods of abstinence.[1] Opioid addiction is regarded to be a major health and social problem in many societies[2] such as our country (Iran), as currently opium and other forms of illegal drugs are used by about 2.5 to 3.5 percent of the society. Most commonly, opium is used in the form of smoking or orally and rarely in the form of injection.[1] Many studies showed that high risk of mortality,[3,4] morbidity,[5] health care costs, law

enforcement costs, family disruption and lost productivity[6] were associated with substance use.

Usually, people who have used opioid for one to two weeks continually, have withdrawal symptoms.[7] Due to severity and invasive nature of withdrawal symptoms, to achieve successful abstinence and detoxification, professional assistance is necessary.[8] Thus, it is important to assist the opiate dependent people to go through the detoxification period of treatment without severe negative withdrawal signs and symptoms. There are a number of different opioid withdrawal management approaches.[2,9] Amato et al reviewed 46 original studies which included 3350 participants.[2] They concluded that Methadone detoxification when compared to adrenergic agonists had higher treatment retention, lower relapse rate and fewer side effects. But comparing different adrenergic agonists showed no significant differences.

In addition to pharmacological approaches for treatment of dependent patients; acupuncture,[10-13] and TENS[14] (Transcutaneous Electrical Nerve Stimulation) may ameliorate opium withdrawal symptoms. Acupuncture is shown to release the endogenous opioid peptides when it is used to treat opiate withdrawal symptoms.[10] This has been supported by experimental researches on animals.[11,12] It is suggested that acupuncture and electrical stimulation by suppressing plasma ACTH, cortisol and c-AMP levels can reduce withdrawal symptoms of addicted subjects.[13] A study by O'Brien et al[15] provided no evidence about effect of TENS on experimental pain threshold or plasma beta-endorphin levels but WU et al[14] found effectiveness of 100-Hz electro acupuncture or 100-Hz transcutaneous electrical nerve stimulation in ameliorating the morphine withdrawal syndrome in rats and human. Based on this experimental study, they suggested that 100-Hz electro acupuncture stimulation increased releasing of dynorphin in morphine dependent subjects and this may elicit an analgesic effect and ameliorating morphine withdrawal syndrome by interacting with kappa-opioid receptor at spinal level. Zhong et al[16] investigated the efficacy of 2 Hz TENS to reduce cue-induced heroin craving and the corresponding cardio vascular responses. Their findings showed that a single-trial 2Hz TENS for 30 minutes could suppress craving induced by a heroin-related cue and abolish totally the cardiovascular activation.

However, substance users in different countries have different characteristics and different expectations of treatment. Thus further studies in various settings and countries are needed. In addition there is no consensus on the best strategy for managing opiate detoxification.[17] Therefore, this study was designed to compare three treatment conditions (methadone, TENS and methadone+TENS) in management of withdrawal symptoms of opiate dependent patients

Methods

This clinical trial study was done in the Baharan psychiatric center of Zahedan (a University hospital) in 2005. It was approved by the local Medical Ethics Committee of the Zahedan University. A total of 45 male patients (aged 20-40); meeting DSM-IV[18] (APA) criteria for substance dependency disorder participated in the study. Patients with schizophrenia, bipolar mood disorder, major depressive disorder, personality disorder and other psychotic disorders were excluded. The participants were randomly assigned to one of the following three treatment conditions after being provided sufficient information to make an informed decision.

Methadone therapy group: The 15 patients (group 1) received methadone treatment with dose of 20-60 mg per day. Dosage of methadone was constant in first 48 hours and was tapered down by 10-20% daily. Methadone dose for each participant was calculated according to usage method, type of substance and percent of morphine absorption.[7]

Methadone+TENS group: The 15 patients of group 2 experienced treatment of methadone. Subjects in this group took 10-30 mg methadone daily that was half of calculated dose. Dosage of methadone was constant in first 48 hours and was tapered down by 10-20% daily, similar to group 1. In addition, TENS was administered twice a day for the first week and tapered down to once a day for the second week.

TENS therapy group: The last 15 patients (group 3) received TENS therapy starting with twice a day for the 1st week and decreased to once per day for the 2nd week. Similar to acupuncture treatment, the TENS was performed with the clipped electrodes on five points of external ears at the center of acupuncture points in the body. Low frequency (2 Hz) TENS was administrated for 30 minutes each time.

The length of treatment across all above mentioned conditions was 14 days and was started at least 12 hours after the last dose of opiate used by the subjects. The number and severity of withdrawal symptoms were assessed based on DSM-IV[18] guidelines. Each individual subject was asked to rate the severity of each withdrawal symptoms on a 5-point scale (0-4) before start of the treatment in the 1st day and in third, fifth, seventh, tenth and fourteenth days after administering methadone and TENS.

Results

About 62.2% of participants used opium, 31.1% used extract of opium and 6.7% used opium and extract of opium combined. The opiates were taken by smoking (48.9%), orally (28.9%) or in both forms (22.2%). The

mean age of participants was 28.1±5.65 years. The mean of methadone dose in the group 1 (treated with methadone only) was 35±2.58mg and in the group 2 (treated with methadone and TENS) was 15±2.58mg. ANOVA analyses showed no significant difference in withdrawal symptoms between all groups before the start of the study. However, there were significant differences between group 3 and groups 1 and 2 on the third day (P<0.05). The mean of number and severity of withdrawal symptoms in three treatment groups are shown in figures 1 and 2.

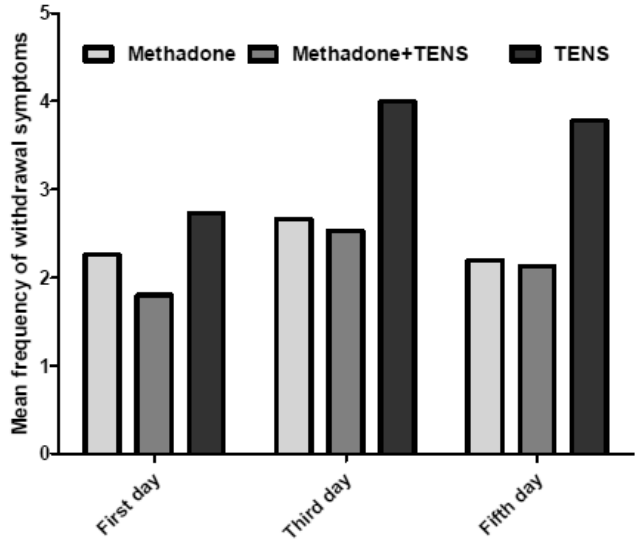

Fig-1: The mean of withdrawal symptoms number in three treatment groups.

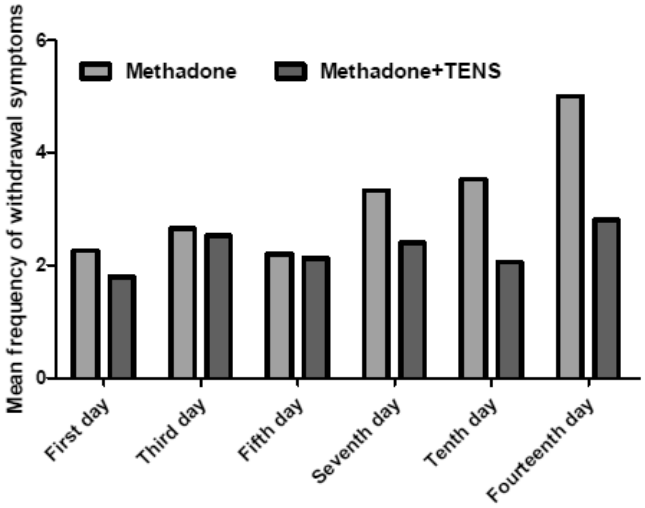

Fig-2: The mean of withdrawal symptoms severity in three treatment groups.

It is worth noting that due to severity of withdrawal symptoms in group 3 (TENS treatment only) after the fifth day of treatment, 10 out of 15 patients stopped participation and only 5 patients completed the course of the treatment. Because of high attrition in third group only the data of remaining two groups (Methadone and Methadone+TENS) are compared in figure 3 for fifth, seventh, tenth and fourteenth days (figure 3). There were no significant

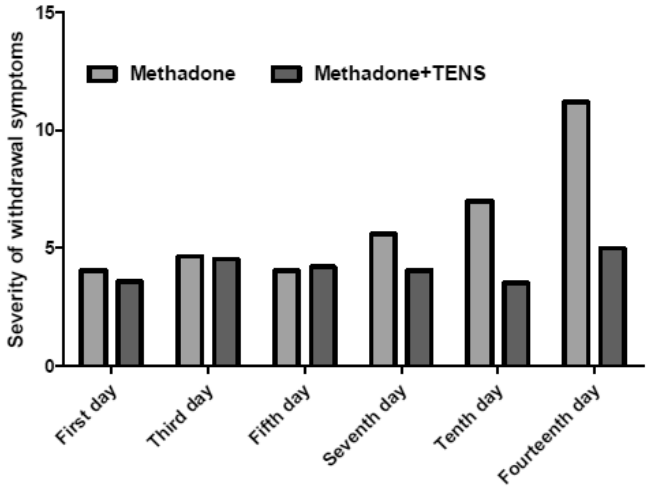

Fig-3: The mean of withdrawal symptoms severity in the two treatment groups.

differences in the number and severity of withdrawal symptoms for these two groups through the seventh day. Comparing these two groups during the 10th and 14th days show a significant difference both in the mean of withdrawal symptoms (P=0.005 for 10th day and P=0.001 for 14th day) and their corresponding severities (P=0.004 for 10th day and P=0.000 for 14th day) with methadone+TENS group being lower than methadone group.

Discussion

The results of this study showed that the most common usage form of opiate usage amongst the participants was opium and the most common method was smoking. The mean dose of administered methadone in methadone group was significantly higher than in the methadone+TENS group.

The severity and number of withdrawal symptoms between the 3 treatment groups were not significantly different prior to the start of treatment; but the number and severity of withdrawal symptoms slightly increased in all 3 groups by the third day. In TENS group increasing in the number and severity of withdrawal symptoms were more than two other groups to the extent that starting the fifth day of treatment the patients in group three left the programme and only 5 patients remained in treatment programme to the end. While all of patients in the methadone group and methadone + TENS group continued the treatment programme. It is worth noting that methadone group's slight increase, but statistically insignificant, in the number and

severity of withdrawal symptoms could be attributed to rapid decrease of methadone in this group. Thus, it is recommended that when methadone reaches 10 mg, some other drugs such as clonidine, NSAID, sedative and hypnotic could be administered, so that patients will be prepared for reduction of final dose.[19]

Because the treatment programmes vary widely, the present study is hardly comparable with earlier studies. Our findings, however, consistent with previous reports[20-22] confirmed the effectiveness of methadone in management of opioid withdrawal. To our knowledge there is no published data about application of TENS in combination with methadone for opiate detoxification. While we observed that methadone +TENS was more effective than methadone alone.

In the present study all patients in the methadone and methadone plus TENS groups completed the treatment programme and were detoxified with low-medium doses of methadone. Whereas the ability of a treatment in retaining patients within the programme can be considered as a proxy of treatment effectiveness. This is with regard to acceptance by the patients and the continuance of treatment to the end of the period, the effectiveness of methadone in management of withdrawal symptoms was more than TENS group. Other studies showed that higher doses (>110 mg methadone) compared with medium doses (60-100 mg) and low doses (40-50) retained more people in the treatment programme.[21] Although Wen[23] and Ellison et al.[24] supported the effectiveness of acupuncture and electrical stimulation in managing opioid withdrawal and rapid detoxification at least for 80% of cases, but in our study about 33% completed TENS treatment course. Han et al.[25] also showed that TENS was very effective in ameliorating the withdrawal syndrome in addicts, which is inconsistent with our findings.

In summary, TENS by itself has no significant effect on withdrawal symptoms. However, when a moderate dose of methadone is combined with TENS it shows a higher effectiveness compared to higher doses of methadone alone. Also, due to lower number and severity of withdrawal symptoms, methadone based treatments were more acceptable to patients compared to TENS alone. Noting the high number and severity of withdrawal symptoms at the end of the treatment, it is recommended that the two-week period of methadone treatment is not enough and a revision in our drug dependency clinic is required in this programme.

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