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The Effect of Acupuncture on the Acute Withdrawal Symptoms from Rapid Opiate Detoxification

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Background: **Rapid Opiate Detoxification (ROD) is among the best treatments for substance abuse. Unfortunately this method is associated with severe withdrawal reaction. The effect of body acupuncture has not been clearly identified during ROD. This study was designed to evaluate the effect of acupuncture on the severity of withdrawal reaction during ROD.**

Methods: **Forty adult male subjects addicted to opioids and scheduled for ROD by naloxone were randomly divided into acupuncture and control groups. In the acupuncture group during three consecutive days immediately before induction of ROD, body acupuncture was performed while in the control group it was exempted. Severity of withdrawal reaction was assessed having recourse to Clinical Institute Narcotic Assessment (CINA) Score and compared between two groups.**

Results: **After induction of ROD, CINA score raised significantly during the consecutive days in both groups compared with baseline values but the rise was significantly lower in acupuncture group.**

Conclusions: **The result of this study shows that body acupuncture reduces the severity of withdrawal symptoms associated with rapid opiate detoxification and it is recommended that this nonpharmacologic method of treatment should be included in ROD program.**

Key words: *Substance withdrawal syndrome. Narcotics. Acupuncture.*

Long-term methadone maintenance has been for many decades the treatment of choice for large groups of opiate addicts.[1] The discontinuation of methadone medication requires a further stage of treatment to complete the process of rehabilitation. In the final stage there occurs the so called methadone withdrawal sydrome, which is associated with severe symptomatology that usually sets in when the daily methadone dose is decreased below 20 mg.[2-4] Prolongation of these symptoms may cause resumption of the abused drug in a high proportion of patients. Opiate antagonists have been added to the therapeutic regimen of these patients in an effort to shorten the phase of abstinence and therefore minimize its complication and especially the relapse rate.[5] This has been called Rapid Opiate Detoxification (ROD), which is usually performed by way of naloxone or naltrexone administration. Usually the administration of an opiate antagonist to an addicted individual during ROD precipitates a severe withdrawal syndrome,[6-8] which necessitates the concomitant use of either general anesthesia or heavy sedation.[9-12] Even after emergence from general anesthesia or heavy sedation the patients may exhibit severe withdrawal symptoms, which require further administration of sedatives, anxiolytics, analgesics and sometimes narcotics.[13] There have been, as reported, at least four cases with fatal outcome[14-16] and numerous life threatening complications[17-18] associated with ROD. Adverse outcomes, as reported, during ROD include serious suicidal attempt,[19] respiratory distress,[18,20,21] vomiting,[19] renal failure, suppression of thyroid hormones,[18] hemodynamic changes and adrenomedullary stimulation with a huge increase in plasma ACTH and cortisol levels.[22,23]

Acupuncture has been used in substance abuse treatment but its effectiveness is controversial. There have been several small randomized trials evaluating the outcomes of adding acupuncture to the conventional treatment of drug abuse, most of which have shown some

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value of acupuncture.[24-27] The effect of acupuncture on the acute withdrawal during ROD has rarely been evaluated in previous studies.[28,29] This study was designed to evaluate the effect of body acupuncture on the severity of withdrawal from opiates during ROD in a group of male addicts.

Materials and Methods

After institutional approval and obtaining patient informed consent 40 male adults addicted to heroin or opium who were referred to the University Rehabilitation Center for the Drug Abuse were prospectively included in the study. The sample size was selected after analyzing the data of a pilot study conducted on a subsample of 10 patients and considering a study power of at least 80% with type II error of 5%. Patients with history of addiction less than 6 month (as stated by the patient) and those with a history of cardiovascular, renal, psychiatric, and severe respiratory disorders were excluded from the study. Patients underwent a program of ROD of a 10-day period beginning with an abstinence period of 24 h (Fig. 1). In the second day patients were placed on oral clonidine regimen at 0.2 mg every 8 h. In the third day, the patients were admitted to the hospital and clonidine dosage was increased to 0.3 mg every 8 h. At 2 p.m. in the third day (the first day of admission) an intravenous line was established and diazepam 20 mg and naloxone 0.4 mg were respectively administered intravenously and intramuscularly every 90 min for four times (a total of 1.6 mg naloxone). Naloxone dosage was raised to 3.2 mg/day in the fourth and to 4.8 mg/day in the fifth days. During naloxone administration continuous ECG and pulse oximetry were monitored, supplemental oxygen was administered, and if necessary ventilation was assisted (with face mask and T-piece system) to maintain oxygen saturation above 92%. From the fifth day clonidine dosage decreased to 0.2 mg/day up till the tenth day when it was completely discontinued. During this ten-day period, adjuvant drugs were given when necessary (as judged by the patient's complaint) to control withdrawal symptoms. These drugs included nonsteroidal anti-inflammatory drugs (NSAID) for myalgia, benzodiazepines for restlessness, barbiturates for insomnia.

The patients were randomly divided into acupuncture and control groups with resort to a computer generated random list. The protocol of ROD was similar for two groups but in the acupuncture group immediately before the first naloxone administration the selected acupoints were needled (Fig. 2), using gauge 30 disposable acupuncture needles. These points were selected after consulting some acupuncture texts and experts on the following functions: LI4: analgesia; PC6 and ST36: treatment of nausea, vomiting, and abdominal discomfort; HT7 and LR3: treatment of restlessness; DU14: an important governing and coordinating point; DU20: harmonizing effect. Even method of manual stimulation (rotating the needle evenly and gently clockwise and counterclockwise) was performed every 10 min for 3 min. The needles were retained in place for 45 min. This acupuncture was given once per day and repeated for three consecutive days beginning from the third day (the first day of admission).

Measurements

An independent observer who was unaware of the allocation of subjects recorded patients' information using a questionnaire. Different demographic information together with characteristics of the patients' addiction was recorded prior to intervention. Severity of with-

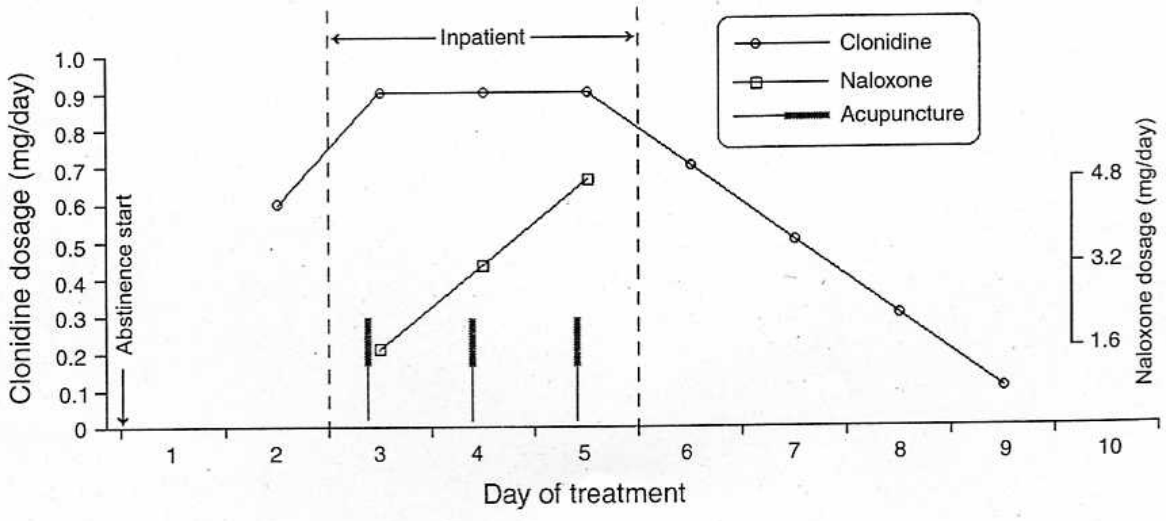

Fig. 1. Time table outline of Rapid Opiate Detoxification protocol.

drawal symptoms and the need of adjuvant drugs during the past 24 h were determined for three consecutive days starting from the second day of treatment. Clinical Institute Narcotic Assessment (CINA) Score as suggested by Peachey *et al.*[30] was used to determine the severity of withdrawal. The CINA is a 13-item opioid withdrawal assessment scale. A score is given to each item based on the severity of withdrawal symptom and sign as follows: nausea and vomiting (0 to 6), tremor (0 to 3), sweating (0 to 3), restlessness (0 to 3), gooseflesh (0 to 3), lacrimation (0 to 2), nasal congestion (0 to 2), yawning (0 to 2), abdominal complaints (0 to 2), feeling hot or cold (0 to 2), muscle aches (0 to 2), (heart rate –80) / 10, (systolic blood pressure –130)/10.

Statistical Analysis

Means of CINA scores were compared within and between two groups using repeated measure analysis of variance. The proportion of patients who needed adjuvant drugs was compared between two groups using Fisher's Exact test. Data are presented as mean ± SD or number (%) where applicable. All comparisons were two-tailed and P value less than 0.05 was considered statistically significant. Data were analyzed using SPSS 10.0 software.

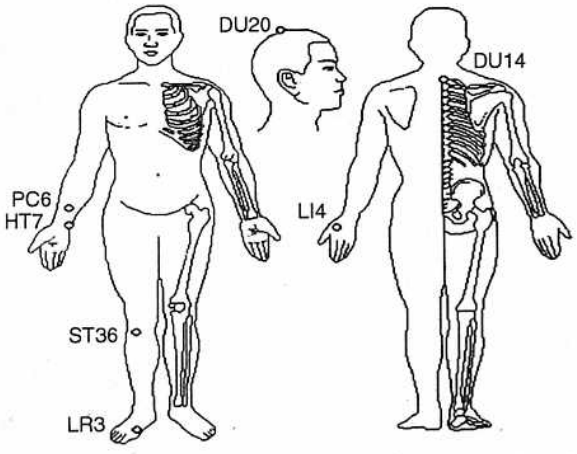

Fig. 2. Location of acupuncture points used in this study. PC6 = Pericardium 6: Between the tendons of palmaris longus and flexor carpi radialis muscles, 2 cun proximal to the transverse crease of the wrist. HT7 = Heart 7: On the transverse crease of the wrist, radial to the flexor carpi ulnaris muscle. ST36 = Stomach 36: One fingerbreadth lateral to the lower border of the tuberositas tibiae, 3 cun below the knee joint. LR3 = Liver 3: Between the first and second metatarsal bones, 2 cun proximal to the margin of the web. LI4 = Large Intestine 4: At the highest point of the adductor pollicis muscle with the thumb and index finger adducted. DU20 = Du Mai 20: Midway of the line connecting the two ear apexes. DU14 = Du Mai 14: Below the spinous process of the vertebra prominens.

Table 1. Demographic and Addiction Characteristics of Patients

	Acupuncture	Control
Age (yr)	32 ± 8	31 ± 9
Weight (kg)	71 ± 9	70 ± 8
Abused Agent		
Opium	10 (50)	13 (65)
Heroin	10 (50)	7 (35)
Addiction Duration (yr)	3.5 ± 1.8	3.8 ± 2
Age when become addicted (yr)	30 ± 6	30 ± 5
Abstinence Duration before ROD (h)	54 ± 2	53 ± 2
Number of Patients with Positive History of Previous Detoxification	8 (40)	6 (30)
Heroin Intake (g/day)	1.2 ± 0.2	1.1 ± 0.3
Opium Intake (g/day)	4 ± 1.2	3.8 ± 1.5

Data are mean ± SD or n (%).
No significant difference between two groups.
ROD = Rapid Opiate Detoxification.

Results

Twenty-three opium and seventeen heroin addicts were studied. Two groups were similar with respect to demographic and addiction characteristics (Table 1).

CINA score raised significantly during the treat-

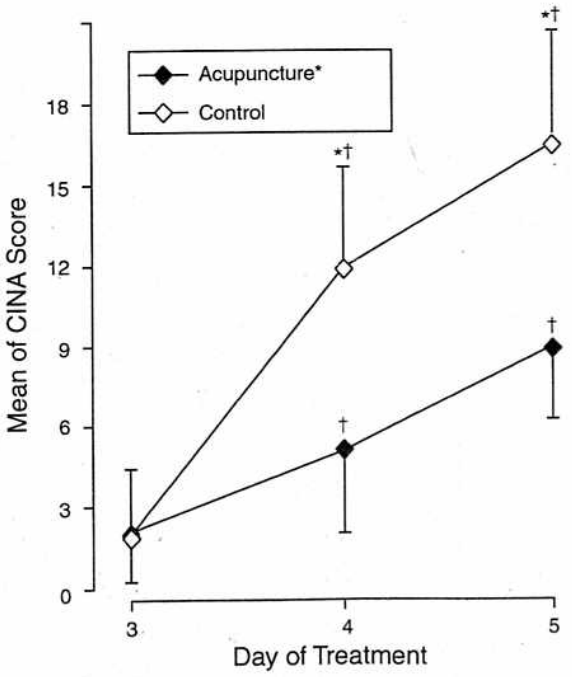

Fig. 3. Severity of withdrawal as measured by CINA Score during day 3, 4, and 5 of treatment in two groups. $*P < 0.001$ (Between-Subjects Effects); $^{\dagger}P < 0.001$ (Within-Subjects Effects); CINA = Clinical Institute Narcotic Assessment.

Table 2. Comparison of Adjunct Drugs Usage between Two Groups during the Acute Withdrawal Phase (third to fifth Days)

Drug	Number of days with a need for drug	Group	
		Control n (%)	Acupuncture* n (%)
NSAID	0	5 (25)	16 (80)
	1	1 (5)	2 (10)
	2	5 (25)	0 (0)
	3	9 (45)	2 (10)
Benzodiazepines	0	0 (0)	15 (75)
	1	0 (0)	2 (10)
	2	0 (0)	2 (10)
	3	20 (100)	1 (5)
Barbiturates	0	14 (70)	20 (100)
	1	1 (5)	0 (0)
	2	0 (0)	0 (0)
	3	5 (25)	0 (0)

NSAID = Nonsteroidal anti-inflammatory drugs.
*$P < 0.05$ compared to control group.

ment course in both groups but the rise in the acupuncture group was significantly less in comparison with the control group (Fig. 3). The need of adjuvant drugs was 50% (95% CI, 30–70%) in the acupuncture group compared with 90% (95% CI, 70–97%) in the control group ($P = 0.007$). The days of need of adjuvant drugs were significantly fewer in the acupuncture group than the control group (Table 2). There was no clonidine-associated side effect. After Diazepam administration a few patients required a brief period of assisted ventilation with mask but no patients developed hypoxia. Neither pulmonary edema nor other severe side effect attributable to naloxone administration was observed.

Discussion

This study shows that body acupuncture decreases the severity of withdrawal from opiates during ROD. Withdrawal reaction in the control group was nearly 3 times severer than that in the acupuncture group and only half of the patients in the acupuncture group needed extra drugs to ease their withdrawal symptoms in contrast to the control group in which almost all of the patients needed some sort of pharmacological support.

In spite of widespread use of acupuncture for treatment of drug and alcohol abuse, however, the opinion concerning acupuncture for the treatment of substance dependency is contradictory and controversial.[31] A number of studies have evaluated the role of acupuncture in opiate detoxification programs; most of them have shown the effectiveness of acupuncture to reduce the severity of withdrawal symptoms.[32] The beneficial effects of acupuncture have not been documented by a randomized trial in clinical setting of ROD.[28,29] Wen *et al.*[28] noted that patients who received acupuncture at the points on the ears (auricular acupuncture) reported fewer symptoms of opium withdrawal, specifically pain, nausea, and vomiting. They subsequently delivered a non-controlled study on the effect of acupuncture to reduce withdrawal symptoms during ROD, which showed a remarkable effect for the acupuncture. Kroenig *et al.*[29] also showed a similar effect when combining electroacupuncture with ROD.

The result of this study confirms that acupuncture can reliably and remarkably reduce the severity of withdrawal reaction. Whether these effects originate from the ability of acupuncture to release endogenous substances, which mimic exogenous opiates such as heroin is not known. A number of studies have shown that the dynorphin which is an endogenous opioid peptide distributed throughout the central nervous system may be responsible for suppressing the morphine withdrawal syndrome via activation of k-opioid receptor in the spinal cod.[33-35] Further studies are required to delineate the mechanisms for acupuncture effectiveness in reducing withdrawal symptoms.

Although acupuncture has been used for different purposes in clinical setting of drug abuse but it seems that the best role of acupuncture treatment during detoxification is to reduce the primary symptoms of withdrawal reaction.

In this present study a limited number of body acupoints have had selected based on the recommendation of classic acupuncture text books.[36,37] It is of course a requirement in designing further studies on other suggested acupoints and especially ear acupuncture to determine the best combination of body and/or ear acupuncture points for the treatment of withdrawal syndrome during ROD.

In conclusion, with respect to the compelling need for improvement of current substance abuse treatment protocol it is recommended that the beneficial role of acupuncture for reducing the withdrawal symptoms should be seriously considered during ROD.

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