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Is Acupuncture Effective in Reducing Opioid Cravings in Detoxifying Opioid Abusing Adults?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

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ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not “Is acupuncture effective in reducing opioid cravings in detoxifying opioid abusing adults?”

STUDY DESIGN: A review of three RCTs published in English, each of which was published in 2009, 2013 and 2014 respectively.

DATA SOURCES: Three randomized controlled trials (RCTs) published in peer-reviewed journals that evaluate the effectiveness of acupuncture to reduce opioid cravings found via PubMed and ScienceDirect.

OUTCOMES MEASURED: Opioid cravings via 100 millimeter analog scale score, the Maudsely craving score consisting of five-point Likert scales and withdraw symptoms as measured by a 4-point scale questionnaire.

RESULTS: Two RCTs found no significant difference between the acupuncture and control groups in opioid withdraw cravings. Chan et al. established a decrease in opiate cravings in both the control and experimental groups, but the decrease was statistically insignificant ($p=0.101$). Moreover, the craving means measured throughout 14 days by Bearn et al. found no statistical difference in placebo vs. auricular acupuncture cravings ($p=0.283$). Conversely, Lua and Talib compared pre and post intervention mean cravings within their experimental acupuncture group, resulting in a significant craving reduction of 20.8% after intervention ($p=0.011$).

CONCLUSIONS: It is not clear the effect that acupuncture has on opiate cravings after detoxification, as two of the RCTs addressed in this paper revealed no improvement and one RCT showed positive results in craving decreases. Additional trials, specifically in countries where acupuncture is less familiar, are necessary to deduce the efficiency of acupuncture as an adjunctive treatment for opiate addiction.

KEY WORDS: Acupuncture, withdraw, opioids, detoxification treatment

INTRODUCITON:

The increasingly high number of opiate overdoses throughout the United States has raised public awareness and concern about the opiate epidemic and its catastrophic consequences. Rampant opioid abuse has placed an ethical and financial responsibility on the American public to manage the opiate crisis and its repercussions. In dealing with this crisis, it is crucial to find a more effective way to treat opiate addiction and prevent relapse. Opioids are used as analgesics that communicate with opioid receptors within the brain. These analgesics are often utilized for moderate to high levels of pain or when patients fail non-opiate therapy for pain control.¹ With receptor activation, the body releases endogenous chemicals such as endorphins that aid in managing a patient's pain perception. However, the activation of these opioid receptors can also create a euphoric effect that has bred misuse and addiction.¹

The National Institute of Drug Abuse (NIDA) estimates that over two million people in the U.S. alone are struggling with opioid dependence.² NIDA also estimates that 115 people die every day in the U.S. due to opiate overdose.² With the amount of dependence and fatalities too large to ignore, President Donald Trump declared the opiate crisis a national public health emergency in 2017.² Since then, the trending combination of potent synthetic opioids such as fentanyl in street drugs has only increased the amount of opiate overdose deaths according to data published in 2018.² The crisis has also placed an economic burden on Americans. Records from July 2016 to September 2017 state there were a total of 142,557 ED visits due to suspected opioid involved overdoses.³ The CEA has also approximated the cost of healthcare, detoxification treatment, decreased productivity after overdose and the involvement of the criminal justice system to be \$72.3 billion per year in the United States alone.⁴

Opioids are known to be highly addictive substances that when misused can lead to dependence, overdose, neonatal abstinence syndrome and the spread of infectious diseases like HIV and hepatitis C.⁵ An addiction to opiates is due to a complex set of influencing factors. First is a patient's environmental dynamics; increased amounts of stress or exposure to opiates and abusing peers influence the likelihood of addiction.¹ Physiologically, utilization of exogenous opiates as described above simulate opioid receptors to release endogenous opiate chemicals throughout the body.¹ These endogenous opiates also stimulate the reward center of the brain, the limbic system, which triggers dopamine to be released in the nucleus accumbens and create a sensation of euphoria. Addicts may chase this eutrophic feeling of pleasure as they begin using, but as opiates are utilized over a long period of time, tolerance and dependence will form.¹

Dependence ensues as opiate abusers' brains become accustomed to having opiates present. Without opiates present, a perceived abnormal environment in the brain does not allow it to work properly and withdrawal symptoms occur.¹ Tolerance arises as opiate receptors become less receptive to a certain opiate, which necessitates an increase in dose or potency of the opiate given to achieve the same effect. Tolerance to opiates pushes opiate dependents to increase their dose, move to a more potent opiate or try new delivery methods (nasal, venous) in order to achieve stronger effects.¹ Tolerance explains why the majority of heroin users abused prescription opioids first. It is the interaction of all of these factors that drives someone to addiction and keeps them addicted to opiates.

Traditional pharmacologic treatment methods, also called Medication Assisted Treatment (MAT) to opioid addiction are first line and include buprenorphine, buprenorphine/naloxone, methadone, and naltrexone.⁶ Buprenorphine and methadone are opiates themselves, working as agonists on the same opiate receptors that illicit opiate substances fit into.⁶ The difference

between street opiates vs. buprenorphine/methadone is that these MAT drugs are long acting, pharmacy controlled dosages that are delivered by mouth. By occupying opiate receptors, patients do not experience withdraw symptoms and can expect decreases in craving to use their opiate of choice after taking buprenorphine or methadone.⁶ Buprenorphine also has a ceiling effect as a partial agonist. At a certain dose there is no longer an increased effect on opiate receptors, which creates less of a risk of MAT misuse.⁶ If patients want to discontinue buprenorphine or methadone, a taper is suggested or withdraw symptoms will occur. Buprenorphine and methadone are also used in short term tapers for patients that want to detoxify from opiates without sudden and extreme withdraw symptoms.⁶

Naltrexone is the newest MAT drug and works as an opioid antagonist.⁶ It effectively blocks opiate receptors, making it impossible to feel any effect from illicit opiates. It is administered once a month in the form of an intramuscular shot. The difficulty with naltrexone is that it must be administered five to seven days after the last use of an opioid because it will oppose any other opiate currently filling opiate receptors, thus sending the patient into instant and dangerous withdrawal.⁶ It is unknown what the most effective length of time is to be on MAT before tapering off in preventing relapse.⁶

MAT works best with the use of simultaneous cognitive behavioral therapy. This type of therapy works with addicts to recognize what may trigger their behaviors and how to avoid those triggers. It also aids addicts to lay out steps to take when feeling urges to use illicit opioids.⁶ Even with the above first-line treatment, relapse rates are estimated to be between forty and sixty percent, creating a necessity to find other additional therapeutic efforts.² The method of adjunctive treatment being discussed in this review would be an additional form of non-pharmacologic symptomatic relief that may aid to decrease relapse rate. Previous research has

found acupuncture to increase the production of endogenous opiates and balance dopamine levels released through the reward pathways of our brain.⁵ Acupuncture involves placing long, thin needles in acu-points around the body. It has been studied and utilized most commonly to relieve chronic pain but has also been found to decrease the frequency and severity of tension/migraine headaches as well as ease chemotherapy side effects.⁷

OBJECTIVE:

The objective of this selective EBM review is to determine whether or not “Is acupuncture effective in reducing opioid cravings in detoxifying opioid abusing adults?”

METHODS:

Three randomized controlled trials (RCTs) published in peer-reviewed journals were used in this review. The population includes men and women over the age of 18 in treatment for opioid addiction. The intervention employed included acupuncture treatment given concurrently with standard methadone treatment, while the control group was only given solely MAT or a methadone taper. The outcomes measured were withdraw symptoms, specifically opioid cravings.

The key words employed to search for the literature used in this review were acupuncture, withdraw, opioids and detoxification treatment. Each of the three articles were published in peer-reviewed journals in English. The articles were found when searching via PubMed and EBSCOhost. Articles were selected when applicable to the clinical question and included patient oriented outcomes (POEMS). Inclusion criteria for this review encompassed RCTs utilizing adults with DSM-IV or similar criteria for opiate dependence. Exclusion criteria included adolescents under 18 years old or recent acupuncture before treatment. A summary of

statistics reported in the reviewed literature included Mann-Whitney *U*-test, Wilcoxon signed-rank test, *p*-values, Cohen's *d*, change from baseline mean, paired *t*-tests and ANOVA.

Table 1: Demographics and Characteristics of included studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Bearn ⁸	Placebo – controlled RCT	93	18 yrs old or greater	DSM-IV criteria for opiate dependence, referral to inpatient detox treatment	Major physical or psych comorbidities, concurrent treatment with antidepressants/neuroleptic meds, pregnancy, ear infection, topical eczema	11	Methadone, group/individual therapy, daily acupuncture for 30 – 40 minutes for fourteen days
Chan ⁵	Single blinded, parallel-group RCT	60	Greater than 20 yrs old	DSM-IV criteria for opiate dependence, receiving methadone treatment for > 1m	Use of antidepressant/neuroleptic meds, acupuncture tx in previous 30 days, developed severe side effects from acupuncture treatment, significant risk of suicide, infection close to the site of selected acupoints, pregnancy, bleeding disorders, HIV positive	2	Methadone, auricular and body electroacupuncture twice weekly for 4 weeks
Lua ⁹	Open label RCT	97	18 yrs old or greater	Opioid dependence determined by the Opiate Treatment Index, volunteered for methadone treatment	Exhibited violent behaviors, suicidal tendencies, psychotic profiles, HIV or Hep B positive, allergic to metal, not giving written consent	28	Methadone, auricular acupuncture three times weekly for two months

OUTCOMES MEASURED:

All three RCTs measured opiate cravings during and after treatment, as reported by patients to evaluate the efficacy of acupuncture as an adjunct for traditional opiate treatment.

Bearn et al.⁸ utilized the Maudsley craving score, an eight item questionnaire consisting of five-

point Likert scales indicating the intensity of craving (scoring of 1 being no craving and 5 being strong craving). Chan et al.⁵ employed a 100 millimeter visual analog scale of opioid cravings, 0 signifying no craving and 100 signifying extreme craving. Lua and Talib⁹ used a withdraw symptom questionnaire including symptoms of opiate cravings on a 4-point scale, 1 demonstrating not present and 4 demonstrating frequent cravings. Each of these studies utilized these measures to evaluate opiate cravings before and after treatment. Bearn et al. also evaluated cravings every day of treatment and produced an average score.

RESULTS:

Chan et al.⁵ conducted a single-blinded RCT, where participants and those evaluating questionnaire data were blinded to treatment groups but the acupuncturist carrying out the treatment was not. This study employed participants from an outpatient clinic in Taiwan, where participants were either referred to the study or volunteered due to advertisements at the clinic.⁵ In order to be included, Chan et al. only accepted individuals that had already been using methadone maintenance treatment (MMT) for one month, as these participants would already have a consistent dose of their methadone established. After exclusion qualifications were elicited, 60 people were randomly assigned to the study.⁵ This random assignment was to true or sham acupuncture treatment groups by a random table generator, with 30 participants in each group.⁵ The intervention consisted of MMT carried out by a separate psychiatrist, who dosed methadone to individual needs. Articular acupuncture (AA) and body electroacupuncture (EA) at the hands and legs of participants was conducted for 20 minute individual sessions, twice a week, for four consecutive weeks.⁵ The control group was given sham AA and body AE through the use of superficial stud needles and EA machines without power. Mild adverse effects to this

study were reported. Three subjects reported small amounts of bleeding at the acupuncture sites and one subject reported an instance of mild hand numbness.⁵

Along with other variables, heroin craving was measured utilizing a 100 millimeter visual analog scale.⁵ Participants were considered compliant and included in the statistical analysis of this study if they were treated with four sessions of acupuncture or more.⁵ Two subjects were lost in each group due to lack of compliance, producing an end compliance of 93%. Paired *t*-tests were employed to investigate statistical significance of craving decreases between baseline and post treatment, shown in Table 2. Indeed there was a significant reduction in opiate cravings in both the control group (44%, $p=0.002$) and the experimental group (72%, $p=0.000$). However, statistical analysis performed using ANOVA to compare true and sham acupuncture post-treatment craving reductions resulted in a statistically insignificant *p*-value of 0.101.⁵ Therefore, the relationship between craving reduction and the specific treatment effect of acupuncture cannot be made.

Table 2 – Chan et al. craving reductions

	VAS baseline (out of 100)	VAS 4 Weeks (out of 100)	Craving reduction	P-value
Control: MMT + Sham AA, AE	44.67 (SD = 34.61)	24.83 (SD = 26.54)	44%	0.002
Experimental: MMT + AA, AE	50.67 (SD = 33.31)	14.14 (SD=22.12)	72%	0.000

Bearn et al.⁸ conducted a single-blinded RCT in an inpatient psychiatric hospital in South London. 93 participants who were referred for detoxification at the inpatient clinic were approached and randomized via a random numbers table to a placebo or AA experimental group.⁸ Those with major psychiatric comorbidities were excluded in order to derive significance from treatment as opposed to cravings exacerbated by other psychiatric illnesses. 11 participants were lost before baseline metrics were measured, thus no intention to treat (ITT) was carried

out.⁸ Therefore, 48 subjects were included in the experimental acupuncture group and 34 were treated with placebo AA. Patients were started on individualized methadone doses and detoxified with decreasing doses of methadone over 10 to 14 days.⁸ 30 to 40 minute sessions of acupuncture was performed in a group setting once a weekday for two weeks.⁸ Placebo metal clips designed specifically for the study aided in blinding participants to their assigned treatment group. No adverse events to treatment were described in this study.

Participant cravings were measured with the 8-item Maudsley cravings scale daily for 14 days, subjects noting their cravings over the last 24 hours.⁸ Analysis between the control and experimental acupuncture group's mean daily cravings was examined by size effect utilizing Cohen's *d* and *p*-values applying paired *t*-tests. Statistical analysis on these data sets were not performed in a pre and post-treatment manner, but rather by evaluating mean craving scores throughout the 14 days of treatment. Results found that there was not a statistically significant change in opiate mean cravings between the experimental and placebo group throughout the study, with $p=0.283$.⁸ There was also a non-significant trend in lower reported opiate cravings in the placebo AA group from day 11–14.⁸ The two group means, as evaluated by $d=0.28$ show a small size effect difference between the two groups. Results are listed below in Table 3.

Table 3 – Bearn et al. craving means

Control: Placebo AA	Experimental: AA	Effect Size	P-Value
13.1 (SD=4.6)	14.6 (SD=5.6)	0.28	0.283

Lau and Talib⁹ conducted an open-label RCT, in which both participants and researchers were aware of treatment group placement. This study utilized three outpatient methadone maintenance treatment facilities in Malaysia.⁹ After screening 376 opiate dependent individuals, 97 participants were enrolled in the study to begin treatment. Subjects with HIV and hepatitis B

were excluded from this study, in order to decrease disease risk for the acupuncturist.⁹ Participants were randomly assigned via interactive voice response to a methadone maintenance control group (42 participants) or to methadone maintenance with auricular acupuncture (55 participants).⁹ Auricular acupuncture was performed for 30 minutes in a group setting of 8-10 participants, consisting of three sessions per week for two months. Data collection instruments were given before and after the two month intervention. The Malay WHOQOL-BREF was used to gauge withdrawal symptoms, including cravings, with responses of 1 (poor) to 5 (excellent) for each symptom.⁹ Participants were considered compliant if they attended eight AA sessions or more, producing an end compliance of 93%. Adverse effects to the AA were considered tolerable, consisting of complaints of dizziness, nausea and pain at the insertion site.⁹

The Mann-Whitney *U*-test was used to compare the two groups at pre and post intervention independently, where the Wilcoxon signed-rank test was utilized for within-group comparisons at pre and post intervention.⁹ These tests were utilized to find the degree of statistical significance of cravings through a *p*-value ($p < 0.05$ significant). Due to the high dropout rate of 28 subjects, analyses were based on the principle of ITT; all participants of each treatment group were included no matter if the participants withdrew from the study.⁹ The mean craving scores compared pre and post intervention in the MMT group insignificantly only dropped from 1.71 to 1.70, a decrease of 0.01% in opiate cravings. The MMT group with auricular acupuncture dropped from a statically significant mean craving score of 2.26 to a post intervention craving score of 1.79, a decrease in opiate cravings by 20.1% that signifies the intervention achieved its intended goal.⁹

Table 4 - Lau and Talib mean cravings

	WHOQOL baseline (out of 5)	WHOQOL 2 Months (out of 5)	Craving reduction	P-Value: Wilcoxon
Control: MMT only	1.71 (SD = 0.81)	1.70 (SD = 0.94)	0.01%	0.685
Experimental: MMT + AA	2.26 (SD = 0.97)	1.79 (SD=0.86)	20.8%	0.011
<i>P</i> -Value: Mann- Whitney	0.005	0.494		

DISCUSSION:

Acupuncture is a practice established through ancient Chinese medicine. In the United States, studies have had the most success utilizing acupuncture for treatment of chronic back and neck pain.¹ The FDA has proposed acupuncture as an adjunctive treatment for chronic pain as a way to reduce opiate prescription writing.⁷ Currently, acupuncture is covered by some insurances for chronic pain treatment in the United States. Although Medicare plans do not cover acupuncture, Medicare Advantage plans may provide coverage.⁷ Acupuncture is regarded as a generally safe treatment, as long as the treatment is provided by a licensed practitioner who is utilizing FDA regulated sterile/nontoxic acupuncture needles.⁷ Treatment complications include minor bleeding at the needling site, dizziness, infection at the needling site and pain with needle insertion.¹ Contraindications for acupuncture treatment involve performing acupuncture on lumbar/sacral points with pregnancy, patients with bleeding disorders, cellulitic or infected skin at the needling site or treatment over wounds.⁷

The question posed by this analysis questions acupuncture and its effect in opiate detoxification. However, Chan et al. and Lau and Talib's RCTs utilize maintenance treatment as a control instead of the proposed tapered detoxification. It is likely that those participants being detoxified would have stronger opiate cravings during treatment than those on methadone

maintenance. Therefore, it is possible that utilizing methadone maintenance created different and less drastic outcomes than may have been produced with detoxification treatment.

There are also some limits to the analyses presented in this paper. Lau and Talib use an open-label design in their RCT.⁹ By allowing open labels and awareness of assigned groups, participants and evaluators may have been more motivated to report reducing cravings when they knew that they were partaking in the experimental treatment. This study also had a very high dropout rate, with 28 participants lost for various reasons from the start of the study.⁹ ITT analysis was employed in attempt to avoid misrepresentative outcomes, but it still may be cause for inaccuracy. The study conducted by Chan et al. allowed subjects to volunteer for the study itself.⁵ This may make the study's outcomes less generalizable, as people volunteering for an AA study may have a greater motivation to quit than the general population of drug users. Lastly, the outcomes in Bearn et al. were measured from a craving average throughout the study, instead of pre and post treatment cravings.⁸ This outcome may not be as applicable to the question posed by this paper, addressing the craving outcome of AA treatment.

CONCLUSION:

In close, acupuncture may reduce opioid cravings in detoxifying opiate abusing adults. Two of the studies reviewed in this paper do not support this hypothesis, while the last had positive findings to the hypothesis. It is promising that the RCTs reviewed in this paper demonstrate acupuncture to be a safe alternative treatment to MAT, as all three studies noted positive findings through the decrease of additional withdraw symptoms other than cravings including fatigue, muscle ache, insomnia and nausea. The majority of research utilizing acupuncture has been conducting in Asia, where acupuncture is a more accepted medical treatment. In the future, more studies would be necessary to perform in Western countries to

evaluate if the findings of these studies are generalizable. Future studies are also necessary to assess not only withdraw symptoms, but how effective acupuncture is in decreasing relapse rates of detoxifying opiate abusing adults long term. The opiate crisis requires superior treatment to current methods, and acupuncture needs to be further studied to investigate its potential.

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