

Randomized Trial of Acupuncture for Nicotine Withdrawal Symptoms

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Background: Acupuncture is frequently used for smoking cessation. Positive results from uncontrolled studies have not been supported by meta-analysis of controlled trials. One possible reason for this is that the optimal acupuncture technique was not applied or that the technique was not repeated sufficiently often.

Methods: A randomized, sham-controlled trial was performed with 2 parallel treatment arms; the participant and the evaluator were unaware of which treatment was received. Seventy-six adults who wanted to stop smoking received either 100-Hz electroacupuncture with needles inserted into the appropriate point in each ear or a sham control procedure over the mastoid bone. Interventions were given on days 1, 3, and 7 of smoking cessation. Nicotine withdrawal symptoms were mea-

sured by visual analog scale scores recorded in a daily diary for 14 days; smoking cessation was confirmed objectively.

Results: There was no significant difference between the mean reduction of withdrawal symptom scores of the 2 groups from day 1 to day 14. Fifteen participants (39%) who received electroacupuncture and 16 participants (42%) who received a sham procedure were abstinent on day 14.

Conclusion: This form of electroacupuncture is no more effective than placebo in reducing nicotine withdrawal symptoms.

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SMOKING IS the largest single cause of preventable death in industrialized countries. A lifelong smoker's chance of reaching age 73 years is half that of a nonsmoker.¹ The government of the United Kingdom declared a target of reducing the prevalence of cigarette smoking in England from approximately 30% in 1990 to 20% by the end of the century.² Numerous methods are available for smoking cessation, but none is fully successful.³ Thus, there is a need for effective programs for smoking prevention and cessation.

A population survey in 1996 suggested that 15% of respondents would use complementary therapies to give up smoking.⁴ Acupuncture is a therapy frequently offered for this purpose. One possible mechanism for an effect was suggested by the finding that acupuncture released endogenous opioid peptides when it was used to treat opiate withdrawal symptoms.⁵ This was supported by findings from different laboratories implying that acupuncture may reduce the withdrawal symptoms of animals that had been rendered dependent on opiates.^{6,7}

Uncontrolled studies with acupuncture have reported smoking cessation rates as high as 95%.⁸ However, results of a meta-analysis of controlled trials were negative,³ which is in keeping with at least 3 possible conclusions: (1) acupuncture operates as a placebo for smoking cessation; (2) acupuncture was not applied optimally in the studies, for example, in not using electroacupuncture (EA); or (3) acupuncture may have an effect on withdrawal symptoms but not on relapse rate. This effect may be overlooked in measuring longer-term smoking cessation rates.

It was originally observed that administration of EA may have an effect on opium withdrawal symptoms.⁹ Use of EA was also assumed to have an effect in tobacco addiction, but this has not been tested. We, therefore, undertook this study to investigate the hypothesis that this form of EA has a specific effect on nicotine withdrawal symptoms.

RESULTS

Seventy-six smokers were randomized, and the baseline characteristics of the 2 groups

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PARTICIPANTS AND METHODS

A randomized trial in which participants and evaluators were unaware of the treatment received was conducted with 2 parallel groups comparing administration of EA at genuine acupuncture points with sham stimulation at sham points.

PARTICIPANTS

Adults older than 21 years who smoked at least 15 cigarettes per day were recruited through media invitations. Those who had been given acupuncture previously were excluded, as were those who were pregnant, breast-feeding, or fitted with a cardiac pacemaker and those who had a known bleeding tendency. Participants were asked to make a deposit of £20, which was refunded on return of the daily symptom diary after 14 days. Signed informed consent was obtained from all participants. The study was approved by the Local Research Ethics Committee of North and East Devon Health Authority, Exeter, Devon, United Kingdom.

PREDICTIVE BASELINE VARIABLES

Baseline characteristics, including those that may predict successful smoking cessation, such as living alone or living with another smoker,¹⁰⁻¹² were obtained via self-completed questionnaires. The Fagerström instrument¹³ was administered to assess nicotine dependency. The participants' attitude toward stopping was assessed by asking them to choose which of 5 statements most nearly matched their opinion, ranging from "I am really confident I can stop smoking now" to "I think I am going to carry on smoking."¹⁰

MASKING AND RANDOMIZATION

A nurse, specially trained for the study and unaware of group allocation of participants, undertook reception duties, coun-

seling, and measurement of outcomes. The acupuncture procedure was performed in a separate room by an acupuncturist (A.R.W.) with 14 years' clinical and teaching experience with acupuncture. The acupuncturist was not involved in counseling but maintained a neutral attitude toward all participants, with minimal verbal and nonverbal interaction.

Participants were randomly allocated to receive genuine acupuncture (group A) or a sham control procedure (group S). Group allocation was based on computer-generated block-randomization codes held in sealed opaque numbered envelopes prepared by departmental staff not involved with the study; the envelopes were opened immediately before the first intervention. Participants were informed that they would receive either low-frequency EA, which they would be aware of, or a high-frequency form, which they would "probably not feel."

ACUPUNCTURE PROTOCOL

All participants were treated in the supine position. In group A, an acupuncture needle (7 × 0.2 mm, Scarborough) was placed in the point known as the "Lung" in each ear. This point lies in a depression in the center of the cavum conchae and was located by inspection. Leads from the EA apparatus (model WQ10-C, Beijing Electronic Factory, Beijing, China) were attached to the needles. The frequency of stimulation was a constant 100 Hz, and the intensity was increased to just above the threshold of sensation.

Group S members were randomized to receive either similar needles placed superficially over the center of the mastoid bone (where no acupuncture point exists) with minimum noxious stimulation or transcutaneous electrical nerve stimulation (TENS) pads fixed with adhesive tape over the mastoid bone. Leads from an inactivated version of the EA apparatus (whose indicator lights flashed without delivering any current) were attached to either needles

Table 1. Baseline Characteristics of the Electroacupuncture (n=38) and Control (n=38) Groups*

Variable	Electroacupuncture Group	Sham Control Group
Age, mean ± SD, y	40.8 ± 10.9	42.5 ± 13.9
Women/men, No.	21/17	18/20
Cigarettes		
≤20	15 (40)	20 (53)
21-30	16 (42)	16 (42)
>30	7 (18)	2 (5)
No. of years smoking, mean ± SD	22.6 ± 9.5	23.8 ± 13.0
Fagerström dependency index, mean ± SD	5.5 ± 2.0	5.1 ± 1.8
Previous attempts to stop smoking, median (interquartile range)	5.0 (0-25)	3.0 (0-25)
Confidence and motivation to stop smoking, mean ± SD	3.7 ± 0.8	3.7 ± 0.8
Aged >40 y	21 (55)	22 (58)
Living alone	3 (8)	3 (8)
Other smoker in household	22 (58)	15 (40)
Advised by physician to stop	14 (37)	12 (32)
Concerned about weight gain	18 (47)	19 (50)
Consider smoking antisocial	18 (47)	13 (34)

*Values are expressed as number (percentage) unless otherwise indicated.

are shown in **Table 1**. The 2 groups had a similar incidence of factors that predict success in quitting, namely, 40 years or older, male, low cigarette consumption, living with spouse or partner, concern about weight gain, medical advice to stop smoking, and the presence of other smokers in the household ($P>.2$). Group A had made more previous attempts to stop smoking ($P=.01$, Mann-Whitney U test).

Fifty-two participants (68%) completed all 3 treatments. Eleven participants (29%) withdrew from group A and 13 participants (34%) withdrew from group S. Three participants stated that they withdrew because of adverse effects: 1 participant (from group S) experienced persistent fainting for the rest of the day after the first treatment; 1 participant (from group A) had momentary pain from excessive current during adjustment in the first treatment and reacted with weeping and anorexia for several days; and 1 participant (from group S) had a headache over the mastoid areas after the first application of TENS pads. Another participant had a similar headache after application of TENS pads but did not withdraw from the study. None of the participants who withdrew stopped smoking. The remaining 21 participants who dropped out did not keep appointments

or TENS pads. Subsequent analysis showed that there was no difference in nicotine withdrawal symptoms in these 2 subgroups of control participants. Therefore, we were satisfied that sham needling had no physiologic effects, and thus we combined outcome data from all participants in group S.

Each procedure lasted 20 minutes. The current in group A was adjusted as necessary every 5 minutes to restore the sensation; this attention was matched in group S by a routine check of the position of the wires and the "setting" of the inactive apparatus. The above procedure was repeated for each participant on days 1, 3, and 7. All participants received a brief standardized description of the reputed role of acupuncture in smoking cessation.

CREDIBILITY OF INTERVENTIONS

As the participants' beliefs in the intervention received are likely to affect the outcome, the credibility of the procedure was assessed by all participants immediately after the first intervention. Participants were asked to record on a Visual Analogue Scale measuring 100 mm long how confident they were that the treatment would help, whether they would recommend it to a friend, how logical it seemed, and how willing they would be to try it for a different problem. This instrument has been validated by Vincent and Lewith.¹⁴ A fifth question was added: "How satisfactory did you find the treatment at the time?"

OUTCOME MEASURES

The primary outcome measure was the daily withdrawal symptom score. Each evening for 14 days, the participants marked a visual analog scale to indicate their responses to 6 questions: "How strong have your cravings been (i.e., your desire to smoke) today?" "How irritable or frustrated have you felt?" "How moody or depressed have you been today?" "How tense or anxious have you been today?" "How much difficulty have you had in concentrat-

ing?" and "How hungry have you felt today?" An example was given of how to use a visual analog scale to score hunger. Measurement of these symptoms of nicotine withdrawal has been used previously¹⁵ and was validated by Hughes and Hatsukami.¹⁶

Smoking cessation was predefined as a secondary outcome measure. It was assessed by self-reports and confirmed by expired air carbon monoxide concentration of 10 ppm or less, measured with the carbon monoxide monitor (Micro Smokerlyser, Bedfont Scientific Ltd, Kent, England).

SAMPLE SIZE

In planning the trial, it was judged that a reduction in the mean withdrawal symptom scores in group A that was 20% greater than that in group S would be clinically relevant. On the basis of the results of Hughes and Hatsukami,¹⁶ in which the SD of symptom scores was 15%, it was calculated that a sample of 24 participants would be needed to demonstrate an effect with 90% power at the 5% level of significance. It was decided to recruit 76 participants to allow for the anticipated high number of dropouts.

STATISTICAL ANALYSIS

Baseline variables were compared by the Student *t* test for continuous data and the χ^2 test for dichotomous data. Changes in mean daily nicotine withdrawal symptom scores in the 2 groups from day 1 to day 14 were compared by independent samples *t* test. An additional descriptive analysis consisted of changes in mean daily withdrawal scores from day 1 to day 3. Credibility scores for the different interventions were compared by the Kruskal-Wallis test. All dropouts were regarded as continuing to smoke, and the analysis was by intention-to-treat. Data were used for all days during which participants remained continuously abstinent. Statistical analysis was performed using a software program (Statistical Package for Social Sciences for Windows v6.1, SPSS Inc, Chicago, Ill).

Table 2. Group VAS Scores (0-100) for 6 Nicotine Withdrawal Symptoms During Smoking Cessation in Participants Receiving Electroacupuncture (Group A) or Sham Acupuncture (Group S)*

Day	Reduction in Mean VAS Score			95% CI for Difference	P
	Group A	Group S	Difference (A - S)		
Participants Who Completed Diaries for at Least 3 Days: Group A (n = 25) and Group S (n = 24)					
2	-0.4	-6.3	5.9	-0.9 to 12.7	.08
3	4.4	-3.5	7.9	-2.1 to 17.9	.12
Participants Who Completed Diaries for 14 Days: Group A (n = 15) and Group S (n = 16)					
2	1.2	-4.5	5.7	-1.7 to 13.1	.13
3	6.1	0.4	5.8	-5.4 to 16.9	.30
4	11.7	3.0	8.8	-6.3 to 23.8	.24
5	10.0	9.0	1.0	-14.8 to 16.9	.90
6	12.2	8.2	4.1	-12.3 to 20.4	.61
7	20.0	10.8	9.2	-8.2 to 26.5	.30
8	20.9	27.9	8.9	-7.6 to 25.4	.28
9	20.1	14.2	5.9	-11.6 to 23.4	.50
10	21.5	11.5	10.0	-7.1 to 27.1	.24
11	23.2	13.9	9.3	-8.9 to 27.4	.31
12	23.3	16.4	6.9	-11.8 to 25.6	.45
13	20.5	15.8	4.7	-14.5 to 24.0	.61
14	21.6	17.3	4.3	-20.9 to 12.3	.60

*Scores are expressed as differences from day 1; negative scores indicate symptoms worse than day 1. VAS indicates visual analog scale; CI, confidence interval.

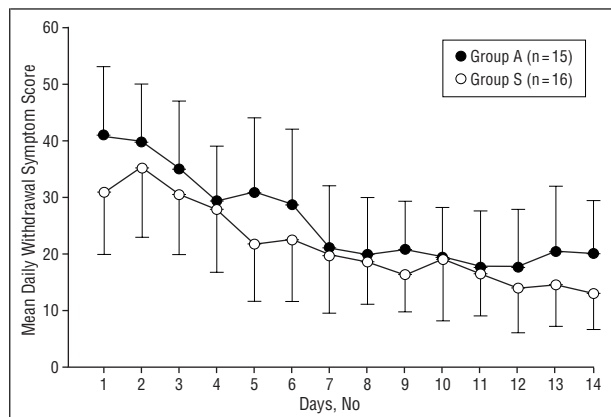
and, as mentioned above, were considered to have resumed smoking.

Diaries were completed for the full 14 days by 15 participants (39%) in group A and 16 participants (42%) in group S who were still not smoking. There were no significant differences between the groups in the reductions in mean withdrawal symptom scores from day 1 to day 14 (**Table 2** and the **Figure**). Furthermore, there were no significant differences when the changes in scores for individual withdrawal symptoms were compared (data not presented). Diaries were completed for the first 3 days by 25 participants in group A and 24 participants in group S who stopped smoking. There were no significant differences between the groups in the reduction in mean withdrawal symptom scores from day 1 to day 3 (Table 2). At 9-month follow-up, only 3 of those quitting at 14 days were still not smoking: 1 participant from group A and 2 participants from group S.

Table 3 gives the scores for participants' responses to the 5 questions used to assess the credibility of the procedures. There was no significant difference between the credibility of the 3 procedures.

COMMENT

This is the first randomized trial that uses a validated measure of withdrawal symptoms to study the effect of acu-



Mean daily nicotine withdrawal symptom scores on the visual analog scale (0-100) in participants who stopped smoking for 14 days after receiving either electroacupuncture (group A) or a sham control procedure (group S). A value of 0 can be assumed for nicotine withdrawal symptoms before participants stopped smoking (baseline). Bars indicate 95% confidence intervals.

puncture in smoking cessation. Its results suggest that EA does not have a specific effect in reducing nicotine withdrawal symptoms.

It has been argued that needling nonmeridian, supposedly "inactive," points on the body may release neurotransmitters and, therefore, is not an appropriate control procedure for acupuncture.¹⁷ However, within group S, we found no difference in outcome between those who received sham acupuncture at nonmeridian points compared with those who received sham TENS. Because the latter is highly unlikely to stimulate the release of neurotransmitters, we do not believe our negative result is because of a specific effect in both arms of the study.

It could be argued that our EA technique was not optimal. Our chosen frequency was close to the 125 Hz used in the original study by Wen and Cheung.⁹ There is no clinical consensus on the optimal frequency, and different investigators have used a range from 1 to 125 Hz.^{9,18} Although there are suggestions that different neurotransmitters are released at different frequencies of EA,¹⁹ it is not possible to select the precise frequency in humans to target specific transmitters. In addition, the roles of different neurotransmitters such as dopamine and the opioid peptides in nicotine withdrawal are still unknown.²⁰ Further trials using different frequencies of stimulation might be considered to resolve these questions.

Would these results have been different if the "Lung" point had been located by a different method, eg, by electrical resistance measurements or tenderness? Margolin et al²¹ showed no difference between the "correct" and nearby "incorrect" points in the sensations or symptomatic effects resulting from stimulation; it has been argued that any benefit of acupuncture in withdrawal symptoms is likely to be caused by neurotransmitter release, and this can be triggered by stimulation anywhere within the area innervated by the vagus.²² Based on the available evidence, we are confident that our result would not have been different if we had used a different technique to locate the point.

Was EA repeated frequently enough for any potential effect to be sustained between treatments? It could be argued that the neurotransmitter effect of acupuncture would be expected to last only 4 to 8 hours and that treatment should be given 3 or 4 times every day. The need for repeated treatments would obviously limit 1 of the potential benefits of the technique, namely, its cost-

Table 3. Group VAS Scores (0-100, Where 100 Is Maximum Credibility) for Participants' Assessment of the Credibility of 3 Interventions by 5 Criteria*

Credibility Question	Acupuncture Group (n=38)	Control Group		P
		Sham Acupuncture (n=19)	Sham TENS (n=19)	
Confident	76.3 (55.9-86.8)	78.9 (63.2-85.5)	73.0 (59.9-86.8)	.90
Recommend	85.5 (55.9-92.8)	89.5 (50.0-96.0)	75.0 (47.4-90.1)	.47
Logical	84.2 (55.9-92.8)	78.9 (69.7-96.0)	75.0 (44.4-94.7)	.46
Different problem	93.4 (85.5-98.7)	93.4 (80.3-97.4)	91.4 (86.9-97.4)	.78
Satisfactory	93.4 (85.5-98.0)	96.1 (81.6-98.7)	92.8 (65.5-95.1)	.33

* Values are expressed as median (interquartile range). See the "Participants and Methods" section for full descriptions of the credibility questions. VAS indicates visual analog scale; TENS, transcutaneous electrical nerve stimulation.

effectiveness. One alternative to repeating the treatments is to maintain continuous stimulation of the auricular point with an indwelling needle or suture; trials using the latter have shown promising results, albeit at significant risk of adverse effects.²³

Short-term (day 14) cessation rates were high in both groups (39% and 42%) and similar to those achieved with nicotine patches (eg, 36% in a study by Schneider et al²⁴). The effects of acupuncture seem to be entirely nonspecific, as shown by the lack of difference between the groups. This suggests that acupuncture is a powerful placebo for this indication and thus (perhaps paradoxically) may have a place clinically as an adjunct in programs of smoking cessation. It seems to have little value in preventing relapse and would need to be used in conjunction with other methods to provide support.

We conclude that the type of acupuncture chosen for this trial is no more effective than placebo in reducing nicotine withdrawal symptoms.

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