Journal of Internal Medicine 1990; 227: 25–30

Effects of acupuncture in moderate, stable angina pectoris: a controlled study

S. BALLEGAARD, F. PEDERSEN, A. PIETERSEN, V. H. NISSEN & N. V. OLSEN

From the Medical Department P, Division of Gastroenterology and Medical Department B, Cardiovascular Laboratory, Rigshospitalet, University of Copenhagen, Denmark.

Abstract. Ballegaard S, Pedersen F, Pietersen A, Nissen VH, Olsen NV (Medical Department P, Division of Gastroenterology and Medical Department B, Cardiovascular Laboratory, Rigshospitalet, Copenhagen, Denmark). Effects of acupuncture in moderate, stable angina pectoris: a controlled study. *Journal of Internal Medicine* 1990, 227: 25–30.

In order to evaluate the effects of acupuncture in moderate, stable angina pectoris, 49 patients were randomized to either genuine or sham acupuncture. In sham acupuncture needles were inserted into points within the same spinal segment as in genuine acupuncture, but outside the Chinese meridian system. The effect was evaluated from exercise tests, anginal attack rate and nitroglycerin consumption. There were no significant differences between the effects of genuine and sham acupuncture either on exercise test variables or on subjective variables. In patients receiving genuine acupuncture there was a significant increase in exercise tolerance (median 9%) and in delay of onset to pain (median 10%). No significant changes were observed in patients receiving sham acupuncture. Within both groups there was a median reduction of 50% in anginal attack rate and nitroglycerin consumption, and there was no significant difference between the results achieved in the two groups. It is concluded that with the present design it was not possible to demonstrate any significant differences between the effect of genuine and sham acupuncture.

Keywords: acupuncture, angina pectoris.

Introduction

Acupuncture is a treatment of disease by insertion of needles through the skin at specific points according to empirical Chinese methods [1].

Transcutaneous electrical nerve stimulation (TENS) has been shown to have the same pain relieving effect as acupuncture [2] as well as a beneficial effect on angina pectoris due to a decreased afterload following peripheral vasodilatation [3]. In a previous study [4] we have examined the effect of acupuncture in severe, stable angina pectoris, refractory to medical treatment. The study showed that genuine acupuncture increased cardiac work capacity, expressed as Delta PRP (difference in pressure-rate product between rest and maximum exercise) and maximum PRP during exercise compared to placebo acupuncture. No difference was found concerning anginal attack rate and nitroglycerin consumption. As the disease was quite advanced among these patients, the present trial was undertaken to evaluate the effect of acupuncture on patients with less severe angina pectoris.

Abbreviations: dPRP = difference in pressure-rate product between rest and maximum exercise, NYHA = New York Heart Association, TENS = transcutaneous electrical nerve stimulation.

Study population

The patients were included consecutively from individuals replying to a public announcement in several newspapers. The inclusion criteria were: clinically stable exercise induced angina pectoris for more than 6 months, two or more anginal attacks per week, consumption of two or more nitroglycerin tablets per week and positive exercise test (1 mm ST-depression in one or more leads). The exclusion criteria were: previous heart surgery, other known

Table 1. General characteristics of study groups

	Genuine acupuncture	Sham acupuncture
No. of patients completing treatment	24	25
Male: female	19:5	19:6
Median age (years) (range)	67 (49–78)	66 (49–75)
Median number of years with angina pectoris (range)	4 (0.5–25)	3 (0.5–13)
Prior myocardial infarction	10	10
Medical treatment		
Beta-blockage	7	4
Calcium-antagonist	7	12
Diuretics	6	8
Nitroglycerin with prolonged effect	3	4

causes of chest pain, intermittent claudication, previous myocardial infarction within the last 6 months, valvular heart disease, severe heart failure, arterial hypertension (WHO groups II and III), treatment with digitalis or anti-arrhythmic drugs, and previous acupuncture treatment for heart disease. Two hundred and fifteen patients replied to the announcement, 97 were excluded during the first interview, and 69 during first examination in the cardiovascular laboratory.

The clinical data for the 49 patients entering the trial are summarized in Table 1. The patients' anti-anginal drug treatment remained unchanged during the study. The patients were instructed not to change their daily habits, exercise schedule or tobacco consumption. All patients gave informed consent before the start of the study, which was approved by the local ethical committee.

Study design

The study period consisted of 3 weeks of pre-treatment control; 3 weeks treatment, during which the patient received either genuine or placebo acupuncture; 3 weeks of post-treatment control. During the entire 9 week period the patient filled in a diary. The first exercise test was performed before the pre-treatment control period to confirm the diagnosis. The second and third exercise tests were performed just before and just after the treatment period. Due to the nature of the treatment a truly double-blind design was impossible, as the acupuncturist (SB) was obviously unblinded. The patients and the doctors in charge of the exercise tests were blinded. The global evaluation was carried out by the other authors on a blind basis.

Acupuncture treatment

The genuine acupuncture was given according to traditional Chinese medicine, each patient receiving 10 treatments in the supine position within 3 weeks. The needles used were Chinese of stainless steel, 30 gauge and 1.5 inches long. After obtaining needle sensation (or the arrival of 'Qi') the needles were left in place for 20 min. The arrival of 'Qi' is described as the reaction the patient feels when the needle is inserted to a certain depth in the acupoint. The sensation is variously described as sore, aching, numb, heavy, distended or swollen and is not to be confused with the pain a needle might produce when it pricks the skin. No electrical or mechanical stimulation of the needle was given. In the control, needles were inserted superficially through the skin, with no attempt to obtain needle sensation, in points within the same spinal segments as the acupoints, but outside the Chinese meridian system and not at triggerpoints. The needles were then left untouched. In all other respects the treatments were identical. The treatment was carried out in the hospital on an out-patient basis. All patients were told that they were receiving genuine acupuncture, and that the study was a comparison between two different kinds of acupuncture. To increase the patients' confidence that they were receiving the correct acupuncture treatment, the acupuncturist employed an electrically-resistant measurement device (APF 700 Biometer, Odense, Denmark), which was adjusted to beep over both genuine and sham points. He then explained to the patient that the beep indicated the exact location of the acupoint and would then confirm the accuracy required for correct needle technique.

Effect evaluation

The effect was evaluated from exercise tests, diaries and a subjective global evaluation by the patient at the end of the trial.

A. *Exercise tests* were carried out on a bicycle ergometer. The patients were told not to drink coffee nor to take nitroglycerin 2 h previous to the exercise tests which were all performed between 14.00 and 16.00 hours. Work load started at 30 W and was increased incrementally by 10 W, exercising 1 min at each step. A twelve-lead ECG was recorded continuously on paper before, during and for 10 min after the test. Blood pressure was measured by cuff every 2 min in the sitting position and after the test in the supine position. The patients were encouraged to exercise to the maximum limit and to express their symptoms. Exercise variables used in the evaluation were: exercise tolerance, maximum PRP, dPRP, heart rate at start of 1 mm ST-depression, time to start of ST-depression, time to end of ST-depression after exercising, size of maximum ST-depression, time with minimum 1 mm ST-depression, time to onset of pain, and postexercise pain duration.

B. *Diaries* were filled out daily by the patients, stating the number of anginal attacks, activity at the time of the pain, nitroglycerin consumption and daily well-being on an ordinal scale, using the terms very good (given value 1), good (2), fair (3), not good (4), bad (5). The dairies were collected after each period, and a final evaluation was made at the end of the entire trial.

C. *After the end of the trial* as well as 6 months later the patients were asked for a global evaluation of the effect of the treatment on an ordinal scale: much improved, somewhat improved, slightly improved, unchanged, slightly worse, somewhat worse, much worse.

Statistics

Between-group differences were evaluated by rank-sum tests for unpaired data (Mann–Whitney). Intra-personal differences were evaluated by rank-sum tests for paired data (Wilcoxon). Five per cent was chosen as the significance level.

Results

There was no significant difference between the two groups with regard to age, sex, prior myocardial infarction, medical treatment (Table 1), exercise test variables (Table 2), anginal attack rate and nitroglycerin consumption (Fig. 1) at randomization. All patients completed the trial.

Exercise test variables

Table 3 shows individual relative changes in exercise variables from pre- to post-treatment exercise tests.

Table 2. Pre-treatment exercise test variables. All values expressed as median (range)

	Genuine acupuncture ($n = 24$)	Sham acupuncture ($n = 25$)	Genuine versus sham (control)
Exercise tolerance ($Wmin^{-1}$)	330 (103–915)	375 (83–1500)	NS*
Maximal PRP ($mmHg\ min^{-1}$)	20.650	22.960	NS
Range	(13.940–29.250)	(16.200–32.195)	
Delta PRP ($mmHg\ min^{-1}$)	9.550	11.830	NS
Range	(3.380–18.810)	(5.920–19.490)	
Heart rate at start of 1 mm ST-depression	104 (81–148)	104 (90–127)	NS
Time to ST-depression (min)	4.36 (1.15–10.45)	4.30 (1.30–11.30)	NS
Time to end of ST-depression (min)	0.45 (0–4.15)	1.0 (0.15–5.30)	NS
Size of maximum ST-depression (mm)	1.5 (1.0–3.5)	1.8 (0.5–5)	NS
Time with minimum 1 mm ST-depression (min)	2.16 (0–8.15)	2.37 (1.0–9.15)	NS
Time to onset of pain (min)	4.59 (2.0–9.0)	5.29 (2.30–9.30)	NS
Postexercise pain duration (min)	1.29 (0.15–4.0)	1.31 (0.25–4.0)	NS

*NS = not significant.

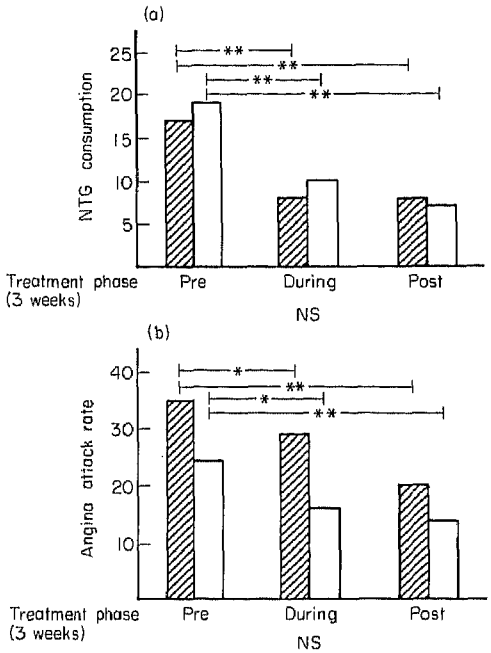

Fig. 1. (a) Nitroglycerin (NTG) consumption and (b) anginal attack rate during study period, expressed as absolute values. $^{*}P < 0.01$, $^{**}P < 0.005$, NS = not significant. Genuine acupuncture, $n = 14$; sham acupuncture, $n = 16$.

Those having genuine acupuncture increased exercise tolerance significantly (median increase 9%, range −25 to +184%) and had a significant delay in time to onset of pain (median delay 10%, range −32 to +107%) when compared to pre-treatment values. Those having sham treatment had no significant change in exercise variables. There were no significant between-group differences.

Subjective variables

In relation to the inclusion criteria the post-study examination revealed an insufficient number of anginal attacks in 19 patients and nitroglycerin consumption in 18 patients. These patients were excluded from this part of the study. However, they all fulfilled the criteria for entry to the study. The individual relative changes in anginal attack rate and nitroglycerin consumption from pre- to post-treatment values did not differ significantly between the two groups (Fig. 1). Within both groups there was a significant decrease in both anginal attack rate and nitroglycerin consumption (Fig. 1). After treatment all patients receiving genuine acupuncture decreased nitroglycerin consumption (median change −54%, range −14 to −100%). Anginal attack rate was reduced in 13 of 14 patients (93%) median change −41%, range +18 to −95%). Nitroglycerin consumption and anginal attack rate were reduced in 15 of 16 patients (94%) receiving sham acupuncture. The median change being −53% (range +20 to −100%) and −55% (range +23 to −100%) respectively. Daily well-being was improved in 14 out of 23 (61%) in both groups (median improvement +1 arbitrary value in both groups). Concerning global evaluation, 75% of the

Table 3. Individual relative changes (%) in exercise test variables from pre- to post-treatment exercise test. All values expressed as median (range). Positive values indicate a post-treatment exercise test value greater than the pre-treatment exercise test value

	Genuine acupuncture ($n = 24$)	Sham acupuncture ($n = 25$)	Genuine versus sham
Exercise tolerance (%)	+9 (−25+184)*	+4 (−16+135)	NS‡
Maximal PRP (%)	−1 (−12+47)	+5 (−22+25)	NS
Delta PRP (%)	+3 (−38+145)	+4 (−28+78)	NS
Heart rate at start of 1 mm ST-depression (%)	−1 (−9+14)	+1 (−7+12)	NS
Time to ST-depression (%)	0 (−42+100)	0 (−40+40)	NS
Time to end of ST-depression (%)	+9 (−75+600)	0 (−58+300)	NS
Maximum ST-depression† (mm)	0 (−1.0+0.5)	0(−1.0+1.5)	NS
Time with minimum 1 mm ST-depression (%)	+15 (−79+490)	+5 (−72+200)	NS
Time to onset of pain (%)	+10 (−32+107)*	+10 (−39+55)	NS
Postexercise pain duration (%)	0 (−47+700)	0 (−77+78)	NS

* $P < 0.05$ (intrapersonal difference).
† Maximum ST-depression expressed as absolute values.
‡ NS = not significant.

patients treated by genuine acupuncture reported improvement in their general condition after the end of the treatment and 6 months later 67% still felt the improvement. Among those treated by sham acupuncture 84% reported improvement and 6 months later 72% still felt it.

Discussion

The present study demonstrates that there is no difference in the effect of genuine and sham acupuncture in patients with mild angina pectoris. In both groups a significant beneficial effect was observed on nitroglycerin consumption, anginal attack rate, and general well-being. Exercise tolerance and time to onset of pain were slightly improved by genuine acupuncture but again with no difference between the groups. The results may be interpreted as if both treatments are effective or as if neither of them is.

It has been suggested that any kind of noxious stimulus attenuates pain through the mechanism of diffuse noxious inhibitory control [5]. Animal studies indicate that a noxious stimulus on the skin has an effect on the interior organs innervated by the same dermathom through a sympathetic cutaneous reflex [6]. Furthermore it has been possible to demonstrate that a noxious stimulus to a triggerpoint of the dermatome of the heart has a beneficial effect on myocardial pain and angina pectoris [7]. Although the sham treatment group in our trial received only superficial acupuncture and thus little noxious stimulus, it has been possible in other trials to show that superficial acupuncture is superior to mock transcutaneous nervous stimulation and that sham acupuncture applied at different spinal segments from the genuine acupuncture produces a significant difference in the effect between genuine and sham acupuncture [8, 9].

The observation of a pronounced, beneficial effect on subjective variables raises the question of the influence of a placebo effect. The effect of drug placebo therapy in patients with chronic stable angina pectoris has been studied by Hartman *et al.* [10] and Khurmi *et al.* [11]. The former group followed 20 patients with exercise tests at 3-month intervals and registration of nitroglycerin consumption during placebo therapy. Nitroglycerin consumption was decreased in 65% of the patients (median reduction 36%). Exercise test variables showed no significant difference. Khurmi *et al.* studied the effect of placebo therapy in 150 patients. Twenty per cent of patients reported subjective relief of their angina. Exercise test variables did not change significantly. Mannheimer *et al.* [3] have studied the placebo effect of TENS in 11 patients with angina pectoris. Each patient performed 10 exercise tests during a 15-week period. Neither placebo nor training effect was observed.

The fact that there was at the time a positive attitude to acupuncture in the newspapers combined with recruitment of patients by advertisements might have increased the placebo effect of the present study. We conclude that with the present design, it has not been possible to demonstrate a difference between genuine and sham acupuncture in patients with moderate angina pectoris and furthermore that it is not possible to determine whether the observed effect is due to placebo effect or due to a specific noxious stimulation of the dermatome of the heart. The study underlines the difficulties of establishing a control group when evaluating acupuncture and thus indicates the need for different scientific designs in future acupuncture trials. One possible way of solving this problem is to include a second control group that is untreated although this does not exclude the placebo effect of receiving a needle treatment in general. Another possibility is that each patient undergoes two trials. In the one trial a clinical acupuncture effect is measured, which therefore involves the influence of the placebo effect. In the other trial the effect of acupuncture is evaluated from variables that are not influenced by placebo effect. By correlating two such trials it might be possible to determine whether an effect a patient observes from acupuncture is due to a placebo effect or to a biological effect of acupuncture.

References

1 Beijing College of Traditional Chinese Medicine. *Essentials of Chinese Acupuncture*. Beijing: Foreign Language Press, 1980.

2 Andersson SA, Carlsson AA, Eriksson M. *Från tro till vetenskab*. Liber Forlag, Kristianstad 1984; 67.

3 Mannheimer C, Carlsson CA, Emanuelsson H, Vedin A, Waagstein F, Wilhelmsson C. The effects of transcutaneous electrical nerve stimulation in patients with severe angina pectoris. *Circulation* 1985; 71: 308–16.

4 Ballegaard S, Jensen G, Pedersen F, Nissen VH. Acupuncture in severe, stable angina pectoris: a randomized trial. *Acta Med Scand* 1986; 220: 307–13.

5 Le Brd D, Dickensson AH, Besson JM. Diffuse noxious inhibitory controls (DNIC): II Lack of effect on non-convergent neurones, supraspinal involvement and theoretical implication. *Pain* 1979; 6: 305–27.

6 Wernøe TB, Vescero-cutane reflex. *Plügers Arch desamte Phys* 1925; **210**: 1–34.
7 Travell J, Rinzler SH. Relief of cardiac pain by local block of somatic trigger areas. *Proc Soc Exp Biol Med* 1946; **63**: 480–2.
8 MacDonald AJR, MacRae KD, Master BR, Rubinb AP. Superficial acupuncture in the relief of chronic pain. *Ann R Coll Surg Eng* 1983; **65**: 44–6.
9 Dundee JW, Chestnutt WN, Ghaly RG, Lynas AGA. Traditional Chinese acupuncture: a potentially useful antiemetic? *Brit Med J* 1986; **293**: 583–4.
10 Hartman KE, Nordstrom LA, Gobel FL. Effect of placebo on exercise response and nitroglycerin consumption. *Minn Med* 1976; **59**: 839–48.
11 Khurmi NS, Fica BS, Bowles MJ. Kohlli RS, Raftery EB. Does placebo improve indexes of effort-induced myocardial ishemia? An objective study in 150 patients with chronic stable angina pectoris. *Am J Cardiol* 1986; **57**: 907–11.

Received 19 April 1989, accepted 9 June 1989

Correspondence: Soeren Ballegaard, MD, Head of Acupuncture Centre, Rigshospitalet, Tagensvej 18 B, 2200 København N, Denmark.