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Efficacy and safety of acupuncture for chronic uncomplicated neck pain: A randomised controlled study ☆

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Abstract

Chronic neck pain is highly prevalent. To determine the efficacy and safety of acupuncture, in comparison with transcutaneous nerve stimulation-placebo (TENS-placebo) in the treatment of chronic uncomplicated neck pain, a single blind prospective study was designed, to be carried out at a Primary Healthcare Centre, with random assignment to two parallel groups and with evaluation and analysis by independent evaluators. A random assignment was made from 123 patients of the 149 initially recruited. These patients had been diagnosed with uncomplicated neck pain and experienced neck motion-related pain intensity equal to or exceeding 30 on a visual analogue scale (VAS) from 0 to 100 mm. The treatment with acupuncture was compared with TENS-placebo, applied over 5 sessions in three weeks. The primary endpoint was the change in maximum pain intensity related to motion of the neck, one week after the final treatment. Sensitivity was analysed per protocol (PP) and variant analyses were by intention to treat (ITT). Adjustment was made for confounders by multiple linear regression, including baseline values and rescue therapy. By ITT analysis, the change in the pain-VAS variable was greater among the experimental group (28.1 (95% CI 21.4–34.7)). The improvements in quality of life (physical aspect), active neck mobility and reduced rescue medication were clinically and statistically significant. In the treatment of the intensity of chronic neck pain, acupuncture is more effective than the placebo treatment and presents a safety profile making it suitable for routine use in clinical practice.

Keywords: Acupuncture; Placebo; TENS; Neck pain; Randomised controlled study

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1. Introduction

Neck pain affects 30% of men and 43% of women at some time in their lives (Borghouts et al., 1998), and is one that becomes chronic among 10% of men and 17% of women. It is the second most common musculoskeletal-related cause of invalidity (Makela et al., 1991; Bovim et al., 1994); the prevalence increases with age, and is greater among women than among men (Cote et al., 2004).

Most cases of chronic neck pain are caused by mechanical factors; although they are usually considered to be related to degenerative cervical processes, no connection has been proven between the patient's complaint and radiological observations (Harrison et al., 2002). Frequently, non-specific neck pain, with no obvious structural cause, is recorded (Bogduk, 1984).

The conservative treatment for uncomplicated neck pain includes physical and pharmacological measures, together with the provision of advice and manual treatments such as mobilisation and manipulation (Irnich et al., 2001). Nevertheless, various systematic reviews have shown that the effectiveness of such interventions is open to question (Aker et al., 1996; Gross et al., 2000; Dziedzic et al., 2005). Acupuncture is frequently applied to treat chronic neck pain, but despite the increase in randomised clinical trials (RCT) there is little evidence for the effectiveness of acupuncture as a treatment for the relief of chronic neck pain (Morey, 1998; White and Ernst, 1999; Smith et al., 2000; White et al., 2002). Systematic reviews have revealed that this lack of evidence is often due to methodological deficiencies such as too small samples, inadequate methods of statistical analysis and the possible physiological activity of placebo (sham) acupuncture (Spitzer et al., 1995; Beaudreuil and Gallou, 2004; Vickers, 2004; Weiner and Ernst, 2004; Paterson and Dieppe, 2005). Moreover, this absence of evidence might arise from the inclusion in some of the reviews of tests examining a wide variety of painful pathologies (White et al., 2002).

In this paper, we present the results of a controlled randomised study to evaluate the efficacy and safety of acupuncture in comparison with transcutaneous nerve stimulation-placebo (TENS-placebo) for the treatment of chronic uncomplicated neck pain with a duration exceeding three months.

2. Methods

2.1. Design of the study

Single blind prospective study with random assignation to two parallel groups, with blind evaluation and statistical analysis by independent evaluators. The study was carried out at the Pain Treatment Unit (PTU) at a Primary Attention Healthcare Centre of the Andalusian Public Health Service (Spain) over a period of two years, from June 2002 to June 2004. The study was approved by the Research Ethics Committee at the reference hospital.

2.2. Participants

All of the general practitioners at the Primary Healthcare Centres in the municipality were informed of the study and their collaboration was requested in recruiting and referring to the PTU patients who met the criteria for inclusion in the study. These were outpatients aged 17 years and over who had been diagnosed with uncomplicated neck pain of over three months' duration (Skouen et al., 2002), symptomatic at the time of examination, with a motion-related neck pain intensity equal to or exceeding 30 on a visual analogue scale of 0–100 mm (pain-VAS), and who had not received any treatment during the week preceding their incorporation into the study. The patients gave their informed consent to participate in the study. The exclusion criteria are listed in Table 1.

2.3. Randomisation

The patients were randomly allocated to two groups: an experimental group that was treated with acupuncture, and a control group given TENS-placebo treatment. The assignation to one or other of the groups was carried out with validated, publicly available software (Silva Ayzaguer, 1993), without using blocking, but sealed, opaque envelopes. Only the doctor who applied the treatment was aware of the group assignment of each patient, and this doctor did not participate in any of the subsequent evaluation phases. A person with no connection with the study was requested to open the envelopes and assign the patients to their respective groups.

The research team adopted appropriate measures to maintain the confidentiality of the participating patients' data, including de-identification of the data contained in the databases created for the analysis.

Table 1
Exclusion criteria

Exclusion criteria
Previous treatment with acupuncture
Pain intensity less than 30 mm on a visual analogue scale (0-100 mm)
Specific diagnosis of neck pain classed as neuropathologic, infectious, inflammatory, neoplasic, endocrine, metabolic or visceral
Cervical fracture or traumatism
Previous spinal surgery
Non-specific fever
Severe psychiatric illness
Severe disorder of overall health state
Infectious feverish disease
Severe or generalized dermatopathy
Any sign of malign tumor
Incompatibility with the medication described in the protocol
Occupation-related lawsuit arising from neck pain
Pregnancy
Prior recommendation for treatment with antineoplasic drugs, corticosteroids, immunosuppressor drugs or opioids
Inability or unwillingness to follow instructions

2.4. Treatment protocols

The treatment consisted of five sessions, applied over a period of three weeks, with two sessions during each of the first and second weeks and one in the third. Both groups were provided with analgesic rescue medication once weekly. The two treatment modes were applied at different times of the day so that the patients should not have the opportunity to exchange impressions in the waiting room.

2.4.1. Acupuncture

A doctor specialising in acupuncture (accredited by the Beijing University of Medical Sciences (China) and by the Scientific Society of Medical Acupuncture (ACMAS Huangdi, Spain)), with over 15 years' clinical experience, selected acupuncture points on the basis of traditional Chinese treatment methods found to be effective for cervical pain (Cobos and Vas, 2000; Stux and Pomeranz, 2000) and administered all of the acupuncture treatments. The points were selected according to the pain characteristics and the accompanying symptoms (Table 2). In every case, the puncture was bilateral, with sterile, single-use needles, $25\,mm \times 0.25\,mm$ or $40\,mm \times 0.25\,mm$, depending on the area to be treated. In every case, the puncture was effected by determining the "Deqi" (an elicitation of needle sensation to check that the puncture was performed in the correct site). The needles were kept in place for 30 min and manually stimulated every 10 min. After removing the needles, Vaccaria seeds were applied in the ear auricle at the points described below, after sterilising the skin, and were taped there until the following treatment session. The patients were told to apply pressure to each ear point for a series of 10 repeats three times per day.

2.4.2. TENS-placebo

The TENS-placebo technique applied is a physiologically inert type of control treatment that has been used previously (Thorsteinsson et al., 1978; Petrie and Hazleman, 1985; Vincent and Lewith, 1995; Lewith and Vincent, 1996; Wood and Lewith, 1998). The technique was applied using TRANSMED 911 [Enraf-Nonius B.V.] transcutaneous nerve stimulation units that had been adjusted beforehand to prevent current passing through the electrodes. With the patient in a prone position, the electrodes were placed at the Jianjing (GB 21) bilateral acupuncture point while the nerve stimulation unit was located in front of the patient for 30 min such that the flashing diode simulating the stimulus was both visible and audible. Every 10 min, the patient's state was checked and the TENS-placebo potentiometer was adjusted.

Although the sham intervention was distinguishable from the experimental technique, the patients had not received acupuncture previously and were given this prior information: "A research project is being carried out at this Healthcare Centre to evaluate and quantify the effects of two non-pharmacological techniques for the treatment of chronic neck pain. One will be applied in a real way, but the other will be false. In a random way, you will be assigned to one or the other group. You will be given medicines that are considered effective for treating your neck pain in case the technique applied does not relieve it".

2.4.3. Rescue medication

The patients in both groups were given a bag containing 21 pills (50 mg) of diclophenac for each of the 3 weeks the study lasted, with the recommendation to take one (50 mg/8 h) if pain relief was not obtained with the treatment given. The unused medication was recovered and quantified. Patients with risk factors received gastroprotective drugs. The patients suffering objectifiable muscular contraction were also given a pill containing tetrazepam (50 mg) every 24 h.

2.5. Assessments

The assessments were made blind, by a medical specialist in rehabilitation before the intervention (T0) and one week after the final treatment (T1, primary end point). The follow up included an assessment at 6 months (week 28) after ending the treatment (T2, secondary end point). At all times, the assessors discouraged the patients from commenting upon the type of treatment received.

2.6. Outcome measures

2.6.1. Primary

Change in maximum pain intensity related to motion of the neck (pain-VAS) assessed at T0 and T1. The patients were asked to rate the maximum pain intensity related to motion of the neck on a visual analogue scale of 0 (no pain) to 100 mm (the maximum pain imaginable).

Table 2
Acupoints selected

Main type of cervical pain	Proximal points	Distal points	Ear points
Muscular, miofascial	Fengchi (GB 20), Jianjing (GB 21)	Taichong (LR 3), Hegu (LI 4), Yanglingquan (GB 34)	Shenmen, Neck, Liver, Muscle Relaxation, Occiput, Thalamus
Arthritic	Tianzhu (BL 10), Dazhui (GV 14)	Houxi (SI 3), Shenmai (BL 62)	Shenmen, Neck, Kidney, Muscle Relaxation, Occiput, Thalamus
Accompanying symptoms	*Additional points*		
Pain in the region lateral to the neck	Xuanzhong (GB 39)		
Anxiety	extra Yintang		
Dizziness with blurred vision	Baihui (GV 20), Sanyinjiao (SP 6)		

GB, gallbladder; LR, Liver; LI, large intestine; BL, bladder; GV, governor vessel; SI, small intestine; SP, spleen.

2.6.2. Secondary

The Spanish version of the Northwick Park neck pain questionnaire (NPQ) (Leak et al., 1994) was used to assess the percentage of discapacity (Gonzalez et al., 2001; Pietrobon et al., 2002) at T0 and T1. One compound index was calculated from the sum of the active cervical mobility (ACM) scores in the 6 possible directions of the spinal column, and another was derived for passive cervical mobility (PCM), measured by goniometry (Gajdosik and Bohannon, 1987), with the patient in a seated position, at T0 and T1. To provide a measure of health-related quality of life, the patients completed the Spanish version of the Short Form-36 Health Survey (SF-36) (Alonso et al., 1995) at T0, T1 and T2; in cases of difficulty in understanding items in the questionnaire, the assessor clarified the doubts. Higher scores indicated a better health-related quality of life. The rescue medication (RM) was quantified at T0, T1 and T2, and categorized into 5 values: 0 (no medication); 1 (less than the prescribed medication); 2 (consumption of the prescribed dose); 3 (consumption exceeding the prescribed medication); 4 (consumption exceeding the prescribed dose with non-prescribed analgesics). The patients were asked at T0 and T2 about visits made to the doctor (general practitioner or specialist) during the previous 3 months (interim medical visits, IMV) as a result of neck pain. At T2, the pain-VAS score was assessed as a secondary result measure.

2.7. Treatment credibility

The patients' degree of confidence was evaluated on a Treatment Credibility Scale (TCS) (Bayreuther, 1994), adapted from one originally proposed by Borkovec and Nau (1972) and validated for use in acupuncture research by Vincent (1990), with 4 items scored on a 7-point scale (from 0, no credibility, to 6, maximum credibility). The first 2 items were scored after the first treatment session:

- Do you believe this treatment could help relieve your pain?
- Does this treatment seem a logical one?

And the other two items were scored at T1:

- Would you recommend this treatment to a friend or relative suffering the same problem?
- Do you believe this treatment might be suitable for dealing with other problems?

2.8. Statistical analyses

The sample size was determined on the basis of a previous pilot study, taking into account the expected differences between the treatment groups, as expressed by their mean scores on the pain-VAS scale one week after the treatment. The mean expected difference was 26.5 (SD 19) for the experimental group and 14 (SD 18) for the control group. For a power of 90% and a level of statistical significance of 5%, 49 patients were thus needed for the experimental group and 46 for the control group. Assuming a loss rate of 20%, the minimum sample size was estimated to be 112, this calculation being made with the freely distributed DSTPLAN software package (Brown et al., 2000).

The values of the sociodemographic and baseline severity variables for the experimental and control groups were compared using measures of dispersion (standard deviation) and of central trend (means). For the primary and secondary result variables, a sensitivity analysis was carried out by comparing the results obtained from the per protocol (PP) analysis and from that of intention to treat (ITT), with imputation of missing data by the worst case method for the experimental group and the best case method for the control group (WBC: when data were missing for a patient in the experimental group, the worst value observed at the end of the follow up of this group was imputed to this patient; when data were missing for a patient in the control group, the best value observed at the end of the follow up of this group was imputed to this patient).

Bivariate results for the pain-VAS and for the secondary result variables are presented by PP analysis and by ITT according to the WBC method (Sackett et al., 2000; EMEA The European agency for the evaluation of medical products 2001). The magnitudes of the differences, for the normally distributed continuous data, were compared using the unpaired Student's t test. Skewed data were compared using the Mann–Whitney test. The chi-squared test was used to analyse the rescue medication variable. The level of statistical significance was assumed to be $p < 0.05$.

The effect size for the raw change scores was evaluated as the difference of mean differences (mean change in control group subtracted from that of the experimental group) divided by the pooled standard deviation of the respective changes (Cohen, 1988), calculated by means of a freely distributed software package (Coe, 2005). The level of credibility was analysed by calculating the mean and its SD for the first two questions (after the first treatment session) and the last two questions (at the end of the follow up), separately, and by comparing the treatment groups.

To adjust for possible confounders and to detect potential interactions, multiple linear regression models were constructed for the result variables, adjusted by the baseline level and using ITT analysis by the WBC method. The group variables (experimental/control) and baseline variables were included in the above, together with new variables, concerning sociodemography (age and sex) and the severity of the process (IMV, past duration of the pain, radiological results, type of pain, NPQ, RM, ACM, PCM, SF-36), using criteria of statistical significance and of confounding (when the introduction of a new variable produced a change in the coefficient of the variable "group" exceeding 10%). The models were constructed again, but this time removing those observations with Cook's distances exceeding the 90 percentile of the distribution, in order to test the consistency of the results. The assumptions of the linear models were tested by a normal probability plot (normality) and by plotting studentized residuals against observed values (constant variance).

3. Results

3.1. Randomisation, progress through the trial and baseline data

Of the 149 patients selected, 15 were rejected because they did not meet the criteria for inclusion

(80% of these patients did not record a score of 30 mm on the baseline pain-VAS); of the remaining 134, eight refused to participate in the study and another three were unable to attend the treatment sessions. Thus, 123 patients were finally randomised for inclusion in the study. Fig. 1 shows the patients' progress during the study and the numbers withdrawing from it. The dropout rate was similar in the two groups, with 3/61 (4.9%) in the experimental group and 5/62 (8.1%) in the control group (χ^2 test $p = 0.50$) being lost.

The baseline characteristics of the samples were found to be balanced among both groups, concerning the patients' characteristics before treatment and with respect to the dropout rates (Table 3).

3.2. Primary outcome measure

The PP analysis between T0 and T1 for the change in the pain-VAS variable was greater in the experimental group (44.1, SD 19.5) than in the control group (12.3, SD 14.6), with the differences being statistically significant in all the subgroups (Table 4).

Table 5 shows the results of the ITT analysis by the WBC method. The difference in the means was 28.1, and the standardised effect size was 1.51 (CI 95% 1.10–1.90).

3.3. Secondary outcome measures

Table 5 shows the results of the ITT analysis of the secondary outcome measures one week after treatment.

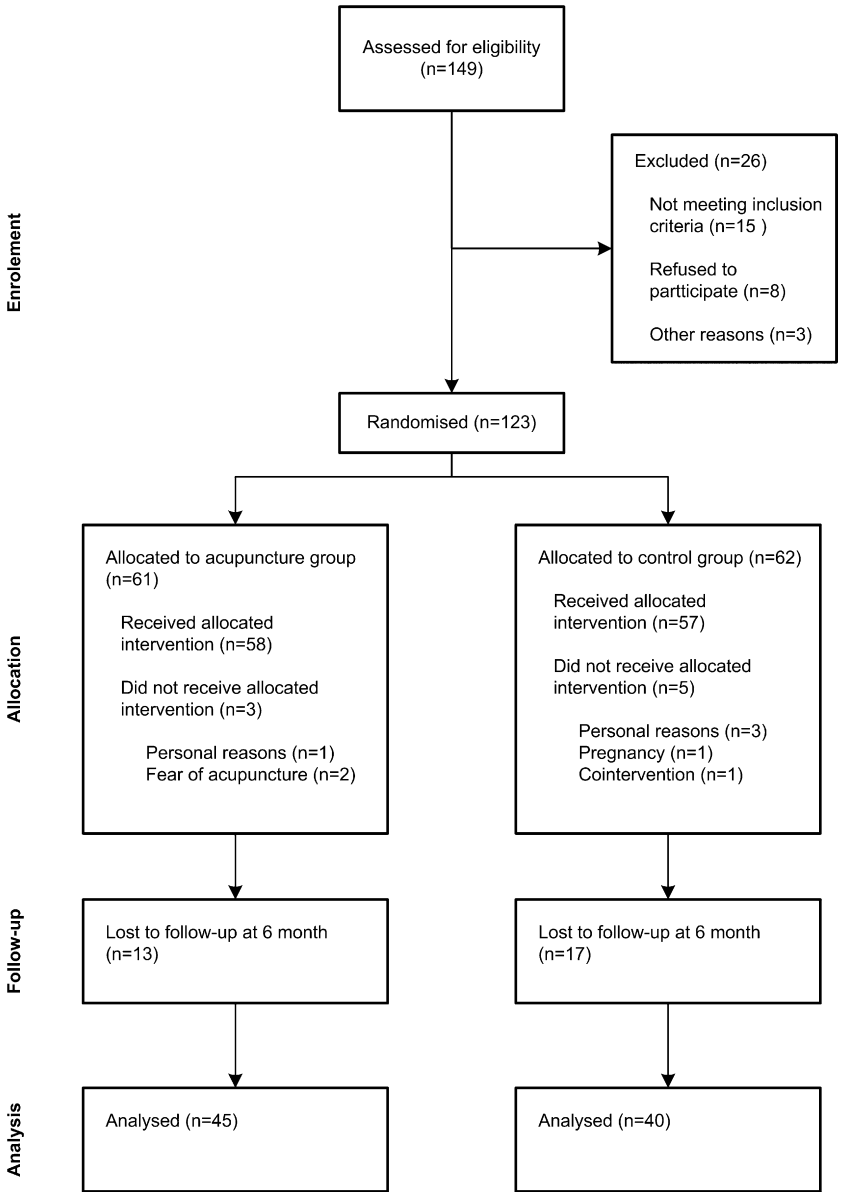

Fig. 1. Flow of participants through each stage and dropouts.

Table 3
Characteristics of the patients before treatment

Outcome measure[a]	Acupuncture group ($n = 61$)	Control group ($n = 62$)	Adherers ($n = 115$)	Dropouts ($n = 8$)	p value (Adherers and Dropouts)
Age (years)	46.0 (13.7)	47.4 (12.8)	47.2 (13.1)	40.3 (14.3)	0.152[b]
Sex, numbers (percentages) of patients					
Men	15 (24.6)	7 (11.3)	20 (17.4)	2 (25.0)	0.587[c]
Women	46 (75.4)	55 (88.7)	95 (82.6)	6 (75.0)	
Pain duration (months)	47.4 (60.3)	43.0 (40.8)	44.3 (51.8)	58.0 (42.4)	0.466
IMV	3.6 (2.8)	4.8 (3.5)	4.2 (3.2)	4.1 (3.4)	0.943
Predominant Rx signs, numbers (percentages) of patients					
Arthritis	34 (55.7)	34 (54.8)	67 (58.3)	1 (12.5)	0.004
Rectification	18 (29.5)	20 (32.3)	35 (30.4)	3 (37.5)	
Non-specific	9 (14.8)	8 (12.9)	13 (11.3)	4 (50.0)	
Type of pain, numbers (percentages) of patients					
Arthritic	34 (55.7)	34 (54.8)	67 (58.3)	1 (12.5)	0.012
Muscular	27 (44.3)	28 (45.2)	48 (41.7)	7 (87.5)	
Frequency of pain, numbers (percentages) of patients					
Occasional	1 (1.6)	–	1 (0.9)	–	0.142
Frequent	8 (13.1)	4 (6.5)	11(9.6)	1 (12.5)	
Very frequent	3 (4.9)	12 (19.4)	12 (10.4)	3 (37.5)	
Continuous	49 (80.3)	46 (74.2)	91 (79.1)	4 (50.0)	
Type of work done, numbers (percentages) of patients					
Sedentary	12 (19.7)	23 (37.1)	34 (29.6)	1 (12.5)	0.519
Moderately active	30 (49.2)	26 (41.9)	51 (44.3)	5 (62.5)	
Physically intensive	19 (31.1)	13 (21.0)	30 (26.1)	2 (25.0)	
Pain-VAS (0–100 mm scale)	68.7 (14.3)	72.3 (15.4)	71.1 (14.7)	61.3 (16.4)	0.070
NPQ (0–100 scale)	52.7 (14.0)	56.5 (13.2)	54.6 (13.1)	54.6 (21.6)	0.996
RM, numbers (percentages) of patients					
None	3 (4.9)	–	3 (2.6)	–	0.946
Occasional	7 (11.5)	6 (9.7)	12 (10.4)	1 (12.5)	
Prescribed dose	36 (59.0)	30 (48.4)	62 (53.9)	4 (50.0)	
Above prescribed dose	10 (16.4)	23 (37.1)	31 (27.0)	2 (25.0)	
Other analgesic medication	5 (8.2)	3 (4.8)	7 (6.1)	1 (12.5)	
ACM (degrees)	240.1 (59.4)	229.8 (59.2)	234.7 (59.0)	237.5 (66.5)	0.139
PCM (degrees)	291.1 (47.3)	288.4 (47.4)	288.5 (47.1)	308.1 (47.9)	0.213
SF-36 PCS (0–100 scale)	36.7 (9.7)	37.6 (7.9)	37.5 (8.4)	32.7 (13.9)	0.365
SF-36 MCS (0–100 scale)	38.7 (13.0)	34.0 (11.4)	35.9 (12.1)	41.6 (16.2)	0.213
TCSa (0–6 scale)	4.6 (0.8)	4.5 (0.8)	4.5 (0.8)	4.6 (0.9)	0.734

Values are means (standard deviations) unless stated otherwise.

[a] IMV, visits during the previous 3 months to GP or specialist because of neck pain; pain-VAS, intensity of neck pain; NPQ, Northwick Park neck pain questionnaire; RM, consumption of rescue medication (one week before inclusion in study); ACM, active cervical mobility; PCM, passive cervical mobility; SF-36, short form-36; PCS, physical component summary; MCS, mental component summary; TCSa, mean of first 2 questions of the credibility score, after first treatment session.

[b] This value correponds to age.

[c] This value correponds to sex.

All the changes in the variables were higher and statistically significant among the experimental group, except the change in PCM and in the Mental Component Summary (MCS) of SF-36.

With respect to consumption of analgesic medication during the experimental period, at T1, 70.5% of the patients in the experimental group had taken no rescue medication, versus 17.7% of the control group, compared with all the other categories (RR = 4.0, CI 95% 2.3–7.0). In the acupuncture group, 8 patients (29.6%) consumed tetrazepam, while in the control group, this was consumed by 19 (67.9%) of the patients. Of the latter, 5 (26.3% of those who consumed it) took more than the prescribed dose. This circumstance was not observed among the experimental group.

At 6 months after ending the treatment (T2), the changes in the result variables with respect to baseline values had decreased in all cases, and only the pain-VAS changes remained statistically significant (Table 6). Of the 17 patients who were lost to the study during the follow up of the control group, 82.3% had taken the prescribed dose of rescue medication or had exceeded it, since T1; in contrast, the patients who left

Table 4
Baseline to post-treatment changes in pain-VAS in subgroups: per protocol analysis

Subgroups (acupuncture patients/control patients)	Acupuncture group	Control group	p value
Pain-VAS (whole group)	44.1 (19.5)	12.3 (14.6)	<0.001
Sex			
Female (44/51)	45.9 (18.5)	12.4 (15.0)	<0.001
Male (14/6)	38.6 (22.5)	11.7 (11.7)	0.013
Duration of process, years			
<1 (15/15)	44.0 (15.0)	12.7 (15.3)	<0.001
1–2 (21/15)	43.3 (22.4)	9.3 (12.2)	<0.001
2.1–4 (8/11)	48.8 (21.7)	16.4 (11.2)	0.003
>4 (14/16)	42.9 (19.8)	11.9 (18.3)	<0.001
Type of pain			
Arthritic (33/34)	46.7 (19.6)	12.9 (14.3)	<0.001
Muscular (25/23)	40.8 (19.3)	11.3 (15.5)	<0.001
Rescue medication (final)			
Not required (43/6)	45.8 (17.2)	20.0 (6.3)	<0.001
Required (15/51)	39.3 (25.2)	11.4 (6.5)	<0.001
Type of work done			
Sedentary – not employed (11/23)	45.5 (16.3)	13.5 (15.8)	<0.001
Moderately active (28/23)	44.6 (19.0)	9.1 (11.2)	<0.001
Physically intensive (19/11)	42.6 (22.8)	16.4 (18.0)	0.003

Values are means (standard deviations).

the experimental group either consumed no RM or did so only occasionally.

The patients' confidence in the technique (measured on the TCS) after the first treatment session was similar among the experimental and control groups (4.6 vs. 4.5, respectively; $p = 0.48$). The patients, therefore, were confident in the treatment being received. On the contrary, the per protocol analysis of the second block of questions revealed a statistically significant difference ($p < 0.001$) between the group treated with acupuncture (mean = 5.1) and the control group (mean = 3.6). This estimate correlated with the pain-VAS results at one week after ending treatment (T1) (Pearson correlation coefficient $r = -0.681$, $p < 0.001$).

The adjustment for unbalanced variables at T0 provided estimators of the T0–T1 change that were slightly different from those arising from bivariate analysis, although the same result variables (pain-VAS, HNP, ACM and Physical Component Summary SF-36) remained statistically significant, as shown in Table 7.

Table 5
Intention to treat analysis for the mean difference between groups and the standardised effect size one week after the final treatment (T1) compared with baseline values (T0)

Variables[a]	Acupuncture $n = 61$	Control $n = 62$	Mean difference (95% CI)	p value between groups	Standardised effect size (95% CI)
Pain-VAS (0–100 mm)	42.1 (21.1)	14.0 (15.7)	28.1 (21.4 – 34.7)	<0.001	1.51 (1.10 – 1.90)
Pain-VAS %	62.2 (28.5)	20.4 (22.5)	41.9 (32.7 – 51.0)	<0.001	1.63 (1.21 – 2.03)
NPQ (0–100 scale)	30.2 (13.6)	12.7 (14.9)	17.5 (12.4 – 2.6)	<0.001	1.23 (0.83 – 1.60)
ACM (degrees)	57.2 (48.4)	33.6 (48.5)	23.6 (6.3 – 41.0)	0.008	0.49 (0.13 – 0.84)
PCM (degrees)	17.3 (40.4)	8.9 (31.3)	8.3 (−4.6 – 21.2)	0.21	0.23 (−0.12 – 0.59)
SF-36 PCS (0–100 scale)	6.3 (11.1)	0.7 (8.2)	5.6 (2.1 – 9.0)	0.002	0.57 (0.21 – 0.93)
SF-36 MCS (0–100 scale)	5.8 (15.4)	6.3 (15.0)	−0.5 (−5.9 – 4.9)	0.861	−0.03 (−0.39 – 0.32)
RM, numbers of patients (percentages)				<0.001[c]	
None	43 (70.5)	11 (17.7)	4.0 (2.3 – 7.0)[b]		
Occasional	11 (18.0)	8 (12.9)			
Prescribed dose	7 (11.5)	29 (46.8)			
Above prescribed dose	–	13 (21.0)			
Other analgesic medication	–	1 (1.6)			

Values are means (standard deviations) unless otherwise indicated.

[a] Pain-VAS, intensity of neck pain; Pain-VAS %, relative change in intensity of neck pain (basal-final/basal); NPQ, Northwick Park neck pain questionnaire; ACM, active cervical mobility; PCM, passive cervical mobility; SF-36, Short Form-36; PCS, physical component summary; MCS, mental component summary; RM, consumption of rescue medication (assessed at 1 week after ending treatment).

[b] RR (CI = 95%) of the patients who took no rescue medication vs. the other RM categories.

[c] χ^2 test.

Table 6
Changes in the results variables from baseline to the end of the follow up (6 months after end of treatment)

Variables[a]	Acupuncture $n = 45$	Control $n = 40$	Mean difference (95% CI)	p value	Standardised effect size (95% CI)
Pain-VAS (0–100 scale)	41.1 (26.9)	26.8 (25.9)	14.4 (2.9 – 25.8)	0.014	0.54 (0.10 – 0.97)
SF-36 PCS (0–100 scale)	9.3 (11.0)	5.3 (8.0)	4.0 (−0.1 – 8.1)	0.054	0.41 (−0.02 – 0.84)
SF-36 MCS (0–100 scale)	8.0 (13.5)	5.2 (14.1)	2.8 (−3.1 – 8.8)	0.351	0.20 (−0.23 – 0.63)
IMV	2.5 (2.6)	1.1 (4.3)	1.5 (−0.1 – 3.0)	0.063	0.40 (−0.03 – 0.83)
RM, numbers of patients (percentages)				0.035[b]	
None	26 (57.8)	12 (30.0)			
Occasional	13 (28.9)	15 (37.5)			
Prescribed dose	5 (11.1)	8 (20.0)			
Above prescribed dose	1 (2.2)	5 (12.5)			
Other analgesic medication	–	–			

Values are means (standard deviations) unless otherwise indicated.
[a] Pain-VAS, intensity of neck pain; SF-36, Short Form-36; PCS, physical component summary; MCS, mental component summary; ICM, visits during previous 3 months to GP or specialist because of neck pain; RM, consumption of rescue medication (assessment at 6 months after ending treatment).
[b] χ^2 test.

3.4. Side effects

The adverse reactions to treatment were mild and affected the experimental and control groups to a similar degree. The acupuncture group reported four treatment-related adverse reactions (swelling of the hand, bruising, pain and ulcer of the ear), while there were two adverse reactions among the control group (cephalea and aggravation of the symptoms).

4. Discussion

4.1. Interpretation of the results

The comparison of the experimental and control groups in this study reveals differences that are statistically significant and clinically relevant in terms of effectiveness in reducing neck pain, measured on a visual analogue scale. The relative change in the mean intensity of neck pain (basal-final/basal) among the acupuncture group was 62.2% (SD 28.5), compared with 20.4% (SD 22.5) among the control group. These differences remained evident in the sensitivity analysis, with per protocol and various forms of ITT analysis. An improvement was also found in all the secondary variables, except MCS SF-36 and PCM.

At six months after ending the treatment, the trend of the results remained in this line, although the effect size was reduced, with the difference being statistically significant only in the case of the pain-VAS variable, the effect size of which varied from intense (1.51) to moderate (0.54), according to the benchmarks proposed by Cohen (1988). The duration of the treatment was estimated on the basis of clinical experience at the PTU. The improvement observed often decreased over the following six months, but remained acceptable for the patients who regularly attended the PTU, enabling the services provided to be optimised. Furthermore, the treatment was safe and produced few, and only mild, side effects.

Table 7
Intention to treat analysis (WC method) in results variables adjusted by basal variables by multiple linear regression models

Variables[a]	Coefficient	CI 95%	p value
1. Basal-final pain-VAS (ITT)	28.474	21.632 – 35.315	<0.001
2. Basal-final NPQ (ITT)	17.980	13.012 – 23.429	<0.001
3. Basal-final ACM (ITT)	28.302	13.418 – 43.185	<0.001
4. Basal-final PCM (ITT)	6.980	−4.648 – 18.608	0.237
5. Basal-final MCS SF-36 (ITT)	2.775	−2.312 – 7.861	0.281
6. Basal-final PCS SF-36 (ITT)	7.824	20.463 – 33.350	<0.001

Adjusted for: 1, RM and basal pain-VAS; 2, Basal pain-VAS and basal NPQ; 3, Basal ACM, radiologic diagnosis and basal PCM; 4, Basal PCM, radiologic diagnosis and basal NPQ; 5, Basal MCS SF-36, basal pain-VAS and RM; 6, Basal PCS SF-36.
[a] Pain-VAS, intensity of neck pain; ITT, intention to treat; NPQ, Northwick Park neck pain questionnaire; ACM, active cervical mobility; PCM, passive cervical mobility; SF-36, Short Form-36; PCS, physical component summary; MCS, mental component summary; RM, consumption of rescue medication.

4.2. Methodological limitations

The groups were homogeneous, according to the baseline evaluation, which indicates that the randomisation procedure functioned well, although the method of using sealed opaque envelopes is not foolproof.

The control measure adopted was an inert technique that produced no stimulus in the patient, unlike other control procedures that have been used, such as sham acupuncture, and is supported by various studies which show that the credibility of this technique is comparable to that of acupuncture (Petrie and Hazleman, 1985). In the present case, the credibility study, after the first treatment session, produced similar results in both

groups, thus confirming the adequacy of the placebo. On the contrary, after the treatment had ended, significant differences were observed between the two groups, in favour of the experimental group; this is a logical consequence of the better results obtained by the latter group. Other studies have reported similar results concerning the improvement in groups given acupuncture treatment (Vincent, 1990) or, if no clinically relevant difference was found, that credibility remained at similar levels among the two groups until the end of the treatment period (White et al., 2004). In our case, the application of the techniques to both groups by the same person made it easier to standardise the procedure; however, although this professional was trained to prevent the patients' noticing any difference in the treatment given to one group or the other, this might comprise a limitation of the study.

Few patients withdrew during the study, and results were unaffected, as shown by the sensitivity analysis with different types of ITT and PP analyses. However, during the subsequent follow up, the differences between the groups diminished, which could be attributed to a dilution of the acupuncture effect. On the other hand, evidence of possible selection bias arose during the follow up of the cohort, with differences being observed between the patients abandoning the study. While in the experimental group, most of those who left the study were taking less rescue medication than that prescribed, in the control group the majority of patients who dropped out were consuming higher than recommended doses of medication. This suggests an alternative explanation to the hypothesis that the acupuncture effect had been diluted in the six months following treatment, as the reduction in the variable-change differences might have been caused, totally or partially, by differences in the characteristics of those abandoning each group. This question should be examined in future studies with a medium-term follow up procedure, as it is reasonable to assume it would also affect patient follow up in standard clinical practice.

An attempt was made to minimize the possibly incorrect classification caused by the above-mentioned effect by using reproducible questionnaires previously tested for use in Spain; moreover, great care was taken at all times to ensure that the assessors worked blind. The effect of possible unbalanced confounders was dealt with by multivariate analysis, which revealed only slight variations in comparison with the raw analysis.

Our original hypothesis was that there is a difference between the pain relief achieved with the acupuncture group, with respect to the control group, of at least 12.5 points on the pain-VAS scale, and this value was, in fact, exceeded. Two variables were found not to be statistically significant, namely PCM and SF-36 MCS. In the case of the former, the possibilities of significant variation between pre- and post-treatment states are minimal, due to the normal limitations of cervical functioning, while ACM is more closely related to the pain experienced by the patient. In the case of MCS, psychosocial variables require more time for significant changes to become apparent; moreover, this scale includes items that are not directly related to the treatment in question, but depend on external social variables. During the 6-month follow up, the MCS measured for the experimental group was found to be better than that of the control group, but this improvement could have been influenced by selection bias.

4.3. Other studies of the question

The latest systematic reviews published (White and Ernst, 1999; Smith et al., 2000; White et al., 2002) showed that the studies made to date continue to present problems of quality, and the authors of these reviews call for new, methodologically acceptable studies to be made. Since the latest review was published, new research efforts have taken place in which the highlighted deficiencies have been addressed. In the study by Irnich et al. (2001), an inert placebo was used, in the same number of sessions as in the present study, and statistically significant differences were found between the group treated with traditional Chinese acupuncture and another group treated with massage, while no such differences were found between the former and the group treated with the placebo. A subsequent analysis in which an adjustment was made for baseline measurements by means of covariance analysis showed pain relief to be greater among the acupuncture group than among those given the placebo, suggesting that acupuncture is beneficial in cases of chronic neck pain, and that this benefit is not achieved with the placebo (Vickers, 2004). White et al. (2004) performed a test with Western acupuncture techniques and obtained results that, although statistically significant, did not achieve a given level of clinical relevance (established by the authors as representing a difference equal to or exceeding 30% between the active treatment and the placebo), as only 12% difference was achieved between the two groups. The greater difference between the latter study and the present contribution results from the combination of ear auricle points, together with a balanced selection of proximal and distal points. Available evidence, together with studies carried out with reference to other sites (Vas et al., 2004), favours the external validity of the use of acupuncture in the treatment of chronic pain. Nevertheless, given the variability of the results produced in different studies, we believe it is necessary to investigate further the number and selection of acupoints on the basis of a diagnosis that is as accurate as possible (according to traditional Chinese medicine). In addition to the above, there are differences between our study and those by White and Irnich that may have

influenced the lack of similarity between the results. The first of these is the baseline level of pain intensity experienced by the patients. In our case, this was 68.7 mm (SD 14.3) among the experimental group and 72.3 mm (SD 15.4) among the control group, with a difference of 14 mm in the best of cases with the values derived from the other two studies. The mean age of the patients in our study was also lower, as was the duration of the illness. Another circumstance that could have led our results to differ from those of the above-mentioned studies is the nature of the organisation where the treatment was implemented, as medical care in the Andalusian Public Health System is totally free of charge and the patient incurs no expense with respect to the treatment received.

5. Conclusions

In the treatment of the intensity of chronic neck pain, acupuncture is more effective than the placebo treatment and has a safety pattern that makes it suitable for standard clinical practice.

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References

Aker PD, Gross AR, Goldsmith CH, Peloso P. Conservative management of mechanical neck pain: systematic overview and meta-analysis. BMJ 1996;313:1291–6.

Alonso J, Prieto L, Anto JM. The Spanish version of the SF-36 Health Survey (the SF-36 health questionnaire): an instrument for measuring clinical results. Med Clin (Barc) 1995;104:771–6.

Bayreuther J. A double-blind cross-over study to evaluate the effectiveness of acupressure at pericardium 6 (P6) in the treatment of early morning sickness (EMS). Complement Ther Med 1994;2:70–6.

Beaudreuil J, Gallou JJ. Acupuncture et cervicalgies chroniques: analyse critique de la littérature. Revue du Rhumatisme 2004;71:721–3.

Bogduk N. Neck pain. Aust Fam Physician 1984;13:26–30.

Borghouts JA, Koes BW, Bouter LM. The clinical course and prognostic factors of non-specific neck pain: a systematic review. Pain 1998;77:1–13.

Borkovec TD, Nau SD. Credibility of analogue therapy rationales. J Beh Ther Exp Pschiat 1972;3:257–60.

Bovim G, Schrader H, Sand T. Neck pain in the general population. Spine 1994;19:1307–9.

Brown BW, Brauner C, Chan A, Gutierrez D, Herson J, Lovato J, Polsley J, Russell K, Venier J. DSTPLAN Calculations for Sample Sizes and Related Problems. (4.2). 2000. Houston, The University of Texas.

Cobos R, Vas J. Manual de Acupuntura y Moxibustión, vol. 1. Beijing: Morning Glory; 2000.

Coe R. Effect size calculator. http://www.cemcentre.org/ebeuk/research/effectsize/Calculator.htm. 1-2-2005.

Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale (NJ): Lawrence Erlbaum Assoc.; 1988.

Cote P, Cassidy JD, Carroll LJ, Kristman V. The annual incidence and course of neck pain in the general population: a population-based cohort study. Pain 2004;112:267–73.

Dziedzic K, Hill J, Lewis M, Sim J, Daniels J, Hay EM. Effectiveness of manual therapy or pulsed shortwave diathermy in addition to advice and exercise for neck disorders: a pragmatic randomized controlled trial in physical therapy clinics. Arthritis Rheum 2005;53:214–22.

EMEA The European agency for the evaluation of medical products. Evaluation of medicines for human use. Points to consider on missing data. http://www.emea.eu.int/pdfs/human/ewp/177699EN.pdf. 2001. 1-3-2005.

Gajdosik RL, Bohannon RW. Clinical measurement of range of motion. Review of goniometry emphasizing reliability and validity. Phys Ther 1987;67:1867–72.

Gonzalez T, Balsa A, Sainz de MJ, Zamorano E, Gonzalez I, Martin-Mola E. Spanish version of the Northwick Park Neck Pain Questionnaire: reliability and validity. Clin Exp Rheumatol 2001;19:41–6.

Gross AR, Aker PD, Goldsmith CH, Peloso P. Physical medicine modalities for mechanical neck disorders. Cochrane Database Syst Rev 2000;CD000961.

Harrison DE, Bula JM, Gore DR. Roentgenographic findings in the cervical spine in asymptomatic persons: a 10-year follow-up. Spine 2002;27:1249–50.

Irnich D, Behrens N, Molzen H, Konig A, Gleditsch J, Krauss M, et al. Randomised trial of acupuncture compared with conventional massage and "sham" laser acupuncture for treatment of chronic neck pain. BMJ 2001;322:1574–8.

Leak AM, Cooper J, Dyer S, Williams KA, Turner-Stokes L, Frank AO. The Northwick Park Neck Pain Questionnaire, devised to measure neck pain and disability. Br J Rheumatol 1994;33:469–74.

Lewith GT, Vincent C. On the evaluation of the clinical effects of acupuncture: a problem reassessed and a framework for future research. J Altern Complement Med 1996;2:79–90.

Makela M, Heliovaara M, Sievers K, Impivaara O, Knekt P, Aromaa A. Prevalence, determinants, and consequences of chronic neck pain in Finland. Am J Epidemiol 1991;134:1356–67.

Morey SS. NIH issues consensus statement on acupuncture. Am Fam Physician 1998;57:2545–6.

Paterson C, Dieppe P. Characteristic and incidental (placebo) effects in complex interventions such as acupuncture. BMJ 2005;330:1202–5.

Petrie J, Hazleman B. Credibility of placebo transcutaneous nerve stimulation and acupuncture. Clin Exp Rheumatol 1985;3:151–3.

Pietrobon R, Coeytaux RR, Carey TS, Richardson WJ, DeVellis RF. Standard scales for measurement of functional outcome for cervical pain or dysfunction: a systematic review. Spine 2002;27:515–22.

Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-based medicine: how to practice and teach EBM. London: Churchill-Livingstone; 2000.

Silva Ayzaguer LC. Muestreo para la investigación en ciencias de la salud. Madrid: Ediciones Díaz de Santos; 1993.

Skouen JS, Grasdal AL, Haldorsen EM, Ursin H. Relative cost-effectiveness of extensive and light multidisciplinary treatment programs versus treatment as usual for patients with chronic low back pain on long-term sick leave: randomized controlled study. Spine 2002;27:901–9.

Smith LA, Oldman AD, McQuay HJ, Moore RA. Teasing apart quality and validity in systematic reviews: an example from acupuncture trials in chronic neck and back pain. Pain 2000;86:119–32.

Spitzer WO, Skovron ML, Salmi LR, Cassidy JD, Duranceau J, Suissa S, et al. Scientific monograph of the Quebec Task Force on Whiplash-Associated Disorders: redefining "whiplash" and its management. Spine 1995;20:1S–73S.

Stux G, Pomeranz B. Fundamentos de acupuntura. Barcelona: Masson; 2000.

Thorsteinsson G, Stonnington HH, Stillwell GK, Elveback LR. The placebo effect of transcutaneous electrical stimulation. Pain 1978;5:31–41.

Vas J, Mendez C, Perea-Milla E, Vega E, Panadero MD, Leon JM, et al. Acupuncture as a complementary therapy to the pharmacological treatment of osteoarthritis of the knee: randomised controlled trial. BMJ 2004;329:1216–9.

Vickers AJ. Statistical reanalysis of four recent randomized trials of acupuncture for pain using analysis of covariance. Clin J Pain 2004;20:319–23.

Vincent C. Credibility assessment in trials of acupuncture. Complement Med Res 1990;4:8–11.

Vincent C, Lewith G. Placebo controls for acupuncture studies. J R Soc Med 1995;88:199–202.

Weiner DK, Ernst E. Complementary and alternative approaches to the treatment of persistent musculoskeletal pain. Clin J Pain 2004;20:244–55.

White AR, Ernst E. A systematic review of randomized controlled trials of acupuncture for neck pain. Rheumatology (Oxford) 1999;38:143–7.

White P, Lewith G, Berman B, Birch S. Reviews of acupuncture for chronic neck pain: pitfalls in conducting systematic reviews. Rheumatology (Oxford) 2002;41:1224–31.

White P, Lewith G, Prescott P, Conway J. Acupuncture versus placebo for the treatment of chronic mechanical neck pain: a randomized, controlled trial. Ann Intern Med 2004;141:911–9.

Wood R, Lewith G. The credibility of placebo controls in acupuncture studies. Complement Ther Med 1998;6:79–82.