Acupuncture vs Streitberger needle in knee osteoarthritis – an RCT

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Abstract

Aims To determine the effectiveness of acupuncture as a therapy complementary to the pharmacological treatment of osteoarthritis of the knee.

Methods Randomised, single blind, placebo controlled trial. Patients with osteoarthritis of the knee were randomly assigned to either 12 sessions of true acupuncture or 12 sessions of placebo acupuncture (Streitberger needle), these sessions taking place once a week. A baseline measurement was carried out, followed by further observations at 4, 8, 12 and 16 weeks. The clinical variables were the WOMAC (Western Ontario and McMaster Universities Osteoarthritis) index, knee pain measured by a visual analogue scale (pain VAS), the weekly consumption of diclofenac and the Profile of the Quality of Life of the Chronically Ill (PQLC). The two groups were compared for each of the clinical variables per protocol and by intention to treat. A multiple linear regression model for the dependent variables was constructed.

Results Ninety seven outpatients were selected, with 88 remaining for the per protocol analysis; the analysis of homogeneity concluded that the lost subjects were not significantly different from those that completed the study. The multivariate per protocol model for the relative pain VAS variable showed a difference in improvement of 43.7% (95% CI 29.4% to 58.0%) for acupuncture, compared with the control group. In an intention to treat analysis, the relative improvement was 32.4% (20.3% to 44.4%). In a per protocol analysis, the total WOMAC showed a relative decrease of 52.0% (34.3% to 69.6%) in favour of the acupuncture group, or 37.6% (22.4% to 52.8%) in an intention to treat analysis.

Conclusions The group treated with acupuncture showed significantly better effects, both clinically and statistically, in the reduction of pain intensity as measured by pain VAS, on the WOMAC index and in decreased consumption of diclofenac.

Keywords

Osteoarthritis, knee, acupuncture, placebo, pain, quality of life, randomised controlled trial.

Introduction

The prevalence and the incidence of radiographic signs and the symptomatology of osteoarthritis increase with age, particularly in the most frequently affected joints such as the knee, distal interphalangeal joints and the hip, and especially in women.[1] The standard pharmacological treatment for osteoarthritis of the knee is associated with a large number of adverse effects, which increase in the elderly. According to a recent survey, patients prefer drugs with fewer adverse effects, even if they are less effective.[2]

Acupuncture is increasingly chosen by patients as a complementary treatment for chronic pain,[3] despite its effectiveness being questioned by researchers due to the heterogeneity of trial results and the difficulty in selecting an adequate control.[4;5]

In this study, we assess the specific effect of acupuncture on osteoarthritis of the knee, calculating

its effect on pain, stiffness and joint function, consumption of non-steroidal anti-inflammatory drugs (NSAIDs) and quality of life.

Methods

Design

We designed a randomised, single blind, placebo controlled trial, which was implemented at the Pain Treatment Unit of a Primary Care Centre within the Andalusian Public Healthcare System over a period of two years (2001-2002). The study protocol was approved by the Clinical Trial Committee of the reference hospital and is described in detail elsewhere.[6]

Patients

All the doctors of the Primary Care Centres in the area where the study took place were informed of the study, and their collaboration was requested for the selection of the patients, according to the criteria included in Table 1. All the patients gave formal consent before taking part in the study.

A computer program was used to assign the patients randomly to one of two groups. These were: 1) an experimental group treated with acupuncture; 2) a control group, to whom placebo acupuncture was applied. The distribution of the treatment numbers was kept in sealed, opaque envelopes and a copy was kept on file with the District Health Board; an administrative assistant, unrelated to the study, was responsible for opening the envelopes which contained the treatment numbers assigning the subjects to the experimental or to the control group. The randomisation sequence and group allocation were kept concealed from all study personnel throughout the entire study, including the data analysis phase, except for the doctor who carried out the treatments and for the administrative assistant.

Appropriate measures were adopted to preserve the confidentiality of the participating patients, including making the data anonymous.

Interventions

The selection of acupuncture points was based on treatments known to be effective for osteoarthritis of the knee,[7-9] and distinguished between the prescription of points local to and distal from the painful area; additionally, a diagnosis was made in accordance with traditional Chinese medicine (TCM). Sterile disposable 30 gauge, 45mm acupuncture needles were used at both local and distal points (Table 2), using the Streitberger ring and adhesive plaster as in the control group. For each point, the sensation of *de qi* was elicited. If both knees were painful, both were treated.

All the needles inserted into local points were stimulated electrically in pairs (apart from *Zusanli* ST36) according to the following protocol: Pair 1) *Yanglingquan* GB34 – *Yinlingquan* SP9; Pair 2) *Waixiyan* (or *Dubi* ST35) – *Neixiyan* (together these points are known as *Xiyan* EX-LE-5). Alternate frequency (2/15Hz) electrostimulation was applied for 20 minutes in each session;[10] the stimulation intensity was as high as tolerable, just below the pain threshold, and was adjusted continuously during the procedure. The patients were given one treatment session a week for 12 weeks (12 sessions).

Table 1 **Eligibility criteria**

Inclusion criteria	Outpatient status
	Age 45 years and older
	Pain in one or both knees for the last three months or more
	Radiological evidence of osteoarthritis of the knee (at least Grade 1 according to the Ahlbäck classification[38])
	Willing and able to complete the study questionnaire
Exclusion criteria	Previous treatment with acupuncture
	Contraindication to medication with diclofenac
	Inflammatory, metabolic or neuropathic arthropathies
	Severe concomitant illnesses that might interfere with the clinical evaluation of the patient
	Severe or generalised skin condition
	Pregnancy
	Existing treatment with antineoplastic, corticoid or immunosuppressive drugs

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Table 2 **Points selected in the study**

	Local points	Depth of needling		Distal points	Depth of needling
Standardised	*Yanglingquan* GB34	1 to 1.6cm		*Hegu* LI4	0.8 – 1.0cm
	Yinlingquan SP9	1 to 2.0cm			
	Xiyan EX-LE-5	1 to 1.2cm			
	Zusanli ST36	1 to 1.5cm			
According to TCM diagnosis			Kidney Insufficiency	*Taixi* KI3	0.5 - 0.8cm
			Blood Stagnation	*Sanyinjiao* SP6	1.0 - 1.5cm
			Phlegm-Damp	*Fenglong* ST40	2.5 - 3.0cm

The placebo acupuncture sessions took place with the same frequency and duration, using Streitberger type needles, situated in the same sites as the true acupuncture, and to which the same pairs of electrodes were attached as in the treatment group (simulating an electrical connection), with the intensity of electrostimulation being modified every five minutes.[11;12] The patients participating in this trial were required not to have received treatment with acupuncture beforehand, the idea being that they should be unfamiliar with the procedure employed.

Both treatments were carried out by the same doctor, a specialist in acupuncture and moxibustion (accredited by the University of Medical Sciences, Beijing, China) with more than 15 years' clinical experience in acupuncture.

Twenty one tablets (50mg) of diclofenac (one tablet every eight hours) were given to every patient in each group every week during the period of the treatment, with instructions to reduce the dose if the symptoms showed signs of improvement. Patients with risk factors for peptic ulcer received gastro-protective medication in addition.

Outcome measures

All the patients completed questionnaires on their own or assisted by an independent evaluator, who was also responsible for giving out the weekly doses of diclofenac and collecting any unused tablets. Questionnaires were completed at the beginning of the study and after weeks 4, 8, 12 (one week after having finished the treatment) and 16 (five weeks after the end of treatment).

The primary outcome measure of the treatment was the change in the WOMAC (Western Ontario and McMaster Universities Osteoarthritis) index, Spanish Version LK3.1 with its three subscales;[13] pain (0 to 20), stiffness (0 to 8) and physical function (0 to 68), from baseline to week 12. Furthermore, the intensity of the knee pain was assessed on a visual analogue scale (pain VAS) from 0 to 100, along with the cumulative dose of diclofenac over the 12 weeks of treatment and, finally, the Profile of the Quality of Life of the Chronically Ill (PQLC) in its six dimensions (physical capacity, psychological function, positive mood, negative mood, social function and social wellbeing).[14] In cases of bilateral osteoarthritis of the knee, the most painful knee was taken as the reference for all assessments. The changes in the WOMAC index and pain VAS were adjusted by the basal variables (relative change).

Statistical analyses

The sample size was determined on the basis of the differences found in a previous pilot study, using as a reference the mean total WOMAC score of 20 (SD 10) for the experimental group, and 33 (SD 28) for the control group. Using two sided analysis, a power of 0.8 and a significance level equal to 0.05, and allowing for a 20% dropout rate, we calculated that a minimum of 83 patients were needed. In the end, 97 were selected (Figure 1).

A basal analysis was carried out on the two groups, both for the general variables and for the result variables. For the dropout analysis we used the Mann-Whitney U test for independent samples.

The analysis of the results was carried out per-protocol (PP) and by intention-to-treat (ITT) for the change in the total WOMAC index and pain VAS. For the ITT analysis, missing data were replaced with the worst observed measurement of that variable for the experimental group and the best observed measurement for the control group. A comparison

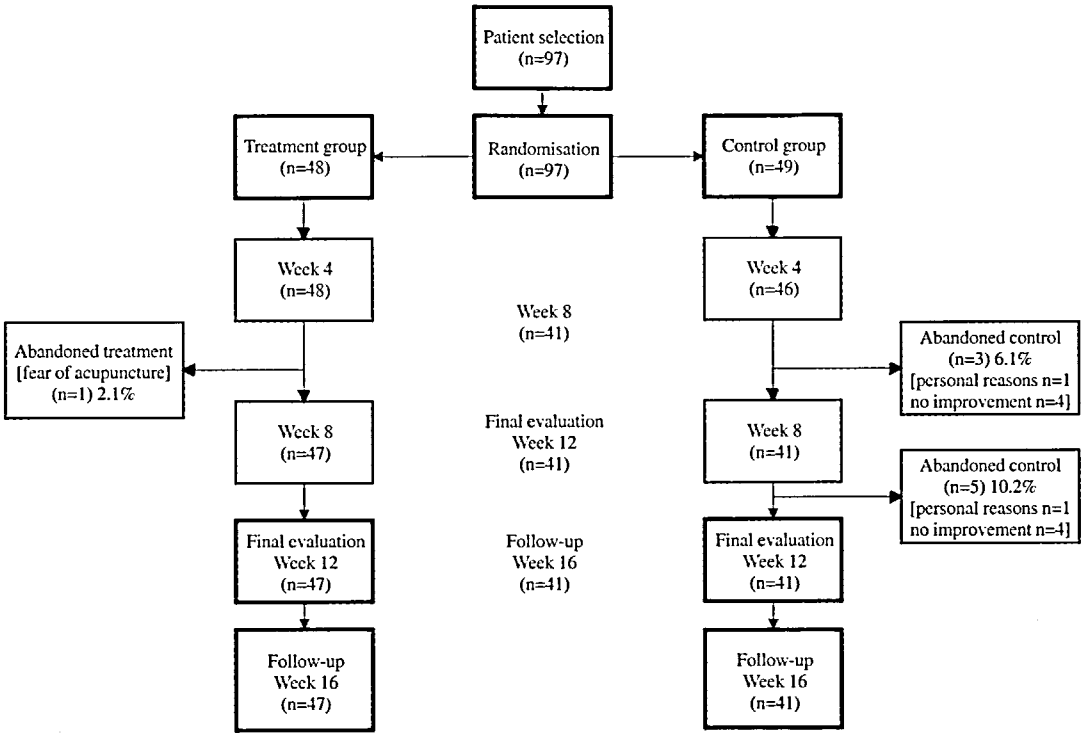

Figure 1 Study flowchart.

of the experimental and control groups was performed for each of the variables and their scales (WOMAC, pain VAS, accumulated diclofenac and PQLC), and the Student's *t* test for independent samples was used. We also analysed the absolute and relative changes of the WOMAC and pain VAS variables. The significance level for all these tests was set at $P<0.05$.

The following multiple linear regression model for the dependent variables was constructed: relative change in WOMAC (WOMAC baseline - WOMAC final / WOMAC baseline * 100) and the relative change in pain VAS (pain VAS baseline - pain VAS final / pain VAS baseline * 100); applied treatment variables (experimental or control group) and total accumulated diclofenac were also forced into the model. Subsequently, potential confounding baseline variables such as sex, age, duration of the condition, location of the osteoarthritis, Ahlbäck index, TCM diagnosis, and body mass index at baseline were introduced by the method of successive steps forwards with an entrance criterion of $P<0.05$ and an exit criterion of $P>0.10$. The model diagnostic was carried out by identifying influential points according to Cook's distance. A new model was constructed, eliminating the observations of Cook's distance above the 90th percentile, in order to identify the possible change in the effect of the treatment. In each of the multivariate models, the interaction between the total accumulated diclofenac and the treatment group was tested. The analyses were carried out using SPSS version 11.5 statistical software.

Results

The characteristics of the 97 patients included in the study are shown in Table 3. The values of the WOMAC index decreased constantly from the start of the treatment until the end, with a slight increase being noticed during the month without treatment (week 16) (see Figures 2-5). The response with respect to the TCM diagnosis is evident in the group treated with acupuncture (relative change in total WOMAC greater than 80%), while in the control group, the degree of relative change was smaller, and moreover with different proportions with respect to the TCM diagnosis (Figure 6). The results of the bivariate PP and ITT analyses have been published previously;[6] the differences in the changes in WOMAC and pain VAS in favour of the experimental

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Table 3 **Baseline characteristics**

Characteristic	Intention to treat population	
	Acupuncture n=48	Control n=49
Age in years, mean (SD)	65.7 (11.0)	68.4 (9.1)
(Age range in years)	(45 to 91)	(48 to 90)
Sex, n (percentage)		
Male	11 (22.9)	5 (10.2)
Female	37 (77.1)	44 (89.8)
Marital status, n (percentage)		
Married	38 (79.2)	29 (59.2)
Separated	1 (2.1)	1 (2.0)
Single	1 (2.1)	-
Divorced	-	1 (2.0)
Widowed	8 (16.7)	18 (36.7)
Education, n (percentage)		
None	14 (29.2)	25 (51.0)
Primary	32 (66.7)	22 (44.9)
Secondary	2 (4.2)	2 (4.1)
Occupation, n (percentage)		
Unskilled	22 (45.8)	15 (30.6)
Skilled	6 (12.5)	1 (2.0)
Public sector	1 (2.1)	-
Self employed	1 (2.1)	-
Farmer	1 (2.1)	5 (10.2)
None	17 (35.4)	28 (57.1)
Currently employed, n (percentage)		
Yes	3 (6.3)	1 (2.0)
No	45 (93.8)	48 (98.0)
Traditional Chinese diagnostic		
Bi + Phlegm-Damp	20 (41.7)	27 (55.1)
Bi + Blood stagnation	19 (39.6)	14 (28.6)
Bi + Kidney deficiency	9 (18.8)	8 (16.3)
Diagnosis, n (percentage)		
Patellofemoral	29 (60.4)	31 (63.3)
Medial tibiofemoral	31 (64.6)	29 (59.2)
Lateral tibiofemoral	14 (29.2)	19 (38.8)
Ahlbäck score, n (percentage)		
1	19 (39.6)	14 (28.6)
2	24 (50.0)	21 (42.9)
3	3 (6.3)	9 (18.4)
4	2 (4.2)	5 (10.2)
Duration of osteoarthritis in years [mean (SD)]	6.5 (8.7)	8.5 (8.4)
Body mass index, mean (SD)	32.4 (6.1)	33.6 (5.8)
Knee affected, n (percentage)		
Right	14 (29.2)	8 (16.3)
Left	10 (20.8)	8 (16.3)
Both	24 (50)	33 (67.3)
pain VAS	58.9 (11.2)	60.3 (13.7)
WOMAC		
WOMAC total	57.1 (16.3)	57.7 (18.6)
WOMAC pain	12.4 (3.4)	12.1 (4.0)
WOMAC stiffness	4.1 (2.6)	4.1 (3.0)
WOMAC function	40.5 (12.2)	41.5 (13.9)
PLQC		
Physical capability	2.1 (0.6)	1.9 (0.6)
Psychological functioning	2.3 (0.5)	2.2 (0.6)
Positive mood	2.1 (0.7)	1.9 (0.8)
Negative mood	2.8 (0.8)	2.8 (0.8)
Social functioning	2.4 (0.5)	2.2 (0.7)
Social wellbeing	3.1 (0.4)	3.0 (0.6)

VAS = visual analogue scale
WOMAC = Western Ontario and McMaster Universities Osteoarthritis index
PLQC = Profile of Quality of Life in the Chronically Ill

group are statistically significant and clinically relevant. The mean differences between the absolute and relative changes are shown in Table 4.

The multivariate PP model for the change in relative pain VAS shows a decrease of 43.7% (95% CI 29.4% to 58.0%) in the experimental group in comparison with the control group. This decrease is lower in the ITT analysis (32.4% [20.3% to 44.4%]). The exclusion of influential points brings the figure down to 23.2%, a difference which is statistically significant. For the relative change in the WOMAC index total, the multivariate PP model shows a relative fall of 52.0% (34.3% to 69.6%), which is 37.6% (22.4% to 52.8%) in the ITT analysis, increasing slightly with the exclusion of influential points from the PP analysis (59.7% [45.9% to 73.6%]) (Table 5). None of the terms of interaction between the diclofenac and acupuncture proved to be statistically significant.

Discussion

The results reported here are comparable to those previously published concerning the main outcome variables,[6] but contribute a greater wealth of information by showing the results of secondary measurements after 4, 8 and 16 weeks, and by analysing the changes observed with respect to the TCM diagnosis made. We see that for the patients in the experimental group there was a relative change exceeding 80% on the WOMAC index in the final assessment, while in the control group patients this change differs depending on the TCM diagnosis, the worst results obtained being the response of the patients with Kidney Insufficiency, followed by those with Blood Stagnation and those with Phlegm-Damp. In a series of previously reported cases,[9] we detected three syndromes in addition to the situation of painful impediment (*Bi* syndrome), namely Kidney Insufficiency, Phlegm-Damp and Spleen Insufficiency. In the study presented here, the Blood Stagnation syndrome can be observed, in most cases caused by the *Bi* syndrome and by Spleen Insufficiency.

By definition, a placebo must be inert, which is why we believe that the control method decided upon (with no piercing of the skin) is the most appropriate; it is intended to eliminate all non-specific effects of the puncture, in the awareness that any stimulus provoked by a needle piercing the skin may

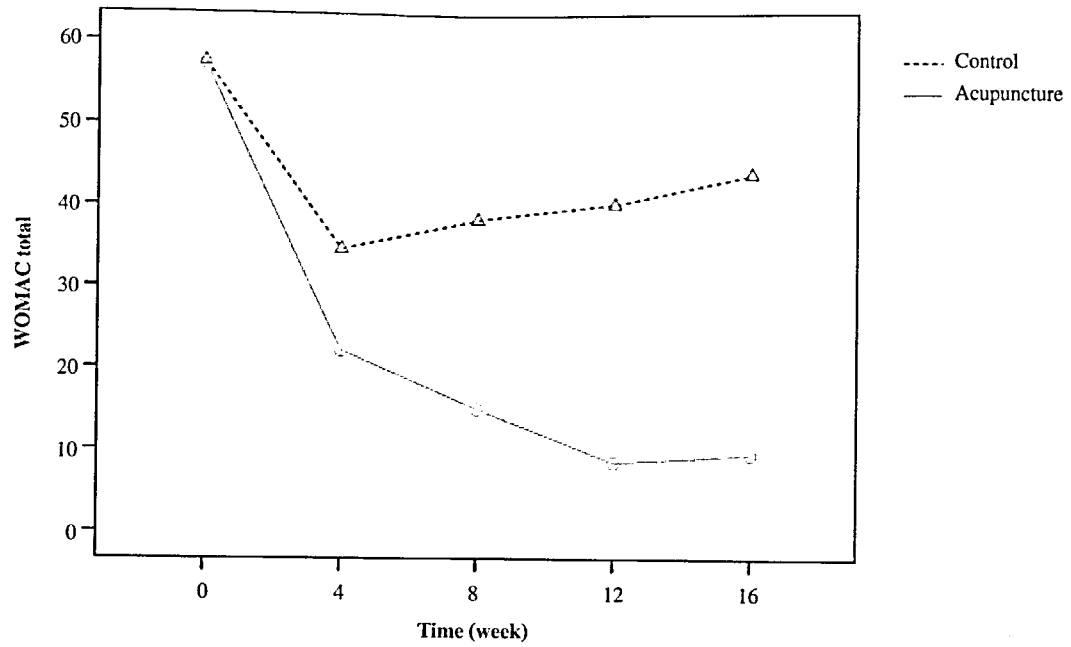

Figure 2 Mean WOMAC total scores from baseline to week 16 (follow-up).

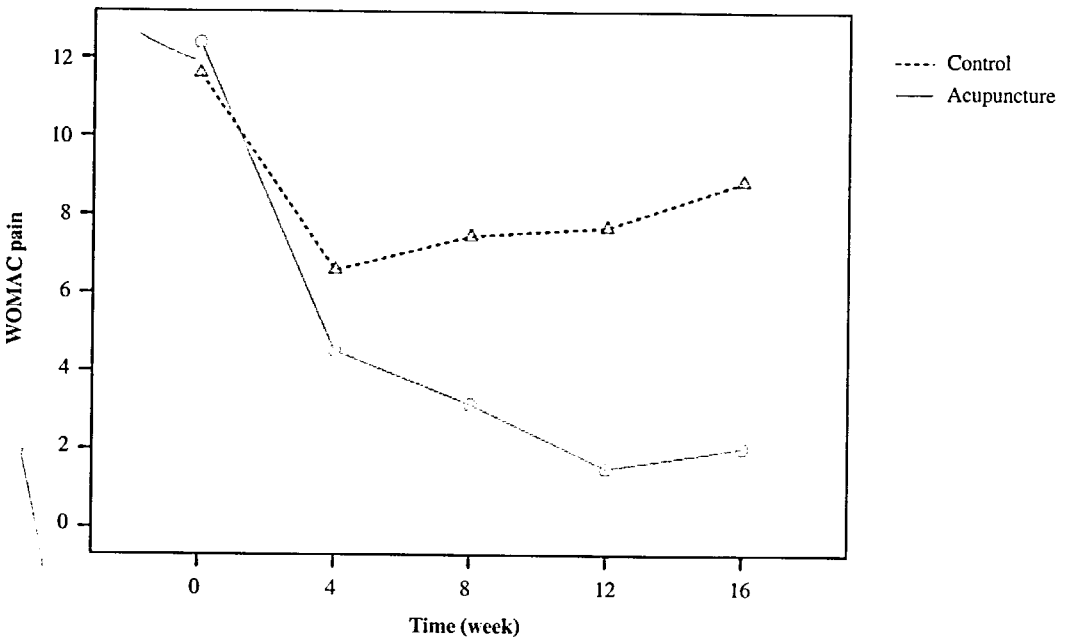

Figure 3 Mean WOMAC pain scores from baseline to week 16 (follow-up).

be capable of activating the spinal nociceptive neurones and sending an excitatory message to the nerve centres, causing a non-specific analgesic effect due among other factors to the activation of the pain suppression system in the spinal cord (diffuse noxious inhibitory controls);[15-17] the credibility of this placebo technique has been demonstrated beforehand,[18,19] although it was not evaluated in the present study.

Although we give the results of the follow up to 16 weeks, after over a month without treatment, this is an insufficient period to assess the effects of the treatment in the medium term. The design is not strictly double blind, given that this would be

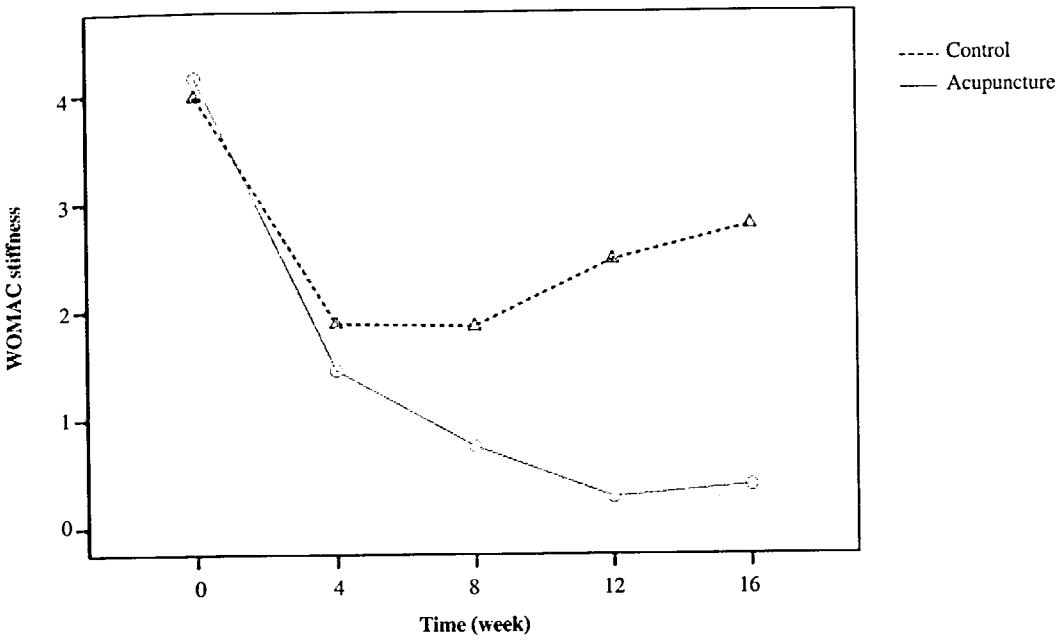

Figure 4 Mean WOMAC stiffness scores from baseline to week 16 (follow-up).

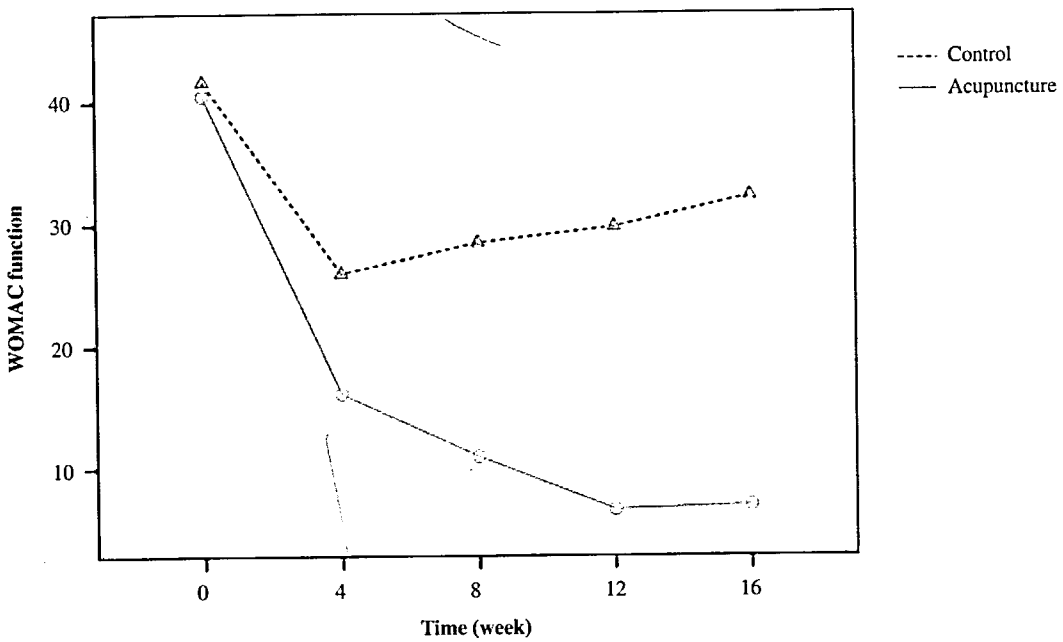

Figure 5 Mean WOMAC function scores from baseline to week 16 (follow-up).

impossible with such complex techniques as acupuncture, but the evaluation of the result variables was independent and blind, and thus the evaluators were unaware of the distribution of the different groups. Among the inclusion criteria was the absence of previous experience of acupuncture, in order to avoid patients recognising the group to which they had been assigned. All participants, both those in the experimental and in the control groups, completed every one of the treatment sessions. The patients who abandoned the control group, whether because their symptoms did not improve or for other, personal reasons, did not state at any time that they were included within the placebo group. Furthermore, the

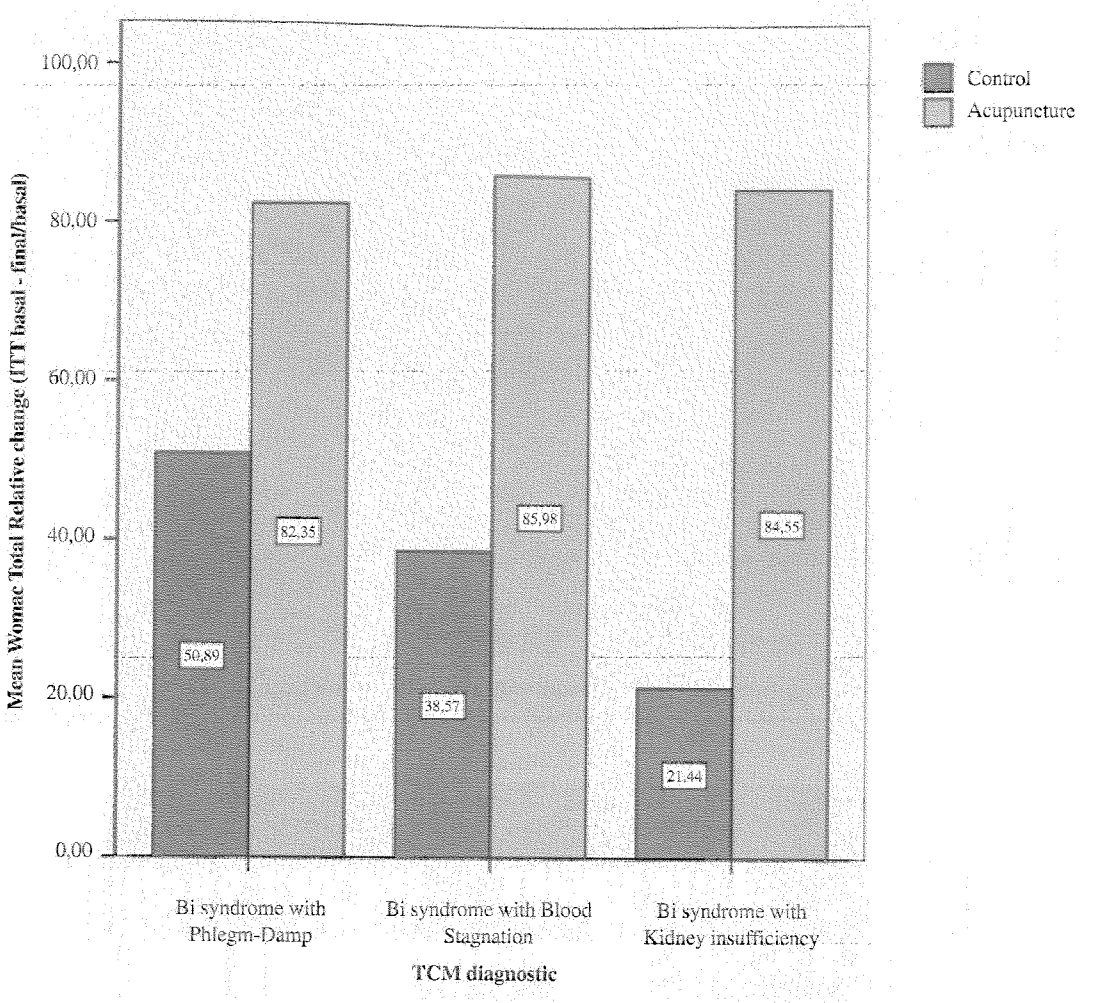

Figure 6 Comparison of the relative improvement in the WOMAC index, with respect to TCM diagnosis.

Table 4 **Bivariate analysis ITT at week 12**

Variable	Acupuncture mean (SE)	Control mean (SE)	Acupuncture vs control mean difference (95% CI)	P value
pain VAS AC	48.33 (1.8)	23.04 (3.7)	25.30 (16.9 to 33.7)	<0.001
pain VAS RC	82.50 (2.4)	36.67 (6.6)	45.82 (31.7 to 59.9)	<0.001
WOMAC total AC	47.60 (2.7)	24.35 (3.8)	23.26 (14.0 to 32.6)	<0.001
WOMAC total RC	84.19 (3.2)	42.56 (6.0)	41.63 (28.1 to 55.2)	<0.001
WOMAC pain AC	10.71 (0.6)	5.69 (0.8)	5.01 (3.0 to 7.0)	<0.001
WOMAC pain RC	86.05 (2.9)	46.10 (6.2)	39.94 (26.3 to 53.5)	<0.001
WOMAC stiffness AC	3.73 (0.4)	2.06 (0.4)	1.67 (0.5 to 2.8)	=0.004
WOMAC stiffness RC	72.58 (6.9)	39.0 (8.1)	33.59 (12.5 to 54.7)	=0.002
WOMAC function AC	33.17 (2.0)	16.60 (2.8)	16.57 (9.8 to 23.4)	<0.001
WOMAC function RC	82.94 (3.4)	39.84 (6.2)	43.10 (29.0 to 57.2)	<0.001

AC = absolute change (baseline – final)

RC = relative change (baseline – final / baseline *100)

VAS = visual analogue scale

WOMAC = Western Ontario and McMaster Universities Osteoarthritis index

Table 5 **Multivariate model for relative changes in WOMAC total score and pain VAS**

Dependent variable	β (95% CI)	P value
Pain VAS RC (PP analysis)		
Constant	55.33 (36.9 to 73.8)	<0.001
Acupuncture vs control	43.68 (29.4 to 58.0)	<0.001
Total diclofenac	-0.19 (-0.3 to -0.1)	<0.001
Cook's distance < 0.12		
Acupuncture vs control	32.96 (22.6 to 43.3)	<0.001
Pain VAS RC (ITT analysis)		
Constant	84.94 (70.2 to 99.7)	<0.001
Acupuncture vs control	32.38 (20.3 to 44.4)	<0.001
Total diclofenac	-0.30 (-0.4 to -0.2)	<0.001
Cook's distance <0.32		
Acupuncture vs control	23.20 (15.1 to 31.2)	<0.001
WOMAC total RC (PP analysis)		
Constant	99.79 (77.0 to 122.6)	<0.001
Acupuncture vs control	51.96 (34.3 to 69.6)	<0.001
Total diclofenac	-0.19 (-0.3 to -0.1)	<0.001
Cook's distance <0.36		
Acupuncture vs control	59.74 (45.9 to 73.6)	<0.001
WOMAC total RC (ITT analysis)		
Constant	137.21 (118.6 to 155.8)	<0.001
Acupuncture vs control	37.58 (22.4 to 52.8)	<0.001
Total diclofenac	-0.49 (-0.6 to -0.4)	<0.001
Cook's distance <0.31		
Acupuncture vs control	37.58 (22.4 to 52.8)	<0.001

Each model includes the effect of treatment after removing observations corresponding to possible influential points (excluding observations with large Cook's distance)

RC = relative change (baseline – final / baseline *100)

VAS = visual analogue scale

WOMAC = Western Ontario and McMaster Universities Osteoarthritis index

six people who dropped out due to a lack of improvement thus reinforced the argument that the placebo really was inert.

The reduction in the consumption of diclofenac is of added importance, given that although the effect has not been quantified, the expenses arising from the treatment of its adverse effects are thus reduced. In our case, as acupuncture is included as a healthcare provision within the Andalusian Public Health Service, studies were carried out to show improvements in the cost/benefit ratio, this resulting mainly from a reduction in the consumption of NSAIDs and analgesics, in addition to the reduced side effects resulting from the latter.[20;21]

Since the completion of our study, diverse trials have been published with varying results,[22;24] none making clear the specific effects of acupuncture, especially in two of these,[23;24] where the differences between true acupuncture and sham acupuncture differ noticeably; one aspect that does distinguish the studies is in the selection of non-acupuncture points. In the latter study, many of the points used for the sham acupuncture group, even though they are not specific for alleviating knee pain, do correspond to acupuncture points, most of these being termed New points or Curious points.[25-27] It would be interesting to be able to analyse the response of patients in relation to the experience of the doctor who applies the true acupuncture technique, and to the number of patients recruited for the study and subsequently treated. Moreover, the puncture at points *Waixiyan* (also known as *Dubi* ST35) and *Neixiyan* requires a special degree of skill; this puncture is normally recommended to be carried out to a depth of 2.5cm, at least, and aimed towards *Weizhong*, BL40; among patients with osteoarthritis of the knee, this technique, if not performed correctly, may damage the articular surface, aggravating pain and stiffness and also worsening the articular functioning of the knee. Taking into consideration the differences

in effects seen in the various studies of acupuncture on the question that have been published, it is necessary to assess the effects in relation to the different types of manipulation and to the depth of the puncture.

Conclusions

Acupuncture is a therapeutic technique that has been found to be effective and safe for the treatment of osteoarthritis of the knee, alleviating pain, lessening stiffness and improving the functioning of the joint to a greater degree than is achieved solely by the use of NSAIDs.

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