Acupuncture vs Streitberger needle in knee osteoarthritis – an RCT

Jorge Vas, Camila Méndez, Emilio Perea-Milla

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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.
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>
<thead>
<tr>
<th>Table 1</th>
<th>Eligibility criteria</th>
</tr>
</thead>
</table>
| **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)  
| | 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 |
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.\textsuperscript{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 gastroprotective 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;\textsuperscript{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).\textsuperscript{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

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**Table 2 Points selected in the study**

<table>
<thead>
<tr>
<th>Local points</th>
<th>Depth of needling</th>
<th>Distal points</th>
<th>Depth of needling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standardised</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yanglingquan GB34</td>
<td>1 to 1.6cm</td>
<td>Hega LI4</td>
<td>0.8 – 1.0cm</td>
</tr>
<tr>
<td>Yinlingquan SP9</td>
<td>1 to 2.0cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xiyan EX-LE-5</td>
<td>1 to 1.2cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zusanli ST36</td>
<td>1 to 1.5cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>According to TCM diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney Insufficiency</td>
<td></td>
<td>Taixi KI3</td>
<td>0.5 - 0.8cm</td>
</tr>
<tr>
<td>Blood Stagnation</td>
<td></td>
<td>Sanyinjiao SP6</td>
<td>1.0 - 1.5cm</td>
</tr>
<tr>
<td>Phlegm-Damp</td>
<td></td>
<td>Fenglong ST40</td>
<td>2.5 - 3.0cm</td>
</tr>
</tbody>
</table>

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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.\textsuperscript{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.

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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
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; the differences in the changes in WOMAC and pain VAS in favour of the experimental
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, 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, 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
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);\textsuperscript{15-17} the credibility of this placebo technique has been demonstrated beforehand,\textsuperscript{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

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

Table 4  Bivariate analysis ITT at week 12

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

AC = absolute change (baseline – final)
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.\textsuperscript{20,21}

Since the completion of our study, diverse trials have been published with varying results,\textsuperscript{22,24} none making clear the specific effects of acupuncture, especially in two of these,\textsuperscript{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.\textsuperscript{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

\begin{table}[h!]
\centering
\caption{Multivariate model for relative changes in WOMAC total score and pain VAS}  
\begin{tabular}{|l|l|l|}
\hline
Dependent variable & $\beta$ (95% CI) & P value \\
\hline
\hline
\multicolumn{3}{|l|}{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 \\
\hline
\multicolumn{3}{|l|}{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 \\
\hline
\multicolumn{3}{|l|}{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 \\
\hline
\multicolumn{3}{|l|}{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 \\
\hline
\end{tabular}
\end{table}

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
Clinical trials

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.

Reference list

Acupuncture vs streitberger needle in knee osteoarthritis – an RCT

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