Acupuncture for Subacute Stroke Rehabilitation

A Sham-Controlled, Subject- and Assessor-Blind, Randomized Trial

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Background: Any adjunctive therapy that may reduce persistent disability after stroke should be considered. Acupuncture is used for this purpose, but there is conflicting evidence on its effectiveness.

Methods: Patients with a recent (<4 weeks) episode of stroke were randomized to receive 12 sessions of either real or sham acupuncture during 2 weeks. The primary outcome was the change in Barthel activities of daily living score at the end of treatment. Secondary outcome measures included National Institutes of Health Stroke Scale score, motoricity index, and quality of life (EQ-5D [EuroQoL-5 Dimensional form] and EQ-VAS [EuroQol—Visual Analog Scale]). Assessments were carried out by blinded physicians.

Results: A total of 116 patients (56 in the real acupuncture group and 60 in the sham group) were randomized, and 98 (real, 48; sham, 50) completed treatment and the 2-week assessment. Patient blinding by means of the sham acupuncture device was successful. Acupuncture was well tolerated except for 1 seizure during a real acupuncture session. The improvements in the Barthel scores were 4 points (interquartile range [IQR], 0-8) vs 3 points (IQR, 0-7) in the real and sham acupuncture groups, respectively (P = .38). The secondary outcome measures also essentially showed no significant effect of acupuncture. Post hoc analysis by baseline severity showed a greater improvement in leg function in the subgroup with baseline Barthel score less than the median (median score, 6): 22 points (IQR, 0-37) vs 4 points (IQR, 0-4) in the acupuncture and sham control groups, respectively (P = .02).

Conclusions: Acupuncture is not superior to sham treatment for recovery in activities of daily living and health-related quality of life after stroke, although there may be a limited effect on leg function in more severely affected patients.

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STROKE REMAINS A MAJOR CAUSE of death and disability worldwide.1-3 The single most effective measure known to reduce mortality and morbidity after acute stroke is multidisciplinary care on an inpatient stroke unit,4 but despite this, major disability persists for many stroke patients. The Perth Community Stroke Study identified a 5-year cumulative risk of new major disability after first-ever stroke of 36%.5 Thus, effective adjunctive therapies that may improve outcome from stroke rehabilitation should be considered.

Acupuncture is used widely in the Far East for stroke rehabilitation,6 but evidence of the effectiveness of acupuncture in the rehabilitation of stroke patients is inconsistent. Two recent systematic reviews have concluded that there is insufficient evidence to support the use of acupuncture for stroke rehabilitation,7,8 mainly because of the poor methodologic quality of most studies, including the particular difficulty in developing an appropriate control. Separating the specific effect of the insertion and stimulation of an acupuncture needle from the wider therapeutic effect of treatment has been controversial.9 To address this issue, we have developed and validated a new nonpenetrating sham acupuncture device.10,11 This has enabled us to conduct a subject- and assessor-blinded, randomized, controlled trial evaluating the effectiveness of manual acupuncture in acute stroke rehabilitation.

METHODS

PARTICIPANTS

We conducted a randomized, controlled clinical trial of acupuncture in stroke rehabilitation in the setting of a large general hospital stroke unit. All stroke patients admitted to the specialist stroke unit at the Royal Devon and Exeter Hospital, Exeter, England, were considered for recruitment. Patients of any age with...
a recent (<4 weeks) clinically or radiologically confirmed stroke (ischemic or hemorrhagic) who were able to give informed consent were eligible for inclusion. Patients were excluded if they had preexisting disability leading to modified Rankin score\textsuperscript{11} of 3 or more, recent history of other serious diseases such as cancer or diseases transmissible by blood, fear of needles, stroke that had occurred under general anesthesia, history of previous acupuncture, or the likelihood of full recovery within 2 weeks. All patients were given full details of the study in both oral and written form. The study received approval from the North and East Devon Research Ethics Committee.

**SAMPLE SIZE**

We estimated that 63 patients were required in each group to detect a clinically relevant 2-point difference in Barthel activities of daily living (ADL) score (scale, 0 [entirely dependent] to 20 [fully independent]) with a power of 80% and an α value of .05. This magnitude of effect was based on an unblinded study of acupuncture in stroke rehabilitation.\textsuperscript{11} Assuming a 30% drop-out rate, we planned to randomize 82 patients to each group. However, recruitment was much slower than planned because many patients were excluded for not meeting the inclusion criteria (stroke too severe or too mild, other abnormality requiring surgery) or not screened because they were admitted to wards other than the main study site for logistical reasons. Recruitment was closed for operational reasons before the required sample size was achieved.

**RANDOMIZATION**

Randomization was stratified by baseline National Institutes of Health Stroke Scale score\textsuperscript{15} of less than 20 or greater than or equal to 20, age less than 70 years or greater than or equal to 70 years, and whether the affected side was dominant or non-dominant. Block randomization was by sequential, sealed, opaque envelopes, and it occurred after the acupuncturist's evaluation (concealed allocation).

**INTERVENTION**

Real acupuncture was performed by means of standard stainless-steel needles (0.30-mm diameter, 40-mm length; AcuPrime; Dong Bang Acupuncture Inc, Chungnam, Korea), manually stimulated to elicit needle sensation (\textit{de qi}). Sham acupuncture was performed with a newly described nonpenetrating sham needle that is blunt and telescopic, giving the impression of insertion but without penetrating the skin (Park Sham Device; 0.30-mm diameter; fully extended length, 40 mm; Dong Bang Acupuncture Inc). This device has been shown not to elicit the sensation of \textit{de qi}, which is believed to be necessary for the therapeutic effect.\textsuperscript{11} Recognized points were used for the real acupuncture group, and sham points at least 1.5 cm away from real points were used for the sham acupuncture group.

In addition to conventional multidisciplinary stroke rehabilitation, all randomized patients received between 9 and 12 sessions of real or sham acupuncture during 2 weeks from a physician of Korean medicine (J.P.) with 5 years' experience in acupuncture. Each treatment session lasted for at least 20 minutes in both groups. Prescriptions of acupuncture points were individually tailored according to 1 of 4 subgroups of Korean acupuncture (defined according to the excess or deficiency of the yin and yang aspect of the patients). Each of the 4 prescriptions comprised 10 points: 6 points determined by the patient's classification (BL66, L11, HT3, HT4, GB43, GB44; LU8, SP3, HT8, HT9, KI17, ST36, LI5, L111, HT7, HT8, SI5; and SP1, SP2, HT8, HT9, LR1, CV4) and 4 points common to all (ST40 [bilateral], CV12, GV20, and GV26). Thus, each treatment involved a total of 11 needles. At the end of 2 weeks of treatment, the success of blinding was tested by asking all patients the following question: “When you volunteered for the trial, you were informed that you had an equal chance of receiving acupuncture or sham (pretend) acupuncture. Which acupuncture do you think you received?”

**OUTCOME MEASURES**

The primary outcome was the change in Barthel ADL score.\textsuperscript{14} Secondary outcome measures included National Institutes of Health Stroke Scale score,\textsuperscript{15} motoricity index,\textsuperscript{16} quality of life (EQ-5D–3 Dimensional form) and EQ-VAS (EuroQol–Visual Analog Scale),\textsuperscript{17} Nottingham Extended ADL score,\textsuperscript{18} Ashworth scale for muscle spasticity,\textsuperscript{19} timed 10-m walk,\textsuperscript{20} 9-hole peg test,\textsuperscript{21} swallowing status ("safe" or "unsafe" swallow based on a bedside swallowing screening test),\textsuperscript{22} and the patient's blinding regarding treatment.\textsuperscript{23} Blinded physician assessors (M.A.J., A.G.H., P.J., or J.C.) screened and recruited patients, and carried out baseline and posttreatment assessments. The first acupuncture treatment was given within 48 hours of screening assessment, followed by the baseline assessment within 72 hours of screening; the posttreatment assessment was done within 2 days of the completion of treatment.

**STATISTICAL ANALYSIS**

Primary and secondary outcome measures were compared between groups on the 2-week data. The analyses were performed on an intention-to-treat basis, with missing data replaced by baseline values. In addition, on the basis of the data from a previous unblinded study,\textsuperscript{11} a post hoc analysis of the primary outcome measure per pair of the real and sham subgroups was performed to look for a differential effect according to baseline severity. Treatment responses were compared between those with baseline Barthel score at or above the median value vs those below the median value (6/20). For within-group comparisons, the Wilcoxon test was used, and for between-group comparisons, either the Mann-Whitney test or \( \chi^2 \) test was used. Blinding indices in both groups were calculated using the method by Bang et al.,\textsuperscript{23} and their statistical significance was tested using 2 independent multinational tests. Most data are presented as median (interquartile range [IQR]) unless otherwise specified, as they were nonparametrically distributed, and \( P<.05 \) (2 sided) was regarded as statistically significant. Statistical analyses were conducted with the SAS software version 9.0 (SAS Institute Inc, Cary, NC).

**RESULTS**

Recruitment commenced on November 20, 1999, and was terminated on August 30, 2003, after 116 patients had been enrolled (56 to receive real acupuncture treatment and 60, sham treatment). Figure 1 shows the flow of participants through the trial. We recruited 9.4% of all patients admitted to the hospital with stroke during the entire study period. End-of-treatment data were complete for 98 (84.5%) of subjects randomized (48 in the real treatment group and 50 in the sham group). Three patients died during the study because their condition deteriorated after randomization, which had been based on the clinical expectation that they would survive. The underlying disease in these deaths was so apparent that the stroke physician in charge ruled out association with acupuncture treatment.
Recent systematic reviews of acupuncture in stroke rehabilitation have not drawn firm conclusions regarding the efficacy of treatment, mainly owing to problems with the quality of previous studies, and have recommended the conduct of adequately controlled and methodologically sound studies.2,28 Previous studies have largely not used blinding, which is a particular difficulty with a physical treatment such as acupuncture, or have been confounded by comparison with another treatment with potential effects.11,24-26 In general, studies of complementary therapies have not been subjected to tests of efficacy and safety equivalent to those for conventional or pharmacologic treatments.27 In this context, our randomized, subject- and assessor-blinded clinical trial of 2 weeks of acupuncture as an adjunct to conventional multidisciplinary stroke rehabilitation has not shown a significant effect of acupuncture on recovery of ADL when compared with control treatment with a novel validated sham acupuncture needle.11 Our results indicate that almost all of the participants either believed they were receiving genuine acupuncture or were unable to tell, and as such we believe our study in stroke rehabilitation to be the first to adequately control for the nonspecific effects of treatment and thus to come as close as possible to testing exclusively the therapeutic effect of needling.

Our principal finding of no difference in the primary outcome measure of Barthel score after 2 weeks of acupuncture or sham acupuncture treatment and thus to come as close as possible to testing exclusively the therapeutic effect of needling.
The timing of assessments affected the result of the effects of acupuncture may be incremental during a longer period. If treatment had been continued longer, as treatment effects may have also been reduced by a lower dropout rate than we anticipated, and our study still represented a welcome secular trend in current UK practice, given that all patients in our study also received specialist stroke unit rehabilitation, but in older studies the lack of an effective intervention for the control group may have cast doubt on the practicality of any treatment in a more favorable light.

We preset the statistical power of 80% at the .05 significance level to test the clinically significant yet plausible treatment effect of a difference of 2 points on the 20-point Barthel score. For comparison, a difference of 1 point on the Barthel score has been regarded as a significant effect of occupational therapy for subacute stroke. 29 The effect size (Cohen’s $d$) of acupuncture in the unblinded Chinese study was 0.72 and 1.29 at 2 weeks and 4 weeks, respectively. 28 We were unable, for various external reasons, to achieve our a priori recruitment target, although this was mitigated by a greater-than-expected improvement in the sham acupuncture group (median [IQR], 6 [3-11] vs 6 [3-7]) of acupuncture in the unblinded Chinese study was 0.72 and 1.29 at 2 weeks and 4 weeks, respectively. 28

<table>
<thead>
<tr>
<th>Outcome Measures</th>
<th>No. of Patients</th>
<th>Real Acupuncture</th>
<th>Sham Acupuncture</th>
<th>Real Acupuncture</th>
<th>Sham Acupuncture</th>
<th>Change Between Baseline and Posttreatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barthel ADL score, median (IQR)</td>
<td>56</td>
<td>11 (5-17)</td>
<td>11 (7.3-15.8)</td>
<td>0 (0-6)</td>
<td>3 (0-7)</td>
<td>0.72 and 1.29 at 2 weeks and 4 weeks, respectively. 28</td>
</tr>
<tr>
<td>NIHSS score, median (IQR)</td>
<td>56</td>
<td>5.5 (2-10.3)</td>
<td>5 (2-9)</td>
<td>3 (0-5)</td>
<td>2 (0-4)</td>
<td></td>
</tr>
<tr>
<td>Motoricity index, median (IQR)</td>
<td>56</td>
<td>6.1 (0-85.3)</td>
<td>71 (21.3-87.3)</td>
<td>0 (0-25)</td>
<td>6.5 (0-23.5)</td>
<td></td>
</tr>
<tr>
<td>Arm score</td>
<td>56</td>
<td>75 (39-99)</td>
<td>75 (54-89)</td>
<td>8 (0-38)</td>
<td>2 (0-23)</td>
<td></td>
</tr>
<tr>
<td>Leg score</td>
<td>56</td>
<td>61 (12-100)</td>
<td>74 (48-100)</td>
<td>12 (0-37)</td>
<td>14 (0-38.3)</td>
<td></td>
</tr>
<tr>
<td>Trunk score</td>
<td>56</td>
<td>16 (13)</td>
<td>11 (2)</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Spastic (ASS $\geq$1), No. (%)</td>
<td>48</td>
<td>48</td>
<td>16 (33)</td>
<td>11 (22)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>NEADL score, median (IQR)</td>
<td>48</td>
<td>6 (12.1)</td>
<td>3 (2-8.5)</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Time to walk 10 m, s</td>
<td>22</td>
<td>22</td>
<td>17 (12-23.5)</td>
<td>24 (17-30)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>9-Hole peg test, s</td>
<td>20</td>
<td>20</td>
<td>37.5 (21.5-92.3)</td>
<td>39 (27.5-121)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>EQ-5D, median (IQR)</td>
<td>48</td>
<td>48</td>
<td>0.64 (0.03-0.8)</td>
<td>0.64 (0.09-0.71)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>EQ-VAS, median (IQR)$^\dagger$</td>
<td>48</td>
<td>48</td>
<td>60 (48.6-72.5)</td>
<td>50 (49.6-70)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: ADL, activities of daily living; ASS, Ashworth spasticity score; EQ-5D, EuroQoL (quality of life)–5 Dimensional form; EQ-VAS, EuroQoL–Visual Analog Scale; IQR, interquartile range; NA, not applicable; NEADL, Nottingham Extended Activities of Daily Living; NIHSS, National Institutes of Health Stroke Scale; VAS, visual analog scale.

$^\dagger$EQ-VAS offers a simple method for obtaining a self-rating of current health-related quality of life by generating a score.

$^*P=0.04.$

$^†$EQ-VAS offers a simple method for obtaining a self-rating of current health-related quality of life by generating a score.

**Table 2. Outcome Measures 2 Weeks After Treatment**

**Figure 2. Change in leg score of motoricity index of subgroups categorized by the baseline severity (greater than or equal to or less than the mean baseline Barthel score [BBS] of 6).**
also a trend with treatment toward a faster (95% confidence interval [CI], 0.33 to 0.61)−0.31 (95% CI, −0.49 to −0.13) (P = .16).

Table 3. Credibility of Sham Acupuncture for Subject Blinding*

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Real</th>
<th>Sham</th>
<th>Do Not Know</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Real acupuncture</td>
<td>21 (22)</td>
<td>0</td>
<td>24 (26)</td>
<td>45 (48)</td>
</tr>
<tr>
<td>Sham acupuncture</td>
<td>19 (20)</td>
<td>4 (4)</td>
<td>26 (28)</td>
<td>49 (52)</td>
</tr>
<tr>
<td>Total</td>
<td>40 (43)</td>
<td>4 (4)</td>
<td>50 (53)</td>
<td>94 (100)</td>
</tr>
</tbody>
</table>

Question Could Not Be Asked, No. Real Sham Do Not Know Total

*Blinding index (acupuncture:sham) = 0.47 (95% confidence interval [CI], 0.33 to 0.61).−0.31 (95% CI, −0.49 to −0.13) (P = .16).


ture although they received the sham treatment. Following the logic of Bang et al.,23 instead of declaring it a failure in blinding, these results indicate high “response bias.” This typifies the situation in which a majority of study participants tends to (or wants to) believe that they were assigned an active or a more effective intervention.35

In conclusion, we contend that our study of the efficacy of acupuncture in subacute stroke rehabilitation, the first of its kind to use a credible sham acupuncture control, has adequately addressed the issue of a specific effect of acupuncture needling alone on recovery of ADL. Our findings are consistent with those from other randomized trials of acupuncture in stroke rehabilitation in identifying no beneficial effect on recovery in ADL and health-related quality of life.24-26 In addition, our data suggest that, should further studies be considered (which would itself be of debatable value), it may be appropriate to confine them to more severely affected patients.

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REFERENCES


