Efficacy of acupuncture for the prophylaxis of migraine: a multicentre randomised controlled clinical trial

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Summary

Background Our aim was to assess the efficacy of a part-standardised verum acupuncture procedure, in accordance with the rules of traditional Chinese medicine, compared with that of part-standardised sham acupuncture and standard migraine prophylaxis with beta blockers, calcium-channel blockers, or antiepileptic drugs in the reduction of migraine days 26 weeks after the start of treatment.

Methods This study was a prospective, randomised, multicentre, double-blind, parallel-group, controlled, clinical trial, undertaken between April 2002 and July 2005. Patients who had two to six migraine attacks per month were randomly assigned verum acupuncture (n=313), sham acupuncture (n=339), or standard therapy (n=308). Patients received ten sessions of acupuncture treatment in 6 weeks or continuous prophylaxis with drugs. Primary outcome was the difference in migraine days between 4 weeks before randomisation and weeks 23–26 after randomisation. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN52683557.

Findings Of 1295 patients screened, 960 were randomly assigned to a treatment group. Immediately after randomisation, 125 patients (106 from the standard group) withdrew their consent to study participation. 794 patients were analysed in the intention-to-treat popoulation and 443 in the per-protocol population. The primary outcome showed a mean reduction of 2·3 days (95% CI 1·9–2·7) in the verum acupuncture group, 1·5 days (1·1–2·0) in the sham acupuncture group, and 2·1 days (1·5–2·7) in the standard therapy group. These differences were statistically significant compared with baseline ($p<0·0001$), but not across the treatment groups ($p=0·09$). The proportion of responders, defined as patients with a reduction of migraine days by at least 50%, 26 weeks after randomisation, was 47% in the verum group, 39% in the sham acupuncture group, and 40% in the standard group ($p=0·133$).

Interpretation Treatment outcomes for migraine do not differ between patients treated with sham acupuncture, verum acupuncture, or standard therapy.

Introduction

Migraine leads to recurrent attacks of mostly unilateral, pulsating headache with associated symptoms such as photophobia, phonophobia, nausea, and vomiting. The International Headache Society differentiates migraine with and without aura.[1] Epidemiological studies from several countries show that migraine has a prevalence of 12–14% in women and 6–8% in men.[2–4] In patients who have frequent migraine attacks preventive therapy is recommended. Although highly effective pharmacological treatments for migraine are available, acupuncture is the most frequently used preventive treatment in Germany despite the apparent lack of efficacy based on evidence from randomised controlled trials.[5] Therefore we undertook a randomised trial to investigate the efficacy of Chinese acupuncture versus sham acupuncture and standard drug treatment in patients who have frequent migraine attacks.

Methods

Participants

The patients with migraine enrolled in the study were recruited from outpatient clinics. The main inclusion criteria were: between two and six migraine attacks in 4 weeks; first migraine attack before the age of 50 years; migraine diagnosis at least 26 weeks before study entry; and duration of migraine attacks 4–72 h without acute medication or at least 2 h with acute medication. Additionally, two migraine characteristics were to be met and at least one of the following: nausea, vomiting, photophobia, or phonophobia. The patient had to be aged 18–65 years, give written informed consent, and be able to read and speak sufficient German. The main exclusion criteria were: severe migraine attacks with inability to go to work on more than 4 days a month; other neurological disease; secondary headache; neuralgia of the face or head; more than 6 days of non-migrainous headache per month; experience with acupuncture for migraine; any body needle acupuncture in the past 12 months; previous unsuccessful treatments with beta blockers; drug abuse; pregnancy; lactation; insufficient contraception; and intake of antipsychotic or antidepressant drugs. Patients were also excluded if they had participated in another clinical trial, taken analgesics on more than 3 days a month for other chronic pain, used prophylactic medication for migraine in the past 6 months, were receiving cortisone treatment, had epilepsy, or had a psychiatric disease.

Procedures

The design of this trial has been described in detail elsewhere.[6] Briefly, the German Acupuncture Trials

(GERAC) migraine study is a prospective, randomised, multicentre, controlled clinical trial in which the patients and the observers were unaware of treatment allocation. The study was undertaken in 149 practices, with patients unaware of the form of acupuncture they received. However, it was not possible to conceal treatment between acupuncture groups and standard therapy. After completing the baseline assessment, which included 4 weeks of headache and medication diary recordings, patients who had between two and six migraine attacks per month were randomly assigned verum acupuncture, sham acupuncture, or prophylactic treatment with beta blockers, flunarizine, or valproic acid in a ratio of 1:1:1 (figure 1). Randomisation was stratified by centre with a block size of nine and was unknown to the trial centre. The randomisation list was generated at the GERAC study centre at the Ruhr-University Bochum and patients were randomly assigned to treatment groups by fax through the study centre. Randomisation was concealed and recorded on a secure central database. Treatment assignment was known to the acupuncturist. The minimum qualification for investigators was completion of 140 h of training in acupuncture and at least 2 years' professional experience as an acupuncturist (median 8·5 years, maximum 36 years).

The study was conducted in accordance with the Declaration of Helsinki and the Guidelines for Good Clinical Practice. The protocol was assessed and approved by the 12 ethics review boards of the participating regions.

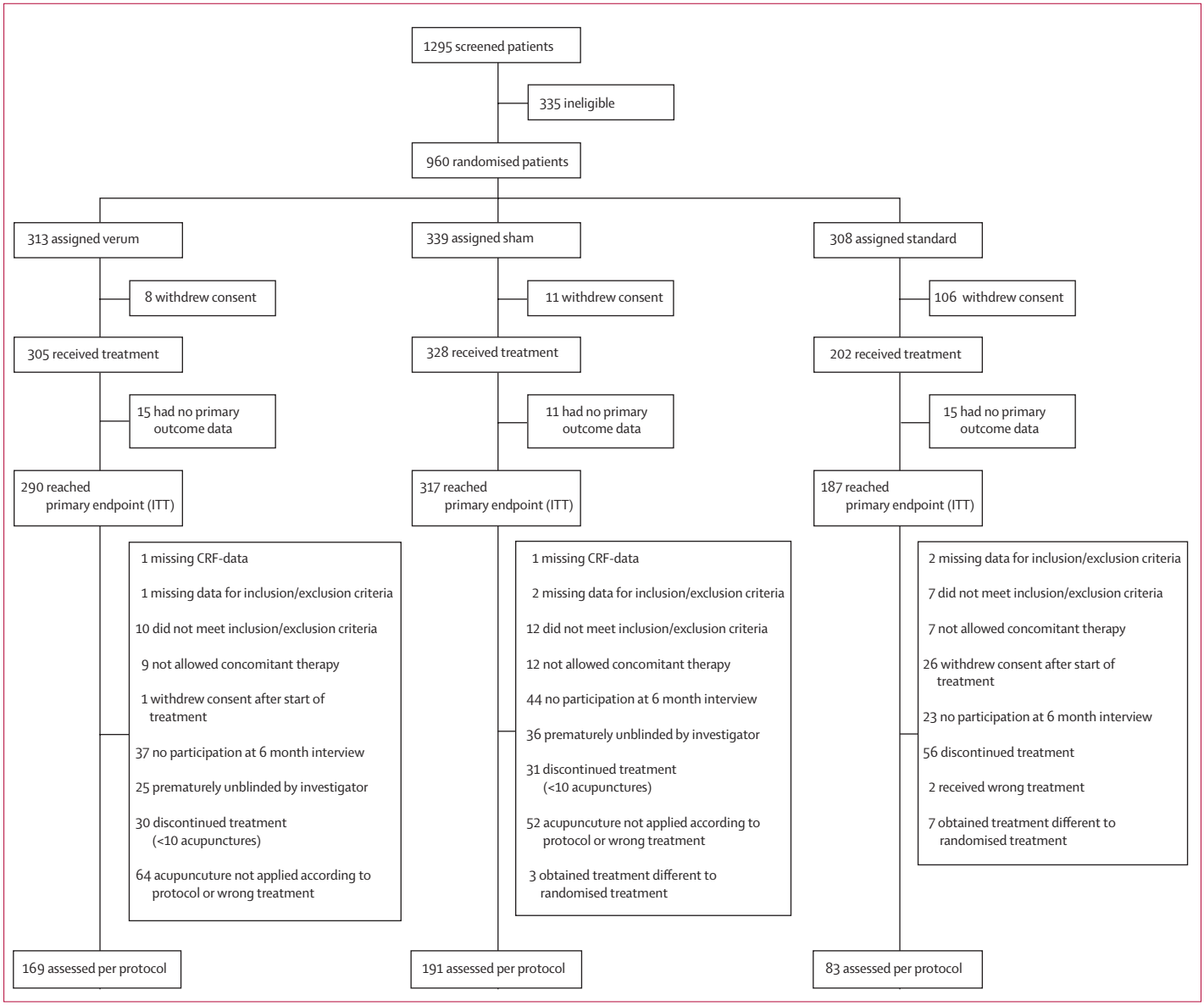

Figure 1: **Trial profile**
CRF=case report form. More than one criterion could be filled.

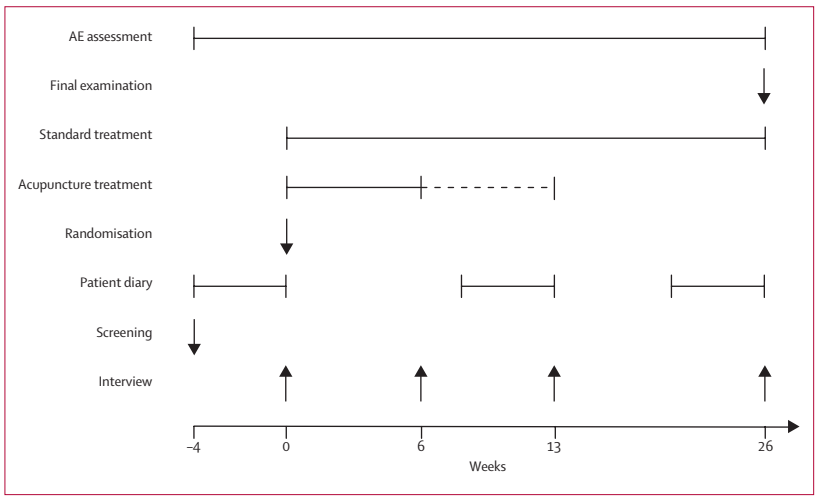

Figure 2: **Study flow**
AE=adverse events.

All study participants provided written informed consent. Consent and source data were verified by independent clinical monitors.

Patients in the acupuncture groups were informed that they would be either treated by Chinese (verum) or "new Western" (sham) acupuncture. Verum acupuncture and sham acupuncture treatments consisted of ten sessions of 30 min duration, administered over 6 weeks, preferably at a rate of two sessions per week (figure 2). Only body needle acupuncture, without electrical stimulation or moxibustion, was allowed. The same number and type of needles (sterile, single-use acupuncture needles, coated, 0·25–0·30 mm thick, 25–40 mm long) were used in both treatment groups. The length of treatment was the same (30 min) and the investigators were instructed to provide the same level of care and attention to both groups of patients. The total number of needles was restricted to a maximum of 25 and a minimum of ten per treatment. Both verum and sham acupuncture points had to be selected from a prescribed list (part standardisation) and needling was bilateral. During acupuncture treatment, communication with the patient was restricted to a minimum of necessary explanations to avoid unblinding of the patient. The sham acupuncture was done on areas of the skin in which no traditional Chinese medicine (verum) acupuncture points are known. Up to six needles were applied superficially on either side of the upper arm, on both thighs, and below both scapulae (depth of needle insertion maximum 3 mm), and no manual stimulation was done. The head has a high density of acupuncture points and was excluded from sham acupuncture.

The verum points consisted of obligatory points and additional points individually chosen by the physicians on the basis of traditional Chinese medicine diagnosis for syndromes (including tongue diagnosis), acupuncture channels related to the individual headache area, and Ah Shi points (locus dolendi points). Needles were inserted 2–20 mm in depth and manual stimulation of the needle was applied to achieve "De Qi" based on subjective reporting of the patient (a numb, radiating sensation thought to be indicative of effective needling).

Since the choice of verum and sham points is controversial,[7] for the purpose of GERAC the acupuncture points, the rules for point selection, and the required Chinese diagnosis were established on the basis of international literature sources and consultation with international experts in the field. The exact mode of acupuncture has been published previously.[6]

To better approximate daily clinical practice in the treatment of migraine, and to comply with the requirements of international acupuncture experts, all patients could receive 15 instead of ten interventions (two per week) if their treatment was graded as only partly successful in the telephone interview at the end of the treatment phase 6 weeks after randomisation (figure 2). The algorithm for deciding whether to extend treatment by five additional sessions was integrated into the interview software, without the knowledge of the investigators and patients. Unsuccessful treatment (reduction in headache days by <20% from baseline) or successful treatment (reduction in number of headache days by >50% from baseline) resulted in discontinuation of acupuncture after ten sessions. All other patients were given the choice of extending their treatment and were informed of this option in the telephone interview. Details of the telephone interview have been described elsewhere.[6] Standard migraine prophylactic treatment in the third study group was undertaken according to the guidelines of the German Migraine and Headache Society.[8] Following these guidelines, the use of beta blockers was the first choice, flunarizine the second, and valproic acid the third. Between six and seven contacts between the investigator and the patient were allowed during the trial to establish the standard treatment.

All patients recorded migraine, other headaches, and use of acute medication in a diary for 4-week periods before assessment by observers during the interviews at baseline (immediately preceding randomisation), at 13 weeks, and at 26 weeks; observers were unaware of treatment allocation. The 26-week interview was the final interview and primary endpoint for all outcomes. Inclusion and exclusion criteria, therapy, adverse events, and co-medication were recorded by the investigators in case report forms.

The primary outcome measure was the difference in migraine days between 4 weeks before randomisation and weeks 23–26 after randomisation. Secondary outcome measures included response, defined as reduction in the number of migraine days by 50% or more compared with baseline, changes in pain intensity, pain-related impairment and pain days according to von Korff,[9–11] changes in health-related quality of life of the patient measured by the German interview version of the short-form health survey (SF12),[12,13] and the patient global assessment of therapy

effectiveness quantified using the grading scale customarily used in German schools (1=very good to 6=fail).[14] These data were assessed during the telephone interviews.

Quality of the acupuncture therapy was assessed according to the amount of time the investigators spent with the patients. To assess whether the acupuncture treatment interventions were comparable in the two groups, the following data were taken from the case report forms completed by the investigator: total treatment period in days; number of sessions completed; and the number of needles used per session. Economic data (eg, number of days of disability before baseline and before final interview) were also obtained. These will be reported elsewhere.

Maintenance of patient blinding was determined at the 26-week interview. In addition to being asked about premature, active unblinding by the physician, patients were asked to guess the type of acupuncture they had received. Verification of the safety of body needle acupuncture was done by the investigators who recorded all adverse events on case report forms. All serious adverse events were faxed to the study centre on special forms.

Statistical analysis

The initial target sample size was 300 patients in each group. All analyses were done on the intention-to-treat population of participants who had at least one treatment and one primary outcome measure. Missing data points (which appeared only at 13 weeks) for days with migraine, pain intensity, and pain-related impairment according to von Korff, patient global assessment, and SF12 were replaced according to the principle of the last observation carried forward. The original power calculation of the study of 95% was based on a difference of 2 migraine days, a drop-out rate of 30%, and a variance analysis to reject the global hypothesis H_0: "There is no difference in the success probability between the three treatment groups." The primary endpoint difference in migraine days between baseline and the 26-week interview was not normally distributed; therefore the data were subjected to confirmatory hierarchical testing with a Kruskal-Wallis analysis to a global significance level of $p<0·05$.

Exploratory analyses were done for the secondary outcome measures, with χ^2 or Kruskal-Wallis tests for categorical or quantitative variables, respectively. An additional per-protocol analysis was undertaken for patients without major protocol deviations up to the final 26-week interview (figure 1). All analyses were done with SAS statistical software (version 9.1).

This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN52683557.

Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

	Verum group N=290	Sham group N=317	Standard group N=187	p*
Age at entry, years	37·1 (10·5)	38·3 (10·4)	36·8 (10·4)	0·135
Women	247 (85%)	257 (81%)	153 (82%)	0·378
Weight, kg	69·3 (14·1)	71·6 (15·7)	71·3 (15·2)	0·138
Migraine attacks/month	3·8 (3·0)	3·8 (3·0)	4·2 (2·6)	0·351
Migraine with aura	150 (52%)	153 (48%)	99 (53%)	0·523
Migraine without aura	139 (48%)	163 (52%)	87 (47%)	0·523
Disease duration, months	201·6 (150·9)	199·5 (131·7)	184·7 (132·5)	0·361
Days with other headache	1·5 (2·9)	2·1 (3·9)	1·6 (3·0)	0·184
Patients using medication for other pain	21 (22%)	32 (27%)	22 (32%)	0·226
Previous exposure to acupuncture >12 months before screening and not because of migraine	41 (14%)	42 (13%)	21 (11%)	0·652

Data are number (%) or mean (SD). *Results from χ^2 or Kruskal-Wallis test for categorical and quantitative variables respectively.

Table 1: **Demographic and clinical characteristics of the intention-to-treat population**

Results

After successful screening, 960 of 1295 patients could be randomly assigned, between April 2002 and December 2004, to the three treatment groups (figure 1). The most common reason for not randomising patients (n=335) was violation of the inclusion criteria. Directly after randomisation 125 patients (106 from the standard group) withdrew their consent for study participation. Therefore only 835 patients received study treatment and constitute the safety population. For 41 patients no data were available for the primary outcome. 794 patients could be analysed as the intention-to-treat population. 443 patients in the intention-to-treat population who had no major protocol violations constituted the per-protocol analysis. Demographic and baseline efficacy parameters did not differ between the treatment groups in the intention-to-treat population (tables 1 and 2). The baseline evaluation of days with migraine in the per-protocol population (table 2) showed a significantly higher value for the standard population.

Patients in the verum acupuncture group were treated with a mean of 15·4 (SD 4·6) needles and patients in the sham acupuncture group with a mean of 13·8 (4·3)

	Verum group	Sham group	Standard group	p*
Days with migraine (ITT)	6·0 (3·2)	5·8 (3·2)	6·4 (4·0)	0·351
Days with migraine (PP)	6·1 (3·4)	5·6 (3·3)	7·1 (4·4)	0·019†
Patients using acute medication for migraine	270 (93%)	292 (92%)	174 (93%)	0·876
Pain intensity (ITT)‡	73·7 (13·3)	73·8 (13·3)	74·5 (12·6)	0·803
Impairment of activity (ITT)§	61·2 (20·6)	62·2 (20·3)	61·6 (21·0)	0·907
Days of pain (ITT)	6·7 (7·1)	7·4 (8·2)	7·1 (6·6)	0·824
Physical health SF-12 (ITT)¶	43·2 (8·4)	42·7 (8·8)	42·6 (8·3)	0·737
Mental health SF-12 (ITT)¶	48·5 (9·5)	48·1 (9·9)	47·6 (10·6)	0·706

Data are number (%) or mean (SD). ITT=intention to treat. PP=per protocol. *Results from $\chi 2$ or *t* test for categorical and quantitative variables respectively. †Verum *vs* sham p=0·231, verum *vs* standard p=0·072, sham *vs* standard p=0·005. ‡Graded chronic pain score (von Korff) questions 1–3. §Graded chronic pain score (von Korff) questions 5–7. ¶Higher values indicate better status.

Table 2: **Baseline data of outcome measures**

needles. The difference was significant (p<0·0001). Patients' mean estimate of the duration of the sessions was 32·5 min (8·3) in the verum group and 32·3 min (17·2) in the sham group (p=0·250), whereas the mean time patients estimated that the physician spent with them was 8·5 min (6·0) in the verum group and 7·7 min (5·6) in the sham group (p=0·079). The mean number of sessions was 10·9 (2·4) for the verum group and 11·0 (2·7) for patients in the sham group (p=0·359). 74 (26%) patients in the verum group and 91 (29%) in the sham group received an extension of five additional acupuncture sessions. Unblinding through the investigator was reported by 9% (25) of patients in the verum group and 11% (36) of the sham-acupuncture patients. 44% (258) of patients treated with acupuncture guessed the type received correctly after 26 weeks (42% [119] verum, 45% [139] sham), 28% (164) guessed wrong (30% [83] verum, 26% [81] sham), and 28% [171] couldn't give any guess (28% [81] verum, 29% [90] sham, three patients missing in each group).

The main outcome measure (table 3, figure 3), the difference in migraine days between 4 weeks before and weeks 23–26 after randomisation in the intention-to-treat population, showed a mean reduction of 2·3 days in the verum group (95% CI 1·9–2·7), 1·5 days (1·1–2·0) in the sham group, and 2·1 days (1·5–2·7) in the standard therapy group. This difference was significant for all three groups (p<0·001). No significant difference was detected between the three treatment groups (p=0·09). An analysis of variance of the number of migraine days at month 6 with treatment groups and number of migraine days at baseline as variables can be regarded as supportive only. The assumption of normally distributed residuals was violated. However, the results were in line with the non-parametric analyses: the mean differences and 95% CIs are 0·57 days (0·09–1·05) for verum versus sham, 0·50 days (–0·06 to 1·05) for verum versus standard therapy, and –0·07 days (–0·62 to 0·47) for sham versus standard therapy.

Explorative analysis revealed a significant difference in migraine days at week 26 compared with baseline (p=0·03) between verum and sham acupuncture (table 3). The per-protocol analysis showed a mean reduction in migraine days after 26 weeks compared with baseline of 2·3 days in the verum group, 1·3 days in the sham group, and 2·7 in the standard group (p=0·031). The difference of 1·0 day between the verum group and the sham group was significant (p=0·017). The responder rate (the percentage

	Time point	Verum	Sham	Standard	p*			
					All groups	Verum *vs* sham	Verum *vs* standard	Sham *vs* standard
Difference from baseline in days with migraine (ITT)	6 weeks	–2·7 (3·2)	–2·4 (3·5)	–2·7 (4·4)	0·548	..	..	..
	13 weeks	–2·2 (3·1)	–1·9 (3·6)	–2·0 (4·1)	0·430	..	..	..
	26 weeks	–2·3 (3·6)	–1·5 (3·8)	–2·1 (4·0)	0·095	0·031	0·202	0·616
Difference from baseline in days with migraine (PP)	6 weeks	–2·7 (3·4)	–2·2 (3·6)	–3·6 (4·7)	0·433	..	..	..
	13 weeks	–2·2 (3·1)	–1·8 (3·8)	–2·6 (4·6)	0·273	..	..	..
	26 weeks	–2·3 (3·5)	–1·3 (4·0)	–2·7 (4·4)	0·031	0·017	0·921	0·055
Response (ITT)	6 weeks	130 (52%)	133 (49%)	62 (39%)	0·038	0·479	0·012	0·052
	13 weeks	128 (46%)	128 (42%)	70 (38%)	0·263	..	..	..
	26 weeks	133 (47%)	121 (39%)	75 (40%)	0·133	..	..	..
Response (PP)	6 weeks	100 (59%)	103 (54%)	46 (39%)	0·598	..	..	..
	13 weeks	83 (49%)	91 (48%)	40 (48%)	0·962	..	..	..
	26 weeks	87 (51%)	84 (44%)	45 (54%)	0·198	..	..	..
GPA success† Yes (ITT)	6 weeks	226 (78%)	237 (75%)	103 (55%)	<0·001	0·657	<0·001	<0·001
	13 weeks	228 (79%)	243 (77%)	114 (61%)	<0·001	0·839	<0·001	<0·001
	26 weeks	215 (74%)	218 (69%)	118 (63%)	0·037	0·144	0·010	0·192
Physical health SF-12 (ITT)	13 weeks	47·6 (7·3)	46·0 (8·2)	45·1 (8·1)	0·002	0·029	<0·001	0·103
	26 weeks	47·3 (8·2)	46·3 (8·7)	47·0 (7·9)	0·300	..	..	..
Mental health SF-12 (ITT)	13 weeks	51·5 (8·4)	50·9 (8·8)	50·2 (9·7)	0·440	..	..	..
	26 weeks	51·4 (9·0)	51·0 (9·4)	50·5 (9·5)	0·513	..	..	..
Pain intensity (ITT)‡	13 weeks	63·5 (19·1)	62·6 (18·9)	67·5 (17·8)	0·010	0·393	0·031	0·002
	26 weeks	57·7 (20·4)	60·9 (20·4)	62·9 (20·8)	0·013	0·045	0·004	0·253
Impairment of activity (ITT)§	13 weeks	40·7 (26·1)	44·3 (26·2)	47·2 (27·2)	0·030	0·112	0·010	0·199
	26 weeks	37·1 (26·2)	40·3 (26·4)	42·4 (27·1)	0·069	..	..	..
Acute medication (ITT)	13 weeks	254 (89%)	272 (87%)	171 (93%)	0·113	..	..	..
	26 weeks	254 (88%)	272 (86%)	167 (90%)	0·344	..	..	..

Data are number (%) or mean (SD). ITT=intention to treat; PP=per protocol. *Results from $\chi 2$ or *t* test for categorical and quantitative variables respectively. †GPA=global patient assessement; success 'yes' =GPA 'excellent' or 'good'. ‡Graded chronic pain score (von Korff) questions 1–3. §Graded chronic pain score (von Korff) questions 5–7.

Table 3: **Outcome measurements**

of patients achieving a reduction of migraine days by at least 50%, 26 weeks after randomisation) was 47% in the verum group, 39% in the sham group, and 40% in the standard group (intention-to-treat population, p=0·133).

The secondary outcome analysis (table 3) showed that all treatments resulted in improvements in secondary outcomes. No differences were recorded between the treatment groups in the summary scales of the SF-12 at 26 weeks. The patient global assessment showed better scores for the acupuncture groups compared with standard therapy. The analysis scores according to von Korff showed a better score for verum after 13 weeks compared with standard therapy in pain-related impairment and significantly better scores for verum patients after 26 weeks in pain intensity than for the other treatment groups. Patients' perception of the received therapy had no effect on the primary outcome (table 4).

During the study, 13 (1%) participants (5 verum, 5 sham acupuncture, 1 standard therapy, and 2 only screened patients) had 16 serious adverse events. 13 cases were classified as having a definitive other cause. One vascular disorder, reported by a patient in the verum group, was classified as not assessable for cause; another one reported by a patient treated with sham accupuncture was classified as the treatment being the possible cause. One case of a hysterectomy was reported from a patient in the verum group 150 days after the end of the treatment with the causality possible. 70 (22%) patients in the verum group, 75 (23%) in the sham group, and 59 (31%) in the standard therapy group had adverse events. Most adverse events were reported as nervous system disorders (verum, n=17 [5%]; sham, 23 [7%]; standard therapy, 15 [8%]) or musculoskeletal and connective tissue disorders (verum, 19 [6%]; sham, 22 (7%); standard therapy, 8 [4%]). The overall pattern of adverse events was similar in all groups.

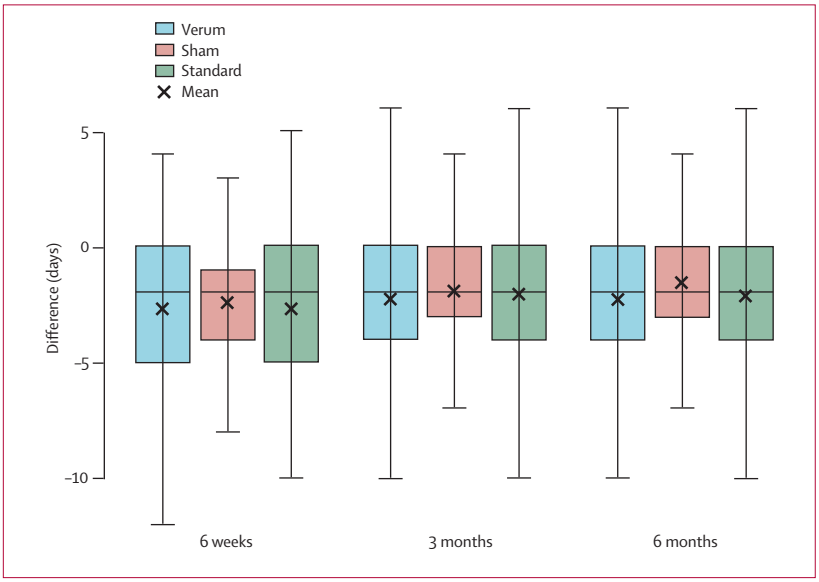

Figure 3: **Difference from baseline in number of days with migraine**
Analysis was by intention to treat.

Discussion

This study was a large and, in terms of study procedures, sophisticated randomised controlled trial, undertaken to investigate the efficacy of acupuncture versus sham acupuncture and standard therapy with prophylactic drugs in patients with migraine. The most important result is that all three treatments were effective and that improvement in the number of migraine days was closely similar in all treatment groups. This finding was also true for most secondary outcomes, such as the patient global assessment. In an explorative analysis verum acupuncture was better than sham acupuncture. The results can be compared with those obtained in a large trial that investigated verum and sham acupuncture.[15] The trial, by Linde and colleagues, had a waiting list group instead of an active control. The small decrease in migraine frequency in the waiting list group shows that regression to the mean does not play a major part in this kind of study design. By contrast with the trial by Linde and colleagues, we showed that after 26 weeks, acupuncture treatment over 6 weeks had a similar efficacy compared with 24 weeks of continuous treatment with standard drug therapy. We identified differences between verum and sham acupuncture that might be due to differences of the acupuncture procedures, the larger power of our trial, or the different endpoints (weeks 10–13 *vs* weeks 23–26).

The strength of our study is the randomised, blinded design, adequate power because of the large patient numbers, selection of highly competent physicians performing acupuncture, and study procedures according to Good Clinical Practice guidelines, including monitoring, data collection in diaries, structured telephone interviews by people not involved in the treatment of patients (to avoid bias in the treating physicians), the small number of unblinded patients, a treatment protocol that reflected clinical practice (variable number of acupuncture sessions), and an active drug treatment control group. Another strength is the semi-standardised acupuncture procedure.

Limitations of the study are that acupuncture was restricted to needling only and that the number of treatments was restricted to ten to 15. Other shortcomings include the relatively high number of patients who dropped out in the drug treatment group (patients expected to receive acupuncture treatment) and the imbalance in

Therapy	Guess	n	Primary outcome, mean (SD)	p
Verum	Verum	119	−2·6 (3·6)	0·183
	Sham	83	−1·8 (3·8)	
	No guess	81	−2·4 (3·4)	
Sham	Verum	81	−1·4 (4·5)	0·346
	Sham	139	−1·3 (3·7)	
	No guess	90	−2·0 (3·3)	

Table 4: **Primary outcome depending on therapy guess**

migraine frequency at baseline. However, patients who withdrew their consent after randomisation to standard therapy were not included in the intention-to-treat analysis (figure 1). If patients who withdrew their consent after randomisation had been analysed as non-responders—ie, as having a difference of 0 days of migraine—the imbalance of dropouts would have resulted in the discrimination of the drug treatment group. Our analysis might therefore have preferred the drug treatment group. Nevertheless both the clinical characteristics and patient disposition in our drug treatment group and the achieved reduction in migraine days are comparable with those from published trials of drug treatment for migraine.[16]

A surprising result was the efficacy of sham acupuncture. Despite being inferior to verum acupuncture in the per-protocol population, needling at non-acupuncture points could exert biological effects similar to the ones achieved when needling specific acupuncture points. A similar finding was reported in trials that investigated the effect of botulinum toxin injected into pericranial and neck muscles in patients with chronic headache.[17,18] This treatment showed a high responder rate, but injection of saline had an almost similar effect. Another possible explanation of the mode of action of acupuncture is a powerful placebo effect. Placebo treatment exerts powerful effects on pain modulating brain structures, as shown by PET and functional MRI studies.[19,20]

Expectancy of real acupuncture was not a major predictor of outcome in this trial. This finding is in contrast with that of a randomised trial of tooth extraction pain in which expected true acupuncture affected pain perception whereas the overall response did not differ between real and sham acupuncture.[21] A comparison of our study with earlier trials of acupuncture for migraine, including those that compared acupuncture with a beta blocker or flunarizine, is difficult.[22] According to modern standards of trial design, these studies were underpowered and biased. However, the high dropout rate in the drug treatment group in our study was due to the disappointment of not being randomised to the acupuncture groups.

Ultimately, one could argue that the efficacy of a treatment, especially a treatment with almost no adverse events or contraindications, is more important than the knowledge of the mechanism of action of this particular therapy. The mode of action of most drugs approved for migraine prophylaxis—eg, beta blockers or antiepileptic drugs—is unknown. The decision whether acupuncture should be used in migraine prevention remains with the treating physician.

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Authors' contributions

HCD was the principal investigator and contributed to the study protocol and study report, and was a member of the steering committee; KK contributed to study coordination, monitoring, and the study report; GB contributed to the study protocol and study report, and was a member of the steering committee; ML did the telephone interviews; CM was a member of the steering committee and did the telephone interviews; AM, MT, and MZ were members of the steering committee; HJT was a member of the steering committee and contributed to the study coordination; R Meinert helped coordinate the study, did the statistical analysis, and was a member of the steering committee.

Conflicts of interest

We have no conflicts of interest.

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