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Treatment in a Randomized Multicenter Trial of Acupuncture for Migraine (ART Migraine)

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Key Words
Acupuncture · Randomized controlled trial · Migraine · Sham acupuncture

Summary
Background: This paper aims to describe the characteristics of physicians and interventions of a large, multicenter randomized trial of acupuncture for migraine (ART Migraine) in order to enable acupuncturists to assess the study interventions. **Patients and Methods:** 302 patients suffering from migraine were randomized to 12 sessions of semi-standardized acupuncture (6 predefined basic points, recommendations for optional individual choice of additional points given), standardized minimal acupuncture (superficial needling of at least 5 of 10 predefined, distant non-acupuncture points) or a waiting list. 30 physicians trained and experienced in acupuncture from 18 centers in Germany participated in the trial. **Results:** The median duration of acupuncture training of trial physicians was 500 h (range 140–1350). Physicians had acupuncture experience for 10 (<1 to 25) years and had treated 200 (60 to >1000) patients with acupuncture in the year preceding trial participation. The 6 basic points were needled in 76–93% of sessions. Compliance with treatment instructions varied considerably among centers in the acupuncture group. In contrast, compliance with the minimal acupuncture protocol was very good. 6 of the 30 physicians stated that they would have treated patients somewhat differently outside the trial, 1 completely differently. The trial found a significant effect of those treated with acupuncture compared to those on the waiting list for treatment, but minimal acupuncture was as effective as acupuncture. **Conclusions:** The treatment protocols for acupuncture and minimal acupuncture in ART Migraine appeared an adequate compromise in the specific situation and for the predefined purposes. However, a relevant minority of participating physicians would have treated patients differently outside the trial.

*All authors participated in the planning of the protocol and revision of manuscript drafts. Specific tasks and responsibilities: general trial coordination: DM, KL, AS, BB, CBW; monitoring coordination: AS, AH; statistical analysis and expertise: WW, KL; acupuncture interventions: MH, JH, DI; general medical and scientific responsibility: SNW, DM.

Schlüsselwörter
Akupunktur · Randomisierte kontrollierte Studie · Migräne · Sham-Akupunktur

Zusammenfassung
Hintergrund: Ziel des vorliegenden Artikels ist es, die teilnehmenden Prüfärzte und die Interventionen in einer grossen, multizentrischen Studie zur Wirksamkeit der Akupunktur bei Patienten mit Migräne (ART Migräne) so zu beschreiben, dass praktizierende Akupunkteure die Qualität der Interventionen bewerten können. **Patienten und Methoden:** 302 Migränepatienten erhielten entsprechend randomisierter Zuteilung entweder 12 Sitzungen semistandardisierte Akupunktur (6 vordefinierte Basispunkte, Empfehlungen für individuell zu wählende Zusatzpunkte), standardisierte Minimalakupunktur (oberflächliche Nadelung an mindestens 5 von 10 vordefinierten, entfernten Nichtakupunkturpunkten) oder vorerst keine Behandlung (Wartelistenkontrolle). 30 qualifizierte Ärzte führten die Behandlung in 18 Prüfzentren in Deutschland durch. **Ergebnisse:** Die mediane Dauer der Akupunkturausbildung der teilnehmenden Prüfärzte betrug 500 Stunden (Range 140–1350 Stunden). Die Ärzte hatten seit 10 (<1 bis 25) Jahren praktische Erfahrung mit Akupunktur und hatten im Jahr vor der Studienteilnahme 200 (60 bis >1000) Patienten mit Akupunktur behandelt. Die 6 Basispunkte wurden in 76–93% der Sitzungen behandelt. Die Erfüllung der Behandlungsvorgaben variierte deutlich zwischen den Prüfzentren. Bei der Minimalakupunktur folgten dagegen alle Ärzte den Behandlungsvorgaben sehr gut. 6 der 30 Prüfärzte gaben an, sie hätten die Patienten ausserhalb der Studie etwas anders behandelt, 1 völlig anders. In der Studie zeigte sich ein deutlicher Effekt der Akupunktur im Vergleich zur Wartelistengruppe; unter Minimalakupunktur gab es jedoch eine ähnlich grosse Verbesserung. **Schlussfolgerungen:** Die Behandlungsstrategien in ART Migräne haben sich als angemessener Kompromiss für die gegebene Situation erwiesen. Ein Teil der Ärzte hätte jedoch ausserhalb der Studie anders akupunktiert.

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Introduction

In 2001, the STRICTA (*ST*andards for *R*eporting *I*nterventions in *C*ontrolled *T*rials of *A*cupuncture) recommendations were published to provide guidance for more precise description of interventions in controlled trials of acupuncture [1]. The recommendations emphasize the need to report details of the rationale for the chosen acupuncture strategy, needling, treatment regimen, co-interventions, practitioner background and control interventions in the publication of a trial. While this is easily possible in single-center trials or studies with standardized interventions, it becomes difficult in multicenter trials with flexible treatment schemes. Such trials are, however, necessary to ensure that results do not only apply to one or a few specialized centers.

We performed a randomized multicenter trial to investigate whether a semi-standardized acupuncture intervention is more effective than either no treatment or standardized minimal acupuncture intervention in patients with migraine (*A*cupuncture *R*andomized *T*rial in Migraine = ART Migraine). ART Migraine was performed within the framework of a larger research program [2] and on request of health authorities in Germany. The trial was sponsored by a group of statutory sickness funds to serve as a basis to decide whether or not to fund acupuncture for migraine. The protocol and the main results have been published elsewhere [3, 4]. This paper aims to describe in detail the characteristics of participating physicians and the acupuncture and minimal acupuncture intervention provided in the trial.

Methods

ART Migraine was a randomized, controlled multicenter trial that compared acupuncture (AC) with minimal acupuncture (MA) and with waiting list (WL) controls who received no acupuncture. In the AC and MA groups, patients were blinded with regard to treatment. Patients with migraine with and without aura (according to the classification of the International Headache Society [5]) fulfilling predefined inclusion and exclusion criteria were randomized centrally (ratio 2 : 1 : 1) to the three groups. Patients who had received acupuncture treatment during the last 12 months or at any time if performed by the participating trial physician were excluded.

Physicians participating in the trial were recruited so as to ensure their qualifications equalled or surpassed those of physicians currently accredited for providing acupuncture by state health funding agencies in Germany. According to the study protocol, trial physicians had to fulfill the following criteria: (1) acupuncture training at least equivalent to an 'A-diploma' from one of the major German acupuncture societies (140 h of acupuncture training); (2) 50% of trial physicians had to have at least a 'B-diploma' (350 h; at the start of current reimbursement programs about 20% of physicians accredited to provide acupuncture had this qualification [6]); (3) 50% had to have experience working in clinical studies; (4) all physicians had to have at least 3 years of practical experience with acupuncture; (5) all physicians had to participate in training sessions for the study, on the trial methods, the interventions tested, and standards for performing clinical trials (ICH-GCP).

The treatment strategies for AC and MA were developed in a consensus process with experienced acupuncture experts (MH, JH, DI) who represented the following two major German societies for medical acupuncture: German Medical Acupuncture Association (Deutsche Ärztegesellschaft für Akupunktur, DÄGfA); International Society for Chinese Medicine (Societas Medicinae Sinensis, SMS). In a first step the three experts developed a proposal which was then presented to more than 30 ex-

Box 1. Acupuncture points used in the ART Migraine.

Basic Points
Gall Bladder (GB) 20
GB 40 or GB 41 or GB 42
Du Mai – Governing vessel (Du Mai, DU) 20
Liver (LIV) 3
San Jiao (SJ) 3 or 5
Extrapoint Taiyang

Optional Points
Mainly frontal headache DU 23, extrapoint Yintang, Bladder (BL) 2, GB 14, Large Intestine (LI) 4, Stomach (ST) 44
Mainly temporal pain: SJ 20, GB 8, GB 12, ST 8
In case of retro-orbital pain: ST 8, SJ 23
Headache associated with menses: Spleen (SP) 6, LIV 2, SP 10
Associated with nausea or vomiting: Conception vessel (Ren-Mai, REN) 12, Pericard (PC) 6
Headache triggered by stress/anger: LIV 2, LIV 5
Triggered by fatigue: ST 36, REN 4

Box 2. Minimal acupuncture points used in ART Migraine (1 cun is defined according to the rules of traditional Chinese medicine as the width of the interphalangeal joint of patient's thumb).

'**Deltoideus'**
In the middle of the line insertion of M. deltoideus (LI 14) and acromion

'**Upper Arm'**
2 cun laterally (radial) of LU 3

'Forearm'
1 cun ulnar of the proximal third of the line between Heart (HE) 3 and HE 7

'**Scapula'**
1 cun laterally of the lower scapular edge

'**Spina Iliaca'**
2 cun above spina iliaca anterior superior in vertical line to the arch of left ribs

'**Back I'**
5 cun laterally of the spine of lumbar vertebrum IV

'**Back II'**
5 cun laterally of the spine of lumbar vertebrum V

'**Upper Leg I'**
6 cun above the upper edge of the patella (between the spleen and stomach meridian)

'**Upper Leg II'**
4 cun above the upper edge of the patella

'**Upper Leg III'**
2 cun dorsally of GB 31 (avoidance of bladder meridian)

Table 1. Characteristics of trial physicians (n = 30)

	Median (range) or n (%)
Acupuncture sessions provided within the trial (per physician)	96 (2–355)
Age, years	43 (29–59)
Sex, female	9 (30%)
Postgraduate specialization ('Facharzt')	22 (73%)
Medical practice, years	16 (1–32)
B-Diploma (≥350 h training)	22 (73%)
Acupuncture training, hours	500 (140–1,350)
Teacher for acupuncture in accredited postgraduate courses	12 (40%)
Use of acupuncture, years	10 (<1–25)
Membership in professional societies	
– Total	27 (90%)
– German Medical Acupuncture Association (DÄGfA)	11 (37%)
– International Society for Chinese Medicine (SMS)	6 (20%)
– German Society for Acupuncture and Neural Therapy (DgfAN)2 (7%)	
– German Acupuncture Society Düsseldorf	2 (7%)
– Research Group Acupuncture and Traditional Chinese Medicine (FATCM)	1 (3%)
Patients treated with acupuncture in the year before the trial	
– Total	200 (60–1,000)
– Migraine patients	50 (15–300)
Therapies used in patients in everyday practice, %	
– Acupuncture	30 (5–98)
– Other traditional Chinese therapies	10 (0–50)
– Other complementary therapies	10 (0–50)
– Conventional medicine	40 (0–95)
Chinese diagnosis before treatment, frequently / always	10 (33%) / 16 (53%)

perts from both acupuncture societies for discussion. The final strategies were defined by the three experts together with the study team and communicated to the external advisors. The final strategies were generally considered as a pragmatic compromise between the need for some standardization and the need for individualization.

Both the AC and MA treatments consisted of 12 sessions of 30 min each, administered over a period of 8 weeks (preferably 2 sessions per week in the first 4 weeks, followed by 1 session per week in the remaining 4 weeks). Patients in the WL group did not receive acupuncture treatment for a period of 12 weeks after randomization. All patients could treat acute headaches as needed.

AC treatment was semi-standardized (box 1): All patients were to be treated at 'basic' points bilaterally unless contraindicated. In addition, physicians were allowed to treat at other points based on a traditional Chinese syndrome diagnosis, personal experience, localization of pain or symptom modalities. Recommendations of additional points (unilateral or bilateral) were made, but acupuncturists were allowed to choose other optional points (including ear acupuncture points, microsystemic or trigger points). The number and name of additional acupuncture points had to be documented. A differentiation of symptoms according to the theory of traditional Chinese medicine was requested, but not mandatory. Sterile one-way needles had to be used, but physicians were free in their choice of needle length and diameter. An irradiating needling sensation ('de qi') was to be achieved if possible. Needles were to be stimulated manually at least once in each session. The total number of needles was limited to 25.

Number, duration and frequency of the sessions in the MA group were the same as for the AC group. In each session at least 5 out of 10 points (see box 2) had to be needled bilaterally (at least 10 needles) and superficially using fine needles. Subcutaneous insertion using fine needles (20–40 mm in length) was recommended. 'De qi' and manual stimulation of the needles was to be avoided. All acupuncturists received oral instruction, a videotape and a brochure with detailed information on MA.

Patients were informed as follows with respect to AC and MA in the study: 'In this study, different types of acupuncture will be compared. One type is similar to the acupuncture treatment used in China. The other type does not follow those principles, but has also been associated with positive outcomes in clinical studies.'

All patients filled in headache diaries in the 4 weeks before randomization (baseline phase), during 12 weeks after randomization and in weeks 21–24 after randomization. In addition, patients were asked to complete a questionnaire [7] before treatment, after 12 weeks and after 24 weeks. The questionnaire included the German version of the Pain Disability Index (PDI) [8]; a scale for assessing sensoric and affective aspects of pain (Schmerzempfindungs-Skala SES) [9]; the depression scale ADS [10]; and the German version of the SF-36 to assess health-related quality of life [11]. The main outcome measure for confirmatory analysis was the difference in the number of days with moderate or severe headache during the 4 weeks before randomization (baseline phase) and in weeks 9–12 after randomization.

Before and after completion of the study a questionnaire was sent to all 30 trial physicians. This questionnaire included questions on training and experience before trial participation as well as questions on how the trial interventions were judged post hoc.

Results

A total of 302 patients were included in the trial; 145 were randomized to AC, 81 to MA, and 76 to WL. 5 hospital outpatient units and 13 private practices participated as study centers. A total of 32 physicians applied acupuncture in the trial, however, 2 provided only one single treatment session while

Table 2. Treatment in the AC group (% or M ± SD) summed up for all sessions and for sessions 1, 5, and 10

	All sessions (n = 1,677)	Session 1 (n = 144)	Session 5 (n = 142)	Session 10 (n = 137)
Basic points, %				
– GB 20	93	94	92	95
– GB 40 or GB 41 or GB 42	78	78	79	80
– DU 20	79	77	79	83
– LIV 3	84	89	87	84
– SJ 3 or SJ 5	84	78	84	82
– Taiyang	76	76	77	76
Number of basic points needled, %				
– < 4	21	19	21	20
– 4	9	13	8	9
– 5	12	12	14	12
– 6	58	56	57	59
Optional points, %				
– LI 4	54	47	56	61
– ST 36	49	38	48	52
– SP 6	48	36	49	48
– ST 8	37	34	38	41
– Yintang	34	32	34	31
– GB 14	26	22	26	28
– PC 6	19	20	22	15
Other classical acupuncture points used, %	41	38	42	40
Microsystem points used, %	11	11	10	10
Ah-Shi points used, %	3	3	4	1
Trigger points used, %	1	1	–	1
Total number of needles, M ± SD	16.6 ± 4.6	15.3 ± 4.6	16.6 ± 4.8	17.1 ± 4.2
Duration of session, min, M ± SD	29.2 ± 4.3	28.8 ± 3.9	28.9 ± 4.3	29.5 ± 4.2
Length of needles used*, mm, %				
– <20	54	57	56	55
– 21–30	85	85	89	86
– 31–40	15	16	18	20
– >40	1	1	2	2
Manual stimulation, %				
– None	38	46	36	34
– Once	48	40	52	51
– More than once	14	14	11	15
'De qi'				
– Easy to elicit	91	82	96	90
– Difficult to elicit	9	18	4	9
– Could be not be elicited	<1	–	–	1

*More than one type of needles could be used in a single patient.

substituting for absent trial physicians. These cases were excluded from further analysis.

The characteristics of the 30 trial physicians are summarized in table 1. The number of AC and MA treatments provided by these 30 acupuncturists varied between 2 and 355 (median 96) per physician. Physicians had had a median of 500 h (140–1,350) of acupuncture training before participating in the trial; 22 (73%) had the B-Diploma. 12 (40%) trial physicians taught acupuncture in accredited postgraduate courses. Physicians had been using acupuncture in their practices for 10 (<1 to 25) years and had treated 200 (60 to >1000) patients with acupuncture in the year preceding trial participation. 2 physicians at a large center had an A-diploma but <3 years of practice in acupuncture (one <1 year and one 2 years). They were supervised by highly experienced acupuncturists from the same center. 26 (86%) physicians frequently or always differentiated symptoms according to traditional Chinese medicine before starting treatment.

Patients in the AC group were treated in a total of 1,677 sessions. On average, 16.6 ± 4.6 (mean and standard deviation, M ± SD) needles were used per session. The number of needles per session slightly increased over treatment courses. The

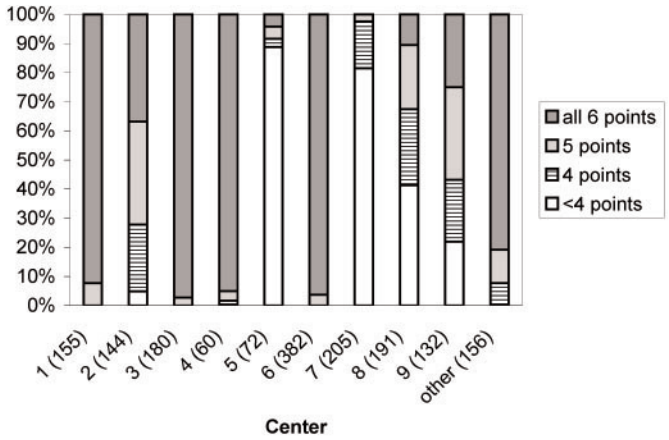

Fig. 1. Compliance with the predefined acupuncture strategy: Proportion of treatment sessions in which all 6, 5, 4 or <4 of the basic points were treated. Displayed are the 9 centers (numbered 1–9) that provided 60 treatments or more; all centers that provided fewer treatments were pooled. The number given in parentheses is the number of treatments performed in the respective center.

single basic points were needled in 76–93% of the sessions (table 2). GB 20 was the most frequently used basic point (93% of all sessions) followed by LIV 3 (84%). In 21% of the sessions <4 of the 6 basic points were treated. Compliance with the treatment instructions varied considerably between centers (fig. 1). The most frequently treated optional points were LI 4 (54%), ST 36 (49%), SP 6 (48%), ST 8 (37%), extrapoint Yintang (34%), GB 14 (26%) and PC 6 (19%). Additional classical points not mentioned as basic or optional points in the treatment instructions were used in 41%, microsystem points in 11%, ah-shi points in 3% and trigger points in 1% of sessions. In 38% of the sessions needles were not stimulated. De qi could be elicited easily in 91% of sessions.

Compliance with instructions in the MA group was very good. Table 3 shows the frequency of use for the single minimal points. Less than 10 needles were used in 14 sessions (1%), 10 needles in 70%, 11 or 12 in 19% and 13 or more in 10% of sessions. The duration of sessions was similar to that in the acupuncture group.

One or more differentiation of symptoms according to traditional Chinese medicine were reported for 90 (63%) of the 144 patients starting acupuncture treatment. The total number of syndrome diagnoses in these 90 patients was 169. The most frequently reported syndromes were rising liver yang, liver qi stagnation (both in 34 patients), spleen qi deficiency (30), blood stasis (22), and kidney yin qi deficiency (18).

The physicians' responses to the questions about how they would treat patients outside of the trial (posed after completion of the trial but before results were available) are reported in table 4. 21 (70%) would have applied acupuncture similarly or exactly in the same way outside of the trial, 6 (20%) differently and 1 (3%) totally different. The criticisms raised most often were the high number of basic points and the selection of basic points. Outside the trial, most physicians would have used additional therapies in at least some patients. A great variety of treatments was mentioned here (most often Chinese herbs, homeopathy, relaxation, nutritional changes). About half of the physicians had ethical problems with providing MA. 25 (83%) explicitly confirmed that they would participate again in the trial, 2 were undecided, and 3 would not participate again. The reasons reported were the use of MA, lack of individualization and the amount of bureaucracy.

Compared to the WL group, patients who received AC scored significantly better in the main outcome measure as well as in almost all secondary outcome measures. However, there were no differences compared to MA (table 5). Clinical outcomes did not vary significantly between centers. The detailed clinical results have been published elsewhere [4]. Results did not differ significantly between centers complying less (centers 5, 7, 8 and 9; fig. 1) or more with instructions for acupuncture.

Discussion

The findings of our analyses can be summarized as follows: (1) The participating trial physicians were a heterogeneous group whose overall qualification was above the average of physicians providing acupuncture within statutory reimbursement systems in Germany; (2) the consensus-based treatment protocol for AC and MA proved feasible and acceptable to physicians, however, a quarter of physicians would have applied acupuncture differently outside of the trial and most would have used additional therapies; (3) in the trial the tested AC intervention was highly effective compared to no treatment but there were no differences between patients receiving AC and patients receiving MA.

Randomized trials of acupuncture are urgently needed to evaluate the effectiveness of this widely used therapy. However, acupuncture is not a uniform intervention that can be standardized easily. Treatment outcomes probably vary depending on the acupuncturist's skills and characteristics of the specific intervention. From a strictly scientific point of view, reduction in variability is desirable, therefore, highly standardized treatment by a single expert in a homogeneous patient sample is reasonable. In routine health care, practitioner skills, treatments provided and patients all vary greatly. To guide decisions, pragmatic trials with flexible treatment provided by a sample of acupuncturists in a sample group of patients representing a defined setting seem more satisfactory. The reader of the report of such a trial, however, has only little idea of the actual treatment provided and whether it is similar to his own practice.

ART Migraine was performed at the request of German health authorities who explicitly required a 'sham-acupuncture controlled' trial to improve the evidence base for the decision whether or not to allow reimbursement of acupuncture by statutory sickness funds. We opted for a semi-standardized

Table 3. Treatment in the MA group (% or M ± SD) summed up for all sessions and for sessions 1, 5, and 10

	All sessions (n = 948)	Session 1 (n = 81)	Session 5 (n = 79)	Session 10 (n = 79)
Point,%				
– 'Deltoideus'	93	93	96	92
– 'Upper Arm'	82	80	81	83
– 'Lower Arm	52	49	46	52
– 'Scapula'	31	33	30	30
– 'Back I'	29	30	28	30
– 'Back II'	23	18	23	28
– 'Spina iliaca'	26	23	28	27
– 'Upper Thigh I'	83	85	80	85
– 'Upper Thigh II'	77	78	76	75
– 'Upper Thigh III'	65	64	66	66
Total number of needles, M ± SD	11.3 ± 2.7	11.1 ± 2.6	11.1 ± 2.6	11.3 ± 2.9
Length of needles used*, mm, %				
– <20	61	54	61	65
– 21–30	46	54	52	44
– 31–40	2	3	–	5
– >40	–	–	–	–
Duration of sessions, min, M ± SD	28.9 ± 3.8	28.6 ± 3.9	28.9 ± 3.7	29.2 ± 4.0

*More than one type of needles could be used in a single patient.

treatment strategy to insure at least basic replicability on the one hand and to allow some flexibility on the other. A large group of experts was involved in the consensus process to ensure that the strategy had relevance at least in a German medical framework. The discussions during the consensus process and with external experts showed that opinions vary strongly on how patients with migraine should be treated. The first question is whether (and if so, how) a syndrome diagnosis according to traditional Chinese medicine should be made before treatment. Obviously, selection of points is also a major issue. For example, some experts consider the acupoint gall bladder (GB) 20 to be mandatory. However, strong stimulation of this point can trigger or aggravate a migraine attack. Several physicians did not needle all predefined basic points in all patients indicating that they felt that some points were sometimes unnecessary. These are only two out of a range of aspects that could be discussed. The trial physicians' responses to the question how they would have treated patients outside of the trial show that the AC intervention in the study did not exactly represent routine practice. We cannot rule out that our treatment protocol was not optimal and we have to emphasize that our results might have been different if another treatment strategy had been chosen. We also performed analyses that were stratified by center to investigate whether outcomes varied between centers (for example, more and less experienced acupuncturists). While such center analyses always have to be interpreted carefully due to the small number of patients per center, we did not find any indication that more experienced or better-trained acupuncturists achieved better results.

A number of centers in our trial did not fully comply with the predefined semi-standardized acupuncture strategy. The physicians in these centers were all highly experienced acupuncturists and tended to use individualized approaches. We do not consider this non-compliance a major drawback of our trial. It even might increase the generalizability of our findings. Outcomes in non-complying centers were similar to those in the other centers.

Acupuncturists criticizing our treatment protocol as suboptimal or inadequate should be aware that it proved highly effective compared to no treatment. Furthermore, a comparison with the data from a large observational study of acupuncture in routine care, which was performed parallel to ART Mi-

Table 4. Acupuncturists questionnaire (n = 30)

	n (%)
How would you have applied acupuncture outside of the trial?	
Exactly the same way	3 (10)
Similarly	18 (60)
Differently	6 (20)
Totally differently	1 (3)
No answer	2 (7)
Would you have used additional therapies outside of the trial?	
Yes, in some patients	19 (63)
Yes, almost in every case	5 (17)
Did you have problems with minimal acupunture?	
Yes, on an ethical level	15 (50)
Yes, technically	2 (7)
Yes, during informed consent	11 (36)
I would participate again in ART Migraine	25 (83)

Table 5. Clinical outcome measures at weeks 9–12 (diary) and the end of week 12 (questionnaire), respectively

	AC group	MA group	WL group	AC vs. MA p	AC vs. WL p
Headache, diary weeks 9–12, M ± SD					
Reduction in days with moderate/severe headache compared to baseline (MOM)	2.2 ± 2.7	2.2 ± 2.7	0.8 ± 2.4	0.96	<0.001
Days with moderate/severe headache	2.8 ± 2.3	2.6 ± 2.4	4.3 ± 2.2	0.58	<0.001
Days with headache	4.9 ± 3.4	4.7 ± 3.4	6.3 ± 3.6	0.76	<0.01
Migraine attacks	1.5±1.2	1.6±1.3	2.3 ± 1.1	0.48	<0.001
Days with medication	3.2 ± 3.0	3.4 ± 2.9	4.4 ± 3.6	0.65	0.01
≥50% Reduction in days with moderate/severe headache, n (%)	74 (51)	43 (53)	11 (14)	0.78	<0.001
≥50% Reduction in migraine attacks, n (%)	78 (54)	43 (53)	13 (17)	1.00	<0.001
Questionnaire at the end of week 12, M ± SD					
Disability (PDI)	20.7 ± 16.6	20.2 ± 15.7	32.9 ± 17.1	0.82	<0.001
Physical health (SF-36)	46.7 ± 7.5	47.5 ± 7.0	42.5 ± 6.6	0.44	<0.001
Mental health (SF-36)	48.6 ± 8.8	47.6 ± 9.6	47.7 ± 10.6	0.47	0.56
Average pain (rating scale 0–10)	3.7 ± 2.0	3.6 ± 2.1	5.6 ± 2.1	0.87	<0.001

p-Values from 2-tailed t tests or Chi^2 tests.
MOM = main outcome measure; for all patients with missing data the value was set to 0. For the secondary outcomes missing values were not replaced.

graine, yielded very similar improvements (manuscript submitted for publication). Response rates in our trial were also comparable to those reported for drugs used for migraine prophylaxis recommended in current guidelines such as beta blockers or calcium channel blockers [12, 13]. The surprising finding in ART Migraine is not an inadequate response in the patients who received AC but the great and lasting improvement in many of those patients who received MA.

This raises the question of whether the consensus-based MA treatment protocol was inadequate. To comply with the request of the health authorities, the trial had to include some sort of sham acupuncture. We were not allowed to use controls such as inactive laser or TENS devices. We did not use 'placebo' (non skin-penetrating) needles as their handling would have been too complicated in a multicenter trial with a long treatment course. Instead, we chose a strategy that deviates from 'adequate' acupuncture in several aspects: superficial needling, non-acupuncture points in distant areas, no manual stimulation, and avoidance of de qi. Still, this strategy proved as effective as our AC intervention. Any intervention involving skin penetration cannot be considered an inert placebo and superficial needling is common in Japan [14]. Although the non-acupuncture points were chosen carefully and physicians could choose between several non-acupuncture points to ensure that potentially active areas could be avoided, we cannot rule out completely that some of the points still might have had some specific activity. However, there can be no doubt that the protocol for MA in our trial would not be considered a good strategy according to classical concepts of acupuncture. The results of similar trials we performed in patients with low back pain and osteoarthritis of the knee [15, 16] suggest that MA is particularly effective in migraine patients. This may be due to the different pathophysiological mechanisms involved in these diseases.

In summary, there are two major potential explanations for the lacking difference between patients who received AC and those who received MA in ART Migraine: (1) The AC treatment had no 'specific' effects (either because our specific treatment strategy was inadequate or because acupuncture, in general, has no 'specific' effect in migraine); (2) the MA intervention was too effective to detect 'specific' effects (either because the MA had 'specific' effects on its own or its 'non-specific' effects were too powerful).

Another important question is whether the response to acupuncture treatment differs among patients with different syndromes according to traditional Chinese medicine. However, it was not possible to investigate this question in ART Migraine. There is no generally accepted taxonomic classification system that can easily be used in multicenter trials involving acupuncturists with very different backgrounds. Furthermore, according to traditional Chinese medicine, migraine is a complex disease and a variety of syndrome diagnoses are possible. As a consequence, the number of patients with a specific syndrome diagnosis in our trial was too small to allow a reliable analysis.

In addition to methodological issues it seems necessary to mention some ethical issues of our trial. Half of the participating trial physicians reported that they found it ethically problematic to provide minimal acupuncture. While on a scientific level the effectiveness of acupuncture might not be proven beyond reasonable doubt most acupuncturists are convinced that their therapy works and that it does matter that they apply it in an adequate manner. It is not fully clear to what extent the resulting internal conflicts influenced the behavior of

trial physicians and whether this had an impact on study outcomes. Another highly critical point is our way of obtaining informed consent. The information we gave on the study interventions suggested to participants that two different types of acupuncture were compared although one was described as not following the rules of Chinese medicine. The words sham, placebo or minimal acupuncture were not mentioned, mainly to avoid that patients tried to find out whether they received the 'true' or the 'fake' intervention. All ethical review boards accepted this approach and the results of the trial might justify it post hoc. Similar ways to obtain consent seem to be frequently used in sham-controlled trials of acupuncture. Still, the ethical problem remains.

In conclusion, we believe that the treatment protocols for AC and MA in ART Migraine were an adequate compromise in the specific situation and for the predefined purposes. Such compromises always have drawbacks. Without the inclusion of an untreated control group, ART Migraine would clearly have been interpreted as a negative trial. The additional comparison with the untreated control group, however, made clear that the issue is complex. We recommend such an additional control group whenever possible in sham-controlled trials of acupuncture.

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Competing Interests

MH, JH and DI have received fees for teaching acupuncture in courses of professional societies. All other authors: none

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