

Credibility of a Newly Designed Placebo Needle for Clinical Trials in Acupuncture Research

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Key Words

Acupuncture research · Placebo · Placebo needle · deqi

Summary

Objective: To test the credibility of a newly designed placebo needle for acupuncture research. **Design:** Analysis of data on credibility of true and placebo interventions of a randomised, placebo-controlled, patient- and evaluator-blind clinical trial. **Patients and Setting:** The study was carried out at a university department for physical medicine and rehabilitation. 68 patients (age 48.1 ± 14.1 years, mean \pm SD) fulfilling the criteria of the International Headache Society for tension-type headache were enrolled into the study. **Interventions:** Group 1 (treatment) was assigned to traditional needle placement and manipulation, whereas in group 2 (control) a new placebo device was used. **Outcome Parameters:** After the first treatment with real or placebo acupuncture, patients were asked to fill in a questionnaire on credibility. In addition, after 3 or 4 treatments, patients were asked for the feeling of needle insertion and deqi. **Results:** No difference between real and placebo acupuncture was detected with respect to the credibility of the treatment ($p > 0.05$). Needle insertion was recognised in all patients in the real acupuncture group and in all but 4 patients of the placebo group ($p < 0.05$). deqi was reported by 84% of patients in the real acupuncture group and by 34% of patients in the placebo group ($p < 0.001$). **Conclusion:** Acupuncture with the placebo needle device described here is of high credibility, and does not differ from that of real acupuncture treatment. However, to achieve comparable prick sensations in both treatment conditions, careful training with the placebo needle is needed. Furthermore, from these results arise new questions with respect to the placebo response of placebo needles. Further investigations are warranted to test if placebo needles are active controls.

Schlüsselwörter

Akupunkturforschung · Placebo · Placebonadel · De-Qi

Zusammenfassung

Fragestellung: Überprüfung der Glaubwürdigkeit einer neu entwickelten Placebonadel für Akupunkturstudien. **Design:** Analyse der Glaubwürdigkeit einer echten Akupunkturbehandlung und Scheinakupunktur in einer randomisierten, plazebokontrollierten, patienten- und untersucherblinden klinischen Studie. **Methode:** Die Studie wurde in der Klinik für Physikalische Medizin und Rehabilitation an der Medizinischen Hochschule Hannover durchgeführt. 68 Patienten (Durchschnittsalter: $48,1 \pm 14,1$ Jahre, Mittelwert \pm SD), die den Kriterien für Spannungskopfschmerz der International Headache Society erfüllten, wurden in die Studie aufgenommen. **Behandlung:** In der Gruppe 1 (echte Akupunktur) wurden die Patienten in Bezug auf die Stichtiefe und Nadelmanipulation mit normale Akupunkturadeln nach den Regeln der traditionellen Chinesischen Medizin akupunktiert, in der Gruppe 2 (Kontrolle) wurde eine neu entwickelte Placebonadel verwendet. **Zielparameter:** Nach der ersten Behandlung füllten die Patienten einen Fragebogen aus, der die Einschätzung der Glaubwürdigkeit der Behandlung ermöglicht. Zusätzlich wurden die Patienten nach der 3. oder 4. Behandlung nach dem Einstichgefühl und dem De-Qi-Gefühl befragt. **Ergebnisse:** Zwischen beiden Behandlungen konnten keine Unterschiede in der Glaubwürdigkeit der Behandlung entdeckt werden ($p > 0,05$). Der Nadeleinstich wurde von allen Patienten der Gruppe 1 (echte Akupunktur) wahrgenommen, 4 Patienten in der Placebo-Gruppe verspürten keinen Einstich ($p < 0,05$). 84% der Patienten berichteten unter echter Akupunktur über ein De-Qi-Gefühl, in der Placebogruppe waren dies jedoch nur 34% ($p < 0,001$). **Schlussfolgerung:** Die Behandlung mit einer Placebonadel erzielt eine hohe Glaubwürdigkeit und unterscheidet sich diesbezüglich nicht von einer echten Akupunkturbehandlung. Für die Auslösung eines vergleichbaren Einstichgefühls bedarf es jedoch eines sorgfältigen Trainings mit der Placebonadel. Des Weiteren ergeben sich neue Fragen im Hinblick auf die Placeboreaktion dieses Verfahrens. Weitere Studien müssen zeigen, ob die sogenannten Placebonadeln nicht in Wirklichkeit eine aktive Kontrollbehandlung darstellen.

Introduction

When classical conservative treatment modalities have been unsuccessful or side-effects have occurred, an increasing number of patients examine the possibilities of complementary and alternative medicine, especially needle acupuncture [1, 2]. In spite of the increased demand for complementary medicine, there is little evidence that needle acupuncture has specific effects in the treatment of most indications for which it is used in daily practice [3]. In particular, when acupuncture is used in pain treatment, it is unclear whether the relief of pain following stimulation of specific acupuncture points is the result of a placebo effect as placebo may well be able to alleviate pain by activating pain-inhibiting mechanisms [4, 5], e.g. by activating the endogenous opioid system [6].

From placebo-controlled trials with drugs it is well known that the mode and manner of administration has a decisive influence on the effectiveness of the placebo, which can even be influenced by the size and colour of the placebo tablet [7]. The patient- and investigator-blind, placebo-controlled study has been established as the golden standard for the quantification of this response in pharmacological studies of effectiveness. Most disparate methods, including for example inactive TENS [8], have been used for as placebo intervention in studies on the effectiveness of acupuncture. Therefore any differences between the effects of these controls and genuine acupuncture could, at least theoretically, be due to differences in placebo effects. In an attempt to reduce this problem of differential placebo response, different placebo needles have recently been developed [9–11].

To carry out a placebo-controlled trial on acupuncture in headache [8], a new placebo needle was designed. This placebo needle was developed because other placebo needles were then not commercially available although some data on placebo needles had been published [10]; however, this study group kept back manufacturing details of their placebo needle.

An essential aspect of the development of new placebo treatments is that there should be as little difference as possible in credibility between placebo and real treatment so that the psychological components of both are comparable [12–14]. In a study on the effectiveness of acupuncture on headache [9], the credibility of a simple new form of placebo needle was investigated in parallel. This methodological section of the headache study is presented here.

Patients and Methods

We included 68 subjects (age 48.1 ± 14.1 years, mean \pm SD) with episodic (21) or chronic (47) tension-type headache (TTH), according to the IHS classification, as previously reported [8]. Previous treatment with acupuncture was not a criterion for exclusion. Subjects were randomly assigned to placebo or real treatment in a patient- and investigator-blind, placebo-controlled trial. The patients gave written informed consent to participate in the study. The study was approved by the local ethics committee.

Measurement of Credibility

Borkovec developed a questionnaire which aims at assessing the credibility of a treatment [15]. We extended this questionnaire by additional items and already used it in an earlier study to investigate the credibility of invasive placebo acupuncture [16]. This is a three-dimensional questionnaire. In the first section, patients are asked about their general interest in and previous knowledge of acupuncture, and their contact to doctors who use acupuncture. The second section focuses on general acceptance of acupuncture as a procedure for treatment and the third section on the credibility and expectancy of patients for the actual treatment. To test credibility, patients filled in this credibility questionnaire after the first treatment. Additionally, after four or five treatments patients were asked to state whether they felt the needle insertion and if a deqi sensation was elicited. Socio-demographic and psychometric data, and information on the intensity, frequency and duration of the headaches have already been reported [9].

Setting

Both the investigator who performed the follow-up examinations and statistical procedures and the patients were blinded to the treatment condition (placebo vs. real acupuncture). After randomisation patients were given appointments during normal out-patient times in a way that patients had no contact with each other. Thus the treatment was carried out in a 'single setting modus', i.e. any contact between patients during the trial was avoided. This was considered necessary because communication between patients can influence the result of treatment in parallel group designs [17]. Before enrolment patients were told that they would be randomly assigned to one of two different forms of acupuncture treatments and that it was not known which of the two forms was more effective. In addition, patients in the placebo group were told that the needles would only be stuck in gently and superficially and that an elastic cube would therefore be necessary to fix the needle.

In order to reduce the influence of the acupuncturist during his contact with the patients, no conversations about the patients' current complaints nor about specific characteristics of acupuncture were carried out during the treatment. Questions from the patients were prevented by instructing them to relax throughout the treatment and that this was particularly important for the effectiveness of acupuncture. At the first treatment, the patients were told that they may feel a prick from the needle. They were also told that a deqi sensation may occur when the needle is inserted, and that this is a feeling of numbness which may be accompanied by warmth and may spread from the site of puncture.

Treatment Modalities

Placebo Acupuncture Needling

We aimed at developing a placebo needle everyone could prepare easily. For preparing the needles, the tip of real acupuncture needles (no. 16, 30×0.3 mm, Asiamed Inc., München, Germany) was removed and the new end was rounded with a diamond polisher. The blunted tip of the placebo needle causes a pricking sensation without actually penetrating the skin. The holding device for the needle is made of sterilised foam and is cube-shaped. The foam is fixed with an O-ring of adhesive tape. To optimise fixation, the skin was cleaned with a disinfecting agent. When the tip touches the skin, the needle is kept adequately in position by the foam. Inserting the needle through the elastic foam blocks the volunteers' view of the point of contact. When the tip of the needle had touched the skin, the needle was gently twisted to enhance the impression of a prick. The patients underwent 2 treatments per week for a total of 10 treatments. Placebo needles were placed bilaterally at acupoints GB20 (medial to the mastoid process), LI4 (first dorsal interosseus muscle of the upper limbs), LR3 (first dorsal interosseus muscle of the lower limbs) and TW5 (between radius and the ulna, proximal to the wrist). The needles were left in place for 30 min. Overall 8 placebo needles were used per session.

Table 1. Sample characteristics (baseline values)

	Placebo		Real acupuncture	
	mean	SD	mean	SD
Number of patients	34		34	
Gender (f/m)	21/14		17/17	
Episodic/chronic TTH	12/22		9/25	
Age, years	48.2	14.6	47.9	13.8
Headache frequency per month, days	20.5	10.3	21.1	10.2
Pain at consultation, numeric rating scale 1-10	6.3	1.9	6.4	2.0
Headache over 4 weeks, numeric rating scale 1-10	4.4	1.3	4.6	1.8
Analgesics/month, tablets	15.6	32.4	9.0	11.1
D-S, range 0-48	9.0	5.7	9.0	8.3
Nottingham Health Profile, range 0-38	28.6	5.7	29.9	7.2
Everyday-Life Questionnaire, range 0-168	116.1	23.8	114.7	25.0
Quality of life scale, numeric rating scale 0-10	5.7	2.6	5.8	2.2

D-S = von Zerssen Depression Scale.

Table 2. Results of the credibility questionnaire

	Mean	95% CI	SD	p value
<i>Section 'interest' (0-1.7)</i>				
Placebo (n = 32)	1.073	0.94-1.20	0.3566	0.789
Real (n = 31)	1.097	0.3463		
Difference	0.0239	-0.1533-0.2010		
<i>Section 'general acceptance' (0-3)</i>				
Placebo (n=31)	2.315	2.07-2.57	0.070	0.673
Real (n=33)	2.242	1.97-2.25	0.6510	
Difference	-0.072	-0.4114-0.2672		
<i>Section 'credibility' (0-3)</i>				
Placebo (n=31)	2.363	2.18-2.54	0.4951	0.178
Real (n=31)	2.508	2.40-2.63	0.3259	
Difference	0.452	-0.0678-0.3581		

Real Acupuncture Needling

Seirin (Neu-Isenburg, Germany) B-type needles no. 8 (0.3 × 0.3 mm) and no. 3 (0.2 × 0.15 mm) were used for real acupuncture. The needles were left in place for 30 min after insertion. A maximum of 15 needles was inserted, but treatment was usually carried out with no more than 6-10 needles as reported elsewhere [9].

Statistics

Differences between the two groups concerning the questionnaire on credibility were tested by student's t-test for unpaired values. Fisher's exact test was used for dichotomous variables (i.e. 'insertion' and 'deqi'). p values of <0.05 were considered statistically significant. The Wilcoxon test was used to qualitatively describe differences between groups in socio-demographic data.

Results

Baseline values of both groups were well comparable concerning headache severity, headache frequency, socio-demographic data and quality of life parameters (table 1).

Out of 68 patients, 64 patients filled in the credibility questionnaires correctly and could be used for further calculation. There were no significant differences between the treatment groups with respect to the three sections of the credibility questionnaire ('interest', 'general acceptance' and 'credibility'; $p > 0.05$). The results are shown in tables 2 and 3. For the item 'Have you felt the needle insertion?' there was a difference between the groups. All patients in the real acupuncture group reported that they felt the needle prick during the treatment. This was not the case in 4 patients of the placebo group. This difference was not significant ($p \geq 0.05$). The difference was more marked and came to significance for the needling sensation. 27 of the 32 patients in the real acupuncture group reported that they had felt a deqi sensation shortly after the prick and in connection with the mechanical stimulation of the needle (twisting). This was reported only by 11 of the 32 patients in the placebo group ($p < 0.001$). Patients who did not feel the prick also did not feel the deqi sensation ($p > 0.05$).

Table 3. Results for feeling insertion of the needle and for the deqi sensation

	Count	yes	no	p value
<i>Insertion of the needle</i>				
Placebo	32	28	4	0.113
Real	32	32	0	
<i>deqi sensation</i>				
Placebo	32	11	21	0.001
Real	32	27	5	

Discussion

In controlled trials acupuncture has been compared with 'placebo' interventions such as mock TENS [8], placebo tablets [18] or with inactivated laser apparatus [19]. To simulate the prick of a needle, some authors used a finger-nail [20], guide tube [21] or cocktail stick [22]. However, these control procedures cannot be considered optimal since they are likely to have a different level of credibility [23]. Acceptance and credibility are considered essential determinants of the placebo response, and it has therefore been suggested that control treatments in acupuncture research should be evaluated on the basis of their credibility [24, 25].

The performances of the two treatment conditions in the present study were not exact the same because the holding device was not used in the real needle group, which causes the risk of unblinding the patients. However, we included patients not having received acupuncture before. Therefore using the holding device in one group can not be judged as information for the patient which kind of treatment he received. The results of the present study show that our newly developed placebo needle exhibited credibility and acceptance similar to that of real acupuncture. With respect to the reliability of applying the new placebo needle, no spontaneous removal appeared throughout the study. Using an adhesive tape to fix the holding device of the placebo equipment on the skin seems thus a suitable method.

The observation that fewer patients in the placebo group felt the insertion of the needle has also been reported previously [9]. One probable reason for this is that the placebo needles are pressed down differently to the skin and that the twisting

of the blunt needle was not sufficient. This problem can however be overcome by adequate training with the placebo needle.

In the placebo group, 11/32 patients reported feeling deqi. There could be a measurement error here since all patients were told before treatment what deqi felt like, possibly biasing the response. Although the real acupuncture group reported deqi more often (27/32 patients), it seems possible that the lack of difference in clinical outcome studies using placebo needles like the one tested here could be attributed to an active 'placebo'. On the other hand, recent functional brain imaging studies have found no modulation of the activities of hypothalamus-limbic systems by *superficial* tactile or pricking stimulation at LI4, in contrast to real acupuncture needle stimulation, indicating that central pain-inhibiting pathways are not activated by the prick of placebo needles [26, 27]. Hsieh et al. [28] demonstrated real needling at a depth of 1 cm to activate the hypothalamus, in contrast to superficial non-stimulated needling. However, it is unknown whether central pain-inhibiting pathways are activated when patients report a deqi from placebo needling at acupuncture points. Therefore it seems to be advantageous to use non-acupoints for placebo needling as in the study of Hsieh et al. [28] no activation of central pathways was seen when deqi stimulation was performed at non-acupoints.

Conclusion

There was no difference with respect to credibility between the placebo needle treatment used in the present study and real acupuncture needling. In addition, compared with other placebo needles, it is certainly the most economical placebo needle equipment. Preparing the needle is easy and does not require any special technical appliance. Using it correctly, requires some experience if all patients are to have the impression of needle insertion. This placebo needle has been used in the present study for the first time. The analysis of these data however call into question the main claim of placebo needles that they only are eliciting a placebo response because deqi, by definition a sensation of real needling, was also registered in the placebo group.

In order to avoid stimulation of central pain-inhibiting pathways with placebo needles, it seems to be appropriate to use non-acupoints which are clear of real acupuncture points. However, further investigations are warranted to demonstrate that placebo needles are not active controls.

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