Pain Medicine 2017; 18: 2235–2247
doi: 10.1093/pm/pnx052

OXFORD

INTEGRATIVE MEDICINE SECTION

Original Research Article

Immediate Pain Relief in Adhesive Capsulitis by Acupuncture—A Randomized Controlled Double-Blinded Study

Sven Schröder, MD, Dr. med. (PhD),* Gesa Meyer-Hamme, MD,* Thomas Friedemann, PhD,* Sebastian Kirch, cand. med.,* Michael Hauck, MD, Dr. med. (PhD),†,‡ Rosemarie Plaetke, PhD,§ Sunja Friedrichs, cand. med.,* Amit Gulati, PhD,§ and Daniel Briem, MD, Dr. med. (PhD)¶

*HanseMerkur Center for Traditional Chinese Medicine at the University Medical Center Hamburg-Eppendorf, Hamburg, Germany; †Departments of Neurology; ‡Neurophysiology and Pathophysiology; §Medical Biometry and Epidemiology; ¶Trauma, Hand, and Reconstructive Surgery, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Correspondence to: Sven Schröder, HanseMerkur Center for Traditional Chinese Medicine at the University Medical Center Hamburg-Eppendorf, Martinistrasse 52, House O55, 20246 Hamburg, Germany. Tel: +49-4041357990; Fax: +49-4041357960; E-mail: schroeder@tcm-am-uke.de.

Funding sources: The study was funded by the HanseMerkur Insurance Group, Germany. SEIRIN Corporation, Japan provided the press tack needles and the press tack placebos.

Conflicts of interest: The authors have no conflicts of interest to declare.

Abstract

Objective. Primary adhesive capsulitis (AC), or frozen shoulder, is an insidious and idiopathic disease. Severe pain is predominant in the first two of the three stages of the condition, which can last up to 21 months.

Design, Setting, and Subjects. Sixty volunteers with primary AC were randomly assigned to acupuncture with press tack needles compared with press tack placebos in a patient- and observer-blinded placebo-controlled study. The participants were subsequently offered classical needle acupuncture in an open follow-up clinical application. Thirty-four volunteers received conservative therapy, including 10 classical needle acupuncture treatments over 10 weeks, 13 volunteers received conservative therapy without classical needle acupuncture. All subjects agreed to follow-up after one year.

Methods. Acupuncture treatment was performed using a specific distal needling concept, using reflex areas on distant extremities avoiding local treatment.

Results. An immediate improvement of 3.3 ± 3.2 points in Constant-Murley Shoulder Score (CMS) pain subscore was seen in the press tack needles group and of 1.6 ± 2.8 points in the press tack placebos group ($P<0.02$). Conservative therapy including classical needle acupuncture significantly improved the pain subscore within 14.9 ± 15.9 weeks compared with 30.9 ± 15.8 weeks with only conservative therapy ($P<0.001$).

Conclusion. The efficiency of distal needling acupuncture on immediate pain reduction was demonstrated in patients with AC and confirmed the applicability of press tack needles and press tack placebos for double-blind studies in acupuncture. Subsequent clinical application observation proved that results obtained with press tack needles/press tack placebos can be transferred to classical needle acupuncture. Integrating acupuncture with conservative therapy showed superior effectiveness with respect to the time course of the recovery process in AC compared with conservative therapy alone.

Key Words. Frozen shoulder; Adhesive capsulitis; Constant-Murley Shoulder Score; Acupuncture; Press Tack Needle; Double-blinded study

Introduction

Adhesive capsulitis (AC), as a particular reason for pain in the shoulder joint, was first mentioned by Codman in

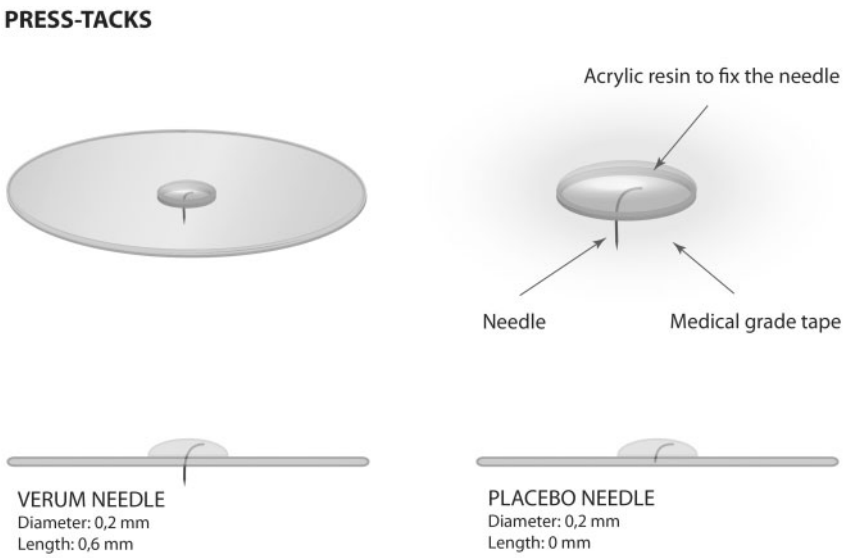

Figure 1 Press tack needle and press tack placebo.

1934 and later on by Neviaser [1]. Primary AC is predominantly an idiopathic condition with no known precipitating event and is associated with diabetes [2,3]. Secondary AC can be provoked by trauma or operations of the shoulder joint and is less frequent [4]. AC is self-limiting for one to four years. It can present in three distinct stages. The first stage is called the freezing or painful stage. This lasts three to nine months, and affected patients have an acute synovitis of the glenohumeral joint. Most patients progress to the second stage—the frozen or transitional stage. The pain does not necessarily worsen and can last between four and 12 months. The third stage is termed the thawing stage. Patients begin to have improved range of motion within 12 to 42 months [5].

Initially, AC is treated by nonoperative treatment programs, including local or systemic administration of corticosteroids, as well as different physiotherapy regimes [6–8]. Manipulation under anesthesia and arthroscopic capsular release are described as surgical approaches; both reveal comparable results [9–11]. However, manipulation under anesthesia may lead to damage of the labrum and humeral head, and recurrent adhesion of the capsule may occur despite surgery [12].

Acupuncture has a long tradition of being applied to patients with painful conditions. It has been successfully accepted as pain management in Western medicine [13]. The common technique in acupuncture is the insertion of needles; its treatment effect can be further enhanced by rotation, lifting and thrusting of the needle, or by the application of electric current or heat [14]. Several investigators agree that this type of manipulation causes a peripheral effect through the release of local tissue substances and transmitters [15]. Designing a controlled trial with a placebo becomes comparatively difficult as patients feel pain as a result of manipulation with acupuncture needles. When designing clinical trials for evaluating acupuncture, this is a major challenge.

Treatment with shallow needles (depth of insertion < 2 mm) traditionally does not include stimulation techniques. It is a treatment that has been described and recommended for pain management in ancient Chinese literature (Chapter 1 of the "Spiritual Pivot," *Huangdi Neijing Lingshu*, 1st cent. BC) [16]. Press tack needles, a special kind of shallow needles, have been primarily developed for the pursuit of a safer and noninvasive method of acupuncture [17]. These needles cause almost no sensation at the time of insertion and can be removed from the puncture site without obvious skin alteration. Using press tack needles for verum acupuncture [18] and press tack placebo needles for sham acupuncture means that double-blind studies can be performed. Press tack placebos look the same for user and patient, but they lack the needle elements (Figure 1). Both types of devices were compared in a randomized controlled trial, and no significant differences were shown concerning the perception(s) of insertion [19].

Until now, no randomized placebo-controlled clinical comparison studies evaluating the efficacy, applicability, and safety of press tack needles compared with press tack placebos for patients with AC have been reported in the literature.

The aim of our study is to evaluate the effectiveness and applicability of acupuncture in the management of AC ("frozen shoulder") by comparing press tack needles with press tack placebos. In this article, we discuss the clinical decision-making process (encompassing clinical expertise and research resources in managing AC), as

well as the transferability of results obtained from press tack needles and press tack placebos to classical needle acupuncture and the outcomes of care for patients with AC.

Methods

Study Design

Clinical Trial

To investigate whether press tack needles can reduce pain in patients with AC, and thus be applied as an additional pain therapy, we conducted a prospective, single center, randomized, placebo-controlled, double-blind trial (two parallel arms) between January 2012 and December 2013.

Follow-up Study

After finishing their assigned treatment, all patients were offered 10 treatments with classical needle acupuncture in an open follow-up study lasting 10 weeks. The last classical needle acupuncture treatment ended in March 2014. Participants' re-evaluation was finished in January 2015.

Inclusion/Exclusion Criteria

To be eligible for the clinical trial, patients had to 1) be at least 18 years old and 2) have primary AC lasting more than one month and with a Constant-Murley Shoulder Score (CMS) pain subscore of 10 (means mild pain) or lower [20].

Patients were excluded from the study if they had 1) prior treatment with press tack needles; 2) a history of major shoulder injury or surgery; 3) a complex regional pain syndrome of the hand or forearm; 4) other disorders possibly influencing existing shoulder symptoms; 5) cervical neuropathy; 6) paralysis or neurological changes of the affected upper limb; 7) fractures or open wounds at the acupuncture application sites; 8) mental disorders possibly affecting their examination and intervening for the diagnosis or evaluation and progression of the disorder; 9) degenerative, inflammatory, or infectious arthritis; 10) history of intra-articular injection pain treatment for their affected shoulder within the last four weeks before recruitment; 11) pregnancy or breastfeeding; 12) noncompliance with the research protocol; and 13) failure to give informed written consent.

In the determination of patients' eligibility for the trial, DB (an experienced shoulder specialist) examined and evaluated them. Patients' clinical diagnosis of AC was confirmed. Other causes (as described above) were excluded by performing a magnetic resonance imaging (MRI) scan of the affected shoulder.

Recruitment of Patients

Clinical Trial

We screened 2,512 patients at the Department of Trauma, Hand and Reconstructive Surgery at the University Medical Center Hamburg-Eppendorf; 2,452 patients were not eligible for the study. This was because they had one of the above described exclusion criteria or did not meet the inclusion criteria. A total of 60 patients (21 males, 39 females) agreed to participate. After giving informed written consent, the patients were randomly assigned to a treatment or placebo group.

Follow-up Study

Thirty-four volunteers agreed to receive classical needle acupuncture treatment (18 from the press tack needles group and 16 from the press tack placebos group). Twenty-six patients did not want to continue because of "lack of time" or "fear of classical needles." However, 13 of them agreed to a re-evaluation of their shoulder pain after one year. Patients were allowed to receive any other intervention to treat pain. All patients were treated conservatively during the follow-up period. The treatment was managed by the shoulder specialist (DB). Figure 2 gives an overview of the study designs and recruitments.

Randomization and Allocation Concealment

Randomization of the 60 patients was performed in two steps.

First, the first 30 recruited patients were randomly assigned to press tack needles or Press tack Placebo treatment according to a randomization procedure with a 1:1 allocation ratio. Randomization was nonstratified and well balanced. Random numbers were generated and assigned to these patients by an independent researcher (TF) using Microsoft Office Excel, Microsoft Corporation, Redmond, WA, USA (2007).

Allocation concealment was implemented by putting the random assignment information within sequentially numbered, opaque envelopes and sealing them. Only study nurse 1 was allowed to open each envelope sequentially after she had written the participant's name on it.

After treatment of the 30 patients, their random assignment was unsealed by TF to obtain necessary information for a power analysis. However, all physicians, other researchers, research nurses, outcome assessors, and patients remained blinded to treatment allocation until the final analysis was completed.

Second, based on this power analysis, the sample size was increased to 60 participants. Subsequently, 30 additional participants were recruited and randomly

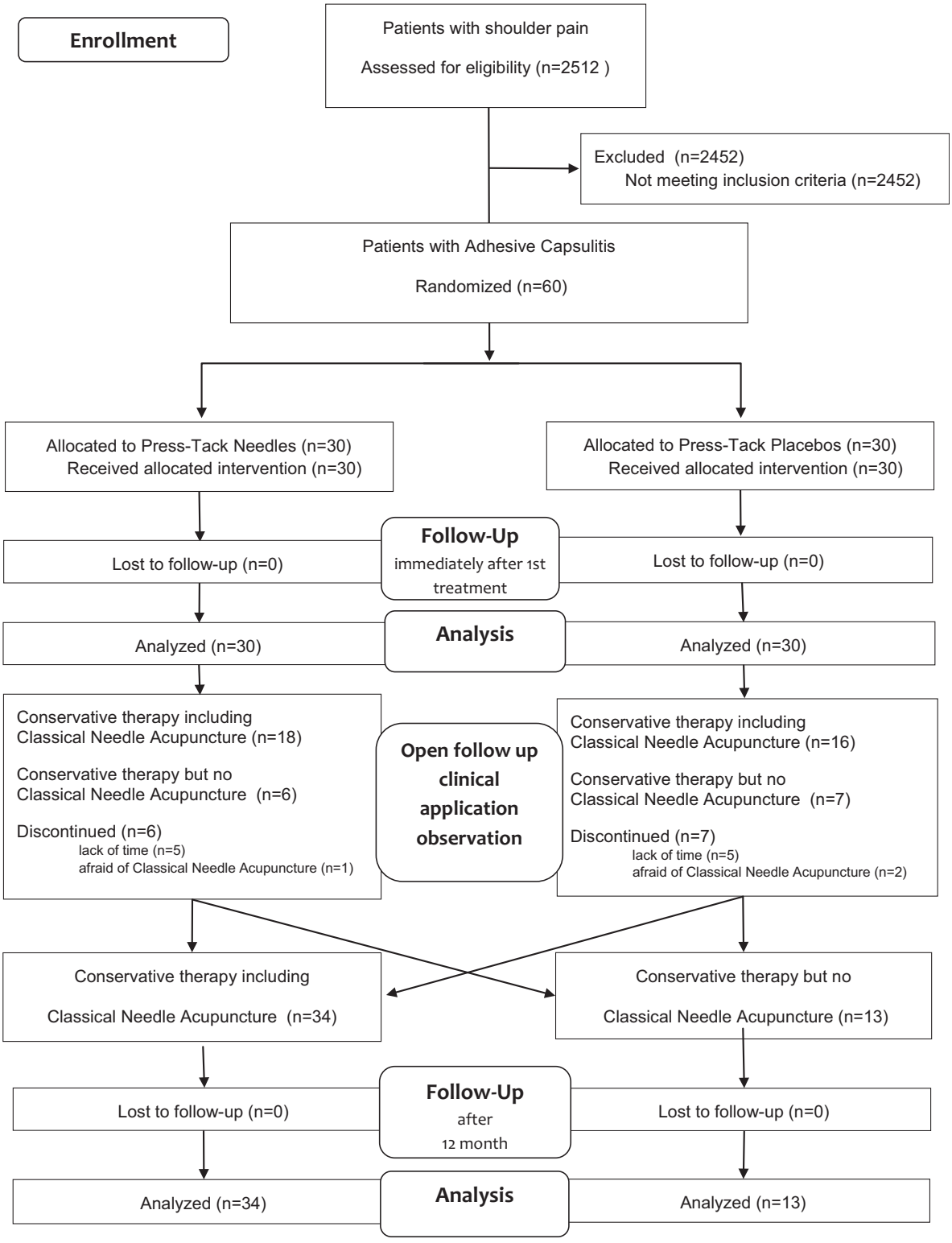

Figure 2 Flow chart of the randomized double-blinded study and the open follow-up observation.

assigned following the same randomization procedures as described above.

Blinding

For each treatment, study nurse 1 opened a patient's opaque, sealed envelope and prepared a tray containing needles according to his/her group assignment. All trays looked alike; press tack needles or press tack placebos were placed in such a way that investigators could not distinguish them from each other. Before treatment, study nurse 2 acquired the tray with press tack needles or press tack placebos, respectively; both study nurses did not communicate with each other. Study nurse 2 gave the tray to the acupuncturist and stayed during treatment. In this way, study nurse 2 and the acupuncturist were able to witness each other's actions and check if patients were complying with the study protocol and not closely examining the needles.

When treatment and examination was completed, study nurse 3 removed the needles. The patient did not see the needles. Study nurse 3 was not allowed to examine these needles and did not talk to the participant(s), nor to any person involved in the study. Removed press tacks were disposed of in a punctured-resistant, rigid container for biomedical waste, whose content could not be accessed at all.

Study Procedures—Clinical Trial

Acupuncture Treatment

For acupuncture therapy, we used press tack needles with a diameter of 0.2 mm and length of 0.6 mm (Pyonex; Seirin Corporation, Shizuoka, Japan). Press tack needles have an adhesive plaster that adheres to the skin for possible long-term placement. Press tack placebos are visually identical to press tack needles; however, their needle elements are removed from the shaft (Figure 1).

The acupuncture concepts and therapeutic strategies for shoulder pain vary depending on the most affected anatomical areas (e.g., frontal, dorsal, or lateral aspect of the shoulder), as well as the painfulness of shoulder movements, in other words, abduction, adduction, internal or external rotation, flexion or extension, and circumduction. In Chinese medicine, the painful areas and movements are assigned to "channels" (syn.: "vessels" or "meridians"). Additionally, Chinese medicine theory defines areas and acupoints on distant extremities and channels as potential reflex areas [16]. The corresponding reflex areas are pain sensitive (so-called *ashi* points) [21]. Accordingly, the most effective treatment areas and acupoints are defined during an examination process. This concept makes it possible to avoid points located in the painful area of the shoulder and to develop an individualized treatment based on the examination prior to treatment.

A detailed description implementing this concept as a treatment protocol is provided in our earlier publications [22,23]. This description consists of selecting a combination of corresponding reflex areas located on extremities, distant to the affected area, by using a somatotopic imaging model. During the orthopedic examination, the most pressure-sensitive areas (*ashi*) and the most painful movements were identified; consequently, the most affected channels were determined. Subsequently, reflex areas on corresponding channels and on corresponding body regions to the shoulder at the extremities were systematically examined for pain-sensitive areas. These identified areas were treated with press tack needles or press tack placebos, respectively. The treatment protocol is described in Table 1. Participants received just one treatment. Two acupuncturists (GMH, SS) with more than 10 years' clinical experience performed the treatment.

Measurements

All participants were assessed by an orthopedic examination including active and passive movement of the shoulder before treatment using the CMS assessment. This is a widely used method to evaluate shoulder syndromes and determine the function of the shoulder. This test has four subscales: pain, activities of daily living, strength, and range of motion. The pain subscale consists of 16 items, each scaled from 15 to 0 (15 means no pain, 10 means mild pain, 5 means moderate pain, and 0 means severe pain). Thus the higher a CMS, the better a shoulder joint can function [20]. The CMS has proven to be a valuable diagnostic instrument and has been validated for AC [24]. Participants were examined just before the treatment procedure and re-examined immediately after the application of the press tacks. Press tacks were applied so that they did not interfere with post-treatment examination. The researcher (SK) performed the examinations, obtained the pain ratings, and recorded the measurements. After the treatment, participants were asked if they received verum or placebo treatment.

Study Procedures—Follow-up Study

Acupuncture Treatment

Participants in the follow-up study received 10 classical needle acupunctures over 10 weeks. Treatments were performed according to the above-described point selection protocol of the clinical trial. Disposable sterile steel needles of 0.30 × 30 mm were inserted to a depth of 10 to 30 mm and remained for 20 minutes.

Measurements

CMS pain subscore was determined before the first of the 10 acupuncture treatments and after 12 months. Patients were (after 12 months) additionally interviewed to find out how long it took them to obtain their status on CMS pain subscore at the time of interview.

Table 1 Treatment protocol

1. Identify the most affected shoulder region by palpation, passive and active movements and define the most affected channel*.

2. Select one unaffected extremity. Investigate channels* that correspond to the one channel* found in step 1. These channels* are examined in specific regions of the extremity (e.g., knee, ankle, contralateral elbow, or wrist) and correspond to the most affected area of the shoulder. Treat the most pain-sensitive acupuncture points (*ashi*).

3. Select another unaffected extremity. Investigate channels* that correspond to those channels* found in step 1 as well as in step 2. These channels* are examined in specific regions of the extremity (e.g., knee, ankle, contralateral elbow, or wrist) and correspond to the most affected area of the shoulder. Treat the most pain-sensitive acupuncture points (*ashi*).

4. Select the remaining unaffected extremity. Investigate channels* that correspond to those channels* found in steps 1, 2, and 3. These channels* are examined in specific regions of the extremity (e.g., knee, ankle, contralateral elbow, or wrist) and correspond to the most affected area of the shoulder. Treat the most pain-sensitive acupuncture points (*ashi*).

5. On the affected arm, examine acupoints on the channel* identified in step 1. However, treatment is only applied to distal regions corresponding to the affected shoulder (e.g., elbow, wrist). Treat the most pain-sensitive acupuncture points (*ashi*). No needles are inserted directly into the shoulder region.

*Channels (syn.: vessels or meridians) are anatomically defined areas on the body surface recognized as potential reflex areas, described by Traditional Chinese Medicine [16,21]; definitions of corresponding channels and corresponding body regions have been described in detail previously [22,23].

Outcomes

Primary Outcome

In both studies, the CMS pain subscore was the primary outcome.

Secondary Outcomes

To measure treatment efficiency, the other items of the CMS (activities of daily living, strength, and range of motion) were selected as secondary outcomes.

Statistical Analysis

Statistical analysis was based on the intention-to-treat principle. Descriptive statistical analysis was used to characterize mean, median, standard deviation, and range. Data was presented as mean ± standard deviation (SD). Hypotheses were tested by applying *t* test for paired or unpaired samples or χ^2 test according to type of data. Homogeneity of variances was tested with Levene's test. Normality of data was tested with Shapiro-Wilk test. If continuous data were not normally distributed, nonparametric tests (e.g., Mann-Whitney U test) were performed. Tests were performed two-sided with a significance level $2\alpha = 0.05$. Statistical analysis was performed with SPSS 21.0 (SPSS, Chicago, IL, USA).

Power Evaluations

An a priori sample size estimate, based on CMS data of the first 30 participants, postulated a two-sided confidence of 95% and a power of 80%. Power was evaluated for a one-sided, two-sample *t* test. We performed an a posteriori evaluation of the power of our study using given sample sizes (N = 30) for each group, our estimates of their means (3.3 and 1.6, respectively), and SD (3.2 and 2.2, respectively). The power to detect a difference of 1.7 between the means with a one-sided, two-sample *t* test is 77% if $\alpha = 0.05$. A posteriori power evaluations were conducted using the PASS statistical software package (NCSS 2008, Kaysville, UT, USA). Based on this evaluation, the sample size was then increased to 60 participants. Subsequently, 30 additional participants were recruited.

Trial Registration and Ethical Approval

The study was conducted in accordance with the principles stated in the Declaration of Helsinki, the Good Clinical Practice (International Conference on Harmonization), and national as well as local regulations. The research protocol was approved by the ethics committee (Ethik Kommission der Hamburger Ärztekammer,

Table 2 Characteristics of study population at baseline

	Group treated with	
	Press tack needles (N = 30)	Press tack placebos (N = 30)
Females/males	20/10	19/11
Age*, y	55.1 ± 10.4 (range = 36–81)	51.9 ± 8.9 (range = 32–66)
CMS pain sub score* (pretreatment)	4.1 ± 2.5	4.3 ± 2.6
Duration of disease*, mo	16.0 ± 23.6	15.6 ± 18.8

CMS = Constant Murley shoulder score.
*Data presented as mean ±SD; differences between both groups were tested with Student's *t* test ($P > 0.05$).

No. PV4255). The study was registered by the German Clinical Trials Register (DRKS00009249). Written informed consent was obtained from all 60 patients prior to performing any study-related procedures. Participants were informed about the study design and that they had the same chance (50%) to be assigned to the treatment or placebo group. When the trial was closed, trial protocol and participants' data were stored for a minimum of 10 years at the HanseMerkur Center for TCM at the University Medical Center Hamburg-Eppendorf.

Study Locations

Initial examination and determination of patients' eligibility for the trial were performed at the Department of Trauma, Hand, and Reconstructive Surgery, University Medical Center Hamburg-Eppendorf. Acupuncture treatments were carried out at the HanseMerkur Center for Traditional Chinese Medicine, University Medical Center Hamburg-Eppendorf.

Results

Participants' Baseline Characteristics

Sixty eligible patients (21 males, 39 females) were randomly assigned to two groups of 30 participants each, that is, to press tack needle treatment (average age = 55.1 years, ±10.4, range = 36–81; 10 males, 20 females) or press tack placebo treatment (average age = 51.9 years, ±8.9, range = 32–66; 11 males, 19 females).

Patients randomized to press tack needle treatment showed an average pretreatment CMS pain subscore of 4.1 (±2.5). Patients in the press tack placebos group had a mean pretreatment CMS pain subscore of 4.3 (±2.5). On average, patients in the press tack needles and press tack placebos groups had the disease for 16 months (±23.6) and 15.6 months (±18.71), respectively.

Both groups were not significantly different regarding age, sex, pretreatment CMS pain subscore, or the duration of disease (all $P > 0.05$, *t* test). Table 2 represents participants' baseline characteristics.

CMS Pain Subscore

The CMS pain subscore in the treatment group was 4.1 ± 2.5 (median = 4, SE of mean = 0.5, variance = 6.2, range = 1–10) before treatment and 7.4 ± 3.7 (median = 7.5, SE of mean = 0.7, variance = 13.4, range = 1–15) after treatment. The CMS pain subscore in the placebo group was 4.3 ± 2.6 (median = 4, SE of mean = 0.6, variance = 12.4, range = 0–10) before treatment and 5.9 ± 3.5 (median = 6, SE of mean = 0.6, variance = 12.5, range = 1–11) after treatment. This implies an improvement of 3.3 ± 3.2 (median = 3, SE of mean = 0.6, variance = 10.2, range = 0–11) points on the CMS pain subscore in the treatment group and 1.6 ± 2.2 (median = 1, SE of mean = 0.4, variance = 4.7, range = −2–6) in the placebo group after treatment. Average changes in CMS pain subscores in both groups differed by 1.7 and were significant ($t(df = 58)$ 2.454503, $P = 0.017$) (Figure 4, suplementary material).

In 11-point pain scales, that is, the pain intensity numerical rating scale (PI-NRS), a two-point improvement is classified as clinically relevant [25]. Analogically, an individual improvement of 3 or more points on the 16-point CMS pain subscale has to be considered as clinically relevant. A clinically relevant reduction of pain was found in 16 of 30 participants in the press tack needles group and in eight of 30 participants of the press tack placebos group. The comparison of both groups reported a statistically significant difference ($P = 0.035$) in results. Figure 3 shows the individual reaction to acupuncture and placebo treatment as measured by CMS pain subscore.

Other CMS Parameters

Comparing pre- and poststatus, no statistical differences were noticed in the other CMS subscores (activities of daily living, mobility, power) and CMS total score.

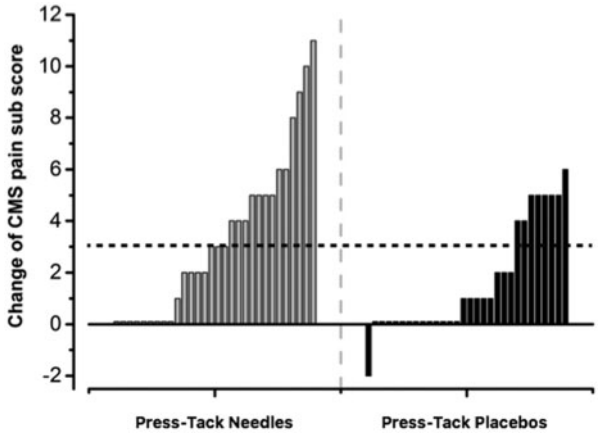

Figure 3 Individual change of CMS pain subscore for all 60 participants. A clinically relevant [25] improvement of CMS pain score of more than 2 points was found in 16 of 30 and eight of 30 participants in the press tack needle and press tack placebo groups, respectively ($P = 0.035$).

Patients' Assumptions and Perceptions of Received Treatment

In the press tack needles group, 15 of 30 participants estimated their intervention as active treatment, and four had experienced a needle sensation. Twelve of these 15 showed an improvement in CMS pain subscore. Nine participants assessed their intervention as placebo treatment. Six of these did not show any or a negative effect, and none of them reported a needle sensation. Six other participants of the press tack needles group could not indicate whether they received an active or a placebo treatment. In the press tack placebos group, 14 participants estimated the intervention as active treatment, and three of these reported a needle sensation. Seven of these 14 participants experienced an improvement in CMS pain subscale after the intervention. Nine participants regarded the treatment as placebo, eight of these experienced no improvement from the intervention, and none reported the sensation of a needle. Seven of the press tack placebos group could not distinguish whether they had an active or a placebo treatment. Comparison of the categories of estimation, that is, whether their treatment was active, placebo, or not identifiable, did not differ significantly between the two groups ($N = 60$, $P > 0.05$).

The acupuncturists estimated the intervention in the press tack needles group as active in 17 of 30 cases. Fourteen of these 17 participants showed an improvement in CMS pain subscore. The acupuncturists estimated the intervention in 10 cases as placebo treatment. Six of these did not show any or a negative effect. In three cases, the acupuncturists could not indicate whether the intervention was an active or a placebo treatment. In the press tack placebos group, acupuncturists estimated the intervention as active treatment in 15 cases. In nine of these 15 cases, the participants experienced an improvement in CMS pain subscale after the intervention. In nine cases, the acupuncturist regarded the treatment as placebo. Four of these participants showed no definite or negative effect. In six cases of the press tack placebos group, the acupuncturist could not distinguish whether they had implemented an active or a placebo treatment. Comparison of methods for measuring the categories of estimation, that is, whether the treatment was active, placebo, or the acupuncturist could not distinguish them, did not differ significantly between the two groups ($N = 60$, $P > 0.05$).

Table 3 represents the assessment of active or placebo treatment of participants and acupuncturists.

Open Follow-up Clinical Application

Thirty-four participants received up to 10 classical needle acupuncture treatments (mean $= 8 \pm 3.1$, range $=$ 2–10) in addition to conservative therapy. This group reported a mean CMS pain subscore of 3.6 ± 2.6 prior to the course of classical needle acupuncture and of 9.3 ± 3.5 one year after the beginning of the acupuncture series. This resulted in an increase of CMS pain subscore of 5.7 ± 3.8 (range $=$ –2 to 12) points. Six of these 34 patients showed no improvement or impairment during this observation period. These six patients reported regular use of nonsteroidal anti-inflammatory drugs (NSAIDs). The other 28 patients showed significant improvement and reported only sporadic intake of oral NSAIDs.

The 13 patients who received conservative therapy without classical needle acupuncture completed the re-evaluation after one year. They reported a mean CMS pain subscore before the experimental study of 5.2 ± 3.4, and of 10.3 ± 4.5 after one year. This resulted in a mean increase in CMS pain subscore of 5.1 ± 4.5 (range $=$ 0–6). Three of these 13 patients did not improve during the observation period of one year. One of these three patients received additional oral opioid therapy, one received transcutaneous electric nerve stimulation (TENS), and one received local steroid injections into the shoulder. Ten patients improved during the observation period. Two of these 10 patients received local steroid injections in addition to regular NSAIDs, while the other eight patients reported only sporadic oral intake of NSAIDs.

Both groups showed no significant difference regarding their values measured before treatment ($N = 47$, $P = 0.223$) and after one year ($N = 47$, $P = 0.293$). Improvement comparison of the mean of both groups was also not statistically different ($N = 47$, $P = 0.783$).

The patients who received conservative therapy including classical needle acupuncture treatment reported that it took them 14.9 ± 15.9 (range $=$ 2–52) weeks to

Table 3 Participants' and acupuncturists' assessment of intervention

Intervention	Assessment of intervention by participant			Assessment of intervention by acupuncturist		
	Active	Inactive	Undecided	Active	Inactive	Undecided
Press tack needles	15	9	6	17	10	3
Press tack placebos	14	9	7	15	9	6

Comparison of participants' and acupuncturists' assessment in both groups showed no statistically significant difference ($P > 0.05$).

reach the final improvement, while the control group that did not receive classical needle acupuncture took 30.9 ± 15.81 (range = 9–52) weeks to reach that status. The duration until improvement occurred was statistically diminished in the classical needle acupuncture group ($N = 47$, $P < 0.001$) (Figure 5, suplementary material).

Safety

None of the volunteers complained of relevant pain, nausea, or cardiovascular symptoms related to the primary study and the open follow-up clinical observation. Furthermore, no relevant skin reaction from the needle or the adhesive plaster was seen.

Discussion

Mechanisms of idiopathic AC are still poorly understood. Many patients will benefit neither from the conservative nor the operative regimes described in the literature. Given this background, the aim of our study was to reveal the effectiveness of press tack needle acupuncture in acute pain management for AC, as well as to investigate the effect of classical needle acupuncture as an addition to conservative therapy in the course of the recovery process in AC patients.

We conducted a randomized, patient- and observer-blinded clinical placebo-controlled study for the assessment of acupuncture effects with press tack needles compared with press tack placebos, followed by an open follow-up clinical application observation with classical needle acupuncture in patients with AC. Participants experienced immediate pain reduction just after application of the press tack needles, which was statistically different from application of press tack placebos. Conservative therapy including classical needle acupuncture eminently influenced the long-term time course of the recovery process in AC patients compared with patients treated with conservative therapy alone.

A recent systematic review on physiotherapy and related techniques recommended that acupuncture and electro-acupuncture were efficient in the management of frozen shoulder [26]. There are four randomized studies dealing with acupuncture treatment for frozen shoulder [27–30]. All these studies indicated positive effects with respect to pain and joint rigidity with acupuncture or electro-acupuncture. However, these results are under debate because all these studies had a high risk of bias [31]. Similar critical results were published in the latest Cochrane study on acupuncture treatment for shoulder pain [32]. The concept of acupuncture is inconsistent between these studies. Most studies favored distant needling at different points for the treatment, that is, Zhongping (extra point on the lower leg one cun [chinese anatomical inch] below ST-36) [33]; Yanglingquan (GB-34) [34–36]; Lingxia (N-LE-17) [37]; or Tiakou (ST-38) [38]. All these points are located on the fronto-lateral side of the proximal lower leg. The application of these distant points at the lower extremity to treating the shoulder shows that acupuncture is a reflex therapy. Our concept and strategy are similar to the approaches mentioned in the previous studies because we have only focused on distant points. This is in accordance with the fact that acupuncture at distant points can be a pain-relieving treatment with immediate onset and can be superior to local needling [33]. However, local treatment has also been shown to be effective in AC, especially if bee venom is injected into local points [39]. Future studies may indicate whether the combination of distal and local acupuncture points may improve the results.

Our concept does not represent a purely traditional Chinese medicine (TCM) theory for decision-making of the acupuncture points [30], which is often not suitable for a Western scientist, nor does it solely originate from empirical knowledge [38,39]. It depicts a systematic and replicable development of an individual treatment pattern [22,23]. Based on identifying painful reflex areas (*ashi* points), our concept offers a rational and reproducible procedure and illustrates the practice of individual acupuncture and avoids uniform treatment procedures. While it is a protocol for immediate effects, studies are cost-effective because of limitation of the number of treatments to just one. Only a few clinical studies so far have described immediate and predominant pain relief following acupuncture treatment, and none of these studies were designed to evaluate AC in a double-blinded manner [33,40,41].

The follow-up clinical application observation (with up to 10 courses of classical needle acupuncture) gave an indication that acupuncture may influence the long-term

course of AC in a very positive manner. Conservative therapy, including classical needle acupuncture, significantly improved the speed of recovery compared with conservative therapy without classical needle acupuncture. Classical needle acupuncture in the open follow-up clinical application observation was limited to 10 treatments over 10 weeks. It took the classical needle acupuncture–treated patients about 14.9 ± 15.9 weeks to reach the final improvement, while the patients treated by conservative therapy without classical needle acupuncture required 30.9 ± 15.81 weeks to reach the relevant clinical improvement. Therefore, extending the use of classical needle acupuncture to more than 10 treatments may improve the time course activity of pain performances in the treatment of AC even more.

Furthermore, such data is evidence that the results obtained with the press tack placebos/press tack needles design can be successfully transferred to classical needle acupuncture and that the special distal needling protocol used in this study has short- as well as long-term effects on pain management. However, not all participants of the double-blinded randomized study participated in the following open clinical application observation, so the number of cases was limited and further trials are necessary to confirm the effectiveness on the course of pain performance in AC.

Stimulation techniques are common in classical needle acupuncture, and the perception of the manipulation called "*deqi*" is asserted as related to the therapeutic effect [42]. However, in the context of clinical studies, perceptive manipulation techniques of acupuncture needles are not suitable for a placebo-controlled design. Shallow needles are traditionally used in Chinese medicine, especially in pain conditions, and have been shown to have specific physiologic effects in controlled clinical trials [43,44]. More importantly, the use of shallow needles does not require stimulation techniques. Therefore, we used press tack needles, special kinds of shallow needles, as the verum therapy and press tack placebos as controls for this study. This allowed the implementation of a placebo-controlled double-blind design for effects specifically associated with metal needle insertion at an acupuncture point. However, press tack needles might have minor effects as classical needle acupuncture [45–47], possibly because of stimulation of superficial layers of the skin only. Despite one study that showed similar therapeutic effects of shallow needles and classical needles in periarthritis of the shoulder [48], most studies found deep needling superior to shallow needling in pain [45] and other conditions [46,47]. These findings are consistent with references from ancient Chinese literature (Chapter 7 of the "Spiritual Pivot," *Huangdi Neijing Lingshu*, 1st cent. BC) [16], where deeper needling is recommended when deep tissue layers are affected. For these reasons, we selected standard needles as treatment for the open follow-up project.

This study first applied the special distal needling protocol in a randomized placebo-controlled design. It shows that press tack needles have an important, major potential role in pain management and can produce immediate effects that are significantly superior to the effects seen when using placebos.

Acupuncture for frozen shoulder is often recommended in combination with physiotherapy [26,49]. A major benefit of using press tack needles is that they remain adherent to the skin for a couple of days, allowing the parallel application of physiotherapy and physical activity for more effective courses of treatment, especially when current therapeutic strategies without local treatment are implemented, as mentioned in this study.

The most consistent explanation for the action of acupuncture is the stimulation of the underlying neural pathways of the peripheral and central nervous system-actions that may account for the physiological effects and clinical responses [50]. While using distal points, especially on the lower extremities, was effective in shoulder pain, we propose that central pain areas play a key role in acupuncture-induced analgesia. The immediate response of acupuncture enhances distinct activity patterns in the brain, particularly in the limbic system; while in the sustained phase, connectivity is found between limbic/paralimbic areas and brainstem nuclei with their neural activity concentrated on endogenous monoaminergic and opoidergic systems, as is shown in functional magnetic resonance imaging studies (fMRI) [51,52].

Our results demonstrate that the use of press tack needles and press tack placebos is an effective way to apply a double-blind placebo-controlled study design because both study groups showed similar results in the estimation of active or placebo treatment and in perception of penetration. Furthermore, the acupuncturist's estimation of active or placebo treatment was similar in both groups (Table 3). This confirms the results of a prior study with 90 acupuncture-naïve participants who were randomly assigned to receive either press tack needles or press tack placebos [19], demonstrating the applicability of press tack needles and press tack placebos for placebo-controlled designs. Our results are consistent with other randomized controlled double-blinded studies with press tack needles and press tack placebos, which have been conducted in patients with lower back pain, shoulder stiffness, muscle soreness in triathlon athletes, and for evaluation of autonomic function [44,22,19,53].

The procedure allows a methodologically efficient tool, which was superior to ones used in most other controlled acupuncture trials that used minimal, superficial, sham, or "placebo" acupuncture as controls for deep needling acupuncture [54,55]. All these concepts permit only a single-blinded approach: Masking of the practitioners is not possible because of the different characteristics of the needles. Another controversial issue is the suitability of so-called nonacupuncture regions as control for defined acupuncture points. Many studies

used points at locations distant from acupuncture points mentioned in textbooks as control groups [56]. However, nonspecific effects have been noted that result from each penetration of the skin [57]. Defining anatomical regions without any influence on other regions seems extremely difficult in view of the above, so needle insertion at locations distant from "real" acupuncture points, defined as minimal or sham acupuncture control, is not suitable as an inert placebo [58].

The results of the press tack placebos group clearly demonstrated that there is a placebo effect (Figure 3) in acupuncture trials, which has to be taken into account for the evaluation of acupuncture-related studies. This is not surprising because sham acupuncture has been shown to increase brain neural activity in fMRI, but the spatial distribution and the insensitivity of signals were much lower compared with acupuncture [52].

Our study provides evidence that acupuncture has a specific impact on AC beyond the placebo effects that may not only be beneficial in reducing short-term pain perception, but may also have a positive long-term influence on the time course of recovery.

Conclusions

Primary AC ("frozen shoulder") is a common disorder associated with pain and significant morbidity in humans worldwide. This first double-blinded (patient- and observer-blinded) study in patients with AC showed the efficiency of our special distal needling protocol [23] by systematic combination of acupoints for immediate pain reduction. The study also confirmed the suitability of press tack needles and press tack placebos as an effective option for double-blind studies in acupuncture. The follow-up clinical observation with classical needle acupuncture confirmed that results obtained with the press tack placebos/press tack needles design can be transferred to classical needle acupuncture. Furthermore, conservative therapy that included acupuncture represented a superior effectiveness on the time course of recovery in AC patients compared with patients treated with conservative therapy alone in a standard clinical setting.

Acknowledgments

Thanks also goes to Sarah Mirza for the production of figures; to study nurse Agnes Urubio; and to clinic staff of the HanseMerkur Center for Traditional Chinese Medicine at the University Medical Center Hamburg-Eppendorf.

Supplementary Data

Supplementary Data may be found online at http://painmedicine.oxfordjournals.org.

References

1 Neviaser JS. Adhesive capsulitis of the shoulder (the frozen shoulder). Med Times 1962;90:783–807.

2 Vastamäki H, Kettunen J, Vastamäki M. The natural history of idiopathic frozen shoulder: A 2- to 27-year follow up study. Clin Orthop Relat Res 2012;470 (4):1133–43.

3 Wang K, Ho V, Hunter-Smith DJ, et al. Risk factors in idiopathic adhesive capsulitis: A case control study. Shoulder Elbow Surg 2013;22(7):e24–9.

4 Evans JP, Guyver PM, Smith CD. Frozen shoulder after simple arthroscopic shoulder procedures: What is the risk? Bone Joint J 2015;97:963–6.

5 Reeves B. The natural history of the frozen shoulder syndrome. Scand J Rheumatol 1975;4(4):193–6.

6 Rill BK, Fleckenstein CM, Levy MS, Nagesh V, Hasan SS. Predictors of outcome after nonoperative and operative treatment of adhesive capsulitis. Am J Sports Med 2011;39(3):567–74.

7 Shin SJ, Lee SY. Efficacies of corticosteroid injection at different sites of the shoulder for the treatment of adhesive capsulitis. J Shoulder Elbow Surg 2013;22(4):521–7.

8 Noten S, Meeus M, Stassijns G, et al. The efficacy of different types of mobilization techniques in patients with primary adhesive capsulitis of the shoulder: A systematic review. Arch Phys Med Rehabil 2016;97(5):815–25.

9 Lewis J. Frozen shoulder contracture syndrome—aetiology, diagnosis and management. Man Ther 2015;20(1):2–9.

10 Grant JA, Schroeder N, Miller BS, Carpenter JE. Comparison of manipulation and arthroscopic capsular release for adhesive capsulitis: A systematic review. J Shoulder Elbow Surg 2013;22(8):1135–45.

11 De Carli A, Vadalà A, Perugia D, et al. Shoulder adhesive capsulitis: Manipulation and arthroscopic arthrolysis or intra-articular steroid injections? Int Orthop 2012;36(1):101–6.

12 Sasanuma H, Sugimoto H, Kanaya Y, et al. Magnetic resonance imaging and short-term clinical results of severe frozen shoulder treated with manipulation under ultrasound-guided cervical nerve root block. J Shoulder Elbow Surg 2016;25(1):e13–20.

13 Chen L. The role of acupuncture in pain management. In: Chen L, Cheng TO, eds. Acupuncture in Modern Medicine. InTech open access, Rijeka, Croatia; 2013.

14 Witzel T, Napadow V, Kettner NW, et al. Differences in cortical response to acupressure and electroacupuncture stimuli. BMC Neurosci 2011;12:73.

15 Goldman N, Chen M, Fujita T, et al. Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. Nat Neurosci 2010;13:883–8.

16 Dun AC. The Yellow Emperor's Inner Classic, Spiritual Pivot (Huang Di Nei Jing Su Wen Jiao Zhu Yu Yi, 1st cent. BC). Chapter 1. Tianjin, China: Tianjin Science and Technology Press; 1989.

17 Yamashita H, Tsukayama H. Minimal acupuncture may not always minimize specific effects of needling. Clin J Pain 2001;17:277.

18 Furuya E, Nayuki T, Yakame M, et al. Effect of press tack needle treatment on shoulder stiffness. JJSAM 2002;52:553–61.

19 Miyazaki S, Hagihara A, Kanda R, Mukaino Y, Nobutomo K. Applicability of press needles to a double-blind trial: A randomized, double-blind, placebo-controlled trial. Clin J Pain 2009;25(5):438–44.

20 Constant CR, Murley AH. A clinical method of functional assessment of the shoulder. Clin Orthop 1987;214:160–4.

21 Sun SM. Thousand Ducat Formulas (Qian Jin Yao Fang), volume 652. Beijing, China: Medical Publishing House; 1955.

22 Schroeder S, Epplee S, Zhang J, et al. Mathematical reflections on acupoint combinations in the traditional meridian systems. Evid Based Complement Alternat Med 2012;2012:Article ID 268237, 10 pages, doi:10.1155/2012/268237.

23 Schroeder S, Meyer-Hamme G, Zhang J, et al. An acupuncture research protocol developed from historical writings by mathematical reflections: A rational individualized acupoint selection method for immediate pain relief. Evid Based Complement Alternat Med 2013; 2013:Article ID 256754, 16 pages http://dx.doi.org/10.1155/2013/256754.

24 Othman A, Taylor G. Is the constant score reliable in assessing patients with frozen shoulder? 60 shoulders scored 3 years after manipulation under anaesthesia. Acta Orthop Scand 2004;75(1):114–6.

25 Farrar JT, Young JPJ, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain 2001;94(2):149–58.

26 Jain TK, Sharma NK. The effectiveness of physiotherapeutic interventions in treatment of frozen shoulder/adhesive capsulitis: A systematic review. J Back Musculoskelet Rehabil 2014;27(3):247–73.

27 Fang JQ, Zhang Y, Xuan LH, Liu KZ, Chen L. Observation on clinical therapeutic effect of transcutaneous point electric stimulation on periarthritis of shoulder at different stages. Zhongguo Zhen Jiu 2006;26(1):11–4.

28 Ma T, Kao MJ, Lin IH, et al. A study on the clinical effects of physical therapy and acupuncture to treat spontaneous frozen shoulder. Am J Chin Med 2006; 34(5):759–75.

29 Cheing GL, So EM, Chao CY. Effectiveness of electroacupuncture and interferential eloctrotherapy in the management of frozen shoulder. J Rehabil Med 2008;40(3):166–70.

30 Sun KO, Chan KC, Lo SL, Fong DY. Acupuncture for frozen shoulder. HKMJ 2001;7:381–91.

31 Maund E, Craig D, Suekarran S, et al. Management of frozen shoulder: A systematic review and cost-effectiveness analysis. Health Technol Assess 2012; 16(11):1–264.

32 Lee MS, Ernst E. Acupuncture for pain: An overview of Cochrane reviews. Chin J Integr Med 2011;17 (3):187–9.

33 Irnich D, Behrens N, Gleditsch JM, et al. Immediate effects of dry needling and acupuncture at distant points in chronic neck pain: Results of a randomized, double-blind, sham-controlled crossover trial. Pain 2002;99(1–2):83–9.

34 Zhang M. Treatment of peri-omarthritis with acupuncture at yanglingquan (GB-34). J Tradit Chin Med 1991;11(1):9–10.

35 Lü J. The clinical application of yanglingquan (GB-34) point. J Tradit Chin Med 1991;13(3):179–81.

36 Liu G, Wang S. Needling at contralateral yanglingquan in treatment of shoulder periarthritis: Report of 115 cases. Int J Clin Acupunct 1993;(4):297–300.

37 Feng Z. 210 cases of shoulder periarthritis treated by needling lingxia and sanjian. J Tradit Chin Med 2003;23(3):201–2.

38 Pothmann R, Weigel A, Stux G. Frozen shoulder: Differential acupuncture therapy with point ST-38. Am J Acupunct 1980;8:65–9.

39 Koh PS, Seo BK, Cho NS, et al. Clinical effectiveness of bee venom acupuncture and physiotherapy in the treatment of adhesive capsulitis: A randomized controlled trial. J Shoulder Elbow Surg 2013;22 (8):1053–62.

40 Park J, Ty Hopkins J. Immediate effects of acupuncture and cryotherapy on quadriceps motoneuron pool excitability: Randomised trial using anterior knee infusion model. Acupunct Med 2012; 30(3):195–202.

41 Stival RS, Cavalheiro PR, Stasiak CE, et al. Acupuncture in fibromyalgia: A randomized, controlled study addressing the immediate pain response. Rev Bras Reumatol 2014;54(6):431–6.

42 Yin CS, Park J, Le JY, et al. Acupuncture perception (deqi) varies over different points and by gender with two distinct distribution pattern of dullness and pain. J Sens Stud 2009;24(5):635–47.

43 Brinkhaus B, Witt CM, Jena S, et al. Acupuncture in patients with chronic low back pain: A randomized controlled trial. Arch Intern Med 2006;166:450–7.

44 Kaneko Y, Furuya E, Sakamoto A. The effects of press tack needle treatment on muscle soreness after triathlon race—sham controlled study. JAM 2009;1:22–30.

45 Ceccherelli F, Rigoni MT, Gagliardi G, Ruzzante L. Comparison of superficial and deep acupuncture in the treatment of lumbar myofascial pain: A double-blind randomized controlled study. Clin J Pain 2002; 18(3):149–53.

46 Yin T, Ni J, Zhu W. Deep needling and shallow needling at three acupoints around ear for subjective tinnitus: A randomized controlled trial. Zhongguo Zhen Jiu 2015;35(10):1015–9.

47 Zhang CY, Wang Y. Comparison of therapeutic effects of deep needling and shallow needling on sudden deafness. Zhongguo Zhen Jiu 2006;26(4):256–8.

48 Chen L. Comparison of therapeutic effects between normal acupuncture and shallow needling with short-needle on periarthritis of shoulder. Zhongguo Zhen Jiu 2006;26(9):647–8.

49 Vas J, Ortega C, Olmo V, et al. Single-point acupuncture and physiotherapy for the treatment of painful shoulder: a multicentre randomized controlled trial. Rheumatology 2008;47:887–93.

50 Longhurst JC. Defining meridians: A modern basis of understanding. J Acupunct Meridian Stud 2010;3: 67–74.

51 Hui KK, Liu J, Marina O, et al. The integrated response of the human cerebro-cerebellar and limbic systems to acupuncture stimulation at ST 36 as evidenced by fMRI. Neuroimage 2005;27:479–96.

52 Liu J, Qin W, Guo Q, et al. Divergent neural processes specific to the acute and sustained phases of verum and SHAM acupuncture. J Magn Reson Imaging 2011;33(1):33–40.

53 Tsumaki M, Saita Y, Ikeda K, et al. Effect of enpishin (press tack acupuncture needles) on autonomic function, WBC count and oxidative stress. Health 2011;7(3):437–43.

54 Park J, White A, Stevinson C, Ernst E, James M. Validating a new non-penetrating sham acupuncture device: Two randomised controlled trials. Acupunct Med 2002;20:168–74.

55 Streitberger K, Kleinhenz J. Introducing a placebo needle into acupuncture research. Lancet 1998;352: 364–5.

56 Lund I, Lundeberg T. Are minimal, superficial or sham acupuncture procedures acceptable as inert placebo controls? Acupunct Med 2006;24:13–5.

57 Linde K, Niemann K, Schneider A, Meissner K. How large are the nonspecific effects of acupuncture? A meta-analysis of randomized controlled trials. BMC Med 2010;8:75.

58 Irnich D, Salih N, Offenbacher M, Fleckenstein J. Is sham laser a valid control for acupuncture trials? Evid Based Complement Alternat Med 2011;2011: Article ID 485945, 8 pages doi:10.1093/ecam/neq009.