Applicability of Press Needles to a Double-blind Trial
A Randomized, Double-blind, Placebo-controlled Trial

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Objectives: Owing to a lack of a suitable needle procedure, it has been impossible to evaluate the efficacy of acupuncture in clinical studies using double-blind testing. We evaluated the applicability of a new kind of press needle (Pyonex) to a double-blind trial by comparing the press needle with a placebo (lacking the needle element).

Methods: The purpose of the study consisted of 2 phases. In the phase 1, to evaluate the applicability and efficacy of the press needles, 90 participants who had never been treated using acupuncture were randomly assigned to receive either the press needle (n = 45) or a placebo (n = 45). The applicability was measured using a questionnaire regarding the perception of penetration, and efficacy was measured using a visual analog scale of low back pain (LBP). When the applicability and efficacy of the press needles were confirmed in phase 1, the mechanism of LBP relief by the press needles was examined in phase 2.

Results: In phase 1, intergroup comparisons showed no significant differences concerning the perception of penetration. In addition, for patients with LBP, the press needles reduced the subjective evaluation of LBP compared with the placebo ($P < 0.05$). In phase 2, visual analog scale results indicated that LBP was reduced significantly more in the press needle group than in the local anesthesia group ($P < 0.05$).

Discussion: The participants could not distinguish between the press needle and a placebo, and the data from the press needle group suggested a specific influence on patients with LBP. These findings imply that the press needle and a placebo provide an effective means of realizing a double-blind setting for clinical studies of acupuncture.

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The authors declare that there is no conflict of interest.

Seirin Corporation participated in random allocation and supplied the press needles (Pyonex) and placebo devices. Maruho Corporation and Nittou Dennkou Corporation (Osaka, Japan) supplied the lidocaine patches (Penles). However, this study was not funded by any corporations or organizations.

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Since the 1990s, several studies have evaluated the specific effects of acupuncture, that is, the effects of the insertion of a needle at an appropriate acupoint.[1–6] However, these studies are insufficient because of 3 main problems. First, although "sham" or placebo needles can be used as a control treatment[7,8] for a single-blind testing method (by masking the treatment allocation from the study participants), masking the treatment from practitioners, which is required for a double-blind testing method, is not possible. Second, the sham needling applied as a placebo needle in previous studies has been referred to as "shallow needling" (depth of insertion < 2 mm) or "contact needling" (a method of obtaining therapeutic effects by holding the needlepoint on the skin surface without penetrating the skin).[9] However, shallow needling has specific physiologic effects,[10] and whereas not as effective as actual acupuncture, it has been proven effective compared with a no-treatment control group.[3,11] Thus, studies using shallow needling as placebo needles for the control group probably produce a skewed interpretation of the specific or placebo effect of acupuncture. Third, the risk for adverse events is very low when acupuncture is applied by qualified professionals,[12–16] and the majority of the adverse events identified from acupuncture clinical trials were of low risk, not mild risk.[2,17–19] However, no study has reported adverse events as a problem in the design and development of acupuncture trials. In addition, interventions using a real needle (lengths from 20 to 40 mm) are painful. A survey of healthcare consumers' perceptions of acupuncture in Japan found that the most frequent response was that it was "painful."[20] Thus, individuals may avoid treatment due to fear of pain. In pursuit of safe acupuncture, Yamashita et al[21] argued that the less-invasive shallow needling and contact needling should not be considered sham or placebo acupuncture but should be acknowledged as safer methods of acupuncture in Japan and worldwide.

The press needles, which are used for a type of shallow needling[22], may allow treatment allocation to be masked from practitioners and study participants; these needles cause almost no sensation at the time of insertion and can be removed from the insertion device without obvious differences. Therefore, the use of press needles may enable double-blind testing for effects specifically associated with metal (acupuncture) penetration of the skin at an acupoint site.

The lack of a suitable placebo needle procedure has prevented double-blind studies from evaluating the efficacy of acupuncture. To evaluate the efficacy, applicability, and safety of press needles, we compared the press needle with a placebo, which was the same device only lacking the needle element. Our findings should be useful in planning double-blind testing of acupuncture.

METHODS

Study Participants

We recruited study participants from among the 811 male undergraduate students who were registered in May 2007 at the Faculty of Sports and Health Sciences, Fukuoka University, Japan. We randomly selected 252 students, aged 20 years or above, and contacted them to ask whether they had ever received acupuncture treatment. At a later date, we provided the 118 students (46.8%) who had not received acupuncture treatment with a written explanation of the study; 90 students (76.3%) agreed to participate. Of the 90 participants, we excluded 9 individuals for physical reasons (n = 4) or noncompliance (n = 5) during the study. Physical reasons encompassed the cases that received medical care for disease or injury. The study protocols were approved by the ethics committee at Fukuoka University, and all interventions were conducted there.

Baseline Characteristics

All participants were validated as follows, for allocation: age, height, weight, body mass index, sitting height, and sit-and-reach distance. Additionally, all participants were questioned about the extent of low back pain (LBP) to establish a baseline (or for allocation): (1) presence or absence of LBP during the past several days (for allocation); (2) visual analog scale (VAS) rating of LBP; (3) duration of LBP based on 10 response categories (0: no pain, 1: <1 wk, 2: ≥ 1 wk and <1 mo, 3: ≥ 1 mo and <3 mo, 4: ≥ 3 mo and <6 mo, 5: ≥ 6 mo and <1 y, 6: ≥ 1 y and <5 y, 7: ≥ 5 y and <10 y, 8: ≥ 10 y and <20 y, 9: ≥ 20 y); (4) days per month with LBP based on 5 response categories (0: no pain, 1: 1 to 3 d, 2: 4 to 6 d, 3: 7 to 14 d, 4 $\geq$ 15 d); and (5) the Roland-Morris Disability Questionnaire,[23] range: 0 to 24.

Procedures

Intervention and Placebo

Figure 1 shows the structure and operation of the press needles used in this study (Pyonex; Seirin Corporation, Shizuoka, Japan); each needle had a diameter of 0.2 mm and length of 0.6 mm. The placebo was identical to the press needle, except the needle element had been removed. The press needles and placebos were packed individually in identical pouches, each of which was assigned a consecutive number. The treatment allocation was not disclosed to study participants, the practitioner, or the evaluator during the period of study.

The press needles and placebo devices were administered (inserted) following the same procedures, according to the product directions, by a single acupuncturist with 10 years of clinical experience. To ensure that the treatment method was masked to the practitioner, the acupuncturist was asked not to check for the presence of a needle during the process of insertion. A different researcher recorded the measurements, and a physician controlled the safety of needle insertion and confirmed that the treatment method was masked.

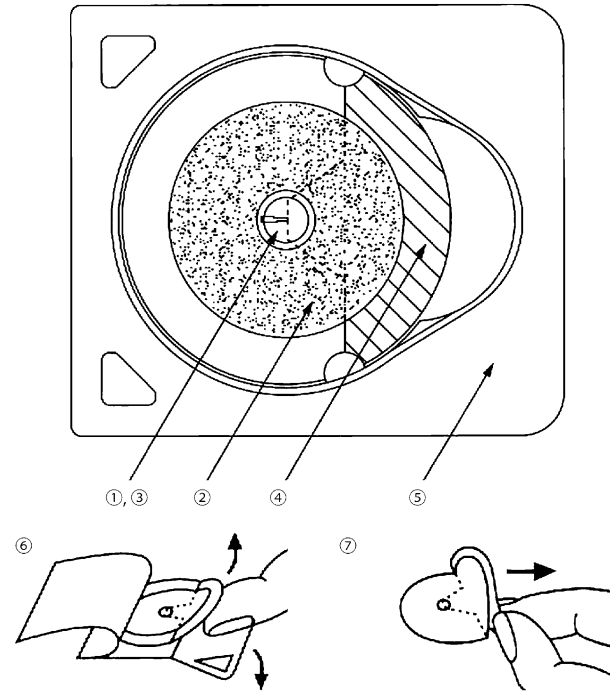

FIGURE 1. Structure and operation of the press needle (Pyonex). The top figure shows the following components: (①) needle (stainless steel), (②) tape, (③) resin, (④) sheath (lunate sheet), and (⑤) cartridge (plastic case). The figure in the lower left (⑥) shows the process of taking the Pyonex needle out of the cartridge (⑤) by picking up the sheath (④) with tape (②). The figure in the lower right (⑦) shows the process of applying the Pyonex needle to an acupoint. It is placed on an acupoint with the sheath (④) attached, pressed down lightly on the top, and inserted. Then, the sheath (④) is stood at a right angle to the skin. Finally, as shown in the figure, the tape (②) is removed.

Study Design

The study consisted of 2 phases. Phase 1 was a double-blind, randomized, placebo-controlled experiment to test the applicability, efficacy, and safety of the press needles. Phase 2 was designed to study the mechanism by which the press needles relieved LBP. Study participants were recruited from September 18 to October 31, 2007. A washout period of at least 4 weeks took place between phases 1 and 2.

Endpoints

The primary endpoint was the applicability as measured by responses to a questionnaire-based assessment for confirming the applicability of the press needles to blind testing. Participants were asked 3 questions regarding the perception of penetration, the perception of de qi (dull sensation), and whether they thought they had received real acupuncture. Participants could choose from 3 responses:

"felt a sensation" (yes), "did not feel a sensation" (no), or "could not discriminate." For the same purpose, pain was evaluated using the short form of the McGill Pain Questionnaire.[24,25]

In addition to applicability, we confirmed the efficacy and safety of the press needles. Efficacy was measured using a VAS of LBP, with the scale ranging from 0 (no pain) to 100 (most intense pain). Measurements were performed at baseline, immediately after administration, and 20 min after administration. Differences from baseline were analyzed. We used previous findings[26] to assess 10 types of possible adverse effects of acupuncture on a 4-point scale of safety from 0 (no risk) to 3 (strong risk).

Acupoint (BL23)

We selected the acupoint at the left side of the BL23. This site is typically used in acupuncture treatment for LBP,[27] and we decided it was the most appropriate site based on factors that might have affected the applicability of the placebo (eg, visual effect).[28] For the same reason, study participants were limited to individuals who had not received acupuncture.

Local Anesthesia Before Needling

Phase 2 of this study was designed to clarify the mechanism for the analgesic effect of the press needles on LBP. Before the insertion of the press needle, a topical anesthetic patch (lidocaine patch; Penles) was applied for 30 min to block the peripheral nerve fibers around the acupoint site. Subsequent analysis compared a group who were treated with the press needles after local anesthesia (LA) and a group who were treated with the press needles without LA.[29]

Statistical Analysis

The allocation of study participants was performed by Seirin Corporation in a randomized manner using a random number generating program (Microsoft Excel). At the time of allocation, baseline data for the participants were gathered from information obtained in advance and were compared between the 2 groups (press needle and placebo). On the basis of an earlier study, we calculated that the necessary sample size was 38 or more cases per group.[8]

Furthermore, participants were stratified according to their LBP status, because the presence or absence of LBP was expected to have a considerable effect on the outcome. We analyzed efficacy using the variation in the VAS scores (difference from baseline measurements) as the dependent variable in a 3-way analysis of variance, with the factors of LBP (presence or absence), time (baseline, immediately after, or 20 min after) and intervention (press needle or placebo). We used Fisher exact test for other intergroup differences in ratios, and a t test for the difference in means. We set the level of significance at 5% for all analyses. All statistical analyses were performed using SPSS (version 11.0J for Windows).

RESULTS

Short Summary of the Main Findings

In phase 1, intergroup comparisons showed no significant differences concerning the perception of penetration. In addition, in patients with LBP, the press needles reduced the subjective evaluation of LBP compared with the placebo ($P < 0.05$). In phase 2, the VAS results indicated that LBP was reduced significantly more in the press needle group than in the LA group ($P < 0.05$).

Applicability or Efficacy (Phase 1)

Figure 2 shows the trial profile. Phase 1 ran from December 12, 2007 to January 11, 2008, and phase 2 ran from January 30 to March 7, 2008. For phase 1, the 90 participants were randomly allocated to either the press needle group (45 cases) or the placebo group (45 cases). Of the 45 participants in the press needle group, 3 dropped out, 1 due to medical treatment and 2 for personal reasons (1 for a sports competition and 1 unknown). Of the 45 participants in the placebo group, 6 dropped out, 3 due to medical treatment and 3 for personal reasons (2 for sports competitions and 1 unknown). The data for the remaining 42 participants in the press needle group and 39 participants in the placebo group were analyzed.

Table 1 shows the baseline characteristics of participants in the 2 study groups. The baseline characteristics were similar in both groups.

Table 2 shows the results concerning the perception of penetration. Four participants (9.5%) in the press needle group (n = 42) and no participants (0.0%) in the placebo group (n = 39) reported a perception of penetration. No participants (0.0%) in the press needle group and 1 participant (2.6%) in the placebo group reported experiencing de qi (dull sensation). Seven participants (16.7%) in the press needle group and 5 participants (12.8%) in the

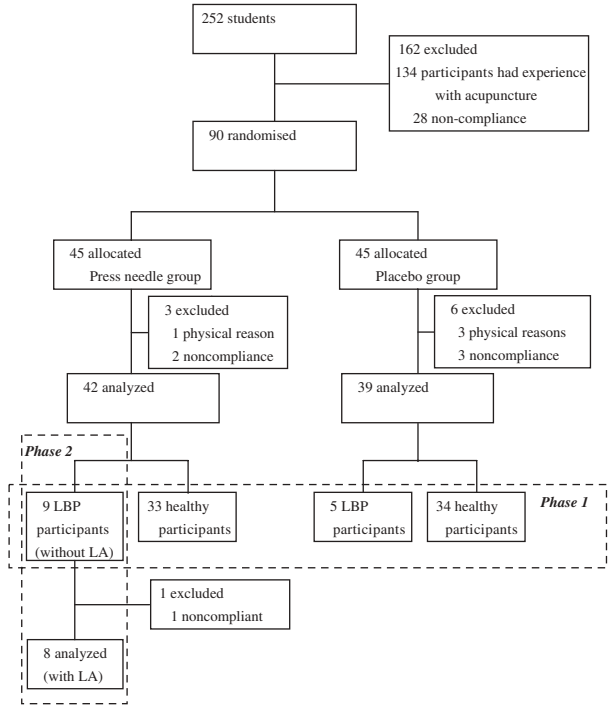

FIGURE 2. Trial flowchart. LBP patients were those having LBP for several days, having LBP at the time of baseline examination, and having a history of LBP for 6 months. LA indicates local anesthesia; LBP, low back pain.

TABLE 1. Baseline Characteristics

Variable	Press Needle Group (n = 42)		Placebo Group (n = 39)	
	LBP Patients (n = 9)	Healthy Participants (n = 33)	LBP Patients (n = 5)	Healthy Participants (n = 34)
Age (years)	20.78 (0.44)	20.88 (0.82)	21.00 (0.71)	20.56 (0.66)
LBP*	6 (66.67)	0 (0.00)	3 (33.33)	0 (0.00)
LBP score (VAS)†	35.56 (21.50)	11.59 (19.90)	35.40 (19.97)	9.73 (12.21)
Duration of LBP‡	4.67 (1.87)	1.66 (2.77)	3.60 (2.70)	1.16 (2.17)
Days per month with LBP§	1.89 (1.17)	0.53 (1.02)	1.80 (0.84)	0.39 (0.90)
RDQ‖	0.44 (0.73)	0.67 (1.45)	2.22 (1.10)	0.74 (3.25)
Height (cm)	178.50 (9.12)	174.31 (6.57)	175.22 (8.69)	173.09 (7.47)
Weight (kg)	72.30 (8.78)	69.74 (8.16)	76.54 (8.88)	68.59 (9.51)
Body mass index	22.71 (2.46)	22.91 (2.01)	25.05 (3.64)	22.88 (2.74)
Sitting height (cm)	95.07 (3.74)	93.59 (2.87)	93.36 (3.47)	92.94 (3.78)
Sit-and-reach test (cm)	47.06 (11.87)	42.97 (8.68)	41.96 (10.73)	42.27 (9.71)

Data are shown as numbers (%) for LBP and mean (± SD) for the other variables.
*The number of patients with LBP during the past several days.
†VAS: 0-100.
‡Ten response categories (0: no pain, 1: < 1 wk, 2: ≥ 1 wk and < 1 mo, 3: ≥ 1 moand < 3 mo, 4: ≥ 3 mo and < 6 mo, 5: ≥ 6 mo and < 1 y, 6: ≥ 1 y and < 5 y, 7: ≥ 5 y and < 10 y, 8: ≥ 10 y and < 20 y, 9: 20 y).
§Five response categories; 0 = no pain, 1 = 1 to 3 days, 2 = 4 to 6 days, 3 = 7 to 14 days, 4 = 15 days or more.
‖RDQ, range: 0 to 24.
LBP indicates low back pain; RDQ, Roland-Morris Disability Questionnaire; VAS, visual analog scale.

placebo group felt that they had received acupuncture using a real needle. Intergroup comparisons showed no significant differences.

Table 3 shows the mean pain scores at the time of needle penetration. The press needle group had a mean total intensity score (based on the short form of the McGill Pain Questionnaire) of 0.10 (± 0.43), and the placebo group had a mean score of 0.10 (± 0.50). The press needle group had a mean VAS of 1.67 (± 5.21), and the placebo group had a mean score of 1.18 (± 2.62). The press needle group had a mean present pain intensity of 0.05 (± 0.22), and the placebo group had a mean score of 0.03 (± 0.16). Intergroup comparisons showed no significant differences.

Using differences in VAS values for LBP at the 3 points (baseline, immediately after, and 20 min after) as the dependent variable, we conducted a 3-way analysis of variance with the factors of LBP (LBP patients vs. healthy participants, where LBP patient may have had LBP for several days, LBP at the time of baseline examination, or a history of LBP for 6 mo), time (baseline vs. immediately after vs. 20 min after), and intervention (press needle vs. placebo; Fig. 3). The results were as follows: [LBP-time–intervention: $F(2,227) = 1.62$, $P = 0.200$; LBP-time: $F(2,227) = 1.92$, $P = 0.149$; LBP-intervention: $F(1,227) = 6.47$, $P = 0.012$; time-intervention: $F(2,227) = 0.66$, $P = 0.520$; LBP: $F(1,227) = 5.27$, $P = 0.023$; time: $F(2,227) = 10.26$, $P < 0.001$; and intervention: $F(1,227) = 2.13$, $P = 0.146$].

As the LBP-intervention interaction was significant, we conducted tests for the simple main effect, and found that the simple main effect of intervention was significant in patients with LBP [$F(1,227) = 4.79$, $P = 0.030 < 0.05$]. This indicates that the press needles reduced the subjective evaluation of LBP (VAS) to a greater degree than the placebo. In addition, the simple main effect of LBP was significant in the press needle group [$F(1,227) = 15.33$, $P < 0.001$].

This finding indicates that patients with LBP in the press needle group experienced a greater reduction in their subjective evaluation of LBP than those without LBP. As the simple effect of time was significant, we conducted a multiple comparison (Bonferroni) and found significant differences in the comparisons of baseline versus immediately after ($P < 0.001$) and baseline versus 20 minutes after ($P < 0.001$), but no significant differences in the comparison of immediately after versus 20 minutes after. A similar analysis limited to patients with LBP in the press needle group showed significant differences in the comparisons of baseline versus immediately after ($P = 0.014 < 0.016$) and baseline versus 20 minutes after ($P = 0.004 < 0.016$), but no significant differences in the comparison of immediately after versus 20 minutes after.

Table 4 summarizes the number of side effects. Only 1 participant in the press needle group developed a side effect (sleepiness).

TABLE 2. Participants' Perception of Penetration and Dull Sensation

	Felt	Did not Feel	Could not Discriminate	Total
Penetration				
Press needle group	4	38	0	42
Placebo	0	37	2	39
Total	4	75	2	81
Dull sensation (De qi)				
Press needle group	0	35	7	42
Placebo	1	33	5	39
Total	1	68	12	81

Penetration was assessed using responses to the following question: "How did you feel when the acupuncture needle was inserted?"
Penetration: no significant differences were observed between the press needle and a placebo (Fisher exact test, $P = 0.074$).
Dull sensation (De qi): no significant differences were observed between the press needle and a placebo (Fisher exact test, $P = 0.493$).

TABLE 3. Variables Concerning Patients' Pain (Mean ± SD)

Variable	Press Needle Group (n = 42)	Placebo Group (n = 39)	P§
SF-MPQ*			
Total intensity scores	0.10 ± 0.43	0.11 ± 0.51	$t(78) = 0.10$, NS
VAS†	1.67 ± 5.21	1.21 ± 2.65	$t(79) = 0.50$, NS
PPI‡	0.05 ± 0.22	0.03 ± 0.16	$t(79) = 0.52$, NS

*SF-MPQ, short-form McGill Pain Questionnaire, 15 pain descriptors rated on an intensity scale as 0 = none, 1 = mild, 2 = moderate or 3 = severe; range: 0 to 45.
†Range: 0 to 100.
‡Range: 0 to 5.
§Two sample t test.
NS indicates not significant; PPI, present pain intensity; SF-MPQ, short form of the McGill Pain Questionnaire; VAS, visual analog scale.

Mechanism (Phase 2)

As patients with LBP in the press needle group experienced a greater reduction in their subjective evaluation of LBP, we conducted additional analyses using 8 of the 9 patients who had LBP and received press needle insertion; we used the LA group as a control (press needle insertion after LA treatment) and compared it with the press needle group (press needle insertion without LA treatment; Fig. 4). We found that the VAS scores for LBP were significantly lower in the press needle group than in the LA group (paired t test: $t = 2.86$, $P = 0.024 < 0.05$, 2-tailed).

DISCUSSION

The results indicate that a methodology using the press needle and a placebo (the same device but lacking the needle element) is suitable for double-blind testing. In addition, we confirmed the safety of press needles, as they did not cause pricking pain among participants (patients) and resulted in almost no adverse effects. Our findings are limited to the BL23 acupoint, so we are unable to confirm the efficacy of the press needles at other single or multiple acupoints; further studies may be necessary.

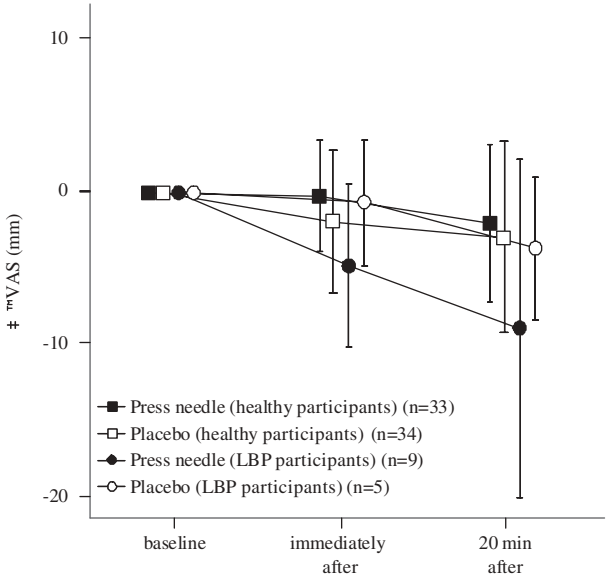

FIGURE 3. Changes in VAS score for LBP. Verticle bars represent the mean ± 1 SD. LBP indicates low back pain; VAS, visual analog scale.

As we showed the efficacy of this methodology in a double-blind setting, we were able to confirm the specific effect of metal (acupuncture) penetration of the skin at the acupoint site. We only observed this effect among patients with LBP, and thus the BL23 acupoint seems to have a specific effect on LBP. This finding supports the use of BL23 as an acupoint in clinical practice. However, acupuncture treatment of BL23 alone may not cure LBP, and actual clinical treatment may require using a combination of multiple acupoints. Concomitantly, the changes we observed in VAS values for LBP were not great enough to be considered clinically effective. In addition, we did not track the duration of this effect.

The use of topical anesthetic treatment as a control is a new research methodology, and previous research has identified problems such as the absorption characteristics of anesthetics.[30] However, these issues did not affect this study because we used only one acupoint, the depth of penetration was as small as 0.6 mm, and the study focused on short-term effects.

The mechanism for the analgesic effect of acupuncture is thought to involve small-diameter afferent nerves, but studies have not yielded sufficient consistent evidence.[31–33] Most studies in this field have focused on acupuncture methods and the resultant de qi, or on electroacupuncture. Almost all physiologic studies that have been conducted on superficial stimulation involve de qi, that is, shallow needling and contact needling. This study is among the first to show the lack of an analgesic effect under topical anesthesia, thereby confirming the involvement of small-diameter afferent nerves in the mechanism for the analgesic effect of superficial stimulation that does not achieve de qi.

With respect to the types of small-diameter afferent nerves, researchers have proposed the possibility of the induction of "limbic touch" through C fibers,[34] and the possibility that suppression at the posterior horn of the spinal cord may reduce the pain transmitted from the same segment of spinal cord through Aβ fibers.[32] These issues are beyond the scope of this study. Additionally, it is necessary to consider the possibility of a "placebo effect," because the patients could recognize having received anesthetic

TABLE 4. Number of Side Effects in the Study

Side Effects	Press Needle Group (n = 42)		Placebo Group (n = 39)	
	Immediately After	20 min After	Immediately After	20 min After
Fatigue or malaise	0	0	0	0
Sleepiness	1	1	0	0
Aggravation of complaint	0	0	0	0
Itching in the puncture region	0	0	0	0
Dizziness	0	0	0	0
Nausea or vomiting	0	0	0	0
Hemorrhage	0	0	0	0
Pain in the puncture region	0	0	0	0
Discomfort in the puncture region	0	0	3	2

treatment. Further study would be necessary to verify this point, and we hope to see advances in this research.

In conclusion, this study showed that the press needle and a placebo were indistinguishable and suggested that the press needle had a specific influence in patients with LBP. These findings imply that the use of the press needle and a placebo can provide an effective means of realizing a double-blind setting for clinical studies of acupuncture. Further studies using other acupoints are necessary to verify these findings and their external applicability.

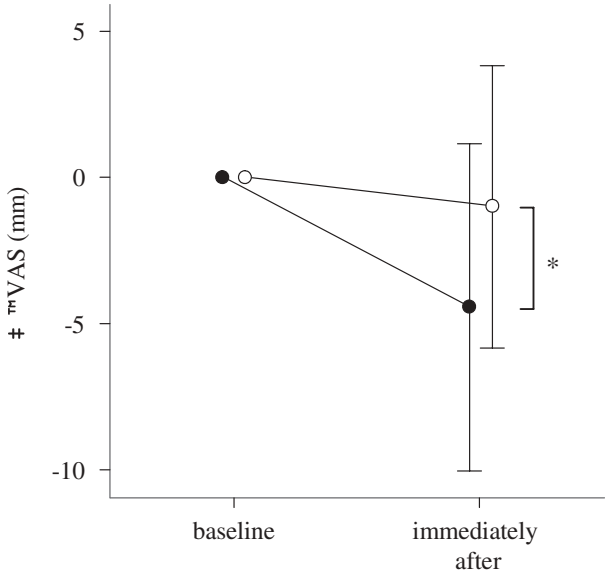

FIGURE 4. Comparison between the control LA group (press needles inserted after LA treatment for 30 min) (○), and the press needle group (press needles inserted without LA treatment) (●). Participants in the control LA group and press needle group were those with LBP in phase 1 (n = 8). In the phase 2, after at least a 4-week washout period, a topical anesthetic patch was applied for 30 minutes to 8 participants from phase 1, to block the peripheral nerve fibers before the insertion of the press needles. Differences in VAS scores at 2 points were compared between the 2 groups, using a paired *t* test [$t(7) = 2.86$, $P = 0.024 < 0.05$ (2-tailed)]. Vertical bars represent the mean ± 1 SD. *$P < 0.05$.

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