Influence of de qi on the immediate analgesic effect of SP6 acupuncture in patients with primary dysmenorrhea and cold and dampness stagnation: a multicentre randomised controlled trial

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ABSTRACT
Objective. The aim of this multicentre randomised controlled trial was to investigate the contribution of de qi to the immediate analgesic effect of acupuncture in patients with primary dysmenorrhea and the specific traditional Chinese medicine diagnosis cold and dampness stagnation.

Method. Eighty-eight patients with primary dysmenorrhea and cold and dampness stagnation were randomly assigned to de qi (n=43) or no de qi (n=45) groups and underwent 30 min of SP6 acupuncture. The de qi group received deep needling at SP6 with manipulation using thick needles; the no de qi group received shallow needling with no manipulation using thin needles. In both groups the pain scores and actual de qi sensation were evaluated using a visual analogue scale for pain (VAS-P) and the acupuncture de qi clinical assessment scale (ADCAS), respectively.

Results. Both groups showed reductions in VAS-P, with no significant differences between groups. ADCAS scores showed 43/43 and 25/45 patients in de qi and no de qi groups, respectively, actually experienced de qi sensation. Independent of original group allocation, VAS-P reductions associated with actual de qi sensation (n=68) were greater than those without (28.4±18.19 mm vs 14.6±12.28 mm, p=0.008).

Conclusions. This study showed no significant difference in VAS-P scores in patients with primary dysmenorrhea and cold and dampness stagnation immediately after SP6 acupuncture designed to induce or avoid de qi sensation. Both treatments significantly reduced VAS-P relative to baseline. Irrespective of group allocation, patients experiencing actual de qi sensation demonstrated larger reductions in pain score relative to those without, suggesting greater analgesic effects.

Trial registration number. Chinese Clinical Trial Registry (ChiCTR-TRC-13003086); Results.

INTRODUCTION
The term de qi, translated as ‘the arrival of Qi’, was first found in Huang Di Nei Jing,1 and has historically been used to evaluate the therapeutic effect of needling. As traditional Chinese medicine (TCM) has developed, it is now considered to represent a sensory response to needling during acupuncture,2 which includes both the patient’s sensation of needling and a feeling experienced by the acupuncturist’s fingers. Traditionally, in both literature and clinical practice, the crucial importance of de qi in acupuncture therapy has been highly emphasised. Nowadays most acupuncturists believe that de qi is key to achieving desired therapeutic effects in acupuncture.3 4 However, the current literature evaluating the role of de qi is insufficient to reach a decisive conclusion.5 It is still unknown whether or not the de qi sensation is essential for the therapeutic effects of acupuncture. After examining published clinical research on the role of de qi in acupuncture, we noted a relative lack of evaluation of actual de qi sensation among subjects, which may hamper the assessment of the real contribution of the de qi sensation to the therapeutic effects of acupuncture. To further elucidate this relationship, further high-quality clinical studies on acupuncture and de qi sensation are required.
Primary dysmenorrhoea is characterised by cramping pain in the lower abdomen that occurs just before or during menstruation\(^6\) in the absence of signs of pelvic disease.\(^7\) It is very common in nulliparous young females, and rarely leads to any complications. Several studies have demonstrated the therapeutic effects of acupuncture in primary dysmenorrhoea.\(^8\)\(^9\)

Our group has particular experience with clinical studies of acupuncture in primary dysmenorrhoea. We have found that the most commonly used acupuncture point for the treatment of dysmenorrhoea using acupuncture is SP6 (Sanyinjiao),\(^10\) in keeping with the findings of a recent review.\(^11\) In our previous studies, acupuncture at SP6 induced significant analgesic effects in patients with primary dysmenorrhoea.\(^5\)\(^6\)\(^12\)

We found that this treatment was especially successful in patients with the specific TCM diagnosis of cold and dampness stagnation.\(^13\)

The aim of this randomised controlled study was to explore the role of the actual *de qi* sensation in the immediate analgesic effect of SP6 acupuncture in patients with primary dysmenorrhoea and cold and dampness stagnation.

**METHODS**

The study was conducted in accordance with the guidelines of the Declaration of Helsinki\(^14\) and was approved by the Ethics Committee of Beijing University of Chinese Medicine (approval no. 2012–040). The trial was prospectively registered in the Chinese Clinical Trial Registry (registration no. ChiCTR-TRC-13003086). The study protocol has been previously published.\(^15\)

**Settings and patients**

A target sample of 96 patients with dysmenorrhoea, aged 18–30 years, were recruited through posters or lectures at Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine, Huguosi Hospital of Traditional Chinese Medicine Affiliated to Beijing University of Chinese Medicine, Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University and Hebei Medical University between March 2013 and January 2015. All the participants received treatment in the acupuncture outpatient clinic of one of these four hospitals.

It was estimated that a sample size of 40 patients per group would be required for this preliminary study. To our knowledge, no similar study has been reported in the literature; thus, due to lack of baseline information about the potential discrepancy between needle manipulation to induce *de qi* and actual *de qi* sensation, a more sophisticated power calculation was not possible. Group sizes were inflated to n=48 (total n=96 subjects), assuming a 20% dropout rate.

Primary dysmenorrhoea was diagnosed according to the criteria outlined in the Primary Dysmenorhoea Consensus Guideline published in the *Journal of Obstetrics and Gynaecology Canada*,\(^16\) while the *cold and dampness stagnation* pattern was diagnosed according to a revised Chinese national consensus guideline on the treatment of primary dysmenorrhoea with new Chinese herbs.\(^17\) All patients included in this study consented to participation, had a duration of primary dysmenorrhoea ranging between 6 months and 15 years, and had suffered from moderate or severe pain (defined as a visual analogue scale for pain (VAS-P) score ≥40 mm) for at least three consecutive menstrual periods. Patients with secondary dysmenorrhoea (eg, due to endometriosis or adenomyosis), irregular menstruation, pregnancy, asthma, psychological diseases or life-threatening conditions (eg, disorders of the cardiovascular, liver, kidney or hematopoietic system) were excluded from this study. Patients with prior knowledge of acupuncture, those who had taken analgesic medication in the 24-hour period before the acupuncture intervention, and those who had potential problems with treatment compliance were also excluded.

Every potential participant was evaluated and informed about the procedures as well as the risks involved with participation in this study at the initial interview, and a full medical and gynaecological history was taken. Candidates who went through the preliminary evaluation and signed consent underwent further examination and ultrasonography. Finally, those who satisfied all the inclusion criteria were enrolled at the clinic. Participants returned on the first day of their next menstrual cycle for treatment when the pain level was confirmed to be ≥40 mm on the VAS-P scale. Baseline demographic data, including current age, age at onset of symptoms, duration of menses, menstrual cycle length and course of disease, were collected.

**Randomisation and blinding**

After completing the baseline evaluation, patients were randomly assigned to either a ‘*de qi*’ group or a ‘no *de qi*’ group in a 1:1 ratio using a centralised telephone randomisation procedure. The random list was generated using the Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS Inc, Chicago, IL, USA) by the coordinator at the Centre for Evidence-Based Chinese Medicine Affiliated to Beijing University of Chinese Medicine. A minimal acupuncture intervention was used in the no *de qi* group as a type of sham procedure (with the intention of avoiding induction of the *de qi* sensation). Patients were informed that they would have a 50% chance of allocation to either group, and that treatment procedures in both groups would be intended to achieve certain potential therapeutic effects. Nonetheless, they were unaware of their group allocation, and were unable to observe the intervention provided by the acupuncturist. Different researchers were in charge of keeping records, recording indices and performing the acupuncture intervention, and no communication regarding the
study was allowed. Data were analysed by professional statisticians who were unaware of the trial procedure or the group allocation.

**Acupuncture intervention**

Participants with menstrual pain scores ≥40 mm on the VAS-P scale received an acupuncture intervention on the first day of menstruation. All treatments were performed by licensed and experienced acupuncturists. Patients received the treatment in the supine position and underwent bilateral needling at SP6 for 30 min. SP6 is located on the tibial aspect of the leg, posterior to the medial border of the tibia, 3 B-cun (proportional bone cun) above the prominence of the medial malleolus.

In the de qi group, sterile disposable stainless acupuncture needles of 0.30 mm calibre and 40 mm length with guide tubes (Zhongyan Taihe, Wuxi Jiajian Medical Instrument Co Ltd, Jiangsu, China) were used. After local sterilisation, the needle was vertically inserted to a depth of 1 cun then manipulated by lifting-thrusting and twirling (180° in both directions, at 1 Hz frequency) for 30 s with the intention of achieving de qi. The manipulation was repeated twice, for 30 s each time, every 10 min. Needles were removed after 30 min.

In the no de qi group, sterile disposable stainless acupuncture needles of 0.18 mm calibre and 13 mm length with guide tubes purchased from the same manufacturer were used. The needle was vertically inserted to a depth of 0.1 cun and no manipulation was applied. Needles were removed 30 min later. In both groups, any adverse reactions associated with the treatment (eg, haematoma, local infection) were documented.

**Outcome measurements**

The primary outcome measure was the change in VAS-P score between baseline and 30 min after the acupuncture intervention was completed. Allowing quantification of the participants’ self-reported severity of pain, the VAS-P score is a continuous variable with a value lying between 0 (no pain) and 100 mm (worst pain ever). VAS-P has high validity and reliability, and has been used in our previous studies. Secondary outcomes included the incidence of adverse events. In addition, given that the experience of de qi depends very much on the subjective feelings of the recipients, actual de qi sensation was measured in both groups using a self-designed acupuncture de qi clinical assessment scale (ADCAS) after the treatment.

Patients were asked to report their experiences of de qi during the treatment, and were reclassified according to actual de qi experience in a secondary analysis.

**Statistical analysis**

Data are expressed as mean and SD. Statistical analysis was performed using SPSS version 22.0 (SPSS Inc). The independent sample t-test or Mann-Whitney U test was used to examine potential differences in baseline demographics and clinical history variables between the de qi and no de qi groups. The paired t-test or Wilcoxon signed-rank test was used to compare VAS-P values before and after the treatment. The independent sample t-test or Mann-Whitney U test was used to compare VAS-P values or the change in VAS-P values between groups. A value of p<0.05 was denoted as significant. Similar statistical methods were employed to perform a secondary analysis looking at the influence of actual de qi sensation on the effects of acupuncture.

**RESULTS**

**Patient enrolment**

During the period of recruitment from March 2013 to January 2015, 350 patients with dysmenorrhoea were interviewed, of which 150 patients received a preliminary diagnosis of primary dysmenorrhoea with cold and dampness stagnation (figure 1). A total of 104 patients signed consent and underwent further examination, of which eight were excluded because they did not meet the formal diagnostic criteria for primary dysmenorrhoea. Finally, 96 patients with primary dysmenorrhoea and cold and dampness stagnation were enrolled in the study and accepted acupuncture treatment. Eight patients were found to have been erroneously included as they had VAS-P scores <40 mm before acupuncture treatment (five in the de qi group and three in the no de qi group) and were therefore excluded from the primary statistical analysis. As a result, data from 88 participants who met the inclusion criteria were analysed.
Baseline data

All participants were unmarried young women aged 23.7±2.37 years (table 1). The average age at onset of painful menstruation was 15.9±2.55 years. Participants had a history of dysmenorrhoea of 93±38.3 months. The pain experienced on the first day of menstruation was 60±15.9 mm on the VAS-P scale.

Primary outcome

When we compared the primary outcome measure, namely change in VAS-P score, between the two groups, there was no significant difference between the de qi and no de qi groups (−27.4±17.75 vs. −24.1±18.86 mm; p=0.306; figure 2). Both groups demonstrated a significant reduction in VAS-P scores post-treatment relative to the baseline in each group. In the de qi group (n=43), VAS-P values reduced from 58.3±12.89 mm before acupuncture to 30.8±17.97 mm after acupuncture, while in the no de qi group (n=45), VAS-P values fell from 61.2±18.41 mm pre-acupuncture to 37.1±23.75 mm post-acupuncture (both p<0.001; figure 3A).

Table 1 Baseline characteristics of participants

<table>
<thead>
<tr>
<th></th>
<th>De qi Group (n=43)</th>
<th>No de qi Group (n=45)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>23.7±2.46</td>
<td>23.7±2.30</td>
<td>0.813</td>
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<tr>
<td>Onset age, years</td>
<td>15.8±2.50</td>
<td>16.1±2.61</td>
<td>0.634</td>
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<td>Menstruation, days</td>
<td>5±1.4</td>
<td>5±1.3</td>
<td>0.677</td>
</tr>
<tr>
<td>Menstruation cycle, days</td>
<td>30±3.2</td>
<td>30±3.2</td>
<td>0.921</td>
</tr>
<tr>
<td>Course of disease, months</td>
<td>95±39.5</td>
<td>92±37.5</td>
<td>0.670†</td>
</tr>
<tr>
<td>VAS-P score</td>
<td>58±12.9</td>
<td>61±18.4</td>
<td>0.694</td>
</tr>
</tbody>
</table>

* By independent sample t-test† or Mann-Whitney U test.

Secondary analysis

All 43 patients randomised to the de qi group receiving active needle manipulation self-reported de qi sensation. However, not all participants randomised to the no de qi group reported its absence. Accordingly, the potential influence of the actual experience of de qi was examined in a secondary analysis. Six patients in the no de qi group exhibited contradiction between the de qi experience and self-reported needling sensation, and thus were excluded from this secondary analysis (figure 1). Of the remaining 39 patients in the no de qi group receiving minimal acupuncture, 25 (64%) self-reported experience of classical de qi sensation, demonstrating a lack of correlation between de qi (non-)intention and de qi experience. The remaining 14 patients were considered not to have been exposed to de qi. Overall, there were 68 patients who felt de qi, and 14 who did not in this study. Within the no de qi group, the 25 patients who reported de qi sensation exhibited a significant reduction in VAS-P values after treatment (33.4±24.92 mm vs. 63.5±21.75 mm at baseline, p<0.001; figure 3B). Similarly, the 14 patients in the no de qi group who did not experience de qi also reported a significant reduction in VAS-P values (61.4±13.79 mm to 46.8±20.30 mm, p=0.001; figure 3B). When analysing all 68 patients who actually felt de qi sensation, regardless of original treatment group allocation, it was evident that VAS-P values were reduced immediately after treatment compared with baseline (31.8±20.65 mm vs. 60.2±16.73 mm, p<0.001; figure 3C). Furthermore, the change in VAS-P scores in these 68 patients was significantly greater than in those 14 patients who did not feel de qi (−28.4±18.19 mm vs. −14.6±12.28 mm, p=0.008; figure 2). Regardless of the treatment group allocation, compared with the 14 patients who did not report de qi, significantly greater reductions in VAS-P scores were observed among those who experienced de qi sensation in both the de qi group.

Figure 2 Reductions in visual analogue scale for pain (VAS-P) scores in 88 patients with primary dysmenorrhoea and cold and dampness stagnation following an acupuncture intervention designed to induce de qi sensation (de qi group, n=43, closed red bars) or avoid it (no de qi group, n=45, closed blue bars). Open red, blue and pink bars indicate secondary analysis based on actual experience of de qi sensation: ‘+’ indicates deep needling with manipulation using thick needles; ‘−’ indicates shallow needling without manipulation using thin needles; ‘+/−’ indicates combined group of patients experiencing actual de qi sensation regardless of initial group allocation. De qi sensation: ‘+’ and ‘−’ indicate whether de qi sensation was felt during the procedure or not, respectively; ‘+/−’ indicates homogeneity of de qi experience in the no de qi group. *p<0.05, **p<0.01 vs. subgroup without de qi sensation. n.s. not significantly different.

Figure 3 (A) Visual analogue scale for pain (VAS-P) scores in 88 patients with primary dysmenorrhoea and cold and dampness stagnation before and after an acupuncture intervention designed to induce de qi sensation (de qi group, n=43, closed red circles, solid line) or avoid it (no de qi group, n=45, closed blue circles, solid line). (B) VAS-P scores before and after acupuncture in patients with red open circles, dashed line) or without (blue open circles and dashed line) actual de qi sensation reported during receiving minimal acupuncture. (C) VAS-P scores before and after acupuncture in all patients reporting actual de qi sensation (n=68) regardless of original treatment group allocation (pink open circles, dashed line). **p<0.01 relative to baseline (de qi). ## p<0.01 relative to baseline (no de qi).
(n=43, -27.4±17.75, p=0.015) and the no de qi group (n=25, -30.2±19.17 mm, p=0.009). Furthermore, among patients who felt the de qi sensation, the original group allocation and the resultant differential treatments did not influence markers of the analgesic effect of acupuncture (p=0.740).

Safety of acupuncture
No adverse effects of acupuncture were documented during the study.

DISCUSSION
The present study was designed to investigate the contribution of de qi to the immediate analgesic effect of acupuncture in patients with primary dysmenorrhoea and cold and dampness stagnation. Comparing the original de qi group (n=43), in which patients were expected to experience de qi by design, with the no de qi group (n=45), in which no de qi sensation was expected, there were no significant differences in our primary outcome and both groups showed similar degrees of reduction in VAS-P scores, suggesting equivalent analgesic effects. Superficial examination of our results may lead to a hasty conclusion that the de qi sensation is irrelevant for acupuncture-induced analgesia. However, it is known that, in clinical acupuncture practice, some patients receiving sophisticated needling techniques sometimes fail to sense de qi, while patients receiving minimal acupuncture interventions sometimes experience de qi nevertheless. We anticipated this uncertainty around the de qi sensation in the design of this study,15 and therefore used the ADCAS score to evaluate the actual de qi sensation after treatment in each group. We found that 64% (25 of 39) of patients in the no de qi group reported de qi sensation; thus, it seems reasonable to suspect that results from these subjects may confound study of the potential influences of de qi sensation on therapeutic outcomes.

For this reason, we decided to focus on the actual de qi sensation, by means of a secondary analysis, and found that the de qi sensation appeared to be associated with a greater therapeutic effect. The average VAS-P score of the 68 patients who actually experienced de qi, regardless of treatment group allocation, was further reduced by approximately 13.8 mm when compared with the 14 patients who did not feel de qi, suggesting that the immediate analgesic effect of acupuncture in the absence of de qi is inferior. As a result, we recommend that the analysis of the exact relationship between needle stimulation with the intention of inducing de qi intention and putative therapeutic effects should take the actual de qi sensation into account. However, there has been relatively little discussion of this potentially confounding factor to date in the acupuncture research community.23

A recent review concluded that the importance of de qi, which is a component of the concept of acupuncture “dose”, is still unclear,1 while our study suggests that it plays a key in the therapeutic effect of acupuncture treatment, at least in primary dysmenorrhoea. Although Xiong et al found that de qi had an effect on immediate menstrual pain, in fact, their study design only allowed for examination of the relationship between the intensity of needle stimulation and the therapeutic effects due to the lack of a tool to judge the level of de qi.24 In the present study, in spite of the different needling methods used in the two groups, there was no statistically significant difference in the immediate analgesic effect between the groups after omitting those who reported the absence of de qi sensation in the no de qi group. This result suggested that de qi sensation might be a major predictor of therapeutic effect in acupuncture, and that needle thickness, needling depth and manipulation are less relevant.

The current study has several limitations. First, although the re-grouping of subjects in the secondary analysis on the basis of the actual de qi sensation allowed us to study the potential contribution of actual de qi sensation to the therapeutic effects of acupuncture, it nonetheless compromised the randomisation and therefore the level of evidence. This compromise is due to the inherent uncertainty of achieving de qi sensation in acupuncture-related clinical studies, and can only be avoided by establishing a better correlation between acupuncture procedures and de qi sensations, which requires the collective endeavour of the acupuncture community. Second, the evaluation of de qi sensation in this study was based on subjective feelings of patients, and more objective indices are needed for confirmation. Thirdly, this study focused on the immediate analgesic effect of acupuncture, and it remains unknown if this pain relief was sustainable. Moreover, the potential role of de qi in sustained analgesic effects has not been examined. Lastly, this study only considered the situation in which recipients of acupuncture could feel evident de qi sensation, and did not explore the possibility of hidden de qi effects or other factors.

CONCLUSIONS
This study showed no significant difference in the intensity of cramping pain in patients with primary dysmenorrhoea and cold and dampness stagnation immediately after acupuncture at SP6, using a regimen designed to induce de qi sensation and minimal needling designed to avoid de qi. Both treatments significantly reduced pain scores relative to baseline. A secondary analysis found that, irrespective of group allocation, patients who experienced actual de qi sensation demonstrated larger reductions in pain score relative to their counterparts who did not experience de qi; this suggests that de qi improves the immediate analgesic effect of acupuncture at SP6 in patients with primary dysmenorrhoea and cold and dampness stagnation.

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Contributors: M-Z and PZ contributed equally to this work. JZ, L-M and PZ conceived and designed the trial. PZ, JL, L-W, WZ, Y-W, Y-S, N-H, CL performed the research. S-H, G-W, Y-W, J-S registered all the data. M-Z analysed the data and drafted the manuscript. PZ and S-J revised the manuscript. JZ and L-M supervised the study. All authors approved the final version of the manuscript accepted for publication.

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Provenance and peer review: Not commissioned; externally peer reviewed.

Data sharing statement: The secondary outcomes of this study, including anxiety levels and temperature changes at SP6, will be reported in a subsequent paper that is yet to be prepared. In the interim, the corresponding author (Professor Jianli Zhu) agrees to make this data available upon request.

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