

# Treating primary dysmenorrhoea with acupuncture: a narrative review of the relationship between acupuncture 'dose' and menstrual pain outcomes

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## ABSTRACT

**Objective** A number of randomised controlled trials have been performed to determine the effectiveness or efficacy of acupuncture in primary dysmenorrhoea. The objective of this review was to explore the relationship between the 'dose' of the acupuncture intervention and menstrual pain outcomes.

**Methods** Eight databases were systematically searched for trials examining penetrating body acupuncture for primary dysmenorrhoea published in English up to September 2015. Dose components for each trial were extracted, assessed by the two authors and categorised by neurophysiological dose (number of needles, retention time and mode of stimulation), cumulative dose (total number and frequency of treatments), needle location and treatment timing.

**Results** Eleven trials were included. Components of acupuncture dose were well reported across all trials. The relationship between needle location and menstrual pain demonstrated conflicting results. Treatment before the menses appeared to produce greater reductions in pain than treatment starting at the onset of menses. A single needle during menses may provide greater pain reduction compared to multiple needles. Conversely, multiple needles before menses were superior to a single needle. Electroacupuncture may provide more rapid pain reduction compared to manual acupuncture but may not have a significantly different effect on overall menstrual pain.

**Conclusions** There appear to be relationships between treatment timing and mode of needle stimulation, and menstrual pain outcomes. Needle location, number of needles used and frequency of treatment show clear dose-response

relationships with menstrual pain outcomes. Current research is insufficient to make definitive clinical recommendations regarding optimum dose parameters for treating primary dysmenorrhoea.

## INTRODUCTION

Dysmenorrhoea can be described as painful uterine cramps of menstrual origin.<sup>1</sup> Primary dysmenorrhoea is menstrual pain in the absence of any organic pathology and is the most common form of period pain in young women,<sup>2</sup> as well as the most frequently under-reported cause of period pain.<sup>3</sup> Prevalence rates among reproductive aged women range from 16.8% to 81%.<sup>4</sup> While standard biomedical treatments, usually non-steroidal anti-inflammatory drugs (NSAIDs) or the combined oral contraceptive pill (COCP), are commonly used and effective for many women,<sup>5 6</sup> approximately 25% have pain that is refractory to one or more of these standard treatments.<sup>7</sup>

Acupuncture has become a popular therapy for treating menstrual disorders in recent years.<sup>8</sup> A recent Cochrane review examined the effectiveness and safety of acupuncture for primary dysmenorrhoea and reported unclear results for the reduction of menstrual pain, mostly due to an inability to combine the data due to evidence of excessive skew.<sup>9</sup> While the review incorporated criteria for assessing the methodological quality of trials, the existence of a possible dose-response phenomenon has not been investigated.

There is both theoretical and empirical support for the hypothesis that alterations

in acupuncture dose have an impact on therapeutic outcomes. Women with primary dysmenorrhoea show reduced uterine blood flow,<sup>10</sup> impedance to which can be improved with both manual acupuncture (MA)<sup>11</sup> and electroacupuncture (EA)<sup>12</sup> in non-pregnant women. Menstrual pain is strongly correlated with reductions in uterine blood flow.<sup>13</sup> Stener-Victorin *et al*<sup>12</sup> found a dose-response relationship between the number of EA treatments and increases in uterine blood flow, which may also be relevant for menstrual pain. There is also evidence of a dose-response relationship when acupuncture and related techniques are used for non-gynaecological pain conditions<sup>14</sup> or subfertility.<sup>15</sup> Other complex interventions such as psychotherapy<sup>16</sup> also show a clear dose-response relationship. While theoretically sound, the current evidence for the existence of a dose-response phenomenon when treating primary dysmenorrhoea is unclear.

We previously used the Delphi process to identify treatment components that are considered to contribute to the 'dose' of acupuncture, including: the number of needles; type of stimulation; retention time; and number of treatments.<sup>17</sup> White and colleagues,<sup>18</sup> in their review on acupuncture 'dosage', found that attempts to discuss whether or not the dose of acupuncture had been adequate included the following components: the number of treatment sessions; the number of acupuncture needles; the length of the session(s); and mode of stimulation. Hao *et al*<sup>19</sup> found that the components of acupuncture dose that affected the outcomes for tension-type headache were mode of stimulation, needle retention time and frequency of treatment.

This review explores the relationship between the components of acupuncture dose and menstrual pain in women with primary dysmenorrhoea. Wherever possible, the effect of varying dose components were compared within the same study, otherwise potential relationships were investigated across studies. Due to the small number of studies examining each component and the issues with meta-analysis encountered in our most recent systematic review,<sup>9</sup> our objective from the outset was to synthesise and report outcomes using a narrative style.

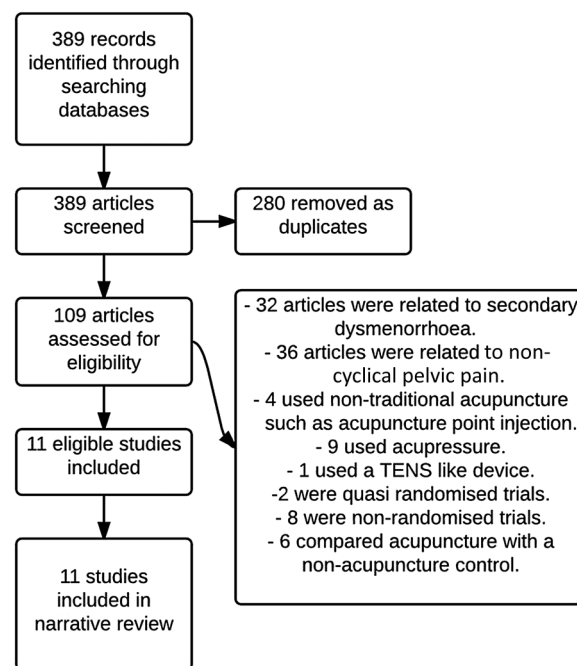
## METHODS

Based on the recommendations of Smith *et al*<sup>17</sup> and White *et al*,<sup>18</sup> as well as the findings of Hao *et al*,<sup>19</sup> we extracted, grouped and reported four different components of acupuncture dose and examined their relationship with menstrual pain intensity: (1) neurophysiological dose reflected by the number of needles, retention time and mode of stimulation (including *de qi*, and intensity and frequency of EA); (2) cumulative dose comprising the total number and frequency of treatments delivered during a treatment course; (3) choice of needle location based on the underlying theoretical framework (often reported in studies as point

location); and (4) timing of treatments. Due to the cyclical nature of menstruation, many studies timed their treatments in relation to the start of menses. Therefore, we also examined for a possible temporal relationship between acupuncture treatment timing and menstrual pain reduction. The two authors extracted dose components and evaluated blinding independently. Any disagreements were resolved by discussion.

## Search strategy

A modified version of the Cochrane search strategy was used. Articles that used acupressure, non-penetrating acupuncture, non-standard acupuncture using microsystems, acupuncture point injections, transcutaneous electrical nerve stimulation (TENS), herbal medicine or moxibustion alone were not included. Only randomised controlled trials (RCTs) were included; quasi-randomised or non-randomised trials were excluded. Databases searched included Medline, PsychINFO, Google Scholar, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, the Cochrane Library menstrual disorders subfertility group, Proquest and Web of Knowledge. All databases were searched from inception until September 2015 using the keywords 'acupuncture' and 'dysmenorrhoea'. Figure 1 outlines the search and selection process. Online appendix A and supplementary material contains detailed search strategies. Papers that either had English full text or an English translation was available were included.



**Figure 1** PRISMA flow diagram of the search strategy. PRISMA, preferred reporting items for systemic reviews; TENS, transcutaneous electrical nerve stimulation.

### Inclusion/exclusion criteria and assessment of methodological quality

To be included, studies had to compare different acupuncture dose characteristics. Any study that did not have at least two verum acupuncture groups was excluded. Studies recruiting participants with a diagnosis of primary dysmenorrhoea or mixed primary and secondary dysmenorrhoea were included; studies of secondary dysmenorrhoea only were excluded. Participants needed to be aged  $\geq 16$  years. All included trials were assessed for risk of bias according to the Cochrane criteria.

### Outcomes

The primary outcome was menstrual pain, measured by visual analogue scale (VAS), numerical rating scale (NRS), Cox menstrual symptom scale (CMSS) or the McGill pain questionnaire. Definitions of 'effectiveness rates' reported by Chinese language studies differed for each study, and did not follow set criteria (see online supplementary table S1 for details of effectiveness criteria for each study).

### Outcome assessment

Follow-up outcome data related to menstrual pain was categorised as immediate (<48 hours after last treatment), short term (2 days to 3 months after the last treatment) and long term (4–12 months after the last treatment). The CMSS<sup>20</sup> records both pain and secondary symptoms, combining the two domains. Therefore, when VAS and CMSS were both present, VAS was used preferentially as this only relates to pain.

## RESULTS

A total of 389 articles were returned, 280 studies were identified as duplicates, and 109 articles were screened for eligibility. Two trials were excluded as they were subsets of the dataset reported in Liu *et al.*<sup>21</sup> In total, 11 RCTs provided data that could be used to explore the relationship between dose and pain outcomes (figure 1).

### Effect of acupuncture dose on menstrual pain

Six studies<sup>11 21–25</sup> investigated the effect of needle location, three studies<sup>26–28</sup> explored the effect of changing mode of stimulation while two studies<sup>29 30</sup> investigated the effect of treatment timing. No studies were found that examined the effect of needle retention time, frequency of treatment or total number of treatments on pain outcomes. Dose components for all included studies are outlined in table 1.

### Neurophysiological dose

Table 2 describes the included studies that examined the impact of changing the number of needles, the retention time or the mode of stimulation. All 11 included studies reported elicitation of *de qi* sensation. One study<sup>26</sup> examined the effect of changing *de qi*

sensation with MA. Acupuncture with strong manual stimulation, as indicated by increased *de qi* sensation, had a greater immediate effect on pain than acupuncture without manual stimulation (minimal *de qi* sensation) for both pain intensity and pain duration. No short-term or long-term follow-up was included. One study<sup>27</sup> examined two styles of MA, one using the 'Qinglong Baiwei' method at LI4 and LR3 compared with standard MA at CV3/CV4 or BL32/SP6. The 'Qinglong Baiwei' method involves inserting the needle obliquely, achieving *de qi* then moving the needle slowly from side to side (as if it were a rudder in a boat) nine times. Immediate pain relief was greatest in the group receiving the 'Qinglong Baiwei' method while short-term pain relief was similar between both acupuncture groups. However, this study varied both needle location and type of stimulation and therefore does not provide useful information about the relative contribution of each component. One study<sup>28</sup> examined MA versus EA using 'superficial' in-dwelling acupuncture and found that EA resulted in a more rapid onset of pain reduction in the 30 min after treatment ( $p < 0.05$ ); however, there was no significant difference between the overall 'clinical effectiveness rate' at the conclusion of the treatment course (91.23 vs 94.74,  $p > 0.05$ ) between MA and EA. No studies examined the effect of changing needle retention time.

### Needle location

Table 3 describes the included studies that examined the effect of changing needle location. Four studies<sup>21–24</sup> examined the effect of EA at SP6, GB39 or an unrelated acupuncture point. All studies concluded that EA had a significant and immediate effect on pain. Studies were inconsistent regarding the importance of point specificity in reducing pain. Immediate pain relief was similar for SP6 and GB39 but superior to an unrelated acupuncture point,<sup>24</sup> with one study showing no difference between points<sup>22</sup> and two studies<sup>21 23</sup> showing SP6 to be superior. Short-term pain relief did not differ between groups.<sup>24</sup>

One study<sup>11</sup> examined the effect of MA at SP6 vs GB39 and found that needling at SP6 resulted in greater immediate pain reduction compared to GB39. One small study<sup>25</sup> examined the effect of MA at traditional acupuncture points versus 'non-channel' points. Examination of responder rates showed that more women in the traditional acupuncture point group achieved  $\geq 50\%$  improvement in pain (90.9%) compared with the non-channel group (36.4%) for long-term pain ( $p < 0.05$ ). However, no significant difference between groups was found for the pain scores themselves, either short- or long-term.

### Treatment timing

Table 4 outlines the included studies that examined the effect of changing treatment timing in relation to

**Table 1** Dose components reported as per STRICTA

Study first location	Number of needles*	Total number of treatments	Frequency of treatments	Timing of treatments	Points selected	Needle retention time (min)	Mode of stimulation	EA frequency and intensity parameters†
Liu <i>et al</i> <sup>21</sup> China	4 (including anchor points)‡	3	1/day for 3 days	First day of menstrual cycle	SP6 or GB39 or 'unrelated acupuncture point'	30	EA	2/100 Hz, intensity 0.5–1.6 mA
Ma <i>et al</i> <sup>30</sup> China	1 or 9	9–21	1/day for 3–7 days per month over 3 months	Either 3–7 days before menses or from first day of menses	SP6, SP8, BL32, <i>Shiqizhui</i> or <i>Shiqizhui</i> alone	30	MA	N/A
Xiong <i>et al</i> <sup>26</sup> China	5	15	1/day for 5 days per month over 3 months	5–7 days before menses	ST36, SP6, CV3	30	MA	N/A
Bu <i>et al</i> <sup>29</sup> China	7	9+	1/day for 3–7 days per month over 3 months	3–7 days before menses	SP6, BL32, SP8, <i>Shiqizhui</i>	30	MA	N/A
Liu <i>et al</i> <sup>24</sup> China	4 (including anchor points)	3	1/day for 3 days	First 3 days of menses	SP6 or GB39 or 'non-acupuncture point'	30	EA	2/100 Hz, intensity 0.5–1.6 mA
Shi <i>et al</i> <sup>22</sup> China	4 (including anchor points)	1	Once	During menses (unclear)	SP6 or GB39	30	EA	2/100 Hz, intensity NR
Ma <i>et al</i> <sup>23</sup> China	4 (including anchor points)	3	1/day for 3 days	First day of menses	SP6 or GB39 or 'non-meridian point'	10	EA	2/100 Hz, intensity highest level tolerable
Yu <i>et al</i> <sup>11</sup> China	2	1	Once	Between 5 days before and 2nd day of menses	SP6 or GB39	5	MA	N/A
Li <i>et al</i> <sup>27</sup> China	≥7	15+	1/day for min 5 days for 3 months	3–5 days before menses until last day bleeding	LI4, LR3 plus CV3/CV4 or BL32/SP6	30	MA	N/A
Zhi <i>et al</i> <sup>28</sup> China	2	3	1 per menstrual cycle for 3 cycles	1st day menses for the first cycle then 3 days before menses for 2nd and 3rd cycle	SP6	30	EA	60 Hz, intensity NR
Helms <sup>25</sup> USA	12	9	3 per month for 3 months	1/week excluding menses	SP4, KI3, ST36, ST30, CV2, CV4, PC6	30–40	MA	N/A

\*Total number of needles used.

†EA stimulation parameters. Single (X) or alternating (X/X) frequency.

‡Anchor points are non-acupuncture points used in conjunction with acupuncture points to facilitate EA.

NR, not reported; EA = electroacupuncture; MA = manual acupuncture; STRICTA, Standards for Reporting Interventions in Clinical Trials of Acupuncture.

**Table 2** Studies examining the effect of neurophysiological dose

Study (# participants)	Intervention	Comparator group(s)	Outcome measure	Treatment outcome for pain
Xiong <i>et al</i> <sup>26</sup> (n=131)	MA with <i>de qi</i> (n=67)	MA without <i>de qi</i> (n=64)	VAS	<i>Immediate:</i> Pain scores decreased in both groups from baseline (p<0.01). Acupuncture with strong manual stimulation produced a greater reduction in both pain intensity (W=2410.0, p<0.01) and pain duration (W=3181.0, p<0.01)
Li <i>et al</i> <sup>27</sup> (n=180)	MA using 'Qinglong Baiwei' method (MAQB) (n=60)	MA (n=60) Herbal medicine: <i>Yueyueshu</i> granules (n=60)	Self-reported improvement scale (cured/marked effect/effective/no effect)	<i>Immediate:</i> MAQB was superior to MA and herbal medicine (p<0.01) <i>Short-term:</i> The cured rate and the total effective rate were 75.0% and 100.0% in the MAQB group, 60.0% and 95.0% in the MA group, and 25.0% and 90.0% in the herbal medicine group, respectively, with MAQB and MA being significantly better than group C (p<0.01)
Zhi <i>et al</i> <sup>28</sup> (n=171)	Superficial EA (ESA) (n=57)	Superficial MA (SA) (n=57) Control group: ibuprofen 300 mg sustained release (n=57)	Self-reported improvement scale (cured/marked improvement/failed)	<i>Immediate:</i> ESA was superior to SA in the onset of pain reduction within 30 min of treatment (p<0.05) <i>Short-term:</i> Total effective rates were 94.74% in the ESA group, 91.23% in the SA group and 77.19% in the control group. The effective rates of ESA and SA groups were significantly higher than that of medication group (p<0.01)

EA, electroacupuncture; MA, manual acupuncture; VAS, visual analogue scale.

the start of menses. One large study<sup>30</sup> varied both the number of needles used and treatment timing. Immediate pain relief, as measured by a VAS, was greatest in the two groups that had treatment during menses regardless of the number of points used (p<0.01); however, the raw numerical data were not published. Treatment before menses at multiple points including SP6, SP8, Bl32 and *Shiqizhui* produced a greater short-term reduction in pain than treatment at the single point *Shiqizhui*. By contrast, when treating during menses the single point was superior to multiple points. Overall treatment before menses at multiple acupuncture points produced the greatest short-term reduction in CMSS scores. One study<sup>29</sup> examined the effect of treatment timing only. MA given 3–7 days before menses was significantly better at reducing short-term pain intensity and short-term pain duration than acupuncture starting from the first day of menses.

#### Cumulative dose

Trials providing ≤3 treatments<sup>11 21–24 28</sup> did not appear to show a trend towards reduced pain compared to those with >3 treatments<sup>25–27 29 30</sup> for immediate, short-term or long-term outcomes.

No studies undertook direct comparisons between the number of treatments.

Trials with either single, weekly or monthly<sup>25 28</sup> treatment did not show a trend towards reduced pain compared to those with daily treatment<sup>21 23 24 26 27 29 30</sup> for immediate, short-term or long-term outcomes.

Furthermore, no studies undertook direct comparisons of the frequency of treatment.

#### Trial quality

Overall risk of bias was moderate to high in all of the included studies (see online supplementary figure S1). Randomisation was performed adequately in all but one study, although allocation concealment was poor in almost two thirds of the included studies. Lack of blinding caused a high risk of bias in over half of the included trials. There was a low risk of bias for incomplete outcome data, while selective reporting and other sources of potential bias were unclear in most studies. Online supplementary figure S2 outlines the risk of bias for each of the included studies. The process of exclusion of secondary dysmenorrhoea, or attempts to distinguish between primary and secondary dysmenorrhoea, were not clearly reported in most trials. Therefore, it is possible that these trials included some women with secondary dysmenorrhoea.

#### DISCUSSION

Overall, few studies included in this review undertook direct comparisons of acupuncture dose, meaning that for most components there was no clear relationship between dose and pain outcomes. Overall, the included studies demonstrated a high degree of variation with respect to the characteristics of the intervention and treatment outcomes, especially in terms of when pain scores were measured. Those studies

**Table 3** Studies examining the effect of needle location

Study (number of participants)	Intervention	Comparator group(s)	Outcome measure	Treatment outcome for pain
Liu <i>et al</i> <sup>21</sup> (n=501)	EA at SP6 (n=167)	EA at GB39 (n=167) or non-acupuncture point (n=167)	VAS VRS	<i>Immediate:</i> SP6 caused a significantly greater reduction (−4.0 mm) in VAS recorded pain than GB39 (p=0.010) or a non-acupuncture point (p=0.012) <i>Short-term:</i> All groups showed improvement in VRS with no between group differences
Liu <i>et al</i> <sup>24</sup> (n=194)	EA at SP6 (n=50)	EA at GB39 (n=50) or non-acupuncture point (n=46) Wait list control (n=48)	VAS	<i>Immediate:</i> All three acupuncture groups showed pain reductions from baseline (p<0.05). GB39 showed a greater reduction than the non-acupuncture point (−7.18 mm, 95% CI −13.84 to −0.51, p=0.035) but no difference to SP6
Shi <i>et al</i> <sup>22</sup> (n=40)	EA at SP6 (n=10)	EA at GB39 (n=10) or non-acupuncture point (n=10) Wait list control (n=10)	VAS	<i>Immediate:</i> All EA groups had a reduction in pain (p<0.05) compared to wait list control. No differences between EA groups
Ma <i>et al</i> <sup>23</sup> (n=52)	EA at SP6 (n=13)	EA at GB39 (n=14) or unrelated acupuncture point (n=12) Wait list control (n=13)	VAS	<i>Immediate:</i> All EA pain reduced from baseline at 5, 10 and 30 min (p<0.001). SP6 had the greatest pain reduction (superior to multiple points, SMD −23.19 mm) compared to control at 30 min post-intervention (p<0.0001)
Yu <i>et al</i> <sup>11</sup> (n=66)	MA at SP6 (n=32)	MA at GB39 (n=34)	Menstrual pain score	<i>Immediate:</i> SP6 group had greater pain reduction at 5 min compared to the GB39 group (SMD −1.31, 95% CI −1.85 to −0.77, p<0.05)
Helms <sup>25</sup> (n=43)	MA at traditional acupuncture points (real) (n=11)	MA at non-channel points ('placebo') (n=11) Standard control: same care as before the study (n=11) Visitation control: increased visits from physician (n=10)	Custom pain scale: 0–6	<i>Short-term:</i> No difference between groups for pain scores. <i>Long-term:</i> Greater proportion of women in the 'real' group (90.9%) showed ≥50% reduction in pain compared to women in the 'placebo' group (36.4%) (p<0.05)

CI, confidence interval; EA, electroacupuncture; MA, manual acupuncture; SMD, standardised mean difference; VAS, visual analogue scale; VRS, verbal rating scale.

**Table 4** Studies examining the effect of treatment timing

Study (number of participants)	Intervention	Comparator group(s)	Outcome measure	Treatment outcome for pain
Ma <i>et al</i> <sup>20</sup> (n=600)	MA at <i>Shiqizhui</i> before menses (n=100)	Treatment before menses at multiple points (n=100) Treatment during menses at <i>Shiqizhui</i> (n=100) Treatment during menses at multiple points (n=100) No treatment control (n=100)	CMSS VAS	<i>Immediate:</i> Both acupuncture groups using treatment during menses had significant reductions in VAS (p<0.01 for both) <i>Short-term:</i> Treatment before menses at multiple points produced the greatest reduction in pain compared with treating at the single point <i>Shiqizhui</i> (SMD −3.22, 95% CI −3.55 to −2.88, p<0.01). When treating during menses the single point was superior to multiple points (SMD −3.55, 95% CI −3.9 to −3.2, p<0.01)
Bu <i>et al</i> <sup>29</sup> (n=80)	Preconditioning acupuncture (PA) 1/day for 3–7 days before menses (n=20)	Acupuncture (A): 30 min 1/day for 3–7 days from 1st day of menses (n=20) Control group: untreated (n=40)	CMSS	<i>Short-term:</i> Acupuncture given before menses (PA) was significantly better at reducing pain intensity (SMD −0.93, 95% CI −1.62 to −0.24, p<0.01) and pain duration (SMD −0.94, 95% CI −1.63 to −0.25, p<0.01) than acupuncture starting from the first day of menses (A). Both groups showed greater pain reduction than the control group (p< 0.05)

CI, confidence interval; CMSS, Cox menstrual symptom scale; MA, manual acupuncture; SMD, standardised mean difference; VAS, visual analogue scale.

that included a no-treatment or wait-list control group showed that the acupuncture intervention appeared to provide an immediate analgesic effect,<sup>22–24 29 30</sup> irrespective of the dose delivered.

The magnitude of the effect of changing mode of stimulation, on the continuum from no stimulation through manual stimulation to EA, was unclear due to the small number of trials. A recent white paper by Langevin and colleagues highlighted the inherent difficulties in comparing MA and EA, as all of the included trials that used EA obtained *de qi* via manual stimulation before the addition of EA; therefore, the included studies may be more accurately interpreted as comparing MA versus MA+EA rather than MA versus EA.<sup>31</sup> The importance of *de qi* in treating menstrual pain is still unclear; while Xiong<sup>26</sup> found an effect on immediate menstrual pain, a more recent analysis on the importance of *de qi* in the treatment of primary dysmenorrhoea casts doubt on this finding.<sup>32</sup> When considering the number of needles used, there were no obvious dose-response relationship across studies; interestingly, however, one study suggested that treatment using a single needle during menses may give better results, whereas multiple needles may be superior before menses.<sup>30</sup> This may reflect an increased sensitivity to acupuncture during menstruation itself.

Needle location differed significantly across trials; however, SP6 was common to all but one trial.<sup>25</sup> The clinical usage of SP6 in trials of traditional Chinese acupuncture is most likely due to its historical usage in dysmenorrhoea,<sup>33</sup> which has been reinforced by experiments in animal models that have provided support for the physiological effects of acupuncture at SP6.<sup>34</sup> The trial that did not use SP6<sup>25</sup> found no differences in pain scores between groups; however, the very small sample size of this trial means that it is difficult to draw any conclusions about the relative importance of needle location.

All trials undertaken in China appeared to consider timing in relation to menses, with treatment starting either less than a week before onset of menses, or at the beginning of menses itself. Justification was not given for this choice but may reflect possible differences in the way acupuncture treatment is delivered in China compared to the rest of the world.<sup>9</sup> Two studies<sup>29 30</sup> found that treatment administered before menses provided greater short-term pain relief than treatment that started on the first day of menses; however, treatment during menses may provide more significant immediate pain relief.<sup>30</sup> Given the more favourable short-term clinical outcomes when treatment was given before menses, rather than at the onset of menses, it is possible that those trials that delivered acupuncture only during menses may have underestimated the treatment effect;<sup>21–24 28</sup> however, this relationship needs to be investigated further.

Examining the relationship between dose components and menstrual outcomes has also provided some

insight into the possible mechanisms underlying acupuncture treatment of primary dysmenorrhoea. Mayor<sup>35</sup> argues that EA implicitly provides a greater dose of stimulation compared to MA alone, based on greater activation of endogenous opioid mechanisms (EOM). The single trial comparing MA with EA showed a more rapid onset of pain relief in the EA group.<sup>28</sup> Both Zhi<sup>28</sup> and Liu *et al*<sup>24</sup> reported the time course of pain reduction following EA and found pain relief peaked within 30 min and, in the case of Liu *et al*, began to decline by 60 min post-treatment, which follows the typical time course of acupuncture-induced endogenous opioid release.<sup>36</sup> Due to the involvement of EOM, the additional pain reduction provided by electrical stimulation is likely to only be transient, with other mechanisms significantly contributing to the observed reduction in overall menstrual pain including changes in uterine blood flow<sup>11</sup> and reduced prostaglandin levels.<sup>28 37</sup> Supporting the influence of multiple mechanisms in addition to EOM, Zhi<sup>28</sup> found that there was no significant effect of changing the mode of stimulation when looking at the overall clinical therapeutic effect. The largest included trial suggested that SP6 offers a greater immediate pain reduction when compared to GB39.<sup>21</sup> This difference is likely due to the fact that SP6 is segmental to the uterus while GB39 is not.<sup>38</sup> This segmental activation at the level of sacral spinal nerve 2 (S2) may lead to reflex sympathetic inhibition of the uterus<sup>12</sup> resulting in increased uterine blood flow.<sup>11</sup> Additional support for immediate pain reduction being mostly secondary to EOM comes courtesy of Ma *et al*,<sup>30</sup> who showed that a greater number of needles causes a more rapid and sustained reduction in pain compared to a single needle when treatment is delivered during painful menstruation. There may also be additional mechanisms by which acupuncture-like treatments can relieve primary dysmenorrhoea; for example, by inactivation of myofascial trigger points on the abdomen using wet needling.<sup>39</sup>

Overall, trial quality was low, which provides several caveats to causally linking the dosing used in these trials (either high-frequency, daily treatment or EA) directly to improved menstrual pain outcomes; there may be a reporting bias in the studies included in this review and some studies have used non-validated outcome measures such as effectiveness scores or CMSS scores, which incorporate multiple domains rather than just pain reduction.

The strengths of this review include its use of all publically available databases plus those provided by the Cochrane Menstrual Disorders and Subfertility Review Group. Data were extracted and checked independently by the two reviewers with any disagreements resolved by discussion. Dose components were assessed based on previously published guidelines. The primary weakness of this review is the limitation on language; only those trials published with full text

in English, or where an English translation had been undertaken during a Cochrane review, were included. This excludes a large body of Chinese language only research. Trials that did not include more than one acupuncture group were excluded from this review. Although this was commensurate with our primary aim of comparing dose between active treatment groups, consequently some high quality studies may have been excluded. Finally, due to skewing of the data, pooled analysis was not possible.

## CONCLUSION

The relationship between acupuncture dose and menstrual pain was unclear, primarily due to the individual variation in the timing of outcome measures that prevented direct comparison. Findings from this review demonstrate that EA may provide more benefit than MA in immediate pain reduction during menses; however, treatment was only delivered on the first day of menses and used an uncommon style of superficial acupuncture. Treatment in the week before menses appears to provide greater benefit than treatment delivered during menses. Overall trial quality was low. Future RCTs should be designed to explore directly the potential effects of variable acupuncture dose on menstrual pain using validated outcome measures.

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# Treating primary dysmenorrhoea with acupuncture: a narrative review of the relationship between acupuncture 'dose' and menstrual pain outcomes

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