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Effects of acupuncture on the symptoms of anxiety and depression caused by premenstrual dysphoric disorder

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ABSTRACT

Objective The objective of this investigation was to evaluate the effects of acupuncture and sham acupuncture on the symptoms of anxiety and depression brought on by premenstrual dysphoric disorder (PMDD).

Methods In a single-blind randomised clinical trial, 30 volunteers with PMDD were assigned alternately to group 1 (acupuncture) or group 2 (sham acupuncture), and completed an evaluation of symptoms of anxiety and depression using the Hamilton Anxiety (HAM-A) and Hamilton Depression (HAM-D) Rating Scales. The procedure was performed twice a week for two menstrual cycles, for a total of 16 attendances for each participant.

Results Before the intervention the mean HAM-A and HAM-D scores did not differ between groups. Following the intervention symptoms of anxiety and depression were reduced in both groups; however, the improvement was significant in group 1 compared to group 2, as shown by a mean reduction in HAM-A scores of 58.9% in group 1 and 21.2% in group 2 ($p < 0.001$). The reduction in the mean HAM-D scores was 52.0% in group 1 and 19.6% in group 2, resulting in a significant difference ($p = 0.012$).

Conclusions The results suggest that acupuncture could be another treatment option for PMDD patients.

INTRODUCTION

Premenstrual dysphoric disorder (PMDD) is a variation of premenstrual syndrome (PMS), affects approximately 2–8% women with PMS^{1–3} and is characterised by a set of symptoms including mood swings, depression, anxiety, behavioural and somatic symptoms, as well as

irritability, emotional instability, tension, and sleep and appetite disturbances. Most of these symptoms begin in the luteal phase of the menstrual cycle and decrease in the follicular phase, hence interfering in a negative and significant manner in the individual's interpersonal and family relationships, and her professional and social life.^{4–5} The impact is proportional to the number of manifestations, mood swings and behavioural changes and is particularly severe when five or more symptoms are present in the luteal phase.^{6–7} Among the therapies employed to treat patients with PMDD are the administration of selective serotonin reuptake inhibitors, benzodiazepine, vitamin supplements, diuretics, progesterone and oral contraceptives, ovulation suppression and acupuncture.^{8–9}

The mechanisms of action of acupuncture, which is based on traditional Chinese medicine (TCM) principles, are not yet fully understood. It is best known for its analgesic effects, but other clinical conditions seem to also benefit from this technique, such as depression and anxiety, and gynaecological dysfunction.^{10–11} Acupuncture's action is based on the activation of afferent A and C fibres in the muscles that transmit signals, via dorsal horn neurons, to the higher centres in the brain, stimulating the release of endogenous neurotransmitters,¹² such as opioid peptides and serotonin (5-hydroxytryptamine, 5-HT).^{13–15}

The treatment of PMS with acupuncture has rarely been investigated in controlled trials⁹; however, the study of Habek *et al* showed positive results, with

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a reduction in physical and emotional symptoms,¹⁶ and a case study described by Taguchi on the same subject indicated an improvement in physical and psychological symptoms, mainly in relation to mood swings, and a decrease in work absenteeism.⁹ The purpose of this present study was to evaluate the effects of acupuncture on symptoms of anxiety and depression brought on by PMDD.

METHODS

Participants and intervention

A single-blind randomised clinical trial was undertaken in the gynaecology and obstetrics department of a physiotherapy clinic in the Union of the Americas Faculty, Foz do Iguacu, Paraná State, Brazil. Thirty women between the ages of 20 and 45 participated, all with regular menstrual cycles (of between 25 and 35 days) and a diagnosis of PMDD as defined by DSM-IV, diagnosed by the criteria of the American Psychiatric Association.³⁻⁹ The criteria relate to four domains: the first defines the characteristics, recurrence pattern, and list of symptoms that may be present in the pre-menstrual and menstrual phases; the second assesses the interference in daily activities caused by the disorder; the third excludes other psychiatric disorders; and the fourth requires confirmation of PMDD through daily self-assessment over at least two cycles. The study exclusion criteria were: pregnancy; irregular menstrual cycles (cycles longer than 35 and shorter than 25 days); use of hormonal contraceptives; use of diuretics or psychiatric medications (psychotropic or tricyclic antidepressant agents, or 5-HT reuptake inhibitors); use of chronic non-steroidal anti-inflammatory drugs; a recent diagnosis of depression or anxiety (in the last 2 years, and not linked to the diagnosis of PMDD); and participation in any type of treatment to reduce PMDD symptoms.

Patients with suspected PMDD were recruited through an article in the media and/or referral from a gynaecologist until the 30 available places were filled. Each then completed a baseline evaluation of their sociodemographic profile. After this, a retrospective evaluation of the menstrual disorder was carried out to confirm the diagnosis of PMDD according to DSM-IV. This was regarded as a provisional diagnosis of PMDD, which was confirmed by the volunteer's diary of daily symptoms. Those without a confirmed PMDD diagnosis were excluded. Patients were informed that they would receive either real or sham acupuncture, as stated in the consent form. After consent was obtained, the symptoms of anxiety and depression were evaluated using the HAM-A and HAM-D Rating Scales. The scales were administered on the first day of menstruation in reference to the preceding 2-week premenstrual phase. After evaluation, the patients were allocated alternately by order of arrival to the acupuncture group or the control group.

Group 1: acupuncture (n=15)

Patients received acupuncture lying supine after acupuncture points were cleaned with 70% alcohol. The technique described by Tam *et al*¹⁷ was used, where a foam cube about 2 cm³ with adhesive material (double-sided tape) covering one face was placed on the skin, exactly above the acupuncture point, as a support for the acupuncture needle. The volunteer was thus not able to see how far the needle penetrated the skin. Dongbang disposable, single-use 0.20×40 mm Korean needles were used. The needle penetrated the skin sufficiently to reach the required depth and elicit *de qi*. The needles remained in situ for 30 min, with gentle rotational movements applied three times.

The procedure was performed twice a week during two menstrual cycles (using as a basis the normal cycle of 28 days), resulting in a total of 16 visits. Each visit, including initial care, needle application and needle retention, lasted about 45 min. The selection of acupuncture points was based on TCM theory and previous publications.¹⁶⁻¹⁸ The points chosen are recommended for the treatment of symptoms of anxiety and depression, as well as for gynaecological disorders, including PMS and PMDD.¹⁶⁻¹⁹

The points used were, bilaterally: *Neiguan* (PC6), *Waiguan* (TE5), *Hegu* (LI4), *Sanyinjiao* (SP6), *Yanglingquan* (GB34) and *Taichong* (LR3).

Group 2: control (n=15)

In group 2 the volunteers received sham acupuncture (simulation) in non-acupuncture points 2 cm either side of the points used in group 1. The foam cube was applied as before, but the needle was only inserted to a depth of 2 mm and then quickly removed, without eliciting *de qi*. The needle was retained in the foam cube to give the patient the impression that it remained in the skin. Dongbang disposable 0.20×30 mm Korean needles were used, the shorter length than in group 1 ensuring that the top of the needle protruded above the cube to a similar extent in both groups. After the end of the intervention, all participants in group 2 received real acupuncture treatment for two menstrual cycles, as described for group 1.

The procedures for groups 1 and 2 were performed by an acupuncturist with more than 5 years of experience.

Evaluations by a psychologist were repeated at the end of two menstrual cycles, using the HAM-A and HAM-D.

This work was approved by the Institutional Review Board/Independent Ethics Committee (IRB/IEC) of the IPA Methodist University Center, under protocol number 287/2009.

Statistical analysis

The paired t test was used for intragroup analysis, and the unpaired t test for intergroup analysis. All results are expressed as mean±SD. Statistical evaluation of

variables was performed using the software SPSS for Windows (V.16.0). *p* Values <0.05 were considered significant.

The total HAM-A score (including all 14 questions of the scale) was used for data analysis. In addition, individual scores were analysed: emotional aspects were evaluated with questions 1 (anxious mood), 2 (tension), 4 (insomnia), 5 (concentration and memory) and 6 (depressed mood), while somatic aspects were evaluated with questions 8–14 (all the somatic items). Questions 3 and 7 from the questionnaire were excluded from the analysis of subscores, as they were not directly related to the aim of this investigation. The HAM-D total was derived from the sum of the 21 items of the scale.

RESULTS

Fifteen of the 45 volunteers evaluated were excluded because the PMDD diagnosis was not confirmed or the symptom diary was not returned. During the investigation, one patient withdrew from group 1 and three from group 2, all due to lack of interest in continuing the study. The investigation procedure is shown in the flowchart (figure 1).

Table 1 presents the sociodemographic characteristics of volunteers and shows there were no significant difference between the groups.

In group 1, of the 10 volunteers admitting to compulsive eating in the luteal phase of the menstrual cycle, six (60%) reported an increased desire to eat sweets in general, three (30%) exclusively craved chocolate and one (10%) reported a general increase in appetite. In group 2, of the nine volunteers admitting to compulsive eating in the luteal phase, seven (77.8%) reported an increased desire for sweets in general and two (22.2%) mentioned an increased appetite in general.

No volunteer, in either group, reported use of illicit drugs or regular use of alcohol; one (8.3%) volunteer in group 2 was a smoker.

When intragroup (table 2) and intergroup (table 3) analyses were combined, group 1 showed a significant difference in the mean HAM-A total between the pre- (27.3 ± 6.5) and post-intervention (11.0 ± 4.17) evaluations, a 59% decrease; and in the sham group there was a fall from 24.8 ± 6.6 to 19.4 ± 5.3 , a 21% decrease. HAM-A 1, 2, 6 and the somatic subscale also showed a significant reduction in the acupuncture group compared with the sham acupuncture group (table 3). Analysis of total HAMA-D scores showed similar changes. In the real acupuncture group, scores pre- (16.30 ± 4.76) and post-intervention (7.64 ± 3.34) decreased by 52%, while in the sham acupuncture group, scores pre- (15 ± 4.9) and post-intervention (11 ± 3.6) decreased by 19% ($p=0.012$).

DISCUSSION

We found a significant decrease in the total HAM-A and HAM-D scores in both groups of women with

PMDD, but acupuncture was more effective in decreasing the symptoms of anxiety and depression compared to sham acupuncture.

There were more withdrawals in group 2 than in group 1, which may indicate that the volunteers dropped out because they did not perceive any change in their symptoms.¹⁷ In both groups, there were reports of increased ingestion of sweets and chocolates and higher calorie intake in the premenstrual period (before the investigation started), demonstrating that the need for carbohydrate consumption in these women could be related to the serotonergic hypofunction characteristic of PMDD.²⁰

Although there is a trend towards increased alcohol consumption in PMDD patients,²¹ in this sample no volunteer regularly consumed alcoholic beverages, and only moderate drinking was reported.

No side effects were observed, which includes hypotension, skin irritation or ecchymosis in the acupuncture points. Although not systematically determined in this investigation, in the re-evaluation three group 1 patients spontaneously reported a reduction in the duration of PMDD emotional symptoms, dropping from a mean of 14 days to only 5 days. No group 2 volunteer spontaneously reported a similar decrease.

Until now, only one study of acupuncture for symptomatic treatment of PMDD has been performed,⁹ and showed an improvement in physical and psychological symptoms, with a decrease in the total score of the Menstrual Distress Questionnaire after treatment, mainly in the score for negative mood, as compared to the period without acupuncture. The hypothesis for this improvement is based on the supposition that the release of substances in the CNS, mainly 5-HT,^{13–15} as a result of acupuncture, could have decreased symptoms because 5-HT dysfunction occurs in PMDD.^{4–9} This present investigation is methodologically different from the previous study as it was a randomised clinical trial. The study duration was shorter, and we observed that it would be hard to conduct a controlled long-term study with sham acupuncture or placebo, as it could be difficult to maintain the patient 'blind' due to the possibility of contact with other patients and the ease of access to information about acupuncture.²² In any case, our investigation corroborates the earlier findings, in that we also found a decrease in psychological and physical symptoms in group 1 compared to group 2.

Although the study objective did not include measurement of 5-HT released as a result of acupuncture, several investigations have demonstrated this physiological response,^{9 23 24} and therefore acupuncture could have modulated the serotonergic system imbalance found in PMDD.¹ This hypothesis is strengthened by analysis of the total scores of the HAM-A and HAM-D, which showed a significant decrease in group 1.

Physical symptoms, although not directly evaluated, were investigated with the HAM-A somatic scale, which showed a decrease in group 1 compared to

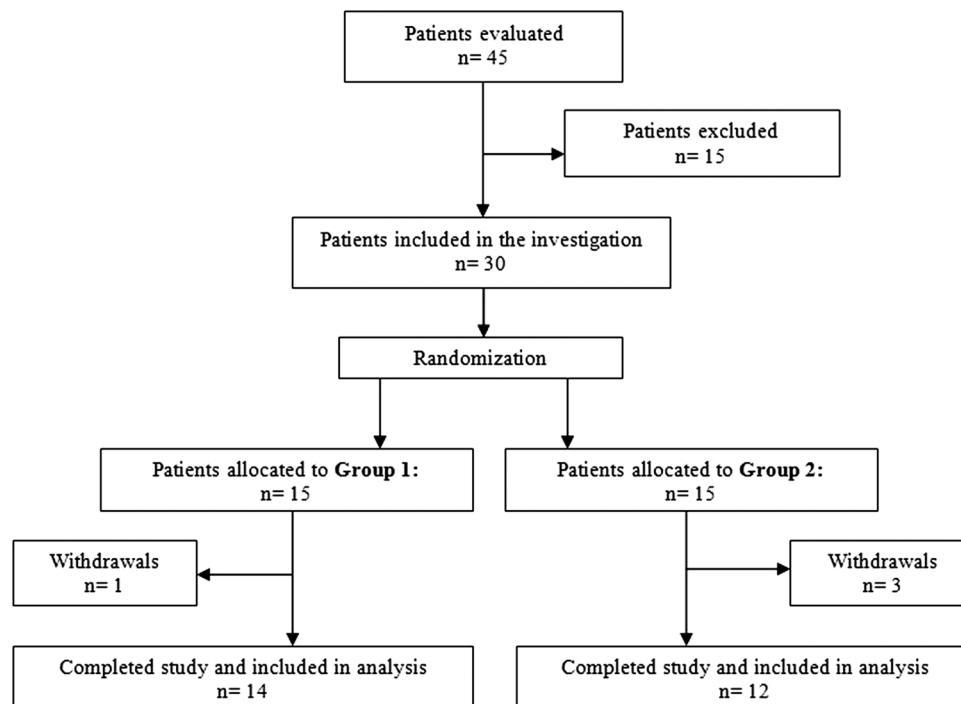


Figure 1 Flowchart for the recruitment of 45 volunteers with suspected premenstrual dysphoric disorder.

group 2, which could be related to the release of opioid peptides in addition to 5-HT.^{13–15} Physical symptoms affect the respiratory, cardiovascular,

sensorial, gastrointestinal, genitourinary, autonomic and muscular systems, and involve pain (in the head and spine) and muscle spasms in the premenstrual phase. One suggested mechanism for the reduced physical symptoms in group 1 is that acupuncture may lessen sympathetic activity, decreasing the release of catecholamine agents, which could be part of the analgesic mechanism of acupuncture.^{25 26} In addition, substance P could be inhibited in the presence of endogenous opioids released by acupuncture.^{15 27}

The improvement in group 2 could be due to: (1) the ‘non-specific physiological effect’ caused by the minimal insertion of the needle, which includes alteration of the local circulation and immune system,²⁸ and (2) the ‘non-specific effect’, that is, the placebo effect caused by the patient’s expectation regarding the treatment and contact with the researcher. Although in both groups a comprehensive effort was made to treat the research volunteers equally, it is possible that a placebo effect occurred in both groups, as in any other therapeutic intervention.²⁹ Even with such effects, the arbitrary analyses of the subscores of HAM-A 2, 5 and 6, which did not show any decrease in symptoms, indicate that the physiological and placebo effects in group 2 were less than in group 1.

The greater decrease in physical than emotional symptoms in group 2 suggests that the non-specific physiological effect produces a greater decrease in pain than in emotional symptoms.¹⁶ It is possible that the small improvement shown in this group is mainly due to the placebo effect. Even if this group presents non-specific physiological responses and placebo effects, these responses are still less than those

Table 1 Sociodemographic characteristics of the participants

| Variables | Group 1: Acupuncture (n=14) Mean (SD) | Group 2: Sham acupuncture (n=12) Mean (SD) |
|------------------------------------|--|---|
| Age (years) | 31.6 (8.6) | 30.7 (6.6) |
| Age at menarche (years) | 12.2 (1.6) | 12.5 (1.5) |
| No. of pregnancies | 1.0 (1.2) | 1.4 (1.1) |
| Menstruation duration (days) | 4.1 (1.2) | 4.1 (1.0) |
| Menstrual cycle (days) | 27.5 (1.7) | 27.1 (1.6) |
| Initial body mass index | 23.2 (3.9) | 25.8 (5.4) |
| | n (%) | n (%) |
| Marital status | | |
| Single | 6 (42.9) | 3 (25.0) |
| Married | 7 (50.0) | 7 (58.3) |
| Separated | 1 (7.1) | 2 (16.7) |
| Ethnic group | | |
| Caucasian | 10 (71.4) | 9 (75.0) |
| Brown | 3 (21.4) | 3 (25.0) |
| Other | 1 (7.1) | 0 (0.00) |
| Physical activity | | |
| Yes | 5 (35.7) | 5 (41.7) |
| Luteal phase alimentary compulsion | | |
| Yes | 10 (71.4) | 9 (75.0) |

Table 2 Intragroup analysis: Hamilton Anxiety and Depression Rating Scale scores before and after the 8-week intervention

| Variable | Group 1: Acupuncture (n=14) | | | Group 2: Sham acupuncture (n=12) | | |
|---------------|--------------------------------|----------|---------|-------------------------------------|----------|---------|
| | Pre | Post | p Value | Pre | Post | p Value |
| HAM-A total | 27.3±6.5 | 11.0±4.2 | <0.001 | 24.8±6.6 | 19.4±5.3 | 0.03 |
| HAM-A 1 | 3.3±0.6 | 1.1±0.8 | <0.001 | 2.9±0.5 | 2.3±0.8 | 0.05 |
| HAM-A 2 | 2.5±0.6 | 1.0±0.6 | <0.001 | 2.7±0.7 | 2.4±0.9 | NS |
| HAM-A 4 | 2.0±1.1 | 0.9±0.8 | <0.05 | 2.2±1.1 | 1.4±0.9 | 0.02 |
| HAM-A 5 | 1.9±1.3 | 1.0±0.9 | <0.04 | 1.5±1.3 | 1.0±1.0 | NS |
| HAM-A 6 | 2.8±0.8 | 1.0±0.8 | <0.001 | 2.2±0.6 | 2.0±1.0 | NS |
| HAM-A somatic | 13.3±4.1 | 5.2±2.6 | <0.001 | 12.0±3.9 | 9.0±4.3 | 0.02 |
| HAM-D total | 16.3±4.7 | 7.6±3.3 | <0.001 | 15.0±4.9 | 11.0±3.6 | 0.02 |

The paired t test was used to analyse data.

HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; NS, not significant.

achieved by acupuncture, where the *de qi* effect is present and specific acupuncture points were used.^{16 17}

The reason for the lack of change in insomnia, memory and cognition between both groups is not known. Acupuncture may be useful in the treatment of insomnia associated with other conditions, such as major depression,³⁰ anxiety disorders^{31 32} and fibromyalgia³³; nevertheless, the mechanisms of the beneficial effects of acupuncture on sleeping disturbances should be more thoroughly investigated.³⁴ Although symptoms in the acupuncture group decreased more than the sham group regarding these topics, the difference was not significant.

Table 3 Intergroup analyses: mean rate of decrease of scores before and after the 8-week intervention

| Variable | Group 1 (n=14), % | Group 2 (n=12), % | p Value |
|---------------|----------------------|----------------------|---------|
| HAM-A total | 59 | 21 | <0.001 |
| HAM-A 1 | 65 | 21 | <0.001 |
| HAM-A 2 | 58 | 9 | <0.001 |
| HAM-A 4 | 54 | 31 | NS |
| HAM-A 5 | 41 | 20 | NS |
| HAM-A 6 | 65 | 5 | 0.02 |
| HAM-A somatic | 58 | 18 | 0.005 |
| HAM-D total | 52 | 19 | 0.012 |

The Student t test was used to analyse data.

HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; NS, not significant.

Summary points

- ▶ Premenopausal dysphoric disorder is characterised by depression and anxiety.
- ▶ In this randomised clinical trial, acupuncture given over two menstrual cycles significantly reduced depression and anxiety.

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Contributors FC was the principal investigator, and the results presented in this study are part of her master's degree dissertation; RV and MPSR were the research supervisors, especially in methodological correction (therapeutics and evaluative instruments) and statistical analysis. KW and ME were responsible for diagnosis, randomisation, and application of the Hamilton Anxiety and Depression Rating Scales; and YAF was investigation supervisor and is a teacher at the Federal University of Health Sciences of Porto Alegre, where part of the study was developed.

Competing interests None.

Ethics approval This study was approved by the Institutional Review Board/Independent Ethics Committee (IRB/IEC) of the IPA Methodist University Center, under protocol number 287/2009.

Provenance and peer review Not commissioned; externally peer reviewed.

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