The impact of meridian balance method electro-acupuncture treatment on chronic pelvic pain in women: a three-armed randomised controlled feasibility study using a mixed methods approach

Introduction: Chronic pelvic pain (CPP) is estimated to affect 6-27% of women worldwide. In the UK over 1 million women suffer from CPP and it has been highlighted as a key area of unmet need. Standard treatments are associated with unacceptable side effects. The meridian balance method electro-acupuncture (BMEA), and traditional Chinese medicine health consultation (TCM HC, [BMEA + TCM HC = BMEA treatment]) may be an effective adjunct to standard treatment.

Aim: The aim of our study was to evaluate the feasibility of a future trial, to determine the effectiveness of the BMEA treatment for CPP in women.

The primary objectives were to determine recruitment and retention rates. The secondary objectives were to assess the effectiveness of the BMEA treatment and acceptability of the study's methodology.

Methods: Women with CPP were randomised into BMEA treatment (group 1), TCM HC alone (group 2) (each intervention administered twice weekly for 4 weeks) or National Health Service standard care (NHS SC, group 3). Primary outcomes were assessed by the proportion of eligible participants randomised, and the proportion of randomised participants who returned follow-up questionnaires. Interventions were assessed by validated pain/physical/emotional functioning questionnaires at baseline (0), 4, 8, and 12 weeks. Focus groups and semi-structured telephone interviews were embedded in the study.

Results: Thirty (30) women (51% of those referred) were randomised over 8-months. Retention rates were 80% (95% CI 74-96), 53% (95% CI 36-70) and 87% (95% CI 63-90), in groups 1, 2, and 3 respectively. Qualitative data suggested a favourable trial experience in groups 1 and 3.

Discussion: Group 2 retention rate was problematic and has implications for our next trial.

Conclusion: Our study suggests that a future trial to determine the effectiveness of BMEA treatment for women with CPP is feasible but with modifications to the study design.

INTRODUCTION

Chronic pelvic pain (CPP) is defined as intermittent or constant pain in the lower abdomen or pelvis of at least six months duration, not occurring exclusively with menstruation or intercourse and not associated with pregnancy[1]. In the United Kingdom, CPP affects over one million women and has been highlighted as a key area of unmet need [2]. An updated systematic review estimated that 6-27% of women worldwide suffer from CPP[3]. Some studies suggest that CPP is responsible for 20% of gynaecological consultations and a 45% loss of work productivity, leading to significant socioeconomic costs[2,4,5]. CPP can be associated with specific conditions, such as endometriosis, but 55% of women have no apparent underlying pathology[6]. If no pathology is identified, the pain is much more difficult to treat, with many women not achieving adequate pain relief, and there is no consensus as to the best management strategies[4]. Non-opioid drugs such as paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) are often the first line of treatment, progressing to a weak (e.g. codeine, co-codamol), then stronger opioid (e.g. oxycodone) if necessary[7]. However, the frequent use of these non-opioid medications can have adverse side effects. Long-term opioid use can be associated with decreased quality of life and physical function[8] as well as tolerance, dependence and the risk of addiction[9].

We believed that the meridian balance method[10] (BM) electro-acupuncture (EA), combined with traditional Chinese medicine health consultation (TCM HC) may be an effective adjunct in the management of CPP. In our study, the combination of BMEA + TCM HC is called BMEA treatment. Unlike most acupuncture studies, we have made a distinction between the acupuncture needling component (BMEA) and the TCM HC of an acupuncture treatment, as well as the context in which a treatment takes place. To our knowledge, there have been no studies that have investigated the use of the meridian BMEA treatment in chronic pain or CPP specifically in women.

There are several acupuncture styles and these include, among others, the meridian balance method (BM), traditional acupuncture (TA) or Japanese acupuncture. The meridian BM acupuncture uses a systematic approach to acupuncture point selections (treatment). Chinese medicine theory posits that the surface of the body has a network of 12 meridians (six yin and six

yang) that connect acupuncture points and internal organs[11]. Pain is believed to be the result of the lack of Qi (vital energy) and Blood and/or stagnation, leading to a blocked meridian and an imbalance in the system. The meridian BM acupuncture treats pain by balancing these meridians, for example, using a yang meridian to balance an affected yin meridian (the yin/yang concept is a comparison of two opposite but complementary states). The meridian network is usefully viewed as a conceptual framework to guide clinical practice[12]. The meridian BM has been described in modern publications[10, 13, 14] as well as the seminal classical Chinese medicine text, the Huang Di Nei Jing[15]. The meridian BMEA forms the first component of an acupuncture treatment.

The second component of an acupuncture treatment is the health assessment which relates specifically to what our study calls TCM HC. It is an integral part of an acupuncture treatment which in itself might have a therapeutic effect[16, 17], hence we wanted to explore the use of TCM HC alone. TCM HC is a structured and patient-centred approach to health assessment through the established clinical practice of Chinese medicine. These include the four examinations (observation, listening, questioning and palpation); and the eight principles (hot/cold, excess/deficient, yin/yang and interior/exterior)[18]. In the four examinations, the participant's general appearance, body language or facial expression are noted. Enquiries are made and discussed on emotional status, diet, sleep quality, energy level and the location as well as the nature of pain. The information obtained is organised according to the eight principles to reflect the whole person. A participant is considered yang deficient, if her pulse is slow and weak, tongue colour and complexion are pale and has a subjective feeling of cold. In this example, she is encouraged to consume cooked and hot food, and fewer cold natured foods such as salads[19].

The third component in which any intervention takes place is called the contextual factors. The context or contextual factors are a complex and indivisible part of any consultation and could nonetheless be clinically meaningful[16]. Examples of contextual factors are the beliefs and expectations of the participant[20] and the healthcare provider, the therapeutic setting and the nature of the patient-healthcare provider relationships[21].

There have only been a few studies of acupuncture for CPP in women. A study using Japanese-style acupuncture and two studies using TA suggested that acupuncture could be effective in managing endometriosis-associated pain[22,23,24]. Larger scale studies comparing TA with sham acupuncture and usual care for other chronic pain conditions, such as osteoarthritis of the knee[25] and tension-type headache[26], have also demonstrated some effectiveness.

Although there have been no studies to show that electro-acupuncture (EA) enhances the analgesic effect of the meridian BM acupuncture, preclinical and clinical evidence suggest that both manual stimulation (MA) of the needle and EA produce an analgesic effect via the release of endogenous opioid peptides in the central nervous system[27]. EA has the advantage that it can be measured precisely, is easier to control and certain parameters such as its frequency and length of stimulation time can be standardised.

Our hypothesis is that the meridian BMEA treatment alleviates pain, improves physical and emotional functioning in women with CPP.

AIM

The aim of this study is to evaluate the feasibility of a future large-scale RCT to determine the effectiveness of the meridian BMEA treatment for CPP in women.

METHODS

Study Protocol

The study protocol was published online [12] prior to participant recruitment.

Ethical Approval

Ethical approval was granted by the Scotland Research Ethics Committee (REC 14/SS/1022) on 22nd August 2014 and was registered with ClinicalTrials.gov (NCT02295111). Informed written consent was obtained from all participants.

Study Design

This was a single centre, open, three-armed parallel randomised controlled feasibility study comparing BMEA treatment (group 1) with TCM HC (group 2) and NHS SC (group 3) that used a mixed methods approach.

Recruitment of Potential Participants

Between October 2014 and June 2015, women aged 18 years and over with CPP who attended the Edinburgh Centre for Pelvic Pain and Endometriosis Care and Treatment Centre (EXPPECT Centre), Simpson Centre for Reproductive Health (SCRH) Royal Infirmary of Edinburgh (RIE), were approached and asked by their Consultant Gynaecologists if they were interested in participating in the study. The gynaecologists' decisions to refer patients were based on their knowledge of the inclusion/exclusion criteria. These were emailed to them at the start of the study and made available to them in all of the outpatient areas. During the recruitment period, the total number of patients who attended EXPPECT was 135. Out of these, 59 (44%) patients were referred to the clinical research team. These patients were approached by a clinical research nurse and given a patient information sheet (PIS) to review at home. Potential participants had at least 24 hours to review the PIS, ask questions and make an informed decision as to whether they wished to participate. After the potential participants had reviewed the PIS, and expressed an interest in participating in the study, they were given an appointment to meet with a member of the research team at SCRH and be screened for eligibility based on the inclusion/exclusion criteria.

Inclusion Criteria

- CPP longer than 6 months duration
- Average pain score on a numeric rating scale (NRS) of at least 4 out of 10 (0-10) in the previous week
- Women aged 18 years or over
- Able and willing to comply with the interventions

Exclusion Criteria

- Pregnancy
- Malignancy
- Severe bleeding disorders (e.g. type 2, 3 Von Willebrand disease)
- Taking regular anti-coagulant
- Severe needle phobia
- A pacemaker in situ

- A history of seizures
- Treatment with EA and meridian BM within the last 6 months
- Moderate to severe psychiatric illness and under the care of a psychiatrist.

Sample Size

A sample size of 30 participants allowed an estimation of the rates of recruitment and retention to within a Standard Error (SE) of at most 10%.

Assessment Tools

Three focus group discussions and a semi-structured telephone interview were conducted post questionnaire collection.

A set of questionnaires was given to all participants at randomisation (0 weeks), 4, 8 and 12 weeks. The questionnaires comprised of:

1. Numeric rating scale (NRS)[28]: The NRS has a 11-point pain intensity scale (0-10, 0 = no pain and 10 = worst pain). Participants were instructed to select a number on the scale that best described the average pain intensity in the previous week.
2. Brief Pain Inventory (BPI)[29]: The BPI has two dimensions: pain intensity and pain interference. Participants were instructed to rate their pain at the time of completing the questionnaire and also pain at its worst, least and average over the past 24 hours, each measured on a 0-10 scale (0=no pain, 10=worst pain). In addition, interference of pain with their general activity, mood, walking ability, normal work, relationships with other people, enjoyment of life and sleep were measured on a 0-10 scale (0=does not interfere, 10=completely interferes).
3. Short Form -12 Version 2 (SF-12v2)[30]: The SF-12v2 is a health related quality of life survey tool. It is a second version of SF12, an abridged version of SF36. SF-12v2 consists of 12 items and has two summary scores: the physical component status (PCS) and the mental component status (MCS). In the PCS, the participants were instructed to rate how much their pain limited their daily activities such as climbing stairs, pushing a vacuum cleaner or playing golf ("yes, limited a lot", "yes, limited a little" and "No, not limited at all"). In the MCS component, participants were instructed to rate how much

any emotional problems interfered with their daily activities or normal work, during the past four weeks. The PCS and MCS are scored from 0-100, with higher scores indicating better quality of life.

4. Hospital Anxiety and Depression Scale (HADS)[31]: The HADS is a self-administered anxiety and depression screening tool for use in non-psychiatric patients. The HADS has 14 items: seven anxiety and seven depression items, both of which focus on the emotional and cognitive aspects. Each item is scored from 0-3 to a combined maximum of 21 for each aspect, with higher scores reflecting a higher symptoms load.
5. Pain Catastrophising Questionnaire (PCQ)[32]: The PCQ is a self-report tool to measure catastrophizing which is understood as a tendency to misinterpret and exaggerate situations that may be threatening. PCQ has 13 items and each item is rated on a 5-point scale: 0 (not at all) to 4 (all the time). The PCQ has three subscales: rumination (Can't stop thinking about how much it hurts), magnification (Worry that something serious may happen) and helplessness (It's awful and I feel that it overwhelms me). A high score indicates higher rumination, magnification and helplessness.
6. Work Productivity and Activity Impairment Questionnaire (WPAIQ)[33]: The WPAIQ measures absenteeism (work time missed), presenteeism (impairment at work), work productivity (work impairment, absenteeism and presenteeism) and activity impairment during the previous seven days. The WPAIQ is self-administered. Higher values (hours or days) indicate greater impairment and lower productivity.
7. Sexual Activity Questionnaire (SAQ)[34]: The SAQ is a self-report questionnaire with three parts: (1) the relationship status (sexually active or not), (2) reasons for sexual inactivity (eight possible reasons) and (3) sexual functioning which has 10 items. If sexually inactive, participants were instructed to complete part 2 and skip part 3. If sexually active, participants were asked to rate their sexual pleasure (desire, enjoyment and satisfaction), discomfort (dryness and pain) and habit (habitual sexual behaviour) during the past month. Sexual pleasure and discomfort are rated on a four-point scale from "very much" to "not at all". A high score indicates high pleasure (range 0-18)/discomfit (range 0-6) and low score indicates low discomfort. A high score in sexual activity ("habit", range 0-

3) indicated a higher degree of sexual activity. Similarly, a high score in the "tired" variable indicated a higher degree of tiredness.

Interventions

After written consent was obtained, eligible women were randomised to receive the meridian BMEA treatment (group 1), TCM HC (group 2), and NHS SC (group 3). Group 1 received 8 BMEA treatment interventions twice a week for 4 weeks. Group 2 received 8 TCM HC interventions twice a week for 4 weeks. The controllable contextual factors in relation to delivery of the intervention to groups 1 and 2 were consistent. For example, the same acupuncturist delivered the interventions to groups 1 and 2, and both groups 1 and 2 had the same TCM HC which was delivered in the same setting". All interventions in groups 1 and 2 were audiotaped to ensure standardisation of procedures and techniques. Group 3 received optimal NHS SC. Participants in groups 1, 2 and 3 were given questionnaires to complete at weeks 0, 4, 8 and 12.

TCM HC intervention: Groups 1 and 2

Groups 1 and 2 shared the same approach to the TCM HC intervention described earlier. Each participant received individualised advice based on her presenting symptoms and needs. The advice given was modified to accommodate each participant's evolving pattern of sleep, pain, or energy levels. Group 2 received TCM HC intervention only. After receiving the TCM HC intervention, group 1 proceeded to receive the second part of the intervention i.e. the BMEA needling.

The BMEA intervention: Group 1

The step-by-step individualised and systematic acupuncture point selections was popularised by Tan[10, 35, 36] and have been described in detail by Chong et al[12]. This systematic step-by-step protocol results in an individualised treatment which is based on the active interaction between the patient and the acupuncturist. Briefly, to diagnose the sick meridian, the acupuncturist asked the participant to point with one finger to where she felt the worst pain. The correct diagnosis of the sick meridian was crucial. Once the sick meridian was identified, the image or mirror method was used to locate the areas of the body to be treated. The image method mapped the relationship

between the limb and the body, e.g. the lower abdomen imaged the forearm or lower leg. The mirror method mapped one limb onto another or one part of the body to another part of the body, e.g. the thumb mirrored the big toe. This kind of mapping is called somatotopy where a specific point on the body can be projected to a specific point in the primary somatosensory cortex of the brain[37]. A healthy meridian was chosen in the area of the body to be treated. The acupuncturist palpated along the chosen healthy meridian for ashii points (tight and tender points) to identify the acupuncture points that provided the most pain reduction as reported by the participant. For example, if when palpating the second ashii point, the participant reported a higher level of pain relief than the first one, acupuncture needles were inserted into the second ashii point.

Depth of Needle Insertion

Sterile, disposable needles (Dong Bang, Korea, Aculine, China) were used. The gauge (thickness) and length of these acupuncture needles were in millimetres. The depth of needle insertion was adjusted to the thickness of the muscles and subcutaneous fatty tissue of each participant. For example, a 0.30mm (gauge, 0.01 of an inch) x 75mm (3 inches in length) acupuncture needle would be inserted to a depth of approximately 25 mm (1 inch) to 50 mm (2 inches) in the gluteal, a 0.25mm x 30mm (1.20 inches in length) needle would be inserted to a depth of approximately 6.35mm (0.25 of an inch) to 19.0mm (0.75 of an inch) in the forearm. The number of needles inserted was individualised based on feedback from the participants.

Electro-stimulation

The negatively charged black lead (to stimulate) of the AS SUPER 4 Digital stimulator (CE 0197, Germany), was connected to the acupuncture needle inserted to the point that gave the most pain relief (therapeutic point) while the positively charged (red) was connected to another needle inserted distal to the therapeutic point. The AS SUPER 4 Digital stimulator emitted a square wave of low frequency (2Hz) for 3-second alternating with high frequency (100Hz). Program 2 was selected and the duration of stimulation was no shorter than 20 minutes and no longer than 30 minutes. These parameters were based on the work of Han and his group[38]. The intensity of the stimulation was adjusted, based on the participant's feedback, to produce a strong sensation without pain or discomfort.

NHS SC intervention: Group 3

Participants continued to follow NHS standard care, defined as care and treatment that patients would normally receive from their general practitioner or the EXPPECT Centre. The EXPPECT team consisted of a Consultant Gynaecologist, chronic pain Consultant, Psychologist and Specialist Nurse. Treatments could include oral analgesics, anticonvulsants, anti-depressants, hormonal approaches (e.g. combined oral contraceptives or progestogens), or surgical intervention (e.g. laparoscopy) if indicated.

Acupuncturist Information

The PI, who had completed at least 3000 hours of acupuncture training, with over 17 years of clinical experience in acupuncture, performed the interventions. She studied the meridian BM acupuncture with the late Dr Richard Tan and has a Master of Science Degree in Acupuncture from an accredited school in New York City, USA. She was awarded a PhD by The University of Edinburgh for her research in Acupuncture in Chronic Pain Management.

Randomisation

A randomised block size of 6 was used. Thirty (30) random numbers were generated by Statistical Package for Social Sciences (SPSS). There were 30 sealed envelopes numbered one to 30, each with a card inside giving the randomly allocated intervention. The first participant who passed the screening, received envelope number one; and the second received envelope number two until all 30 envelopes were used. For transparency, each envelope was opened in front of each participant at the time of randomisation. Participants who were randomised to receive the BMEA treatment and TCM HC, received the appropriate first intervention on the same day. Participants who were randomised to receive NHS SC were instructed to continue with their NHS standard care.

Primary Objectives

The primary objectives were to determine recruitment and retention rates in EXPPECT NHS Lothian within defined inclusion/exclusion criteria.

Secondary Objectives

The secondary objectives were to determine the effectiveness and acceptability to participants of the proposed methods of recruitment, randomisation, interventions and assessment tools.

Primary Outcomes

Recruitment and retention rates were assessed by the proportion of eligible participants randomised into the study and the proportion of participants who returned questionnaires at the follow-up weeks 4, 8 and 12 respectively. The research team kept an electronic log of women who were referred to the study, fulfilled the eligibility criteria, were invited to participate, as well as the return of follow-up questionnaires and reasons for no show for any intervention.

Secondary Outcomes

- Acceptability to the participants of the method of recruitment and randomisation: assessed using data from recruitment history and semi-structured telephone interviews
- Acceptability to the participant of assessment tools: assessed by data completion and patterns of missing data in the questionnaires and semi-structured telephone interviews
- Acceptability of interventions: assessed by the proportion of treatment interventions completed by participants in the groups 1 and 2 as well as semi-structured telephone interviews
- Effectiveness of the interventions on CPP: assessed by the completed data from questionnaires and focus group discussions

Statistical Analysis

For primary outcomes, we estimated the proportion of eligible women randomised, and of those randomised who were followed up at weeks 4, 8 and 12 with 95% confidence intervals. Our study was not powered to allow comparisons, however, differences between baseline and subsequent time points (weeks 4, 8 and 12) among the 3 groups, and per group were statistically analysed using a one-way analysis of variance (ANOVA). Differences from baseline within each group were also tested for clinical significance in the NRS and BPI. Clinical significance was also analysed as a binary variable (significant vs no significant reduction). Fisher's Exact Test was used to test the differences in rates between groups, due to the small numbers. Clinical significance is defined as a reduction of $\geq$30% or $\geq$2 points on a 0-10 scale,[39] in the relevant score from baseline to weeks 4, 8 and 12. A one-point reduction from baseline to weeks 4, 8 and 12 in the BPI-sleep is considered clinically significant. Due to small sample size, a statistically significant response was not expected. No additional adjustments for multiple testing were made

for a pilot study. The statistician was blinded to the groups at the time of analysis. For acceptability of assessment tools, we assessed data completion and patterns of missing data in each questionnaire. Information on effectiveness and acceptability of the study methods not covered in the questionnaires was captured in the semi-structured telephone interviews.

Qualitative Analysis

Focus group discussions to ascertain the participants' trial experiences were conducted by an independent researcher, for groups 1, 2 and 3, post week 12 questionnaires completion. The discussions were audiotaped, transcribed and thematically analysed. Overall most participants did not report any negative trial experiences, however, data on the acceptability of recruitment, methods of randomisation and of questionnaires were unavailable. Consequently, semi-structured telephone interviews were conducted by the PI. The interview questions consisted of four main parts: acceptability of the recruitment and randomisation methods, acceptability of the questionnaires and overall experience of the study. The participants were asked to rate these questions from 1 to 5 on a 5-point scale from positive to negative or acceptable to unacceptable. Each interview lasted about 10-15 minutes. The data from the interviews were aggregated into most acceptable/unacceptable and positive/negative scales.

RESULTS

Recruitment and retention

Of the 135 women who attended the EXPPECT Centre during the recruitment phase, 59 (44%) were referred to our study. Of those referred, 30 (51%, 95% CI 38%-63%) were randomised into the study. Ten women were randomised into the group 1, 10 women to group 2 and 10 women to group 3 (Figure 1, CONSORT flowchart). There was no evidence to suggest any differences in baseline characteristics between the randomised groups (Table 1).

The retention rates were 80% (95% CI 74-96), 53 % (95% CI 36-70) and 87% (95% CI 63-90) in groups 1, 2 and 3 respectively. This showed a borderline significant difference between the groups (χ^2 test, p= 0.08), which was unexpected due to the small number of participants in the

trial. Of the 30 follow-up questionnaires sent to each group over the follow-up period (weeks 4, 8 and 12), group 1 returned 24, group 2, 16 and group 3, 26.

Acceptability to participants of the methods of recruitment/randomisation/ interventions/ assessment tools

Table 2 and Table 3 show the number of interventions attended and the number missed by the participants in groups 1 and 2 respectively. The TCM HC intervention appeared to be less acceptable. Of the planned 80 interventions, group 1 attended 72 (90%) compared to 45 (56%) who attended in group 2 (χ^2 test, $p<0.001$). Two participants from group 2 were lost to follow-up (attended and completed questionnaires at Week 0 only).

There were no missing data points for BPI, SF12v2, HADS and PCQ. The WPAIQ had the highest missing data points (39%), followed by the SAQ (31%) and the NRS (7%). There was a statistically significant difference (at 10%) in questionnaires returned between the 3 groups (χ^2 test, $p= 0.08$), group 3 returned the highest (87%, 95% CI 63-90), followed by groups 1 (80%, 95% CI 74-96) and 2 (53 %, 95% CI 36-70).

Of the 30 participants, 21 (70%) responded to the 10-15 minutes telephone interviews. The majority of the participants responded favourably to the methods of recruitment, randomization, intervention and assessment tools. Two participants in group 2 expressed disappointment at not being randomised to the BMEA treatment. One participant in group 1 found the questionnaire challenging due to dyslexia.

Estimates of clinical significance, effectiveness per group and between groups

This was a feasibility study and did not have an adequate sample size to produce reliable estimates of intervention effects. However, outcome measures between groups and per group were analysed to give an indication of which measures might be likely to show an intervention effect in a larger RCT. Table 4 gives a summary of the analyses of clinical significant in NRS-pain, BPI-pain subscale, interference and sleep. A higher proportion of the participants in group 1 who received the BMEA treatment had a clinically significant reduction in the NRS-pain, BPI-pain and interference subscales along with sleep at weeks 4 and 8 when compared to the groups 2 and 3. Fishers' Exact test did not show a statistically significance difference.

Estimates of effectiveness per group suggested a trend towards improvement in group 1 at week 4 in almost all scores. Group 2 showed some signs of improvement in some scores such as BPI severity and interference and SF12v2-MCS. There was little change in group 3, except in the HADS-total mean change by week 8 and 12, where the participants showed a statistically significant increase (mean difference=4.0, 95% CI 0.2 to 7.8, p=0.04; and mean difference=3.4, 95% CI 0.2 to 6.7, p=0.04), i.e. more depressed and anxious, while group 1 achieved a significant (mean difference=-2.5, 95% CI -7.4 to -0.4, p=0.04) change from baseline to week 4 in the opposite direction i.e. less anxious and depressed.

Adverse Events

No adverse events were observed or reported that were directly related to the interventions. Three participants from group 2 were admitted to hospital for conditions which were not related to the intervention.

Focus Groups: Key Findings

A full description of the key findings will be reported in a separate paper however, a summary is offered here. Both groups 1 and 2 perceived a reduction in pain, enhancement in sleep, energy level and sense of wellbeing with group 1 (n=6) reporting higher therapeutic benefits than group 2 (n=2). Participants in group 3 (n=3) expressed frustrations at, and dissatisfaction with the ineffectiveness and significant unwanted side effects of their medications. These findings may have been biased due to self-selection and low attendance.

DISCUSSION

Overall, our pilot study supports the feasibility of a future large-scale phase 3 RCT to determine the effectiveness of the meridian BMEA treatment in the management of CPP in women, on the basis of recruitment, retention, questionnaire completion and acceptability of the study to participants. Our ability to recruit and randomise 30 women over 8 months (51% of those referred to the study) and at 12 weeks follow-up, retain 23 participants (77%) is encouraging. The recruitment rate fulfilled our expectation of 50% or over and is comparable to other acupuncture pilot studies[40,41,42].The caveat is that group 2 has not demonstrated feasibility.

Analysis of the semi-structured telephone interview data regarding the methods of recruitment, indicated randomisation and interventions were generally acceptable to the participants. The attendance rates between group 1 and group 2 differed. The attendance rates for both the TCM HC intervention and focus group discussions were specifically problematic in group 2. The explanations for the 5 poor attenders for the TCM HC intervention were a mix of hospitalisation and no reasons given. It is possible, (and this was our impression) that these participants would have preferred to be in group 1. These results have important implication on our next RCT design.

Interpretation of pain and other outcomes in an inadequately powered study has to be cautious. As expected with any clinical pain study, there were some changes in all groups. It is, however, reassuring to note that most of the chosen pain tools seemed appropriate and those randomised into the BMEA treatment might perform better than those randomised into TCM HC and NHS SC. With regards to missing data in the returned questionnaires, the SAQ and WPAIQ had the highest missing data points. In the WPAIQ, missing data were primarily due to the higher unemployment rate of group 2.

Importantly, consistent with most acupuncture studies, there were no adverse events to acupuncture treatment reported or observed in our study[43].

Reflection on any aspects of the study which may have had a negative impact on outcomes of a larger study is important. In particular, in the light of both low attendance and low rate of questionnaire return in group 2, we will modify the design by eliminating the TCM HC arm. In considering the questionnaires, we might exclude the SAQ and WPAIQ which had high missing data points but will include a questionnaire on the expectation of acupuncture treatment.

The patients were all recruited from a multidisciplinary specialist clinic and future recruitment from similar pools of patients would be important.

For our next phase 3 RCT, the design will need to change significantly, and we are considering BMEA versus sham BMEA. Our pilot study suggests that 5/9 patients in group 1 have a fall of 30% in worst pain score from the BPI (responders), whereas only 2/9 patients in group 3 were responders. However, due to the small sample size, these figures should be treated with caution.

Thus, erring on the side of caution, we would assume that fewer participants might respond in the BMEA group than the 56% seen in the pilot, and more might respond in the new sham BMEA group. To this end, if we assume 40% in BMEA group and 30% in sham BMEA group, we would need 152 completing participants per group to adequately power our next RCT.

CONCLUSION

In conclusion, significant modifications to our pilot study design are necessary before we can move forward to a full large-scale phase 3 RCT to evaluate the effectiveness of the meridian BMEA treatment for CPP in women.

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Table 1. Baseline Characteristics of the Three Groups

Deprivation Score: http://www.nhslothian.scot.nhs.uk/publichealth/2005/ar2003/dataset/depcats.html
Last accessed on 6th November 2017

Age	BMEA treatment Intervention, group 1	TCM HC intervention, group 2	NHS SC group 3
Mean **Range**	34.7 (SD± 9.0) 23-50	31.4 (SD± 9.9) 21-51	33.5 (SD± 8.8) 23-44
Ethnicity			
Caucasian **Mixed (Mexican & Scottish)**	9 (90%) 1 (10%)	10 (100%)	10 (100%)
Deprivation Score			
Affluent (1-2) **Intermediate (3-4)** **Deprived (5)** **Very deprived (6-7)**	1(10%) 5 (50%) 2 (20%) 2 (20)	1 (10%) 6 (60%) 1 (10%) 2 (20%)	2 (20 %) 5 (50%) 2 (20%) 1 (10%)
Diagnosis			
Endometriosis **Unknown aetiology**	8 (80%) 2 (20%)	6 (60%) 4 (40%)	7 (70%) 3 (30%)
Education			
Tertiary **Secondary**	7 (70%) 3 (30%)	8 (80%) 2 (20%)	10 (100% 0 (0%)
Employment Status			
Unemployed	3 (30%)	6 (60%)	1 (10%)
Employed	7 (70%)	4 (40%)	9 (90%)

Table 2. Number of BMEA Intervention Attended and Missed: Group 1

	Number of Participant	Number of Intervention attended	Number of Intervention missed	Reasons for Missed Intervention
	6	8/8	0	Traffic, Unwell, Holiday
	1	7/8	1	
	2	6/8	4	
	1	5/8	3	
Total	**10**	**72 (90%)**	**8 (10%)**	

Table 3. Number of TCM HC Intervention Attended and Missed: Group 2

	Number of Participant	Number of Intervention attended	Number of Intervention missed	Reasons for Missed Intervention
	2	8/8	0	Cold, work, hospitalised for pain and asthma, no reason
	1	7/8	1	
	1	6/8	2	
	1	5/8	3	
	1	4/8	4	
	1	3/8	5	
	1	2/8	6	
	2	1/8	14	
Total	**10**	**45 (56%)**	**35 (44%)**	

Table 4. Analyses of NRS and BPI Scores

Participants with clinically significant change (reduction of ≥30% or ≥2 points on a 0-10 scale)
Sleep (clinically significant is a change of one point or more)

		ARMS/INTERVENTIONS		
NRS		**BMEA treatment group 1**	**TCM HC group 2**	**NHS SC group 3**
Baseline	N Mean (SD)	10 7.2 (2.1)	10 6.1 (2.0)	10 7.9 (1.5)
Week 4 ## N (%)	N Mean change (SD)	9 -2.78 (2.6) 5 (56%)	6 -1.5 (2.9) 2 (33%)	8 -1.1(1.2) 3 (38%)
Week 8 ## N (%)	N Mean change (SD)	7 -1.6 (1.0) 4 (57%)	4 -0.8 (1.2) 1 (25%)	8 -0.4 (1.5) 1 (25%)
Week 12 ## N (%)	N Mean change (SD)	7 -0.9 (2.0) 1 (14%)	6 -0.2 (2.1) 2 (33%)	9 -1.1 (1.8) 2 (22%)
BPI-pain severity				
Baseline	N Mean (SD)	10 5.6 (1.6)	10 5.0 (1.6)	10 6.2 (1.0)
Week 4 ## N (%)	N Mean change (SD)	9 -1.3.(2.8) 5 (56%)	6 -1.0 (2.6) 2 (33%)	9 -0.17(1.6) 2 (22%)
Week 8 ## N (%)	N Mean change (SD)	7 -0.9 (1.6) 3 (43%)	4 0.0 (1.2) 0 (0%)	8 -0.3 (1.4) 1 (13%)
Week 12 ## N (%)	N Mean change (SD)	7 -0.2 (2.7) 2 (25%)	6 -0.6 (1.9) 3 (50%)	9 -1.0 (1.8) 2 (22%)
BPI-Interference				
Baseline	N Mean (SD)	10 5.5(3.0)	10 5.6(2.1)	10 5.9(1.4)
Week 4 ## N (%)	N Mean change (SD)	8 -1.3(3.9) 5 (63%)	6 -1.9(3.1) 2 (33%)	9 -0.3(1.3) 2(33%)
Week 8 ## N (%)	N Mean change (SD)	7 -0.7(1.6) 3(43%)	4 -0.7(1.1) 1(25%)	8 -0.3 (1.9) 2(25%)
Week 12 ## N (%)	N Mean change (SD)	8 -0.1(2.6) 1 (13%)	6 -0.5 (2.2) 2(33%)	9 0.5(2.0) 1(11%)
BPI-sleep				
Baseline	N Mean (SD)	10 6.4(3.1)	10 6.0(3.3)	10 6.3(2.6)
Week 4 ## N (%)	N Mean change (SD)	9 -2.2 (4.9) 6 (67%)	6 -1.0(4.3) 2 (33%)	9 -1.1(2.8) 6(67%)
Week 8 ## N (%)	N Mean change (SD)	7 -0.4(3.2) 4 (57%)	4 2.5(3.7) 1(25%)	8 -0.8(2.1) 2 (25%)
Week 12 ## N (%)	N Mean change (SD)	8 -1.0(3.0) 3(38%)	6 0.5(2.4) 2(33%)	9 0.1(2.7) 3(33%)