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ORIGINAL ARTICLE

Acupressure and vitamin B6 to relieve nausea and vomiting in pregnancy: a randomized study

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Abstract
Objective To compare the effectiveness of acupressure and vitamin B6 in the outpatient treatment of nausea and vomiting in early pregnancy.
Study design Pregnant volunteers with symptoms of mild to moderate nausea and vomiting between 6 and 12 weeks' gestation participated in a 7-day clinical trial. Participants were randomly assigned to receive a device for acupressure therapy and placebo drug or an otherwise identical but non-stimulating placebo device and vitamin B6. The primary outcome measure was self-recorded symptoms according to Rhodes index. Secondary outcome measures were weight gain and medication use.
Results The mean change in Rhodes index was not significantly different between the two groups. There were no statistically significant differences in weight gain and medication use between the two groups.
Conclusion Acupressure therapy is not more effective than vitamin B6 in reducing nausea and vomiting in symptomatic women in the first trimester of pregnancy.

Keywords Acupressure · P6 or Neiguan point · Vitamin B6 · Wristband · Rhodes index

Introduction

Nausea and vomiting of early pregnancy (NVP) is a common complaint affecting approximately 50–80% of pregnant women [9]. Although these symptoms are generally self-limited, and rarely severe enough to cause hyperemesis, they can cause considerable distress and temporary disability that can impact both the pregnant women and their families. Various treatments have been empirically recommended for this disorder, reflecting many theories as its cause. Nevertheless, a pregnant woman is often reluctant to take antiemetic drugs because of a fear of possible teratogenic effects. Also, medications that are effective in relieving nausea and vomiting cause symptoms of sleepiness [8], which can interfere with a woman's ability to work as well as other activities of daily living.

Stimulation of the median nerve at the P6 or Neiguan acupuncture point by applying pressure to specific area of the wrist (acupressure) has been studied as one of many alternative modalities to alleviate symptoms of nausea and vomiting. Various trials have been reported about the effectiveness of acupressure at P6 point compared to the placebo group in reducing nausea and vomiting in pregnancy [1, 3].

Vitamin B6 is commonly prescribed as first-line therapy in the outpatient management of nausea and vomiting in pregnancy and there is evidence from a few randomised control trials that revealed the effectiveness of vitamin B6 (pyridoxine) in reducing these symptoms [13, 14].

To date, there have been no randomised studies that compare the effectiveness of these two non-pharmacological and pharmacological therapies. Thus, the aim of our study is to compare the effectiveness between acupressure and vitamin B6 in reducing nausea and vomiting in pregnancy.

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Materials and methods

The study was approved by the Research Ethics Committee of the Faculty of Medicine, Chulalongkorn University. Between 1 September 2005 and 30 June 2006, 66 patients consented to participate in a single-blind randomized study for seven consecutive days. The subjects were recruited from the antenatal clinic at the Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. The inclusion criteria are as follows: (1) singleton pregnancy, (2) suffered from mild to moderate nausea and/or vomiting, (3) gestational age between 6 and 12 weeks, with date confirmed by ultrasound, and (4) age 20–35 years at the time of entry into the study. We excluded pregnant women who: (1) had other medical disorders such as hepatitis or gastrointestinal diseases that might manifest with nausea or vomiting, (2) had taken other medications in the past few weeks that might aggravate or alleviate nausea or vomiting, (3) were mentally retarded or had language barriers, (4) were unable to take the medication or apply the instrument as prescribed, or (5) were unable to return for the follow up visit in 1 week.

Nerve stimulation therapy was accomplished with the acupressure wristbands (Sea-Bands), which had a button to provide pressure on Neiguan point. Neiguan or P6 point is a Chinese acupuncture point located three fingerwidths up from the wrist crease, between the tendon of the flexor carpi radialis and palmaris longus muscles on the medial aspect of one forearm. The dummy point was located at the same level on the forearm as P6 point. However, the button was placed over the radius of the forearm. This location was chosen because it appears similar to the treatment (P6) point but is not near the treatment or any other acupressure point. One trial reported that there were no statistically significant differences in reduction of nausea and vomiting symptoms between the groups of unilateral and bilateral pressure on Neiguan point [3].

Participants were given a demonstration on the technique to apply the wristbands as well as oral and written instructions. Each of them was asked to wear the band on the wrist as continuously as possible from the beginning on the day of participation until the evening of study day five.

The symptoms were evaluated by Rhodes index of Nausea and Vomiting form 2 [12]. This form is an eight-item, 5.0 Likert-type, pencil-and-paper instrument that measures the prevalence and amount of distress caused by nausea with or without vomiting or retching over a 12-h period. Three of the items measure nausea (scores ranged from 3 to 15) and the remaining five items measure vomiting and retching (scores ranged from 5 to 25). The form was translated into Thai and tested for its reliability and validity by experts.

Volunteers who met inclusion criteria received a written explanation of the study and signed a written informed consent. They underwent a general physical examination and routine obstetric evaluation. Randomization was done into two groups (acupressure and vitamin B6 groups) by an independent remote researcher had no prior knowledge of the patients by using a block of four technique. A ticket that indicated the group was drawn in a sealed opaque envelope before the study was begun, and the group assignment was performed by picking the envelope sequentially.

All participants were given a package containing 15 copies of Rhodes index of Nausea and vomiting, and they were also instructed to evaluate their symptoms every 12 h (on the day of participation and twice daily for seven consecutive days). They were also asked to record the use of rescue drug (dimenhydrinate 50 mg) and the hours of applying the device. They were instructed to use oral dimenhydrinate 50 mg every 6 h when they had nausea and vomiting. The patients in the acupressure group were advised to apply Sea-Bands on P6 point and identical looking tablets were used as placebo in the same regimen as vitamin B6. Those in vitamin B6 group were advised to apply Sea-Bands on the dummy point and 50 mg tablets of vitamin B6 were prescribed every 12 h for 5 days. Patients in both groups were informed to divide their meals into frequent small ones rich in carbohydrates and low fat. They were also advised not to take any other medications except the rescue drug prescribed by the researchers. Compliance was assessed by pill count, and at the end of the trial we asked the patients to rate their satisfaction of the provided treatments.

The primary study outcome was assessment of nausea and vomiting by Rhodes index score. Secondary outcome variables were weight gain or loss over the study period, and medication use. The first hypothesis tested whether acupressure and vitamin B6 were different in terms of reducing nausea and vomiting symptoms, and this would be indicated by the statistically significant difference of the mean score changed between the groups from baseline of Rhodes index of nausea and vomiting scale.

The sample size calculation was based on data from a pilot study ($n = 10$). The mean reduction of Rhodes Index scores were 3.0 and 2.0 in acupressure group and vitamin B6 group, respectively. To reject the null hypothesis of a reduction in symptoms with a power of 80% and a significant level of 5%, a minimum sample

size of 30 women per group was required. With adjustment for a withdrawal rate of 10%, a minimum of 33 women per group were required. Student *t*-test was used to compare differences between groups. The means of pre-treatment nausea and vomiting scores and continuous variables were analyzed. A significance level of $p < 0.05$ was used for all tests.

Results

A total of 66 patients were enrolled in the study. All subjects were included in the intention to treat (ITT) analysis. Six patients (9.1%) did not complete the study (three in acupressure group and three in vitamin B6 group). One patient from the withdrawal group was lost to follow up, one patient complained about the irritation while wearing the device and quit the trial, two patients lost the acupressure devices, and two patients did not complete 15 copies of the Rhodes Index form. Finally, there were 30 patients in acupressure group and 30 patients in vitamin B6 group (Fig. 1). Baseline characteristics of the patients did not demonstrate any statistically significant differences between the two groups (Table 1). There were no significant differences in initial Rhodes index score.

Since six patients did not complete the study, an intention to treat analysis, counting all withdrawals as treatment failures, was performed. The measurement of the primary outcome throughout this trial, we found statistically significant in the improvement of nausea, retching, and vomiting symptoms in both acupressure ($p < 0.001$) and vitamin B6 group ($p < 0.001$) (Fig. 2). There were no statistically significant differences in the reduction of Rhodes index scores between the baseline score and the end of the treatment score (in the evening of the fifth day) between both groups ($p > 0.05$). After the discontinuation of the treatment (in the evening of the seventh day), there were also no statistically significant differences in the rising score during this 24 h period in both acupressure group ($p > 0.05$) and vitamin B6 group ($p > 0.05$).

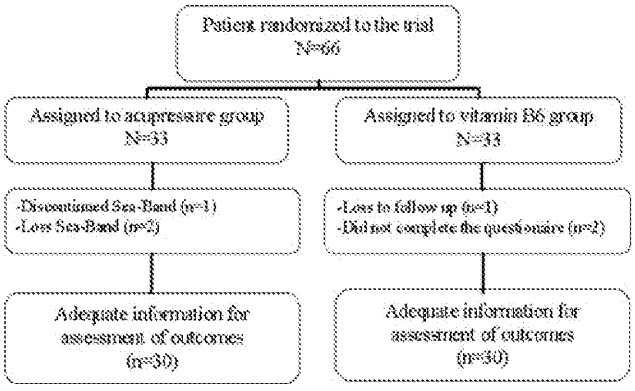

Fig. 1 Profile of patient recruitment and follow-up following randomization to either acupressure or vitmain B6 group

Table 1 Baseline characteristics of the patients

Characteristics	Acupressure ($n = 33$)	Vitamin B6 ($n = 33$)
Age (years)	28.2 ± 5.1	28.1 ± 5.6
Gestational age (weeks)	8.1 ± 1.7	8.9 ± 3.5
Pretreatment weight (kg)	52.4 ± 7.0	49.9 ± 4.7
GA of onset (weeks)	6.2 ± 1.0	6.8 ± 1.5
Initial Rhode index score	14.3 ± 3.3	15.4 ± 3.0
Parity		
Nulliparous (*n*)	19 (57.6%)	14 (42.4%)
Multiparous (*n*)	14 (42.4%)	19 (57.6%)
Education		
None	1 (3.0%)	2 (6.1%)
Primary school	3 (9.1%)	2 (6.1%)
Secondary school	20 (60.6%)	21 (63.6%)
University	9 (27.3%)	8 (24.2%)
Occupation		
Employee	13 (39.4%)	14 (42.4%)
Merchant	9 (27.3%)	8 (24.2%)
Housewife	7 (21.2%)	6 (18.2%)
Civil servant	4 (12.1%)	5 (15.2%)

Data are presented as %, mean ± SD or *N*

Evaluation of secondary outcome variables, the mean change of maternal weight which recorded for three times (pre-pregnancy weight, weight on the participation day, weight at the end of the trial) in both groups is shown in Table 2, but no differences of weight gain were observed between these groups comparing between weight on the participation day and weight at the end of the trial ($p > 0.05$). The use of medication (rescue drug) and the satisfactory rating of both interventions were not different also (0.6 ± 1.6 tablets vs. 2.8 ± 4.7 tablets; $p > 0.05$ and 3.0 ± 1.0 vs. 2.6 ± 0.7; $p > 0.05$ in acupressure group and vitamin B6 group, respectively).

In general, the majority of the patients did not have any trouble in wearing Sea-bands and felt the pressure on their wrists despite variation on their wrist sizes. All of the patients were able to wear the devices more than 18 h per day and take the vitamin B6 completely. One patient, however, complained about the irritation and finally quit the trial.

Discussion

To our knowledge, this is the first randomised, prospective trial to compare the effectiveness of acupressure and vitamin B6 in the outpatient treatment of

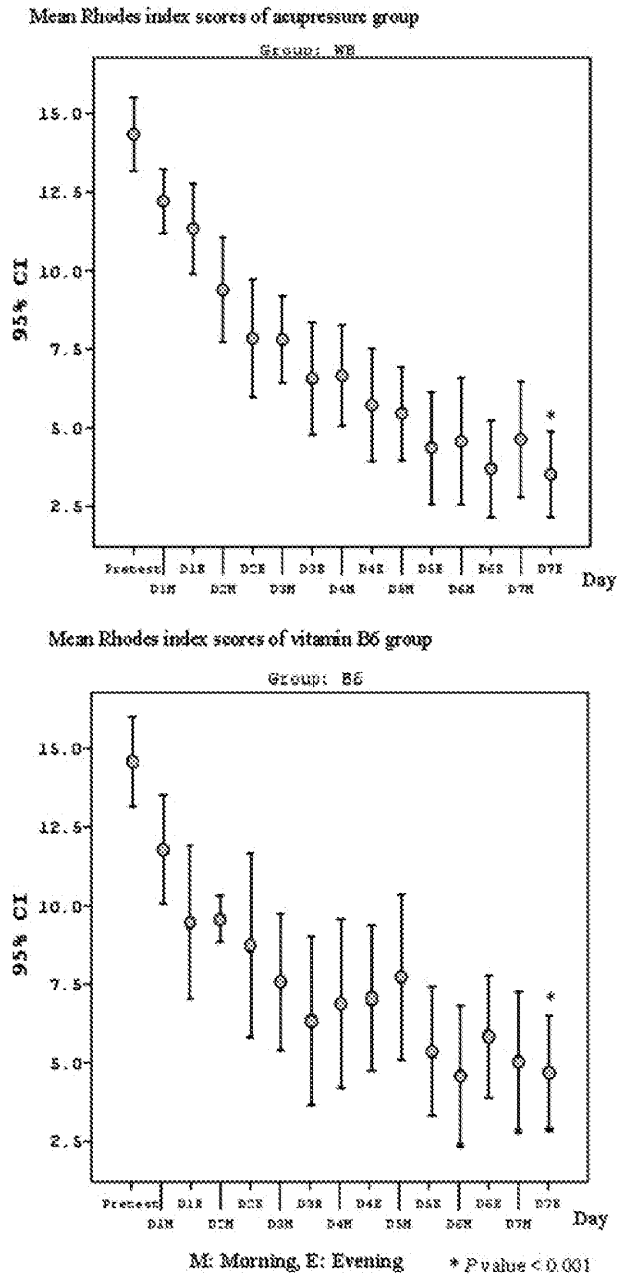

Fig. 2 Rhodes index of nausea and vomiting scores throughout the 7 days of the trial in acupressure and vitamin B6 groups

NVP. Our study revealed no statistically significant differences in the reduction of nausea and vomiting between these two groups. All patients had their symptoms relieved and gained weight during the trial.

Nausea and vomiting are common complaints during the first trimester. Most patients have mild to moderate symptoms; less than 1% of them turns out a severe form of hyperemesis gravidarum [11].The actual etiology is not well understood. Elevated levels of pregnancy related chemicals, such as chorionic gonadotropin has been implicated in this occurrence [6]. A progesterone effect has been implicated by some, especially in the relation to relaxation of the esophageal-gastric sphincter. Social and psychological factors can also contribute to the severity of the nausea [4].

In our study, Sea-Bands (Sea-Band UK Ltd., Leicester, UK) were chosen as acupressure devices because they produced more constant pressure than manual acupressure and they were also easy to use. There were a lot of studies that provided the information of the management of this condition, both pharmacological and non-pharmacological therapies. Vitamin B6 has usually been selected as the first-line drug for outpatients who experienced NVP and its safety has been proven when used in appropriate dose [10]. Acupressure is a non-invasive procedure which was proposed for its effectiveness in reduction of NVP and it may be also considered an alternative treatment for some patients who are reluctant to take medication of any reasons. Not only that, as there are no theoretical concerns about the safety of acupressure in pregnancy, a recent study concluded that acupressure by Sea-Bands was well tolerated and not associated with an increase in perinatal morbidity or death [7]. In the current studies, no subject informed about any lingering effect of acupressure; there is a study of acupuncture on the prevention of nausea and vomiting from chemotherapy which revealed its antiemetic effect that lasted for about eight hours [5].

The major part of the study is the interpretation of the subjective symptoms such as nausea and vomiting to objective measurement. In our study, we translated

Table 2 Change in mean of maternal weight

	Acupressure group	Vitamin B6 group	*p* value
Pre-pregnancy weight (kg)	52.4 ± 7.0	49.9 ± 4.7	NS
Weight on the participation day (kg)	53.5 ± 7.6	50.7 ± 4.5	NS
Weight at the end of the trial (kg)	55.1 ± 7.4	50.7 ± 4.6	NS
Weight on the participation day—pre-pregnancy weight (kg)	1.2 ± 2.0	1.0 ± 2.2	NS
Weight at the end of the trial—weight on the participation day (kg)	1.5 ± 1.2	0.8 ± 0.6	NS

Data are present as mean ± SD

Rhodes index form 2 into Thai language, which was tested for reliability and validity by the experts. A variety of visual analogue scores, self-reporting tools, and patient interview methods have been used in previous trials. In October 1998, an expert group of clinicians determined that a standard, validated tool should be used to allow comparisons between studies, and Rhodes Index was an optimal tool for this purpose [2].

Most of these symptoms normally regress when gestational age reached 12 weeks and it might be one of the confounding factors. In our study, the mean gestational age at entry (acupressure group = 8.1 ± 1.7; vitamin B6 group = 8.9 ± 3.5 days) was still relatively early. After controlling for improvement due to time limit, we found a significant reduction in the symptoms of nausea and vomiting in both the acupressure group and vitamin B6 group, but there were no statistically significant differences when compared to each other. The improvement of nausea and vomiting in present study may be spontaneous due to a placebo effect, the additional medication used, or either of the treatments.

The improvement of nausea and vomiting observed in this study may be a result of the combination of acupressure with the rescue drug. It is possible that the rescue drug provided a large reduction of the symptoms but the exclusion of the rescue drug could not be permitted due to ethical reasons.

Furthermore, we found that all the patients gained weight after the treatment in both groups. The explanation of this result may be the enrollment of the patients who had only mild to moderate symptoms and were able to be managed as outpatients.

In further clinical research, the objective data such as laboratory and pathophysiologic tests may be accomplished to support the efficacy of both treatments. Because of time limitation, the perinatal outcomes were not included in the results; however, for future studies, these aspects should be evaluated to ensure the safety of acupressure in pregnancy.

In conclusion, acupressure therapy is not more effective than vitamin B6 in reducing nausea and vomiting in mild to moderate symptomatic women in the first trimester of pregnancy.

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