

**BRIEFING PAPER No 10**

# **OBSTETRICS (1)**

## **NAUSEA AND VOMITING IN PREGNANCY**

**The evidence for the effectiveness of  
ACUPUNCTURE**



Edited and produced by the **Acupuncture Research Resource Centre**  
Published by the **British Acupuncture Council**  
August 2004

The Evidence Series of Briefing Papers aims to provide a review of the key papers in the literature which provide evidence of the effectiveness of acupuncture in the treatment of specific conditions. The sources of evidence will be clearly identified ranging from clinical trials, outcome studies and case studies. In particular this series of briefing papers will seek to present, discuss and critically evaluate the evidence.

## **NAUSEA AND VOMITING IN PREGNANCY: THE EVIDENCE FOR THE EFFECTIVENESS OF ACUPUNCTURE**

### **Summary**

This paper presents a summary of the evidence for the effectiveness of acupuncture in the treatment of pregnancy-related nausea and vomiting. The available sources provide some evidence that acupuncture is an effective treatment for these conditions. However, there are only a few clinical trials, with a wide variability in the type of acupuncture and methodological design. There are more studies on the use of acupressure than acupuncture (12:4) and most show a positive outcome with the point Pericardium 6.

### **Introduction**

Nausea and vomiting during pregnancy affects up to 80% of all pregnant women, and has a significant impact on the quality of life of those who experience it (Hollyer 2002). It is most common between 6 and 14 weeks gestation. For many women, it is necessary to have time off work, and there is a marked effect on family life and relationships.

The severity can range from mild nausea to frequent or even severe vomiting (*Hyperemesis Gravidarum*) leading to hospitalisation for intravenous administration of fluids to prevent further dehydration. Pharmacological treatments are available, but concerns over the perceived teratogenicity of these has made them unpopular following the Thalidomide disaster of the 1960s. For this reason, women generally prefer non-pharmacological methods to alleviate nausea and vomiting of pregnancy, and may try several modalities including herbal remedies such as ginger, and acupressure with Sea Bands. They will often seek help from professionals and be willing to try anything "as long as it is safe for the baby".

Professor Dundee and co-workers were among the first to research the effects of acupuncture and acupressure on nausea and vomiting, particularly using the point Pericardium 6 (P6). Dundee observed acupressure being used in an obstetric outpatient clinic in China as a preventative for morning sickness and this led him to

carry out several studies using P6 with acupuncture stimulation, electro-acupuncture, transcutaneous electric nerve stimulation (TENS) and acupressure. The studies were for nausea and vomiting from various causes including postoperative, morning sickness, cancer chemotherapy and travel sickness. His trial on morning sickness used only acupressure on 350 women attending a Belfast antenatal clinic, (Dundee et al 1988) but his prolific output of papers on the antiemetic effects of P6 prompted many of the further studies. There are many more studies using acupressure for morning sickness, and these are presented in tables and included in the reference list. This briefing paper is primarily concerned with the use of acupuncture, even though there are only a few trials suitable for review.

## Literature search

A search was made using the ARRC database, as well as further searches on AMED, MEDLINE, CINAHL and COCHRANE databases, using the key words "pregnancy (+obstetric etc)", "nausea", "vomiting", "sickness", "*hyperemesis*", plus acupuncture. Articles in foreign languages, letters, commentaries and reports related to practice rather than research were excluded. This left 23 articles which included 4 randomised controlled trials evaluating acupuncture, 12 studies on acupressure, 5 review articles, 1 safety outcome article and 1 outcome study.

## Controlled trials with acupuncture

A summary of the acupuncture trials identified in the literature search is given in Table 1.

### Carlsson et al (2000)

The first trial to look specifically at the effect of acupuncture on pregnancy sickness was conducted in Sweden. A placebo-controlled, randomized, single-blind, crossover study was carried out on 33 women with *Hyperemesis Gravidarum* or severe vomiting of pregnancy. The study was conducted over a two-year period, and patients were offered participation in the study following admission to hospital for hyperemesis, having failed to respond to conventional out-patient treatment. Following random allocation to either group "A" or group "B", the study was undertaken over 8 consecutive days for each patient. On days 1,2,5 and 6, the acupuncture treatments were given. No acupuncture was given on days 3 and 4, regarded as a "wash-out-period". Group A received the active acupuncture first, whereas Group B started with the placebo-acupuncture. After the "wash-out" period, treatments for the groups were switched. During the study, the women received intravenous nutrition with 5% glucose.

The acupuncture treatments were given for thirty minutes, three times daily on treatment days. In the active acupuncture group, the point P6 was needled and de-qi obtained, with further stimulation every 10 minutes. The placebo, or superficial acupuncture group had a needle inserted 10 cm from the wrist on the thumb side of both forearms, just 1-2 mm depth, and no deqi sensation was obtained, but the needles were "twisted a little" every 10 minutes.

The women estimated their degree of nausea daily, 1 hour after the last acupuncture treatment of the day, or at the same time on the days that acupuncture was not performed using a visual analogue scale (VAS). Instances of vomiting and intake of meals were recorded by the patient, and the ward staff documented the amount of intravenous fluid every day.

### **Results**

Crossover analyses showed that there was a faster reduction of nausea, though the difference was not statistically significant, and more women who stopped vomiting (this was significant) after active acupuncture than after placebo acupuncture. The increase in food intake from day 0 to day 2 was significant in group A. The amount of intravenous fluids fell swiftly in both groups from admission to discharge, and no side effects were seen during or after the study.

### **Comment**

This is a difficult patient group to treat, in that their condition was severe enough to warrant hospital admission and intravenous therapy. Although acupuncture was given more frequently (three times per day) than would tend to be the case in general practice, there were only two days of active treatment, and the only point used was P6. During the study period, 72 women were admitted with hyperemesis, 32 were not randomised for various reasons, which left 40 patients who underwent randomisation, and out of these, 7 did not complete the study. It would be a difficult study to replicate in this country mainly due to the practical constraints to providing acupuncture three times per day to hospital in-patients. The acupuncture was performed by midwives who did not belong to the usual ward staff, and were only present to perform the treatments. Crossover designs are usually inappropriate for acupuncture trials as the effects of the treatment can be cumulative and long-lasting. This may not be so with this acute condition, but the authors do not make the case for their 2-day wash-out.

### **Knight et al (2001)**

The second trial to be published was conducted in the maternity unit at Exeter hospital and compared acupuncture with sham (placebo) acupuncture for treatment of nausea and vomiting of pregnancy. It was a subject- and observer-blinded trial in which 55 women who were between 6 and 10 weeks gestation, were randomly assigned to receive genuine traditional-style acupuncture, or sham treatment with a cocktail stick on three or four occasions over 3 weeks. The acupuncture points used varied according to the traditional Chinese diagnosis, and included St36, Ren12, P6, Sp4 and St44.

Sham treatment consisted of tapping a blunt cocktail stick, supported by a guide tube, over a bony prominence in the region of each acupuncture point. After removing the cocktail stick, the guide tube was left in situ but concealed by a dressing. Needles or sham were left in position for about 15 minutes. Both genuine and sham acupuncture were given twice in the first week and once weekly for 2 weeks. The primary outcome measure was nausea score, as determined by subject report on a visual analogue scale. Anxiety and depression were also assessed using the Hospital Anxiety and Depression scale. Although the sample size of 55 had been calculated to have a 95% power to discriminate between acupuncture and control, five women withdrew for medical

reasons or dropped out before the second treatment. Six other women did not have a fourth treatment session.

### **Results**

Nausea scores decreased from a median of 85.5 to 47.5 in the acupuncture group and from 87.0 to 48.0 in the sham treatment group. There was strong evidence of a time effect ( $p < .001$ ) but no evidence of a group effect. Similarly, there was evidence of time effects in scores for anxiety and depression but no group differences. The conclusion was that acupuncture was as effective as a sham procedure in treating nausea of pregnancy.

### **Comment**

This was the only one of the four randomised controlled trials to show no advantage at all for the true acupuncture group over the sham. There are possible reasons – the sham not being inactive, sub-optimal spacing of treatment sessions (due to limitations on availability of the acupuncturist and social or work commitments of the participants) and too few participants – but mostly these apply to the other trials as well. Indeed, this trial had some apparent advantages, including individualised treatment and a non-inserting sham that also avoided the actual points. In retrospect, the inclusion of a non-treatment control arm may have shed more light on the results, as was the case with the next trial reviewed.

## **Smith et al (2002)**

The largest study in terms of sample size is a trial conducted by a research team from Adelaide University, Australia, which looked at acupuncture to treat nausea and vomiting in early pregnancy. The study randomly assigned 593 women, who were less than 14 weeks into their pregnancy, with symptoms of nausea or vomiting, to four groups. The first group received individualised acupuncture, the second group acupuncture to point "Neiguan or P6", the third, sham acupuncture, and the control group- no acupuncture. Diagnosis and treatment were performed according to a standardized protocol guiding the interaction with women, including diagnosis, acupuncture and sham acupuncture and needling techniques. Participation in the trial was for 4 weeks. Women allocated to the 2 acupuncture groups and sham acupuncture group were advised to attend for treatment twice weekly for the first week and then to attend weekly. Women allocated to the traditional acupuncture group were administered a treatment based on their traditional Chinese medicine diagnosis, using a variety of points. Women allocated to the P6 study group received this single point only. The sham acupuncture group received acupuncture needles inserted into an area close to, but not on, acupuncture points. A no acupuncture group was included to control for the effect of spontaneous remission of symptoms. The primary outcomes were nausea, dry retching, vomiting and health status. Comparisons were made between groups over 4 consecutive weeks.

### **Results**

Data was received from 534 (90%) of women at the end of the first week of the trial, and from 443 (75%) at the end of the fourth week of the trial.

Compared with no treatment, women receiving individualised acupuncture reported significantly less nausea throughout the trial (i.e. weeks 1-4) and less dry retching

from week two onwards. 9% of them were free of nausea by the end of the first week compared to 4.3% of the untreated women, and they reported the bouts of nausea to be less frequent and of shorter duration. In respect of both nausea and retching the individualised group improved faster than either the P6 or sham acupuncture groups. P6 was ahead of sham for nausea but similar for retching.

However, by the end of the trial there was little difference in nausea scores between the two 'real' acupuncture groups (3.4 and 4.0 points) and the sham group (3.7 points). The no treatment group was worst (5.0), but nevertheless it had improved substantially over the trial period (from 8.4 at baseline). Dry retching showed a similar pattern.

The women's health status measurement showed the greatest effect from traditional acupuncture with improvements on five SF36 domains; this happened on only two domains for P6 acupuncture and one for no acupuncture. Sham acupuncture improved two domains, women's emotional well-being and social function.

The conclusion was that acupuncture is an effective treatment for women who experience nausea and dry retching in early pregnancy, and that the individualised approach is superior to single point P6 application. There was a greater improvement in women's health status in the acupuncture groups, especially with traditional acupuncture.

### **Comment**

This is the only study to compare traditional acupuncture with P6, and it is interesting to see the faster response with the traditional group. Note that the particular benefit of individualised acupuncture seemed to be to give early relief to more women, whereas by the fourth week it was no longer significantly ahead of standard P6 or even sham acupuncture. It can also be seen that even with no intervention at all there was a substantial improvement in symptoms over the four-week period, a change that was much larger than any of the between group differences. This fits with the pattern seen in Knight et al's results, but Smith had much larger groups, greatly increasing the chances of finding some significant effects.

It is a comprehensive report that used the Rhodes Index of Nausea and Vomiting Form, a 5-point Likert scale, as well as the SF36 to measure women's health status. It is the only published paper that measured the effect of acupuncture for nausea and vomiting on women's health status during early pregnancy. There is plenty of detail regarding statistical analysis and the research methodology was generally sound. The comprehensive discussion includes a comparison with other trials, and comments on the optimum treatment frequency for this condition. There is acknowledgement of the lack of external observation and possibility of practitioner bias, though the subjects were asked to comment on the credibility of the treatment, (i.e. whether they felt they were having true or sham points).

### **Follow-up safety study**

Smith et al (2002) looked at pregnancy outcome in the women who participated in the above study. The objective was to assess the risk of adverse effects of acupuncture administered during pregnancy. Outcome measures included data on perinatal outcome, congenital abnormalities, pregnancy complications and other infant outcomes. Their findings suggested that no serious adverse effects arise from acupuncture administered during early pregnancy.

## **Habek et al (2004)**

The most recent study is a prospective, randomised, placebo-controlled trial from Croatia, which aimed to evaluate the antiemetic effect of acupuncture and acupressure of point Neiguan (P6) in women with hyperemesis gravidarum (HG). Thirty-six women (all primigravidae) were divided into four groups. In group one, 10 women had bilateral manual acupuncture to P6 with deqi effect, over 7 days for 30 minutes per day. In group two, 11 women had bilateral acupressure to P6, applied by the women themselves for 30 minutes whenever they felt nausea throughout the day. Group three consisted of 8 women who had superficial intracutaneous placebo acupuncture using the same type of needles but without deqi effect. In group four, 7 women applied placebo acupressure for 30 minutes 3 cm above the wrist without acupoints. The median gestational age at the occurrence of hyperemesis symptoms and the beginning of treatment was 7 weeks in group 1 and 8 weeks in groups 2,3 and 4. Neither the women nor the physician assessing therapeutic efficacy were aware of patient allocation to the acupuncture, acupressure or placebo groups. Women with a more serious HG picture with electrolyte imbalance were administered intravenous infusions for 3 days with anti-emetics. The outcome criteria for acupuncture or acupressure treatments were disappearance of nausea and vomiting, and no need for medical therapy. Therapeutic efficacy was based on patient report and independent gynecologist's evaluation of the patient's clinical condition.

### **Results**

Four women from group 1 and seven women from groups 2,3 and 4 required intravenous fluid and electrolyte supplementation. The antiemetic metoclopramide was administered intravenously to one woman in group 1, two in group 2, six in group 3, and four in group 4. Promethazine (an antihistamine used for HG) was administered to one woman from groups 2 and 3, and three women from group 4. The efficacy of treatment was judged to be 90% with acupuncture to P6, 64% with acupressure to P6, 12.5% with placebo acupuncture and 0% with placebo acupressure. These results show that the use of P6 bilaterally could significantly reduce the occurrence of HG, either with acupuncture ( $p < 0.0001$ ) or acupressure ( $p < 0.01$ ). The author's conclusion was that both are effective non-pharmacological methods for the treatment of HG.

### **Comment**

The authors acknowledged the small sample size and stated that although the study produced favourable preliminary results, they need to be confirmed in a larger group of subjects. They considered the study reliable in terms of its double-blind design in that the evaluating physician was blinded to the method of acupuncture treatment and the patients receiving placebo acupuncture were unaware of it. However, there is no specific description of the location of the placebo acupuncture, merely that it was at points without deqi effect, and it is not clear whether this was to P6 or other points.

Why should this trial have produced such positive results, so different from Knight et al (2001)? Although this may be due just to chance effects in small samples a likely cause may be found in the amount and frequency of the acupuncture given. Seven treatments in seven days may well be more effective in this situation than three or four

in three weeks. It would certainly accord more with the Chinese approach (see the next section).

## **Outcome studies**

### **Zhou Cong-lian (1999)**

A short paper from China reports on 30 patients with pregnancy sickness.

Acupuncture points Neiguan (P6), Zusanli (St 36) and Gongsun (Sp4) were routinely used. The needles were retained for thirty minutes and "twisted" every five minutes, using strong stimulation and reduction at Neiguan and Zusanli, and moderate reinforcement and reduction at Gongsun. Treatment was given once per day, with one week making up a course. A second course was given after a rest of three days if the patient was not cured.

### **Results**

Cure was designated as total disappearance of nausea, vomiting and dizziness. Among the 30 patients in the series, 26 were cured after one course and 4 were cured after 2-3 courses. The overall cure rate was 100%.

### **Comment**

The treatment given in this trial was very intensive, 7 sessions over 7 days, plus another 7 later if needed. This may explain the very positive results.

In the discussion, the author explains the choice of points according to TCM theory. There is some confusion though, regarding the safety of "reduction manipulation" on Gongsun (Sp4). The beginning of the paragraph states "The use of reduction manipulation would not jeopardize the course of pregnancy" and at the end: "Yet, it should be noted that reduction manipulation is likely to lead to rupture of the membranes and initiate parturition". This highlights the difficult issue of "Forbidden points of pregnancy" about which there is much debate, and which is not in the remit of this briefing paper.

## **Acupressure trials**

12 trials on acupressure for nausea and vomiting of pregnancy were located in the literature. Nine were controlled. Nine definitely used P6, but it is unclear in the others, which just mention "a point on the wrist". (In Vickers' (1996) review, he clarifies the use of P6 in Evans' (1993) trial, having contacted the author!). In ten trials, there was a positive outcome for the treatment groups, in one there was no difference and in another the results favoured the control group (Stone, 1994). There is wide variation in the sample sizes.

The trials are summarised in Table 2.

## Reviews and systematic reviews

A systematic review of acupuncture antiemesis trials was conducted by Vickers in 1996. Seven related to pregnancy sickness but all used acupressure or TENS stimulation (and the point P6) rather than acupuncture. The majority showed a greater positive effect from the active treatment as compared to the placebo and control groups.

More recent reviews on this topic (Meltzer,2000; Mazotta,2000; Hollyer,2002) have included one or more of the acupuncture studies described above, but the bulk of the material refers to acupressure. Mazotta's review included 7 of the acupressure trials and commented that P6 acupressure significantly reduces persistent nausea by at least 50% but that methodological flaws (primarily lack of blinding) meant that no confidence could be placed in the demonstrated effectiveness of this treatment. Roscoe's 2002 review looked at acupressure and acustimulation bands for control of nausea with emphasis on nausea of pregnancy. He stated that the literature supported the conclusion that P6 stimulation by acupressure and acustimulation wrist bands for nausea relief is efficacious for many patients.

## Discussion

The four randomised acupuncture trials cannot be directly compared. The Carlsson hyperemesis group were hospitalised and sufficiently dehydrated to need intravenous infusion, making their condition more severe than in the other studies. They also received acupuncture very frequently (three times per day) even though it was only for two days.

The Adelaide trial (Smith et al, 2002) used a far greater sample size, compared traditional point prescription with just P6, and included a control group to take account of spontaneous remission of nausea and vomiting. It is also the first published trial to measure the effect of acupuncture for nausea and vomiting on women's health status during early pregnancy.

Habek's hyperemesis trial was on a small sample size, with only 7-11 subjects per group. It did show a clear positive outcome, which is promising for this severe form of pregnancy sickness, and it would provide a good pilot for a large scale study. It is the only study to include and compare acupuncture and acupressure in the same group of patients.

Knight's trial did not show positive results, possibly due to small sample size, poor spacing of treatments or active effects from the sham treatment.

Three out of the four randomised controlled trials produced positive results and there are so many variable factors that it is not possible to say why the fourth completely failed to do so. The most likely explanation may lie with the amount and intensity of treatment given in relation to the measurement end point. Smith's work showed that the most marked effect of acupuncture seems to be in the speed of the change rather than the overall amount of change at the end of the day. Hence an intensive course of treatment assessed after one week may give a better response than weekly interventions assessed after a month. If it is impractical to treat frequently then perhaps acupuncture should be combined with self-help acupressure.

For external purposes there is a need for more large trials of the sort conducted by Smith et al (2002). For informing practice the best approach may be a number of small studies that look at variations in parameters such as the intensity and duration of treatment, the number and type of points, the needle action and the value of auxiliary interventions.

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**TABLE 1. ACUPUNCTURE STUDIES FOR PREGNANCY SICKNESS**

STUDY	TRIAL DESIGN	SAMPLE	INCLUSION CRITERIA	ACUPUNCTUR	CONTROL	TREATMENT FREQUENCY	OUTCOME MEASURES	RESULTS	DISCUSSION
<b>Carlsson et al 2000</b>	Randomised single-blind, crossover, controlled	40 (33 completed)	Women with hyperemesis, otherwise healthy	P6 for 30 minutes with deqi obtained every 10 minutes	Superficial sub-cutaneous sham point	3 times daily for 2 days, with two day "wash-out" period before crossing over to other arm of trial	Daily VAS for nausea; diary of vomiting and intake of meals	Significantly faster reduction of nausea VAS and cessation of vomiting in active acupuncture group than placebo.	Patient group required intravenous infusion. How replicable in terms of staff input?
<b>Knight et al 2001</b>	Randomised controlled subject and observer masked	55 (44 completed)	Women at 6 to 10 weeks gestation with nausea, with or without vomiting	According to traditional diagnosis	Sham using cocktail stick on bony regions near to the points	Twice in first week, then weekly for 2 weeks	VAS for nausea. Hospital anxiety and depression scale	Acupuncture was as effective as sham procedure	Poor optimal spacing of treatment sessions. Sample size too small for this design.
<b>Smith et al 2002</b>	Single blind	593 534 (90%) completed first week 443 (75%) completed to final fourth week	Women under 14 weeks gestation with symptoms of nausea and vomiting	Traditional based on TCM diagnosis or P6	Sham needling to an area close to acupoints. Second control group had no acupuncture.	Weekly for 4 weeks	Nausea, vomiting, dry retching. Health status, Rhodes index, SF36.	No difference in vomiting in any group. Less nausea throughout trial in traditional acupuncture group and from 2nd week in P6 group.	
<b>Habek et al 2004</b>	Prospective randomised observer-masked controlled	36	Women with hyperemesis	P6 for 30 minutes with de-qi effect. Also, an acupressure group, self-administered, to P6	Placebo acupressure to non-acupoints and placebo acupuncture with no de-qi effect	Daily for 7 days, 30 minutes per day.	Disappearance of nausea and vomiting and no need for medical therapy.	Both acupuncture and acupressure groups had significant reduction in symptoms and required much less medical therapy.	Small sample size and insufficient detail of which placebo acupuncture points used.

- VAS = visual analogue scale-ie subjects score severity of symptom on a linear scale

**TABLE 2. ACUPRESSURE STUDIES FOR PREGNANCY SICKNESS**

STUDY	TRIAL DESIGN	SAMPLE SIZE	ACTIVE TREATMENT	CONTROL	TREATMENT FREQUENCY	RESULTS
<b>Bayreuther et al 1994</b>	Double-blind, cross-over.	16	P6 acupressure from wrist-band	Placebo band	N/A	Nausea score: P6=32%, placebo = 49% ( $P<0.019$ )
<b>Belluomini et al 1994</b>	Randomised, blinded.	60	Manual pressure to P6	Manual pressure to dummy point on hand	For 10 minutes every 4 hours. 4 day run in period, 3 days treatment.	Improvement in nausea significantly better in active treatment group. No difference in vomiting between the 2 groups.
<b>DeAloysio et al 1992</b>	Randomised.	54	Acupressure wristbands to P6	Placebo band	N/A	Symptoms reduced or absent: treatment group 64-69%, placebo 29-21% ( $P<.005$ )
<b>Dundee et al 1988</b>	Randomised, controlled.	350	Self- administered manual stimulation to P6	No treatment or dummy point near elbow	5 minutes pressure, 4 hourly, for 4 days.	Significantly less troublesome sickness in P6 group compared to control groups ( $P<0.0005$ )
<b>Evans et al 1993</b>	Crossover	23	Sensory affect stimulation device to surface of wrist	Placebo band worn same position with pressure, but no electrical stimulation	48 hours each device, 24 wash-out then crossover for 48 hours	Improved symptoms for 20 (87%) women with SAS device and 10 (43%) with placebo. ( $P<.05$ )
<b>Hyde 1989</b>	Randomised, crossover design	16	P6 wrist band	Wrist band with no stud	Pressure for 5 days followed by crossover, order reversed for half the patients.	Using VAS , significant reduction in nausea ( $P<0.05$ )from acupressure with relief of symptoms in 12 of 16 subjects.
<b>Miller et al &amp; DeVeciana et al 2001</b>	Randomised	230, of which 187 finished	Acustimulation wrist-band	Placebo band	Three weeks	Mixed findings. Effective in reducing mild to moderate n & v (n=114) but not severe(n=73)
<b>Norheim, Pederson et al 2001</b>	Randomised, double-blind, placebo-controlled	97	Wrist-band to P6	Wrist band with no stud	4 day run-in, 4 days intervention, 4 days follow-up.	71% in intervention group had less intensive sickness and shorter duration of symptoms. Placebo group, 59% less intensity, 63% shorter duration Significance level only reached in duration ( $P=0.018$ )
<b>O'Brien et al 1996</b>	Randomised	149	Bi-lateral acupressure wrist-band to P6	Sham point and no band	Continuously for 3 days	Significant decrease in vomiting or retching in both study and control groups
<b>Stone 1993</b>	Non- randomised, controlled	42	"Sea bands" to P6	Dummy "sea bands"	N/A	Change in nausea score: P6 = 0.232, control = 0.399 ( $P= 0.052$ in favour of control)
<b>Werntoft and Dykes 2001</b>	Randomised, controlled.	60	P6 wristband.	No treatment or acupressure to placebo point	2 weeks	Significant reduction in nausea ( $P<0.05$ ) one day after starting treatment, in both P6 and placebo; but effect in placebo group only lasted 6 days compared to 14 days in P6 group.