Does acupressure help reduce nausea and vomiting in palliative care patients? A double blind randomised controlled trial

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ABSTRACT

Introduction Nausea and vomiting are common symptoms for patients with advanced cancer. While there is evidence for acupuncture point stimulation for treatment of these symptoms for patients having anticancer treatment, there is little for when they are not related to such treatment.

Objective To determine whether acupressure at the pericardium 6 site can help in the treatment of nausea and vomiting suffered by palliative care patients with advanced cancer.

Materials and methods Double blind randomised controlled trial—active versus placebo acupressure wristbands. In-patients with advanced cancer in two specialist palliative care units who fitted either or both of the following criteria were approached: Nausea that was at least moderate; Vomiting daily on average for the prior 3 days.

Results 57 patients were randomised to have either active or placebo acupressure wristbands. There was no difference in any of the outcome measures between the two groups: change from baseline number of vomits; Visual Analogue Scale for ‘did acupressure wristbands help you to feel better?’; total number of as needed doses of antiemetic medication; need for escalation of antiemetics.

Conclusions In contrast to a previously published feasibility study, active acupressure wristbands were no better than placebo for specialist palliative care in-patients with advanced cancer and nausea and vomiting.

INTRODUCTION

Nausea and vomiting are problems for up to 70% of patients with advanced cancer. Management of these patients rests on trying to treat any underlying cause. If this is not possible, and while the underlying cause is being treated, antiemetics are used. Careful patient assessment allows clinicians to choose an appropriate first-line antiemetic based on what is thought to be the underlying neuropharmacological mechanism.

While this is a widespread approach there is little evidence for the drugs commonly used for these symptoms in this patient group. A recent study has challenged whether this mechanistic approach is correct and whether symptom control could be just as good using one drug.

Acupuncture originated in China over 2000 years ago and is now used globally. It is a technique where needles are inserted in predetermined areas (or acupuncture points) in the body. For nausea, while many acupuncture points have been described for prevention or treatment of nausea, the most commonly described is P6 (pericardium 6). This point is located two cun (a Chinese measurement equal to approximately 3 cm) proximal to the midpoint of the transverse crease of the wrist between the tendons of palmaris longus and flexor carpi radialis. There is mixed evidence for acupuncture point stimulation for control of nausea in pregnancy and postoperative nausea. For patients with cancer, the majority of studies relate to chemotherapy or radiotherapy.

Acupressure is an attractive alternative to acupuncture involving pressure on acupuncture points. There is methodological heterogeneity for randomised controlled trials of acupressure and when sham acupressure is used there are a number of alternatives for the sham intervention including acupressure at non-acupuncture points or sham acupressure at real points.
In a large study of patients with chemotherapy-induced nausea, patients were randomised to active wristbands, sham wristbands or no wristband. Patients in all groups received antiemetics. Both sets of wristbands were elasticated with a small stud which could apply pressure to an acupuncture point. In the active group, this would be placed at P6, in the sham group, the bands were placed so that the stud faced outward, not putting pressure on P6. In this large study, 500 patients were randomised. There were no statistical differences between the outcomes for the groups although slightly less nausea in the active and sham groups combined when compared with no band, and slightly lower healthcare costs for those who had bands.

We wished to see whether acupressure wristbands placed at the P6 site can help patients with terminal cancer who are suffering from nausea and vomiting. There are a number of reasons why acupressure would be a useful choice for such patients if it helped their symptoms. First, it is relatively easy to apply. Patients (or their carers if they were too fatigued) can place the bands after receiving simple instruction allowing them some control over treatment. Second, this can be done at home without the need for a trip to the hospital or hospice for medication. Third, this technique can be used safely in patients with clotting disorders, thrombocytopenia and neutropenia when acupuncture would be contraindicated. Fourth, it is a technique which is extremely well tolerated. Very few patients have side effects from wearing the bands and those who do complained only of sensations of tightness, swollen hands and itchy wrists although blistering at the site of the stud has been reported. We know of no reports of serious adverse effects of acupressure in patients.

There have been very few investigations of acupressure wristbands for patients with cancer where the cause of the nausea has not been chemotherapy or radiotherapy and only one randomised trial. In this small feasibility study, 10 patients were randomised to active or placebo acupressure wristbands. That study allowed power calculations to inform the study presented here. As in the feasibility study, patients were allowed antiemetics alongside the acupressure intervention.

**PATIENTS, MATERIALS AND METHODS**

**Inclusion criteria**

Between 17 June 2010 and 1 January 2018, adult in-patients at two specialist palliative care units were approached if they met the following inclusion criteria:

1. Diagnosis of advanced cancer with an estimated prognosis of less than 1 year but more than 3 days.

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**Figure 1** Consolidated Standards of Reporting Trials diagram.
Original research

2. Nausea as at least moderate on a none/mild/moderate/severe scale OR had at least one vomit per day for the last 3 days.
3. Have an underlying cause for their nausea thought to be irreversible OR the patient has made an autonomous choice not to proceed with treatment for any potentially reversible cause (eg, surgery for bowel obstruction or drainage of ascites).
4. If patients are taking corticosteroids the dosage should be stable for 3 days before and during the trial.

Exclusion criteria
1. Arm lymphoedema.
2. Weakness, fatigue or confusion sufficient that patient is unable to take part.
3. Previous history of acupuncture/acupressure for nausea or vomiting, or history of use of acupressure by a close relative.
4. History of parkinsonism or parkinsonism on examination (as metoclopramide included in treatment escalation schedule for patients with suspected gastric stasis)

Table 1  Baseline characteristics

|                      | Active (n=28) | Placebo (n=27) | P value |
|----------------------|--------------|----------------|---------|
| **Age, years; median (IQR)** | 65.5 (57.5–75.0) | 67.0 (59.0–71.0) | 0.743  |
| **Females**          | 24 (85.7)    | 24 (88.9)      | 0.724  |
| **Diagnosis**        |              |                | 0.615  |
| Upper gastrointestinal tract | 4            | 6              |      |
| Lower gastrointestinal tract | 3            | 4              |      |
| Pancreas/gall bladder | 6            | 4              |      |
| Lung                 | 6            | 4              |      |
| Ovary                | 3            | 5              |      |
| Breast               | 2            | 2              |      |
| Other                | 4            | 2              |      |
| **Nausea level**     |              |                | 0.970  |
| None                 | 4 (14.3)     | 5 (18.5)       |      |
| Mild                 | 7 (25.0)     | 7 (25.9)       |      |
| Moderate             | 14 (50.0)    | 12 (44.4)      |      |
| Severe               | 3 (10.7)     | 3 (11.1)       |      |
| **Baseline nausea VAS, median (IQR)** | 28.5 (12.5–56.5) | 38.5 (13.0–58.0) | 0.580  |
| **Pattern of nausea**|              |                | 0.589  |
| None-mild            | 8 (28.6)     | 6 (22.2)       |      |
| Sudden onset         | 20 (71.4)    | 15 (55.6)      |      |
| Movement related     | 11 (36.3)    | 11 (40.7)      | 0.912  |
| Obstructive          | 11 (36.3)    | 9 (33.3)       | 0.646  |
| Medication related   | 5 (17.9)     | 1 (3.7)        | 0.092  |
| Constipation         | 12 (42.9)    | 8 (30.8)       | 0.358  |
| **Regular antiemetic at baseline**|  | | |
| None                 | 2            | 0              |      |
| Cyclizine            | 6            | 7              |      |
| Metoclopramide       | 17           | 14             |      |
| Haloperidol          | 13           | 18             |      |
| Levomepromazine      | 23           | 19             |      |
| Ondansetron          | 3            | 0              |      |
| **Route of antiemetic administration**| | | |
| Orally               | 25           | 20             | 0.551  |
| SC injection         | 38           | 17             | 0.001  |
| CSCI                 | 16           | 23             | 0.098  |
| **Regularity**       |              |                | 0.433  |
| PRN only             | 2            | 0              |      |
| Once a day           | 2            | 4              |      |
| Twice a day          | 0            | 1              |      |
| Three times a day    | 8            | 4              |      |
| CSCI                 | 16           | 23             |      |

CSCI, continuous subcutaneous infusion; VAS, Visual Analogue Scale.
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5. Sharing a room with another patient taking part in the study.
6. Unable to read or comprehend the questionnaires or Visual Analogue Scale (VAS).

If patients were positive about participation the study was described to them by a member of the research team and a patient information leaflet given to them. They were given a minimum of 1 hour to consider participation. If after this time they were happy to proceed they were asked to sign a consent form.

A baseline assessment was then completed by a member of the research team documenting the likely clinical picture or cause for nausea. The patient was asked to complete a baseline VAS nausea rating.

Pairs of active or placebo acupressure wristbands had previously been placed in sequential numbered envelopes according to a sequence derived from randomization.com. The bands were provided free of charge by Sea-Band Ltd. They appeared the same when in place, the difference being that active bands have a spherical bead exerting pressure while sham bands have no such bead.

The bands were placed on participants’ wrists at the correct P6 points by a member of the research team not involved with clinical decision making for the patient.

Patients’ antiemetics were not altered on day 0 and they continued their current antiemetic regimen which could be as needed, regular oral or subcutaneous medication, or a constant infusion via subcutaneous syringe driver.

For the next 3 days, the patient was assessed by a clinician (blinded to the type of acupressure bands in place) and asked if the patient felt that their nausea/vomiting control was good enough. If not, the clinician could escalate the patient’s antiemetics according to a predefined treatment escalation schedule. This schedule took account of the most likely clinical picture. If regular oral antiemetics did not give adequate symptom control patients were offered a constant infusion via a subcutaneous syringe driver.

In-patient unit nursing staff reminded patients to complete their daily nausea assessments and estimate of efficacy. Patient participation in the study finished on day 3. Wristbands were then removed, and patients had the option of wearing a normal pair of acupressure wristbands if they wished.

### Outcome measures

Primary outcome measures were determined by the feasibility study:
- Change from baseline number of vomits.
- VAS for ‘did acupressure wristbands help you to feel better?’
- Total number of as needed doses of antiemetic medication.
- Need for escalation of antiemetics.

Secondary outcome measures were:
- VAS of nausea measured daily.
- Duration of perceived nausea over previous 24 hours.
- Adverse effects of acupressure.

### Statistical analysis

Descriptive statistics were used to characterise the cohort. The frequency with percentages is reported for categorical outcome measures and median with IQR values is reported for the continuous variable outcome measures. The non-parametric Mann-Whitney U and Fisher’s exact test were used to compare outcomes.

### RESULTS

Fifty-seven patients were recruited to the study (30 in the active arm and 27 in the placebo arm). Two patients in the active arm became too unwell before they could contribute any data so they have not been included in analysis. For Consolidated Standards of Reporting Trials diagram, see figure 1 and baseline characteristics see table 1. Patients in the placebo arm had a higher average baseline nausea VAS but this was not of statistical significance. There was no difference between the numbers of patients receiving oral medication or via a syringe driver but there were more patients in the active arm receiving injections of antiemetics.

Results for primary and secondary outcome measures are in tables 2 and 3, respectively. For each of days

| Table 2  | Primary outcome measures results for interventions |
|----------|--------------------------------------------------|
|          | Active (n=28) | Placebo (n=27) | p value |
| Total no of study days | 84 | 75 | 0.940 |
| Day 1    | 28 | 27 |       |
| Day 2    | 28 | 24 |       |
| Day 3    | 28 | 24 |       |
| Average no of vomits at baseline (previous 3 days), median (IQR) | 2 (1–3) | 2 (1–3) | 0.9112 |
| Average no of vomits during 3-day study period, median (IQR) | 1.2 (0.5–1.8) | 0.7 (0.3–2.0) | 0.5657 |
| No with missing data on vomiting | 4 | 3 |       |
| Difference in average no of vomits | −0.7 (-1.7–0) | −0.8 (-1.5–0.3) | 0.9288 |
| Do you think the acupressure wristbands helped you to feel better? mm, median (IQR) | 35 (11–63) | 46.5 (8–80.5) | 0.7528 |
| Day 1    | 47 (18.5–73) | 30 (4–82) | 0.4181 |
| No with missing value | 4 | 2 |       |
| Day 2    | 32 (6–54) | 53 (14–87) | 0.2199 |
| No with missing value | 1 | 8 |       |
| Day 3    | 43 (10–66.5) | 52 (14–62.5) | 0.9861 |
| No with missing value | 4 | 7 |       |
| Total no of PRN doses | 65 | 50 | 0.1317 |
| Escalation of antiemetic |       |       | 0.957 |
| No | 70 | 60 |       |
| Yes | 14 | 13 |       |
| No with missing value | 0 | 2 |       |
1–3, there was no difference between the groups with regard to any of the outcome measures.

The main adverse event was that the bands felt too tight and this led to one patient in each arm withdrawing from the study before day 3. Levels of missing data varied from 4.4% to 15.1% for different outcome measures.

**CONCLUSIONS**

This is the first adequately powered randomised controlled trial of active versus placebo acupressure wristbands for nausea and vomiting in a terminally ill palliative care population where the focus was not chemotherapy or radiotherapy. The study took longer to recruit to than hoped. Most patients admitted did not fit the inclusion criteria. The most common reasons were because nausea or vomiting was not severe enough; or that patients did not fit the prognostic criteria. There were different levels of missing data in our study. The reason for missing data was largely when patients became too unwell to complete assessments or misinterpreted how to complete VAS, although there were instances where nurses did not document the number of vomits per day.

Missing data are increasingly recognised as a problem in palliative care research.\(^2\) While any missing data are disappointing, levels in this study were lower than those reported in a recent systematic review.\(^2\) It is likely that this was because of a relatively short study over 3 days with outcome measures that are straightforward to complete.

Adverse events were not severe and only two patients withdrew because of them.

In a recent systematic review examining the role of acupressure for chemotherapy-induced nausea and vomiting, acupressure reduced the severity of acute and delayed nausea.\(^2\) However, in their subgroup analyses non-sham-controlled trials tended towards significance while the sham-controlled trials did not, suggesting that sham acupressure had a placebo effect. In another study, patients were asked whether they expected wristbands to work and those that did had more chance of an effect, which the authors say may be another pointer to a placebo effect.\(^2\) This and another study showed variable effects of gender on response with one showing better efficacy in men\(^2\) and another in women.\(^2\)

In our study, there was no evidence of a sham placebo effect as neither group showed an improvement in any of the outcome measures.

So, where does this leave the use of acupressure wristbands for palliative care patients? This study shows that in this hospice in-patient unit population active bands are not better than placebo. It is difficult to argue that medication worked well for this population as symptoms did not improve greatly in either arm. The number of vomits per day decreased in both arms but this did not reach statistical significance. There are some interesting questions which remain. It is unclear whether acupressure would have worked better for one mechanism of nausea and vomiting rather than another (eg, biochemical nausea rather than gastric stasis). There were not enough patients in each group

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**Table 3** Secondary outcome measures results for interventions

|                       | Active (n=28) | Placebo (n=27) | P value |
|-----------------------|--------------|---------------|---------|
| Nausea VAS mm (all 3 days), median (IQR) | 22.5 (6.5–58) | 21 (7–43) | 0.5736 |
| Baseline (day 0)      | 28.5 (12.5–56.5) | 38.5 (13.0–58.0) | 0.580 |
| Day 1                 | 23.5 (8–50.5) | 28 (6–55) | 0.9035 |
| No with missing VAS   | 4            | 4            |         |
| Day 2                 | 24.5 (8–55) | 17 (3–37) | 0.21146 |
| No with missing VAS   | 2            | 7            |         |
| Day 3                 | 18 (2–71) | 26 (7–42) | 0.9387 |
| No with missing VAS   | 2            | 5            |         |
| Time nauseated over last 24 hours (all 3 days) | | | 0.769 |
| < ¼                   | 42            | 31            |         |
| ¼–½                  | 15            | 17            |         |
| ½–¾                  | 11            | 10            |         |
| ¾–1                  | 8             | 8             |         |
| No with missing value | 8             | 9             |         |
| Adverse event         | 15            | 13            | 0.299  |
| Side effect type      |              |               | 0.166  |
| Dug in                | 1             | 0             |         |
| Giddy                 | 1             | 0             |         |
| Itchy                 | 3             | 0             |         |
| Tired                 | 1             | 0             |         |
| Too tight             | 9             | 13            |         |

VAS, Visual Analogue Scale.
to be able to ascertain this. Perhaps wristbands would have worked better for less symptomatic patients, for example, those seen as outpatients or at home. They do not appear to work in this highly symptomatic population. For now, we will advocate the use of wristbands only for those palliative care patients who are keen to try an intervention that does not involve drugs with the explanation that there is little evidence to support their use.

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Contributors PP conceived the study and designed it along with AB. AP collected most of the data along with BD. RKA was responsible for data analysis. All authors critically revised drafts of the paper. PP is the guarantor.

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