

The effectiveness and cost-effectiveness of acupuncture for the control and management of chemotherapy-related acute and delayed nausea: Assessment of Nausea in Chemotherapy Research (ANCHoR), a randomised controlled trial

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Scientific summary

Assessment of Nausea in Chemotherapy Research (ANCHoR) trial

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Scientific summary

Background

Although chemotherapy-related vomiting is relatively well controlled with current antiemetics, nausea remains a significant problem for patients and a difficult symptom for clinicians to manage. The role of complementary therapies, and particularly acupressure at the P6 (Neiguan) point, as adjunctive treatments to pharmacological antiemetics has been investigated in a number of studies in the past. Both positive and negative results have been reported in the literature, providing highly suggestive but not conclusive evidence. Many past studies, however, are hampered by methodological problems, including small sample sizes, minimal control of risk factors for chemotherapy-related nausea and vomiting and no control of the antiemetic drugs used. Hence, there is a need to clarify whether or not acupressure is effective and cost-effective in the management of chemotherapy-related nausea and vomiting using a robust methodological design with a well-powered sample size.

Objectives

Primary objective

1. To assess the clinical effectiveness of self-acupressure using wristbands in addition to standard care compared with standard care with sham acupressure wristbands and standard care alone in the management of chemotherapy-induced (acute and delayed) nausea.

Secondary objectives

2. To assess the cost-effectiveness and extent of use of usual care in patients using acupressure wristbands in addition to standard care compared with that in patients undergoing standard care with sham acupressure wristbands and standard care alone for the management of chemotherapy-induced nausea.
3. To assess the quality of life of patients using acupressure wristbands in addition to standard care compared with that of patients receiving standard care with sham acupressure wristbands and standard care alone in the management of chemotherapy-induced nausea and vomiting.
4. To assess the clinical effectiveness of self-acupressure using wristbands in addition to standard care compared with that of standard care with sham acupressure wristbands and standard care alone in the management of chemotherapy-induced (acute and delayed) vomiting.
5. To ascertain for which emetogenic level of chemotherapy regimen (i.e. high, moderate or low) self-acupressure using wristbands in addition to standard care is more or less effective in terms of nausea compared with standard care with sham acupressure wristbands and standard care alone.
6. To ascertain whether or not any improvement in chemotherapy-induced nausea and vomiting from using acupressure wristbands is different between men and women.
7. To ascertain whether or not there is an age effect from the use of acupressure wristbands in relation to chemotherapy-induced nausea and vomiting.

Methods

A randomised three-group sham-controlled trial (Assessment of Nausea in Chemotherapy Research or ANCHoR) was designed to test the effects of acupressure in the management of chemotherapy-related nausea and vomiting. Patients with heterogeneous cancer diagnoses receiving chemotherapy of low, moderate and high emetogenic potential were randomised to receive acupressure wristbands in addition to standardised antiemetics, sham acupressure wristbands in addition to standardised antiemetics or

antiemetics alone. The randomisation method used consisted of minimisation with a random element (stochastic minimisation), balancing for gender, age (16–24, > 24–50, > 50 years) and three levels of emetogenic chemotherapy [low, moderate and high according to international American Society of Clinical Oncology (ASCO) and Multinational Association of Supportive Care in Cancer (MASCC) classifications]. Patients were instructed to wear the wristbands throughout the day for the first 7 days during each cycle of chemotherapy. The primary outcome assessment using the Rhodes Index of Nausea, Vomiting and Retching was carried out daily for 7 days per chemotherapy cycle over four cycles. Other assessments, completed at day 6 of each of the four cycles, included the MASCC Antiemesis Tool, the European Quality of Life-5 Dimensions (EQ-5D) utility scale and the Functional Assessment of Cancer Therapy – General (FACT-G) quality-of-life scale. At baseline participants completed measures of anxiety and depression, nausea/vomiting expectation and expectations from using the acupuncture wristbands. An economic evaluation was also carried out based on drug and health service utilisation from the perspective of the health and social care provider and presenting incremental cost-effectiveness ratios with quality-adjusted life-years as the outcome. Finally, a nested qualitative interview study was incorporated to shed more light on the quantitative findings.

Results

In total, 500 patients were randomised in the study arms (166 standard care, 166 sham acupuncture and 168 acupuncture) and data were available for 361 participants for the primary outcome. The primary outcome analysis (nausea in cycle 1) revealed no statistically significant differences between the three groups, although nausea level in the patients using wristbands (both real and sham) was somewhat lower than that in the antiemetics only group (median nausea experience scores for the four cycles: standard care arm 1.43, 1.71, 1.14, 1.14; sham acupuncture arm 0.57, 0.71, 0.71, 0.43; acupuncture arm 1.00, 0.93, 0.43, 0). Adjusting for gender, age and emetic risk of the chemotherapy, the odds ratio (OR) of a lower nausea experience was 1.18 for the acupuncture group and 1.42 for the sham acupuncture group. A gender interaction effect was evident in the data ($p = 0.002$), with women responding more favourably to the use of sham acupuncture wristbands than men (OR 0.35 for men and 2.02 for women in the sham group; 1.27 for men and 1.17 for women in the real acupuncture group). This suggests a placebo effect. No significant differences were detected in relation to vomiting outcomes, anxiety and quality of life. The cost-effectiveness evaluation revealed no significant differences (t -tests) between the costs of each arm. Total costs (all drug and NHS costs) were £70.66 for the acupuncture group, £111.13 for the standard care group and £161.92 for the sham acupuncture group. However, caution is needed in interpreting these results because of very small changes in utility and the influence of a few high-cost outliers. A total of 26 subjects from all three groups took part in in-depth qualitative interviews. Four themes emerged from the data: 'Deciding to participate', 'Perceptions and experiences of complementary therapies', 'Experience of taking part in the trial' and 'Experience of using the wristbands'. The qualitative data overall suggested that the participants perceived the wristbands (both real and sham) as effective and helpful in managing their nausea experience during chemotherapy. Minor and transient side effects from the use of the wristbands were observed.

Conclusions

No clear conclusions can be made about the use of acupuncture wristbands in the management of chemotherapy-related nausea and vomiting as the results did not reach statistical significance. However, the differences observed may be of clinical importance for patients and may potentially lead to lower health-care utilisation. The use of wristbands was safe and perceived to be effective by patients. Before rejecting this intervention we need to consider the therapeutic effect of placebos in situations such as the management of nausea, when low-cost and safe interventions may enhance the effect of antiemetic drugs even in the absence of clearly statistically significant effects. The study provided encouraging evidence in relation to an improved nausea experience as well as a suggestion of potential health resource-use

benefits; further consideration of the use of acupressure wristbands both in practice and in further clinical trials is therefore warranted.

Trial registration

This study is registered as ISRCTN87604299.

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