

# COMMENTARY ON THE COCHRANE REVIEW OF STIMULATION OF THE WRIST ACUPUNCTURE POINT P6 FOR PREVENTING POSTOPERATIVE NAUSEA AND VOMITING

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**Background:** Postoperative nausea and vomiting (PONV) are common complications following surgery and anaesthesia. Drugs to prevent PONV are only partially effective. An alternative approach is to stimulate the P6 acupoint on the wrist. This is an update of a Cochrane review first published in 2004.

**Objectives:** To determine the efficacy and safety of P6 acupoint stimulation in preventing PONV.

**Search Strategy:** TWe searched CENTRAL (*The Cochrane Library*, Issue 3, 2008), MEDLINE (January 1966 to September 2008), EMBASE (January 1988 to September 2008), ISI Web of Science (January 1965 to September 2008), the National Library of Medicine publication list of acupuncture studies, and reference lists of articles.

**Selection Criteria:** All randomized trials of techniques that stimulated the P6 acupoint compared with sham treatment or drug therapy for the prevention of PONV. Interventions used in these trials included

acupuncture, electroacupuncture, transcutaneous nerve stimulation, laser stimulation, capsicum plaster, an acu-stimulation device, and acupressure in patients undergoing surgery. Primary outcomes were the risks of nausea and vomiting. Secondary outcomes were the need for rescue antiemetic therapy and adverse effects.

**Data Collection and Analysis:** Two review authors independently assessed trial quality and extracted the data. We collected adverse effect information from the trials. We used a random-effects model and reported relative risk (RR) with associated 95% confidence intervals (95% CI).

**Main Results:** We included 40 trials involving 4,858 participants; four trials reported adequate allocation concealment. Twelve trials did not report all outcomes. Compared with sham treatment P6 acupoint stimulation significantly reduced: nausea (RR 0.71, 95% CI 0.61 to 0.83); vomiting (RR 0.70, 95% CI 0.59 to 0.83), and the need for rescue antiemetics (RR 0.69, 95% CI 0.57 to 0.83). Heterogeneity among trials was moderate. There was no clear difference in the effectiveness of P6 acupoint stimulation for adults and children; or for invasive and noninvasive acupoint stimulation. There was no evidence of difference between P6 acupoint stimulation and antiemetic drugs in the risk of nausea (RR 0.82, 95% CI 0.60 to 1.13), vomiting (RR 1.01, 95% CI 0.77-1.31), or the need for rescue antiemetics (RR 0.82, 95% CI 0.59-1.13). The side effects associated with P6 acupoint stimulation were minor. There was no evidence of publication bias from contour-enhanced funnel plots.

**Authors' Conclusions:** P6 acupoint stimulation prevented PONV. There was no reliable evidence for differences in risks of postoperative nausea or vomiting after P6

acupoint stimulation compared to antiemetic drugs.

## COMMENTARY ON THE COCHRANE REVIEW

The Cochrane review by Lee and Fan provided a comprehensive summary of recent research investigating the role of stimulation of P6 acupoint in preventing postoperative nausea and vomiting.<sup>1</sup> The authors performed a thorough literature search and identified 40 randomized controlled trials (RCTs) conducted between 1986 and 2008 involving 4858 patients. Meta-analysis of these RCTs showed that compared with sham treatment, P6 acupoint stimulation induced significant reduction in postoperative nausea and vomiting (PONV), and reduced the need for rescue antiemetic medication. There was no significant difference between P6 acupoint stimulation and antiemetic medication in reducing PONV and the need for rescue antiemetic medication. Importantly, no significant adverse effects of P6 acupoint stimulation were identified. The authors concluded that P6 acupoint stimulation reduced PONV and showed no significant difference from antiemetic medication. This commentary takes a closer look at this systematic review and identified a few important issues to consider before bringing the results generated from this meta-analysis into clinical practice.

This systematic review summarized the results of recent RCTs on the efficacy of a novel intervention, P6 acupoint stimulation, on preventing common postoperative complications—nausea and vomiting. Antiemetic medication has limited preventative effect and may be associated with significant adverse effects. P6 acupoint stimulation is a

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simple, inexpensive, and relatively noninvasive intervention with minimal side effects. The research question is significant and the intervention is novel. The review itself is well conducted and follows the rigorous Cochrane systematic review methods for reviewing and summarizing RCTs. In addition, the reviewers evaluated the risk of bias of the RCTs according to the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions and assessed for and found no evidence of significant publication bias.

The results generated from this meta-analysis demonstrated the superiority of P6 acupoint stimulation over sham treatment in reducing the risk of PONV. It is important to point out the significant heterogeneity among the RCTs in all three main outcome analyses, with  $I^2 = 60\%$  for PON, 53% for POV, and 43% for rescue antiemetic medication usage, where  $I^2$  values of 25%, 50%, and 75% represent low, moderate, and high heterogeneity. The authors explained that the moderate heterogeneity observed in this systematic review is mainly the result of different sample sizes; different types of surgeries; different type, timing, duration, and intensity of P6 acupoint stimulation; and different follow-up times to assess PONV. As even though most trials followed patients for 24 hours after surgery, some only followed them for 2 hours. This moderate heterogeneity suggests the inconsistency of the studies, which limits the generalizability of the findings of this meta-analysis.<sup>2</sup>

In addition, in order to integrate P6 acupoint stimulation into clinical practice and make it part of standard care to prevent PONV, it is important to identify the optimal stimulation type, timing, duration, and intensity. Among the 40 RCTs included in this review, 10 types of P6 acupoint stimulation were studied, including needle acupuncture, infiltration of dextrose, semipermanent needles, electrical stimulation of needles, transcutaneous electrical nerve stimulation, laser stimulation, acupoint stimulation device, peripheral nerve stimulation, capsicum plaster and acupressure.<sup>1</sup> Subgroup analysis comparing the effect of invasive P6 acupoint stimulation with noninvasive P6 acupoint stimulation versus sham therapy in preventing PONV showed no significant difference between invasive versus noninvasive stimulation. Seventeen out of 40 trials used acupressure, the

most common type of noninvasive stimulation, to stimulate P6 acupoint. Because acupressure is noninvasive, requires minimal training, and is inexpensive, it may be the most cost effective stimulation method to use in practice. Further efficacy and cost effectiveness analysis research need to be conducted to identify the optimal type of P6 acupoint stimulation.

Once the preferred stimulation method is established, it is important to determine the optimal stimulation duration to prevent PONV. Among the 40 RCTs included in this review, duration of P6 acupoint stimulation varied from 15 minutes when using electroacupuncture to 24 hours when using acupressure. In acupressure trials, some applied acupressure at P6 acupoint for 6 hours and others for 24 hours. Further research to determine if there is a dose-response relationship between duration of P6 stimulation and response to intervention is needed. Furthermore, the optimal timing of P6 stimulation should be identified as well. Timing of P6 acupoint stimulation in the 40 RCTs summarized ranged from application before anesthesia to application after the patient had regained consciousness following surgery.

Subgroup analyses on patients with high versus low baseline risk of PONV suggested that patients undergoing high risk PONV surgeries tend to benefit more from P6 acupoint stimulation than patients undergoing low risk PONV surgeries.<sup>1</sup> This finding brought up an important question: what is the patient population that would benefit the most from P6 acupoint stimulation? In identifying the subgroup of patients that would benefit the most from P6 acupoint stimulation, we would then be able to further improve the cost effectiveness of such intervention and avoid the unnecessary cost and discomfort resulting from applying the intervention to patients who would not benefit. It is important to conduct research to determine if there are any differences in treatment response in patients undergoing different types of surgery, or in patients with different attitudes towards acupuncture and complementary and alternative medicine.

This systematic review demonstrated that there is no significant difference between P6 acupoint stimulation and antiemetics in preventing PONV. Further research needs to be conducted to determine if the combination of antiemetics and P6 acupoint stimulation works better than each component alone.

Indeed, an animal study showed that combination therapy of electroacupuncture (EA) at P6 acupoint with ondansetron, droperidol, or metoclopramide prevented emesis more significantly than EA or any of the medications alone.<sup>3</sup> These data suggested that EA and anti-emetic medication work synergistically.

Last, the mechanism of P6 acupoint stimulation in preventing PONV needs to be studied. Although studies have not been able to fully explain the mechanism of acupuncture, it has been proposed that acupuncture worked through its effect on neurotransmitters and neurohormones.<sup>4</sup> In addition, modern human neuroimaging studies have suggested that stimulating acupuncture points resulted in responses in cortical and subcortical areas in the brain.<sup>5</sup> An animal study showed that the anti-emetic effect of EA at P6 acupoint was diminished by naloxone pretreatment. This supports the implication that central opioid receptors are involved in the P6 acupoint stimulation anti-emesis pathway.<sup>6</sup>

## REFERENCES

1. Lee A, Fan LTY. Stimulation of the wrist acupuncture point P6 for preventing postoperative nausea and vomiting. *Cochrane Database Syst Rev* 2009, Issue 2. Art. No.: CD003281. DOI: 10.1002/14651858.CD003281.pub3.
2. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557-560.
3. Lao L, Zhang G, Wong RH, Carter AK, Wynn RL, Berman BM. The effect of electroacupuncture as an adjunct on cyclophosphamide-induced emesis in ferrets. *Pharmacol Biochem Behav* 2003;74:691-699.
4. Han JS. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. *Trends Neurosci* 2003;26:17-22.
5. Dhond RP, Kettner N, Napadow V. Neuroimaging acupuncture effects in the human brain. *J Altern Complement Med* 2007;13:603-616.
6. Tatewaki M, Strickland C, Fukuda H, et al. Effects of acupuncture on vasopressin-induced emesis in conscious dogs. *Am J Physiol Regul Integr Comp Physiol* 2005;288:R401-R408.

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