

Review

# Acupuncture for nausea and vomiting: An update of clinical and experimental studies

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## Abstract

The objective of this overview is to summarize existing knowledge about the effects of acupuncture-point stimulation on nausea and vomiting. Systematic reviews on postoperative nausea and vomiting, chemotherapy-induced nausea and vomiting, and pregnancy-related nausea and vomiting exist. Several randomised trials, but no reviews, exist for motion sickness. For postoperative nausea and vomiting, results from 26 trials showed acupuncture-point stimulation was effective for both nausea and vomiting. For chemotherapy-induced nausea and vomiting, results of 11 trials differed according to modality with acupressure appearing effective for first-day nausea, electroacupuncture appearing effective for first-day vomiting, and noninvasive electrostimulation appearing no more effective than placebo for any outcome. For pregnancy-related nausea and vomiting, results were mixed. Experimental studies showed effects of P6-stimulation on gastric myoelectrical activity, vagal modulation and cerebellar vestibular activities in functional magnetic resonance imaging. There is good clinical evidence from more than 40 randomised controlled trials that acupuncture has some effect in preventing or attenuating nausea and vomiting. A growing number of experimental studies suggest mechanisms of action.

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*Keywords:* Acupuncture; Nausea and vomiting

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## 1. Introduction

Scarcely any other ancient therapy has gained as much interest from the scientific medical community as acupuncture. Stimulation of special acupuncture points on the body surface with needles, heat or pressure has been used in China for more than 2500 years to treat diseases and relieve pain. The traditional theory behind this therapy includes non-Western concepts such as meridians, Qi, Yin and Yang, and other aspects of Chinese philosophy. These ideas appear to be incompatible with the modern, Western view of life. Nevertheless, the West has been intrigued with acupuncture, and spectacular reports about surgery with acupuncture-induced analgesia in China have appeared in the Western press since the 1950s. Research interest ignited in 1971 when a New York Times reporter wrote about his postoperative pain relief by means of acupuncture.

Experimental studies in the 1970s showed an influence of needle stimulation on the endogenous opioid system, which seemed to explain the analgesic effect of acupuncture (Pomeranz and Chiu, 1976; Mayer et al., 1977). Since then, many other mechanisms of acupuncture action have been researched and postulated (Kaptchuk, 2002). Numerous clinical trials have been published on the effects of acupuncture, mostly on different pain conditions (Ezzo et al., 2000) and on nausea and vomiting (Lee and Done, 2004).

The interest in acupuncture for nausea and vomiting goes back to 1986 when Dundee first reported in the *British Medical Journal* that an acupuncture point, P6, located near the wrist had been used as prophylaxis for postoperative nausea and vomiting in minor gynaecological operations (Dundee et al., 1986). In a previous visit to China in 1983, Dundee was impressed by the use of acupressure as prophylaxis against vomiting in early pregnancy, and he became fascinated by the idea of using acupuncture of P6 for prevention of postoperative nausea and vomiting. Because of the good effect and easy standardisation of the therapy with only one acupoint, P6 gained a reputation as being a model acupuncture point for investigating acupuncture.

Ten years after Dundee's initial publication, a systematic review summarized 33 controlled studies of P6 stimulation for nausea and vomiting, with 27 showing the efficacy of P6 stimulation using a variety of modalities, including acupuncture, electroacupuncture, transcutaneous electrical nerve stimulation, and acupressure (Vickers, 1996).

Influenced by this review, a National Institute of Health Consensus Conference on Acupuncture in 1997 concluded that "promising results have emerged showing the efficacy of acupuncture in adult postoperative and chemotherapy induced nausea and vomiting" (National Institute of Health, 1998). However, some of the existing studies had methodological limitations and control group problems. There were also questions about the optimal mode of P6 stimulation. Thus, research continued and more trials and more systematic reviews have been done to examine the effect of acupuncture-point stimulation on nausea and vomiting.

The aim of this review is to provide a general overview of the clinical and experimental work on acupuncture-point stimulation and nausea and vomiting. We searched Cochrane Library and Medline for reviews using the keywords 'acupuncture', 'pericardium 6' ('P6', 'PC6', 'Neiguan'), 'nausea and vomiting'. We also searched for randomised controlled trials which had been published since the most recent reviews and for experimental studies of acupuncture and nausea and vomiting. For each nausea and vomiting condition, we first summarize the systematic reviews. If additional trials have been published since the most recent systematic review, these trials are described after the reviews.

## 2. Acupuncture techniques

### 2.1. P6 (Pericardium 6)

The acupuncture point P6 is the most important acupuncture point for nausea and vomiting. It is located approximately 3 cm proximal to the wrist between the tendons of the M. flexor carpi radialis and M. palmaris longus. P6 (or PC6) is the abbreviation of pericardium 6, meaning it is the sixth point at the pericardium meridian. The original Chinese name is *Neiguan*, which means the inner pass or gate. According to traditional Chinese medicine, P6 calms the shen (spirit), harmonizes the stomach, and regulates the triple energizer, which includes all internal organs.

In the traditional Chinese medicine system, other acupuncture points also have antiemetic effects. However, none have been studied to the extent of P6. A few studies suggest that other additional acupuncture points might be helpful (Shen et al., 2000; Somri et al., 2001; Ming et al., 2002; Reindl et al., 2005).

## 2.2. Alternatives to P6

While some studies have suggested adjuncts to P6, other studies have suggested alternatives to P6. [Kotani and colleagues \(2001\)](#) suggest that intradermal needles applied on the back at points along the bladder meridian are effective for both postoperative pain control and postoperative nausea and vomiting. However, compared to P6 stimulation, this procedure is time consuming and not very practical in a perioperative setting.

Three studies have shown that Korean hand acupressure may be comparable to P6 in preventing postoperative nausea and vomiting ([Schlager et al., 2000](#); [Boehler et al., 2002](#); [Kim et al., 2002](#)). Two Korean acupuncture points have been described: K-K9 on the palmar side of the ring finger and K-D2 on the dorsal side of the forefinger. Auricular acupuncture has not been well evaluated; a single trial has demonstrated some positive effect ([Kim et al., 2003](#)).

## 2.3. Stimulation

Acupuncture points can be stimulated with different methods including invasive and noninvasive stimulation. The SeaBand® (Sea-Band Ltd., Leicestershire, England) is one of the most popular forms of P6 stimulation because it is noninvasive and easy to apply. This band includes a plastic button or pearl which can be placed at P6 to apply pressure, which is then defined as acupressure. Originally, SeaBands were developed to treat seasickness by providing continuous acupressure at P6. Acupressure can also be applied by pressing on acupuncture points with one's fingers. In recent studies, the ReliefBand® (Woodside Biomedical, Inc., Abbott Park, IL; Maven Laboratories, Citrus Heights, CA) has been used. This band looks like a wristwatch and includes a device which applies surface electrical current at the acupuncture point. Transcutaneous electrical stimulation also is used. Both are broadly called electrostimulation.

Invasive stimulation usually includes insertion of thin acupuncture needles which can be stimulated manually (manual acupuncture) or electrically by connecting with electrodes (electroacupuncture).

There has been much debate on the optimal time to apply stimulation to prevent nausea and vomiting. For chemotherapy-induced illness, P6 stimulation prior to chemotherapy is considered most effective. For postoperative nausea and vomiting, P6 stimulation prior to induction of anaesthesia has been considered most effective in the past ([Vickers, 1996](#)). However, in more recent studies, intraoperative and postoperative stimulation have also been successful ([Rusy et al., 2002](#); [Wang and Kain, 2002](#); [Kim et al., 2003](#)).

## 2.4. Control groups

Nausea is a highly subjective symptom, and researchers must rely solely on patients' self-reports. Highly subjective outcomes can be prone to placebo effects if the patient knows

the treatment group assignment. Therefore, ensuring that patients do not know their treatment group assignment by using a sham (fake), procedure as a control is an important aspect of trial designs of treatments for nausea.

Two types of sham controls have been used in acupuncture trials. (1) *Sham acupuncture* involves needling (i.e., puncturing the skin) in a minimal way such as needling real or wrong points or non-points shallowly with minimal stimulation. Critics of sham needling suggest that even minimal needling produces some physiological effects and is not a truly physiologically inert procedure. (2) *Placebo acupuncture* uses a noninserted needle with a telescopic function or a needle encased in a cartridge so that the patient cannot tell whether the needle has been inserted or not. Unlike sham acupuncture, placebo acupuncture offers a presumably almost physiologically inert placebo ([Streitberger and Kleinhenz, 1998](#)). Controls in studies of other stimulation methods than needle insertion also include stimulation at nonpoints (sham acupressure) or apparent but not real stimulation at acupuncture points (placebo laser, placebo electrostimulation).

## 3. Postoperative nausea and vomiting

Postoperative nausea and vomiting still is the “big little problem” for anaesthetists. While postoperative nausea and vomiting is not life threatening, it can lead to increased recovery room time, unanticipated hospital admissions ([Fortier et al., 1998](#)), and more discomfort than postoperative pain ([Macario et al., 1999](#)). The overall incidence of postoperative nausea and vomiting is approximately 30% ([Watcha and White, 1992](#)), increasing up to 79% in high-risk patients ([Apfel et al., 1999](#)). Recommended strategies for minimising the incidence of postoperative nausea and vomiting include identification of high-risk patients, avoidance of emetogenic stimuli, and a multimodal therapy ([Gan, 2002](#)).

The most effective antiemetics appear to be serotonin antagonists, droperidol and dexamethasone, alone or in combination. However, droperidol use has been nearly abandoned due to a recent warning from the Food and Drug Administration, USA, about possible cardiac arrhythmia. Other antiemetics, such as promethazine, dimenhydrinate or scopolamine are not as effective or cause postoperative sedation. The most recent recommendations include non-pharmacological techniques like acupuncture, acupressure, and transcutaneous nerve stimulation ([Gan et al., 2003](#); [Habib and Gan, 2004](#)).

### 3.1. Postoperative nausea and vomiting anti-emesis: reviews

The first review on an antiemetic effect of acupuncture was published in 1996 by Vickers, and included 21 trials for postoperative nausea and vomiting of which 16 showed positive results for acupuncture, electroacupuncture, transcutaneous electrical nerve stimulation, or acupressure at the acupuncture point P6 ([Table 1](#)). Despite the positive results obtained in the studies, it

Table 1  
Reviews about acupuncture and nausea and vomiting

Indication	Author	Number of studies (stimulation)	Results
CCT	Ezzo et al. (2005)	11 RCT (mixed)	Metaanalysis: EA pos. for acute vomiting Aps pos. for acute nausea ES no pos. results
PONV	Lee and Done (2004)	26 RCT (mixed)	Metaanalysis: Pos. for nausea, vomiting and need for rescue antiemetics
PONV	Lee and Done (1999)	19 RCT (mixed)	Metaanalysis: Pos. for early vomiting (NNT=5) and early nausea (NNT=4)
PONV, CNV, PRNV	Vickers (1996)	33 CCT (mixed)	27 pos. (11 of 12 S-Control) 16 pos. 5 pos. 7 pos.
PRNV	Jewell and Young (2003)	4 RCT (mixed)	Pos. compared to no treatment; continuous data equivocal
PRNV	Aikins (1998)	7 RCT (6 APs, 1 EA)	APs 5 pos., 1 neg. EA 1 pos.

AP=acupuncture, Aps=acupressure, CCT=controlled clinical trials, CNV=Chemotherapy-induced nausea and vomiting, ES=Electrostimulation, EA=Electroacupuncture, P=Placebo, PONV=Postoperative nausea and vomiting, PRNV=Pregnancy-related nausea and vomiting, RCT=randomised controlled trials, S=Sham, w=wake, a=anesthetized, MTC=Metoclopramide, SA=Serotonin-antagonists, Drp=Droperidol, N=nausea, V=vomiting, ns=not significant, NNT=number needed to treat, pos.=positive results.

was difficult to draw clear conclusions due to methodological limitations in existing studies, and further research followed.

A meta-analysis of 19 randomised controlled trials (Lee and Done, 1999) seemed to confirm the effectiveness of P6-stimulation to prevent postoperative nausea and vomiting (Table 1). However, in some of the studies, multiple statistical testing was performed resulting in positive and negative results for different outcomes in the same trial. There were discrepancies in the effectiveness between early and late vomiting and nausea, and some of the negative outcomes were thought to be related to P6-stimulation during anaesthesia or to occur in studies including only children.

The authors subsequently updated their review using 26 trials (Lee and Done, 2004) (Table 1). They concluded that P6 acupoint stimulation is effective in reducing the risk of postoperative nausea and vomiting, stating that “the effect of P6 acupoint stimulation for the prevention of postoperative nausea (RR 0.72, 95% CI 0.59 to 0.89) is similar to

the prevention of vomiting (RR 0.71, 95% CI 0.56 to 0.91).” The effect was similar between children and adults, and between invasive (acupuncture) versus noninvasive (acupressure and electrostimulation) modalities. When P6 was compared with antiemetic medication, the pooled results across antiemetic subgroups showed that P6 conferred a greater reduction in the risk of nausea but not vomiting than did the antiemetic group. However these results should be interpreted with caution because the pooled antiemetics included a variety of drugs including metoclopramide, which is not viewed as effective for postoperative nausea and vomiting prophylaxis.

Patient populations at higher risk for postoperative nausea and vomiting had more benefit. For example, if in the control group the postoperative nausea and vomiting rate was 70% the number needed to treat for acupoint stimulation was five.

### 3.2. Postoperative nausea and vomiting: recent randomised controlled trials

#### 3.2.1. Acupressure

Randomised controlled trials published since the most recent Cochrane review (Lee and Done, 2004) are presented in Table 2. Since that review, three acupressure trials have been published (Samad et al., 2003; Schultz et al., 2003; Klein et al., 2004). Two of those trials showed equivocal results (Samad et al., 2003; Schultz et al., 2003). The third showed no overall effect, but found acupressure had a better effect in women (Klein et al., 2004).

#### 3.2.2. Acupuncture

One acupuncture trial was published since Lee and Done’s (2004) review. Findings were equivocal for incidence of postoperative nausea and vomiting and/or antiemetic rescue medication within 24h after surgery. Rescue medication is medication used if the patient feels sick and wants to relieve the symptoms. For vomiting alone, acupuncture had a greater effect than placebo. This trial included 220 gynaecologic or breast surgical female patients. It was a placebo-controlled, patient- and observer-blind design (Streitberger et al., 2004). The control used a noninvasive placebo needle which simulated skin penetration at a non-acupuncture point. Subgroup analysis by type of surgery showed greater reduction in postoperative nausea and vomiting with acupuncture compared to placebo for gynaecological surgical patients than for breast surgical patients. An additional analysis showed that subgroups receiving acupuncture before induction of anaesthesia had no better results than those receiving acupuncture after induction.

#### 3.2.3. Electrostimulation

Two recent studies have shown a positive effect of electrostimulation. In the first trial, electrostimulation using



Table 2  
Recent randomised controlled trials about acupuncture and nausea and vomiting (not reported in previous reviews)

Indication	Author	n	Therapy	Control	Results (outcome)
CNV Pediatric oncology	Reindl et al. (2005)	11	Individual AP+SA	No AP+SA	ns (V) s (rescue)
CNV Breast cancer	Roscoe et al. (2005)	96	P6 ES+SA	S-ES+SA No ES+SA	ns (N, V) ns (N, V)
PONV Gynecologic+Breast surgery	Streitberger et al. (2004)	220	P6 AP (w / a)	P-AP	ns (PONV) s (V)
PONV Pediatric surgery	Butkovic et al. (2005)	120	P6 Laser (w)	P-laser MTC	s (PONV 0–2h), ns (PONV 2–6h) ns (PONV 0–6h)
PONV Gynecologic surgery	Schultz et al. (2003)	143	P6 APs+Drp APs+P-Drp	P-APs+Drp P-APs+P-Drp	ns (PONV) ns (PONV)
PONV Laparoscopic CCE	Samad et al. (2003)	50	P6 APs (w)	P-APs	ns (PONV)
PONV Cardiac surgery	Klein et al. (2004)	152	P6 APs (w)	P-APs	ns (N, V)
PONV Female laparoscopy	Khan et al. (2004)	42	P6 ES	S-ES	s (PONV 24h)
PONV Major breast surgery	Gan et al. (2004)	77	P6 ES	SA S-ES	ns (PONV 24h) s (PONV 24h)
PONV Pediatric tonsillectomy	Kabalak et al. (2005)	90	P6+CV13 ES	SA No-ES	ns (V 24 h) s (V 24 h)

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an alternating current of 2 and 100 Hz was more effective than sham for postoperative nausea and vomiting and pain when applied 30 min before surgery until end of surgery (Gan et al., 2004). In another study, the anaesthetists used a neuromuscular monitoring device (TOF-watch) applied to P6 to reduce postoperative nausea and vomiting (Khan et al., 2004).

#### 3.2.4. Laser

A 2005 pediatric trial showed a significant reduction of postoperative nausea and vomiting within 0–2 but not 2–6h using laser stimulation compared to metoclopramide and sham (Butkovic et al., 2005).

## 4. Chemotherapy related nausea and vomiting

The American Society of Clinical Oncology (ASCO) recommendations include giving potential 5-HT<sub>3</sub> receptor antagonists plus corticosteroids before chemotherapy to patients receiving chemotherapy that are at high risk of emesis. Nevertheless, many patients still experience nausea and vomiting related to chemotherapy. Therefore, the expert panels emphasize the need for evaluation of additional ways to reduce these symptoms (Gralla et al., 1999; Hesketh et al., 1998). The need for additional relief has led to interest in nonpharmacological adjuncts to drugs like acupuncture or acupressure. Chemotherapy-induced nausea and vomiting is classified as either ‘acute’ (within 24h postchemotherapy) or ‘delayed’ (greater than 24h but less than seven days postchemotherapy).

### 4.1. Chemotherapy-induced nausea and vomiting anti-emesis: reviews

#### 4.1.1. All modalities combined

The pooled results of 11 randomised controlled trials evaluating acupuncture-point stimulation plus antiemetics for chemotherapy-induced nausea and vomiting showed a significant reduction in the proportion of patients experiencing acute vomiting, RR=0.82 (95% CI 0.69, 0.99,  $p=0.04$ ), and a trend towards significance for reducing acute nausea severity (Ezzo et al., 2005) (Table 1). This is consistent with the review of Vickers (1996), who reported five studies showing acupuncture and chemotherapy-induced nausea and vomiting to be effective.

In contrast to the review of postoperative nausea and vomiting (Lee and Done, 2004), the review of chemotherapy-induced nausea and vomiting (Ezzo et al., 2005) indicated noteworthy differences as a function of modality of stimulation.

#### 4.1.2. Acupressure

Acupressure showed a protective effect for both mean acute nausea severity SMD=−0.19 (95% CI −0.37, −0.01,  $p=0.04$ ) and most severe acute nausea score SMD=−0.20 (95% CI −0.39, −0.02,  $p=0.03$ ). Acupressure showed no protective effect for acute vomiting or chemotherapy-induced nausea and vomiting. None of the pooled studies involved a placebo control. All acupressure trials gave concomitant modern antiemetics to both groups.

#### 4.1.3. Acupuncture

Manual and electroacupuncture trials combined reduced the proportion of patients experiencing acute vomiting (RR=0.74, 95% CI 0.58, 0.94  $p=0.01$ ). When analyzed separately, electroacupuncture showed a benefit of reduced acute vomiting (RR=0.76, 95% CI 0.60, 0.97,  $p=0.02$ ), but manual acupuncture did not. However, the manual acupuncture trial gave modern antiemetics with acupuncture, and the electroacupuncture trials gave antiemetics, but none were modern ones by today's standards. For acute nausea, manual acupuncture was equivocal, and no data were reported for electroacupuncture. No acupuncture trials had data on delayed nausea and vomiting.

#### 4.1.4. Electrostimulation

Acute and delayed chemotherapy-induced nausea and vomiting outcomes were not significantly improved by non-invasive stimulation compared to placebo. All electrostimulation trials gave concomitant modern antiemetics to both treatment and control groups.

### 4.2. Chemotherapy-induced nausea and vomiting: recent randomised controlled trials

#### 4.2.1. Acupuncture

In a recent pediatric trial of individualized acupuncture, rescue medication was significantly reduced in the acupuncture-plus-antiemetics group compared to no acupuncture (Reindl et al., 2005). The vomiting was reduced but not significantly (Table 2).

#### 4.2.2. Electrostimulation

Roscoe et al. found no difference in the antiemetic effects of real versus sham electrostimulation wrist bands for chemotherapy-induced nausea and vomiting (Roscoe et al., 2005) (Table 2).

## 5. Pregnancy-related nausea and vomiting

More than 50% of women in Western societies are affected by nausea and vomiting in early pregnancy. This is generally self-limited. However, in the symptomatic period, considerable distress, temporary disability, and even dehydration may occur (Vellacott et al., 1988). Because of concerns about potential teratogenic effects, drugs usually are avoided during the critical embryogenic period. Therefore, many women try alternative therapies such as acupuncture or acupressure.

### 5.1. Pregnancy-related nausea and vomiting anti-emesis: reviews

#### 5.1.1. All modalities combined

Two early reviews (Vickers, 1996; Aikins, 1998) suggest that P6 stimulation reduces nausea and vomiting related to pregnancy (e.g., morning sickness). However, the most

methodological rigorous trial using 161 patients revealed no differences in pregnancy-related nausea and vomiting between acupressure and placebo (O'Brien et al., 1996).

A Cochrane review (Jewell and Young, 2003) which included four randomised controlled trials into analysis, showed that for dichotomous data assessing the presence or absence of morning sickness, P6 was significantly more effective than no treatment (odds ratio=0.25, 95% CI 0.14 to 0.43,  $p<0.01$ ) or sham treatment (odds ratio=0.35, 95% CI 0.12 to 1.06,  $p=0.06$ ). The review concluded that "These effects are comparable to those obtained with drugs." However, findings for continuous data (severity of nausea, frequency of vomiting) were equivocal. Therefore, the authors cite the evidence as "mixed."

#### 5.1.2. Acupressure

A systematic review of seven acupressure trials also noted conflicting results (Roscoe and Matteson, 2002). For example, one trial in that review showed the duration but not severity of nausea was significantly reduced with acupressure compared to a placebo band (Norheim et al., 2001). However, another trial showed acupressure to be more effective than placebo bands in reducing moderate but not severe nausea and vomiting (Miller et al., 2001).

Although each of these reviews have noted methodological flaws in the individual trials, most came to the conclusion that P6 stimulation, usually with acupressure, might be a beneficial, low-cost option for pregnancy-related nausea and vomiting.

## 6. Motion-related nausea and vomiting

The SeaBand® originally was designed to prevent and treat motion related nausea and vomiting. However, currently there are no reviews of acupuncture treatment for motion related nausea and vomiting. Only single controlled studies with small sample sizes and contradictory results have been published.

### 6.1. Motion-related nausea and vomiting anti-emesis: controlled studies

#### 6.1.1. Electrostimulation

Two electrostimulation trials had contradictory results (Bertolucci and DiDario, 1995; Miller and Muth, 2004). The first trial showed P6 had a positive effect compared to sham stimulation in a small cross over study of nine healthy volunteers on the open sea (Bertolucci and DiDario, 1995). However, another study of 77 volunteers showed that P6 stimulation either by electrostimulation or acupressure could not prevent motion sickness induced by optokinetic drum exposure (Miller and Muth, 2004).

#### 6.1.2. Acupressure

Of five studies of acupressure at P6, two showed significant results favoring acupressure (Hu et al., 1995; Stern et al., 2001),

and three did not show significant results (Bruce et al., 1990; Warwick-Evans et al., 1991; Alkaissi et al., 2005). The two studies that showed significantly less nausea also showed less abnormal gastric myoelectric activity compared to sham acupressure and no treatment (Hu et al., 1995; Stern et al., 2001). In the third study, acupressure reduced significantly the time to moderate nausea during eccentric rotation compared to no treatment, but there was no significant difference compared to sham acupressure (Alkaissi et al., 2005). The remaining two studies, with 36 and 18 subjects, respectively, showed no effect of acupressure (Bruce et al., 1990; Warwick-Evans et al., 1991).

A recent study compared Korean hand acupressure at K-K9 with sham acupressure in 100 geriatric patients during ambulance transport (Bertalanffy et al., 2004). There was a significant difference in nausea scores and in the overall patient satisfaction.

## 7. Experimental studies

Nausea and vomiting can be induced by many physiological and pathological factors, as well as drugs or ingested toxins. Nausea and vomiting is primarily controlled by the vomiting centre, an area in the brainstem in the dorso-lateral reticular formation of the medulla that integrates responses and initiates the vomiting reflex. This centre is influenced by afferent stimuli from the central nervous system including the cerebral cortex, vestibular and cerebellar nuclei and the chemoreceptor trigger zone. The chemoreceptor trigger zone is comprised of a group of cells close to the area postrema on the floor of the fourth ventricle. The chemoreceptor trigger zone is very sensitive to stimuli from chemoreceptors and pressure receptors in the gut, and to circulating chemicals like opioids or other emetic drugs. Histamine, serotonin,

dopamine, acetylcholine, and opioid receptors are found in the chemoreceptor trigger zone.

Several mechanisms of action have been proposed for the effect of P6 on nausea and vomiting (Table 3). One proposed mechanism is that P6 works through neurotransmitters. Many experimental studies have shown that acupuncture influences the endogenous opioid system (Han and Terenius, 1982) as well as serotonin transmission via activation of serotonergic and noradrenergic fibers (Mao et al., 1980; Takeshige et al., 1992).

A second proposed P6 mechanism is through direct influence on the smooth muscle of the gut. Electrostimulation of P6 has reduced gastric tachyarrhythmia in induced motion sickness studies (Hu et al., 1995; Stern et al., 2001) and enhanced the percentage of regular slow waves seen by electrogastronomy (Lin et al., 1997). Electroacupuncture at P6 and St36 (located approximately 3 cm below the patella at the lateral side of the lower leg) together have decreased period-dominant frequency in the electrogastronomy; P6 alone reduced period-dominant power, and St36 alone increased period-dominant power (Shiotani et al., 2004). Electroacupuncture at P6 but not at control points suppressed retrograde peristaltic contractions and reduced vomiting episodes in seven conscious dogs with vasopressin-induced emesis (Tatewaki et al., 2005). This effect was abolished by naloxone, so the authors concluded that a central opioid pathway was involved.

A third proposed mechanism is that P6 works through a somatovisceral reflex. Electrostimulation at P6 has inhibited the rate of transient lower esophageal sphincter relaxations triggered by gastric distension in healthy volunteers while sham acupuncture did not (Zou et al., 2005). In contrast to the previous study (Tatewaki et al., 2005), this effect was not

Table 3  
Experimental studies about acupuncture and nausea and vomiting

Author	Participants	Treatment	Measurement	Results
Zou et al. (2005)	14 healthy volunteers	ES at P6 vs S-ES	Rate of transient lower esophageal sphincter relaxations	40% reduction, not naloxon reversible no effect by S-ES
Tatewaki et al. (2005)	7 dogs (vasopressin induced emesis)	EA at P6, BI21, St36	Episodes of vomiting and retrograde peristaltic contractions	Reduced, naloxon reversible by P6, no effect by BI21 and St36
Shiotani et al. (2004)	8 healthy volunteers	EA at P6 and St36 vs S-EA	Electrogastronomy: Period dominant frequency (PDF) and Period dominant power (PDP)	PDF decreased by P6+St36 PDP reduced by P6 and increased by St36
Huang et al. (2005)	121 healthy volunteers	AP at P6 vs S-AP vs no treatment	Heart rate variability	No effects by S-EA Increased in high frequency power (vagal modulation) only by AP
Li et al.(2005)	29 male healthy volunteers	AP at P6 and LI4 vs superficial S-AP	Heart rate variability	Increase in high frequency and decrease in low frequency by AP
Lin et al. (1997)	9 healthy Chinese	ES	Electrogastronomy: Gastric myoelectrical activity	ES significantly increased regular slow waves
Yoo et al. (2004)		AP at P6 vs S-AP vs tactile stimulation	functional magnetic resonance imaging	Modulation of cerebellar vestibular neuromatrix only by P6

AP=acupuncture, ES=Electrostimulation, EA=Electroacupuncture, S-AP=Sham-acupuncture, vs=versus.

inhibited by naloxone, thus, suggesting a non-opioid mechanism. Zou and colleagues (2005) speculate that a somatovisceral reflex, which has been previously demonstrated to affect gastric motility in rats (Sato et al., 1993), could be involved.

A fourth proposed mechanism is that P6 works through **sensory input inhibition**. According to this theory, when **sensory input from gastric distension is inhibited**, it leads to an inhibition of the frequency of transient lower esophageal sphincter relaxations. Because acupuncture had no influence on the residual lower esophageal sphincter pressure or on the duration of lower esophageal sphincter relaxations, it seems unlikely that acupuncture acts primarily on the efferent motor pathway (Zou et al., 2005).

A fifth mechanism suggests P6 stimulates a **somatosympathetic reflex** that induces gastric relaxation. The reflex centre is within the **medulla, and the ventrolateral medulla** neurons may play an important role (Tada et al., 2003).

A sixth proposed mechanism is that P6 can **increase vagal modulation**. Huang and colleagues (2005) proposed that vagal modulation could be examined through heart rate variability analysis. Normalized high-frequency power was used as the measure of vagal modulation. Normalized high-frequency power increased in the P6 group but not the sham acupuncture or no-treatment groups, thus, suggesting vagal modulation through P6 (Huang et al., 2005). Similar results were observed for acupuncture at P6 in combination with a second acupuncture point (Li4) compared to a sham procedure (Li et al., 2005).

A seventh proposed mechanism is that P6 may **influence the cerebellar vestibular neuromatrix**. In an functional magnetic resonance imaging study, acupuncture at P6 **selectively activated the left superior frontal gyrus, anterior cingulate gyrus, and dorsomedial nucleus of thalamus** whereas sham acupuncture or tactile stimulation did not (Yoo et al., 2004). P6 acupuncture also selectively activated several structures in the cerebellum suggesting that P6 for motion sickness may work through the cerebellar vestibular system.

## 8. Psychological aspects of acupuncture and nausea and vomiting

The impact of psychological factors on nausea and vomiting is widely acknowledged, and the efficacy of influencing these psychosomatic aspects, e.g. by behavioural therapy or hypnosis, has been demonstrated (Mundy et al., 2003). Thus, a psychological effect of acupuncture treatment has been hypothesized, because (in addition), acupuncture appears to be effective for depression (Allen et al., 1998; Eich et al., 2000) and for psychosomatic disorders of the gastrointestinal tract (Rohrbock et al., 2004; Schneider et al., 2005a). In the case of depression, these effects could be derived by the influence of acupuncture on the autonomous nervous system (Chambers and Allen, 2002). However, significant placebo effects also must be addressed, as was shown recently for irritable bowel syndrome (Enck and Klosterhalfen, 2005; Schneider et al.,

2005a). Determinants of placebo response could be high disease coping capacities (Schneider et al., 2005a), expectations (Vase et al., 2003), and suggestibility (De Pascalis et al., 2002). Additionally, the treatment response seems also to be related to cognitive aspects (Kreitler et al., 1987) and perception of bodily sensations during the acupuncture treatment (Schneider et al., 2005b). As the relations among these variables of treatment and placebo response remains unclear, further studies need to be done to evaluate the psychological impact of acupuncture on nausea and vomiting.

## 9. Adverse effects

Reviews of the adverse effects of acupuncture confirm that acupuncture, in the hands of qualified practitioners, is safe (Lao et al., 2003). Serious adverse effects like pneumothorax, cardiac tamponade, lesions of abdominal viscera and the nerve system are anecdotal and could have been avoided by careful practice and knowledge of the anatomy (Peucker et al., 1999). Transient nonserious adverse events include needling pain, hematoma, minor bleeding, orthostatic problems, forgotten needles, and local skin irritation (MacPherson et al., 2001; Melchart et al., 2004).

Despite P6 proximity to the median nerve, adverse effects of P6 stimulation are very rare. Only one report exists concerning neuropathy of the median nerve caused by a broken acupuncture needle in the carpal tunnel adjacent to P6 (Southworth and Hartwig, 1990). Discomfort with the acupressure band, skin irritations, transient pain and swollen wrists are described in some single studies of nausea and vomiting (Lee and Done, 2004; Ezzo et al., 2005).

## 10. Discussion

There is good clinical evidence from more than 40 randomised controlled trials that acupuncture-point stimulation at P6 has some effect in preventing or attenuating nausea and vomiting. A growing number of experimental studies suggest mechanisms of action.

Of the four nausea and vomiting-related conditions explored in this review, the studies are the most robust with respect to postoperative nausea and vomiting. Data from 26 trials show that P6 reduces the risk of both nausea and vomiting at a level similar to medication; that benefits are consistent for both children and adults, and that invasive and noninvasive modalities are equally effective. Given this, the postoperative patient can select the least invasive modality such as acupressure bands or electrostimulation wristwatch-like devices. For those opting to apply acupressure with their fingers, the literature suggests that the benefits of acupressure last about two hours, and then must be reapplied. For surgical patients at high risk of nausea and vomiting, manual acupuncture at P6 applied by an experienced acupuncturist just before induction of anaesthesia might be the best way to achieve postoperative nausea and vomiting prophylaxis. The effect might be enhanced by electrical stimulation or use of



additional acupuncture points like St36. Because both are time consuming, these methods might not be applicable routinely in the perioperative setting.

Most postoperative nausea and vomiting trials to date have focused on P6 compared to sham, or P6 compared to medication, but not P6 added to medication. Future postoperative nausea and vomiting trials should ascertain whether acupoint stimulation *plus* medication is superior to either alone, especially for those patients at highest risk.

For chemotherapy-induced nausea and vomiting, unlike postoperative nausea and vomiting, the effectiveness of P6 stimulation appears to be modality dependent. Acupressure appears to reduce chemotherapy-induced acute nausea but not vomiting and, therefore, might offer a no-cost, convenient, self-administered intervention for chemotherapy patients to reduce nausea on the first day. However, given that these trials lacked a sham control, placebo effects cannot be ruled out. Interestingly, two of the pregnancy-related nausea and vomiting trials also showed significant benefits of acupressure compared to sham wristbands only for nausea but not vomiting (Bayreuther et al., 1994; Belluomini et al., 1994). Reasons for this discrepancy are unclear.

For chemotherapy-induced acute vomiting, only electroacupuncture was effective. However, while the effectiveness of electroacupuncture provides proof of principle, studies that combine electroacupuncture with state-of-the-art antiemetics are needed to determine if electroacupuncture can confer additional benefit to modern antiemetics and to refractory patients. For chemotherapy-induced nausea and vomiting, electrostimulation seemed to be no better than placebo (Ezzo et al., 2005).

The most conflicting results emerge in reviews of pregnancy-related nausea and vomiting (morning sickness) where dichotomous data showed a protective effect of P6 stimulation, but the continuous data did not. It is unclear what accounts for this inconsistency. More research needs to be done to ascertain dose, characteristics of responders, differences among modalities, or other factors that determine response.

Additional questions remain. What is the optimal site of stimulation? P6 is the most highly documented point, but Korean hand acupressure may be a promising alternative or adjunct. Other acupuncture points like St36 might be helpful adjuncts to P6 but need more investigation.

What is the optimal time of stimulation? For the prevention of postoperative nausea and vomiting, stimulation should be performed before induction of anaesthesia to enhance psychological effects. However, it is possible that treatment afterwards might sometimes be a better option, especially for children or patients with needle phobia. For chemotherapy-induced nausea and vomiting, stimulation is mostly performed before the application of chemotherapy and is repeated in between the treatments. For motion- and pregnancy-related nausea and vomiting, treatment with stimulation bands can be used prophylactically or after onset of first nausea and vomiting.

Further large, high-quality clinical trials are important to identify the clinical value of the method, the most practical and effective techniques, and identification of the kinds of patients who will benefit most.

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