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Acupuncture facilitates neuromuscular and oculomotor responses to skin incision with no influence on auditory evoked potentials under sevoflurane anaesthesia

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Background: More sevoflurane was recently found to be required to prevent movement in response to surgical incision in anaesthetized patients subjected to electro-acupuncture (EA) than to sham procedures. The present study was designed to compare differences in movement, dilatation of the pupils, divergence of the eye axes and activity of auditory evoked potentials (AEPs) between patients given and those not given EA under standardized sevoflurane anaesthesia.
Methods: Neuromuscular, oculomotor and AEP responses to skin incision were assessed with and without a bilateral 2-Hz burst EA in patients under steady-state anaesthesia maintained with 1.8% of sevoflurane. Forty-five healthy patients, scheduled for laparoscopic sterilization, were randomized for EA (n = 22) or sham (n = 23) procedures between induction of anaesthesia and start of surgery. Middle latency AEP activity was recorded and interpreted by the A-line ARX (autoregression with exogenous input) index (AAI).
Results: More acupuncture than sham patients were found to respond to skin incision with movement of the neck or limbs (77% vs. 43%; $P = 0.021$), dilatation of the pupils (77% vs. 39%; $P = 0.001$) and divergence of the eye axes (72% vs. 39%; $P = 0.023$), whereas there was no difference in AAI response.
Conclusion: Electro-acupuncture facilitates physiological responses to nociceptive stimulation under sevoflurane anaesthesia. Differences in neuromuscular and oculomotor responses between acupuncture and sham patients under general anaesthesia are probably not associated with interaction between EA and the depth of anaesthesia, as AEP activity was similar in the two groups.

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Key words: Acupuncture; anaesthesia, inhalational; auditory evoked potentials; minimal alveolar concentration; pain; sevoflurane, surgery.

Double-blind clinical studies on acupuncture vs. sham procedures have to be carried out under general anaesthesia despite the risk of pharmacodynamic interaction of anaesthetic drugs with acupuncture. Electro-acupuncture (EA) failed to attenuate physiological responses to incision under general anaesthesia in two recent studies of patients (1) and volunteers (2) and even more volatile anaesthetic was found to be required to prevent motor response to skin incision in the latter study.

The present double-blind randomized study was designed to compare physiological and auditory evoked potential (AEP) responses to skin incision in anaesthetized patients subjected to EA or sham procedures.

Methods

Following approval by the Human Research Ethics Committee of the Medical Faculty, Lund University, Sweden, we included 46 adult female patients admitted for endoscopic sterilization at the Department of Gynaecology and Obstetrics at Helsingborg Hospital, Sweden.

Exclusion criteria were ASA (American Society of Anaesthesiologists) physical status III or IV, regular use of analgesics, body mass index greater than $35\,kg\,m^{-2}$ and language difficulties. All patients received written and oral information at home in advance by mail and telephone and had given written consent to participate in the study. They were prepared for surgery according to the clinical routines of the department, but received no premedication.

Adhesive, transparent dressing with securing tape (Tegaderm™, 3M Health Care, Borken, Germany) was applied onto the skin at all acupuncture points possibly stimulated after induction. A vertical drape was used to prevent the anaesthesia nurse, positioned at the head, from observing the rest of the patient (Fig. 1). After induction of anaesthesia using a face-mask with 6–8% of sevoflurane in 6 l min^{-1} of oxygen, the patients were subjected to either EA (n = 23) or sham (n = 23) procedures according to a list designed by randomization in blocks of 10. Anaesthesia was maintained by facemask with sevoflurane in an oxygen-air mixture containing 30–40% of oxygen.

In acupuncture patients, stainless steel EZY-5 (Carbo Trading Co. Inc, Scarborough, Ontario, Canada) acupuncture needles (dimension 25G, length 25 mm) were inserted intramuscularly to a depth of 5–15 mm. An ACUS II stimulator (Cefar Medical AB, Lund, Sweden) was used to generate a square pulse pattern with alternating polarity (duration 180 ms, intensity 2 mA, burst frequency 2 Hz including 80 Hz of frequency pulse-trains), previously found to be well-tolerated by conscious volunteers (unpublished observations, NK, October 2001). Bilateral stimulation was given at three pairs of acupuncture points – LI4 (hegu) and PC6 (ximen) [to avoid accidental and unattended puncture of the radial nerve in these anaesthetized patients, a point located approximately 1 cm radial to the traditional point PC6 was stimulated with penetration to periosteal tissue of the radial bone (3)], ST36 (zusanli) and SP9 (yinlingquan), LR3 (taichong) and SP6 (sanyinjiao) (Fig. 1). These acupuncture points were chosen for their general analgesic potency according to traditional Chinese principles of EA under anaesthesia (personal communication from anaesthesiologist active during The Cultural Revolution in China, wishing to be anonymous, 2001).

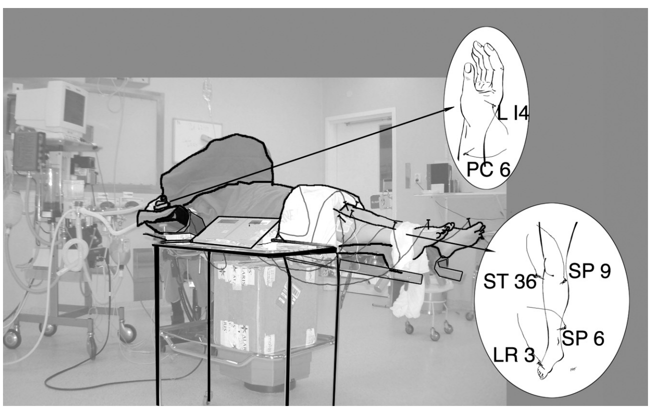

Fig. 1. Clinical set-up with study patient in the operating room. Acupuncture points are shown in circles.

In the sham patients, the electrodes were taped onto the skin, without needle insertion, at the above-mentioned points. The electrodes were not connected to the EA device during the sham procedures. The EA and sham procedures were continued for approximately 20 min, allowing the alveolar concentration to reach a steady-state level, defined as a difference of 0.2% or less between inspiratory and expiratory concentrations of sevoflurane. The steady-state expiratory sevoflurane concentration of 1.8% attained in all patients has been found to abolish half of all neuromuscular responses to surgical incision in a similar recent study (1) in agreement with previous finding in patients aged 20–40 years (4). All electrodes (together with needles in acupuncture patients) were removed immediately after the completed stimulation, and the acupuncture points were covered with Band-Aids.

Physiological reactions to skin incision in terms of neck or limb movements, pupil dilatation and divergence of the eye axes were assessed by an independent observer who was not allowed to enter the operation room until immediately before the start of surgery. Corresponding heart rate and blood pressure responses were recorded by an S-5 anaesthesia monitor (Datex Ohmeda, Helsinki, Finland).

Bilateral click sound stimuli of 65-dB sound pressure level intensity, 2-ms duration and 9-Hz repetition rate were delivered through a pair of headphones. The AEP signals were detected by three silver/silver chloride electrodes (A-Line™, Danmeter AS, Odense, Denmark) – positioned at the median forehead (positive), left mastoid (negative) and left forehead (reference) – and continuously recorded with an AEP monitor (Alaris Medical Systems Inc., San Diego, CA). Mid-latency 4-Hz AEP signals were extracted from the electroencephalogram (EEG) by autoregression with exogenous input (ARX) modelling (5, 6). Changes in mid-latency AEP, reported to correlate with the depth of anaesthesia (5–9), are reflected by the A-Line ARX index (AAI). The AEP signals were recorded throughout the anaesthetic period in the last 35 patients included and later analyzed in 32 of them (16 belonging to each group) by subtracting the average AAI level before the incision from the maximal value immediately after the incision. One patient was excluded because the first page of her records was lost postoperatively, and the AEP recordings could not be adequately interpreted in a further two patients because of technical disturbances.

In all patients the same two investigators were responsible for the induction and initial maintenance of anaesthesia (CC) and for the acupuncture or sham procedures (NK, an experienced acupuncturist).

Surgery was then carried out under general intubation anaesthesia including propofol, fentanyl, nitrous oxide and sevoflurane according to established local clinical guidelines.

Results are given as mean $\pm$ 1 standard deviation (SD) for parametric data and as median with 25th and 75th percentiles in parenthesis for non-parametric data. Parametric variables were analyzed with unpaired two-sided Student's *t*-test. Differences in non-parametric variables were analyzed with the Mann–Whitney *U*-test. The SPSS software for Windows, release 11.0.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analyses. The level of statistical significance was set at $P < 0.05$.

Results

The mean age of the acupuncture patients was 35 ± 5 years and for the sham patients 38 ± 5 years, with body mass index values of 23.2 ± 3.0 and 24.7 ± 3.2 kg m^{-2}, respectively. The duration of the acupuncture and sham procedures was 21 ± 1 and 23 ± 3 min, respectively.

There were no significant differences in the responses of the mean arterial pressure and heart rate to skin incision between the study groups (Table 1).

Skin incision was associated with head or major limb movements, pupil dilation and with divergence of the eye axes in more of the acupuncture than sham patients (Figs 2–4). Of those patients with dilatation of the pupils and divergence of the eye axes, 76% had both responses simultaneously.

The difference in median AAI change in response to skin incision between acupuncture and sham patients, 20 (6, 31) and 10 (2, 40), respectively, was found to be statistically non-significant ($P = 0.59$).

The mean difference between the inspiratory and expiratory concentrations of sevoflurane at steady-state was 0.2 ± 0.1% at an expiratory concentration of 1.8%.

Discussion

The main finding of this study is that the anaesthetized patients given EA reacted more to the surgical incision than those subjected to sham procedures. This does not seem to correlate with the depth of anaesthesia, as there was no difference between the study groups in AEP activity.

In the present study, acupuncture patients – exposed to the same concentration of sevoflurane as sham patients – reacted more to skin incision with respect to movements of the neck and limbs, dilatation of the pupils and divergence of the eye axes. These results are in agreement with those of a recent double-blind randomized study of similar design (1), where more sevoflurane was found to be required to prevent physiological responses to surgical incision in patients given EA than in sham patients. In contrast, no difference in the minimal alveolar concentration of desflurane was found between the volunteers subjected to the acupuncture or sham procedures before noxious skin stimulation in another double-blind randomized cross-over study (2). Major differences in study design may explain these divergent findings.

In the present and previous (1) studies in patients anaesthetized with sevoflurane, the effect of EA given at three pairs of acupuncture points – ST36 + SP9 and LR3 + SP6 on the legs, and LI4 + PC6 on the arms – for approximately 20 min was assessed from physiological responses to abdominal skin incision, i.e. far from the points stimulated. In the present study, EA was given as a bilateral 2-Hz burst stimulation with 2.0-mA intensity. In the previous clinical study (1) patients had unilateral continuous 2-Hz stimulation with 2.5-mA intensity.

In another study (2) in volunteers anaesthetized with desflurane, the effect of EA stimulation at three acupuncture points on the legs – ST 36, GB 38 and BL 60 – during a period of time not reported was

Table 1

Changes in mean arterial pressure and heart rate in response to skin incision in the study groups.

	Acupuncture group (n = 22)	Control group (n = 23)	*P*-value
Baseline mean arterial pressure before skin incision (mmHg)	80 ± 9.0	78 ± 10	0.47
Change of mean arterial pressure on skin incision (mmHg)	2.6 ± 1.3	7.1 ± 12	0.23
Baseline heart rate before skin incision (min^{-1})	82 ± 19	73 ± 12	0.082
Change of heart rate on skin incision (min^{-1})	18 ± 15	17 ± 23	0.92

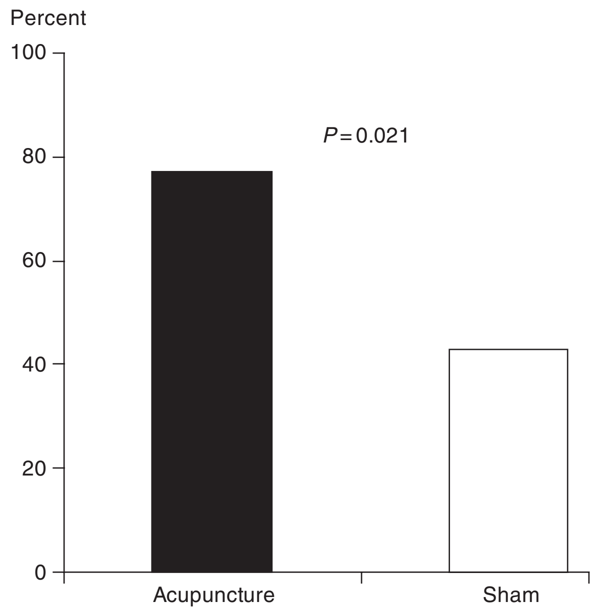

Fig. 2. Movement of the head or limbs in response to skin incision in the study groups.

assessed from the physiological response to repeated local noxious electrical stimulation at the thigh, i.e. close to the points used for EA stimulation. The EA was given as a bilateral mixed 2-Hz and 100-Hz stimulation with 2-mA initial intensity, which was then gradually increased to a level just below that inducing muscle contractions, but the final level of EA intensity is not reported.

We believe that special emphasis should be drawn to the mode of stimulation applied in these studies on EA. Simultaneous use of alternating bursts of

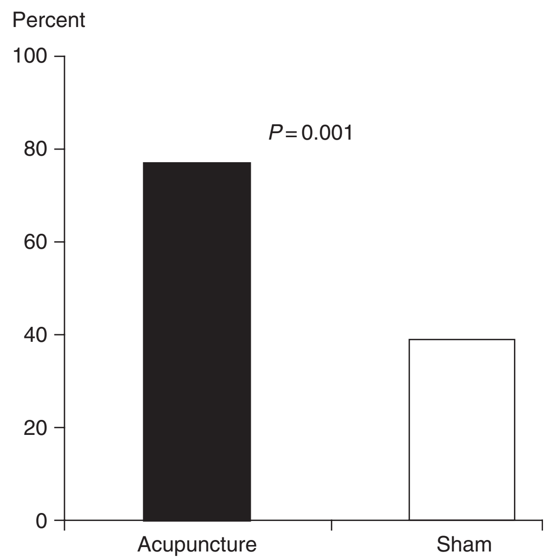

Fig. 3. Dilatation of the pupils in response to skin incision in the study groups.

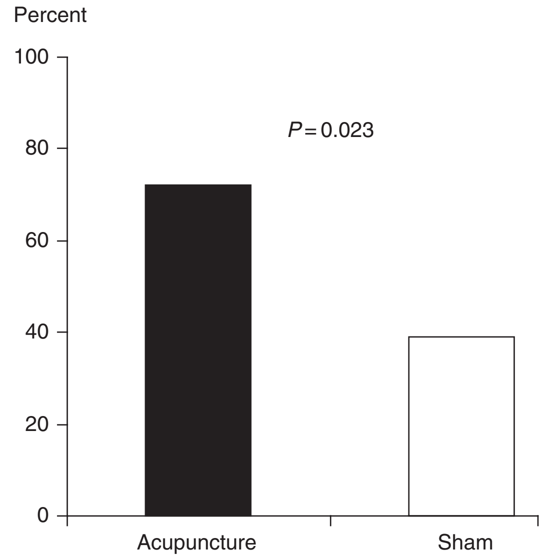

Fig. 4. Divergence of the eye axes in response to skin incision in the study groups.

low-frequency and high-frequency stimulation, as in the study by Morioka et al. (2), might promote the activation of different receptor systems in the CNS. Low-frequency (2 Hz) stimulation has been found to mediate analgesia by activating μ-receptors, whereas high-frequency (100 Hz) stimulation has been reported to activate κ-receptors in two studies on EA in animals (10, 11) as well as in a study on transcutaneous electrical nerve stimulation (TENS) in humans (12). Combined high- and low-frequency stimulation under general anaesthesia might activate different endogenous transmitter systems in the CNS, which under these circumstances could have opposing effects on the response to nociceptive stimulation. It is possible that a more generalized and mainly algesic effect of low-frequency stimulation on nociception under general anaesthesia – indicated by the results obtained in the present and previous (1) studies – is counteracted by a more localized and mainly analgesic effect of high-frequency stimulation (2) under general anaesthesia.

Low-frequency burst EA under general anaesthesia could be assumed to facilitate nociception by promoting the release of endogenous opioid antagonists, as EA has been reported to be associated with increased levels of these compounds (13). Lack of attenuation of nociceptive stimulation could also be explained by no or delayed release of endogenous opioid agonists. Nonetheless, increased levels of endogenous opioid agonists have been found within 20 min of low-frequency EA stimulation (14, 15), i.e. the duration of EA or sham procedures chosen in the present and previous (1) studies. Either procedure was interrupted immediately before skin incision to allow the observer to evaluate physiological responses under blinded conditions, and the antinociceptive effects of low-frequency EA have been reported to persist for up to 30 min after stimulation (15–17). Based on available reports (14–17) the study design used here, in which low-frequency EA stimulation was maintained over a 20-min period, followed by skin incision within a few minutes, would allow physiological responses to nociceptive stimulation including possible changes in endorphin levels to be adequately compared between patients given and those not given EA.

Another possible explanation for the different results obtained in our present and previous studies (1) compared with those obtained by Morioka et al. (2) is the difference in distance between EA and noxious stimulation. In our studies, patients in the acupuncture groups were given low-frequency EA far from the site of surgical nociceptive stimulation, whereas in the study by Morioka et al. (2), volunteers were given high- and low-frequency EA close to the site of electrical nociceptive stimulation. It cannot be excluded that the high-frequency component of EA applied at the site of nociceptive stimulation (2) by involving the gate control mechanism might counteract the algesic effects of low-frequency stimulation reported in the present and previous (1) studies.

Anaesthetized patients given EA at the ear together with TENS have been found to require less fentanyl than control patients to maintain a similar heart rate and mean arterial pressure during retroperitoneal lymph node dissection (18). It is tempting to presume that TENS rather than EA was responsible for the reduced peroperative use of opioids found in these patients, particularly considering that abolished or even opposed antinociceptive effects of acupuncture alone have been found under general anaesthesia in the present and previous (1, 2) studies. Accordingly, less anaesthetic gas has been reported to be required during high-frequency TENS than during sham procedures in two randomized double-blind studies, where the electrodes were placed either regionally during hand surgery (19) or in front of the ear during experimentally induced pain (20). The beneficial effect in the latter study is somewhat surprising, considering that TENS electrodes were applied far from the site of noxious stimulation. It cannot be excluded that electrostimulation of cranial nerves (20) may differ from that involving spinal dermatomes (1,2) with respect to general antinociceptive effects.

The lack of an antinociceptive effect of acupuncture in anaesthetized patients and volunteers in the present and two previous (1, 2) studies is in agreement with findings in anaesthetized patients given acupuncture to prevent emesis (21–24). Although an antiemetic effect of P6 acupuncture was found by Vickers in a meta-analysis of 33 clinical studies in the mid-nineties (25), he simultaneously proposed a lack of antiemetic effect of acupuncture given under general anaesthesia.

In the present study, differences between the study groups regarding major movements of the head or limbs, dilatation of the pupils and divergence of the eye axes in response to skin incision were found not to be associated with a corresponding difference in the AAI level reflecting AEP activity. It has recently been shown that an AAI value of less than 30 is associated with an anaesthetic level of sevoflurane found to abolish a neuromuscular response to surgical incision in virtually all patients (8). Provided that AEP activity reliably reflects the depth of sevoflurane anaesthesia (5, 7–9), there is no considerable interaction of acupuncture with the anaesthetic effect of sevoflurane. Our results suggest that mechanisms by which acupuncture facilitates neuromuscular and oculomotor responses to nociceptive stimulation under sevoflurane anaesthesia do not include reduction of the anaesthetic depth produced by the volatile agent itself.

In conclusion, we have shown that bilateral 2-Hz burst stimulation with EA under general anaesthesia facilitates various physiological responses to skin incision. The present study indicates that these facilitated responses seem not to result from a reduced anaesthetic depth reflected by the AAI level or from contralateral hyperalgesia following ipsilateral stimulation. Further studies on mechanisms by which electro-stimulation facilitates physiological responses to noxious stimulation under general anaesthesia are needed.

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References

1. Kvorning N, Christiansson C, Beskow A, Bratt O, Åkeson J. Acupuncture fails to reduce but increases anaesthetic gas required to prevent movement in response to surgical incision. *Acta Anaesthesiol Scand* 2003; **47**: 818–22.
2. Morioka N, Akca O, Doufas AG, Chernyak G, Sessler DI. Electro-acupuncture at the Zusanli, Yanglingquan, and Kunlun points does not reduce anesthetic requirement. *Anesth Analg* 2002; **95**: 98–102.
3. Mann F. *Textbook of Acupuncture*. Oxford: Heinemann Medical, 1987.
4. Mapleson WW. Effect of age on MAC in humans: a meta-analysis. *Br J Anaesth* 1996; **76**: 179–85.
5. Alpiger S, Helbo-Hansen HS, Jensen EW. Effect of sevoflurane on the mid-latency auditory evoked potentials measured by a new fast extracting monitor. *Acta Anaesthesiol Scand* 2002; **46**: 252–6.
6. Litvan H, Jensen EW, Revuelta M et al. Comparison of auditory evoked potentials and the A-line ARX Index for monitoring the hypnotic level during sevoflurane and propofol induction. *Acta Anaesthesiol Scand* 2002; **46**: 245–51.
7. Litvan H, Jensen EW, Galan J et al. Comparison of conventional averaged and rapid averaged, autoregressive-based extracted auditory evoked potentials for monitoring the hypnotic level during propofol induction. *Anesthesiology* 2002; **97**: 351–8.
8. Kurita T, Doi M, Katoh T et al. Auditory evoked potential index predicts the depth of sedation and movement in response to skin incision during sevoflurane anesthesia. *Anesthesiology* 2001; **95**: 364–70.
9. Thornton C. Evoked potentials in anaesthesia. *Eur J Anaesthesiol* 1991; **8**: 89–107.
10. Chen XH, Han JS. Analgesia induced by electroacupuncture of different frequencies is mediated by different types of opioid receptors: another cross-tolerance study. *Behav Brain Res* 1992; **47**: 143–9.
11. Huang C, Wang Y, Han JS, Wan Y. Characteristics of electroacupuncture-induced analgesia in mice: variation with strain, frequency, intensity and opioid involvement. *Brain Res* 2002; **945**: 20–5.
12. Han JS, Chen XH, Sun SL et al. Effect of low- and high-frequency TENS on Met-enkephalin-Arg-Phe and dynorphin A immunoreactivity in human lumbar CSF. *Pain* 1991; **47**: 295–8.
13. Han JS. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. *Trends Neurosci* 2003; **26**: 17–22.
14. Kitade T, Odahara Y, Shinohara S et al. Studies on the enhanced effect of acupuncture analgesia and acupuncture anesthesia by D-phenylalanine (2nd report) – schedule of administration and clinical effects in low back pain and tooth extraction. *Acupunct Electrother Res* 1990; **15**: 121–35.
15. Romita VV, Suk A, Henry JL. Parametric studies on electroacupuncture-like stimulation in a rat model: effects of intensity, frequency, and duration of stimulation on evoked antinociception. *Brain Res Bull* 1997; **42**: 289–96.
16. Chung JM, Fang ZR, Hori Y, Lee KH, Willis WD. Prolonged inhibition of primate spinothalamic tract cells by peripheral nerve stimulation. *Pain* 1984; **19**: 259–75.
17. Chung JM, Lee KH, Hori Y, Endo K, Willis WD. Factors influencing peripheral nerve stimulation produced inhibition of primate spinothalamic tract cells. *Pain* 1984; **19**: 277–93.
18. Kho HG, Eijk RJ, Kapteijns WM, van Egmond J. Acupuncture and transcutaneous stimulation analgesia in comparison with moderate-dose fentanyl anaesthesia in major surgery. Clinical efficacy and influence on recovery and morbidity. *Anaesthesia* 1991; **46**: 129–35.
19. Bourke DL, Smith BA, Erickson J, Gwartz B, Lessard L. TENS reduces halothane requirements during hand surgery. *Anesthesiology* 1984; **61**: 769–72.
20. Greif R, Laciny S, Mokhtarani M et al. Transcutaneous electrical stimulation of an auricular acupuncture point decreases anesthetic requirement. *Anesthesiology* 2002; **96**: 306–12.
21. Weightman WM, Zacharias M, Herbison P. Traditional Chinese acupuncture as an antiemetic. *Br Med J (Clin Res Ed)* 1987; **295**: 1379–80.
22. Dundee JW, Milligan KR, McKay AC. Influence of intraoperative acupuncture and droperidol on postoperative emesis. *Br J Anaesth* 1988; **61**: 117–8.
23. Yentis SM, Bissonnette B. P6 acupuncture and postoperative vomiting after tonsillectomy in children. *Br J Anaesth* 1991; **67**: 779–80.
24. Yentis SM, Bissonnette B. Ineffectiveness of acupuncture and droperidol in preventing vomiting following strabismus repair in children. *Can J Anaesth* 1992; **39**: 151–4.
25. Vickers AJ. Can acupuncture have specific effects on health? A systematic review of acupuncture antiemesis trials. *J R Soc Med* 1996; **89**: 303–11.

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