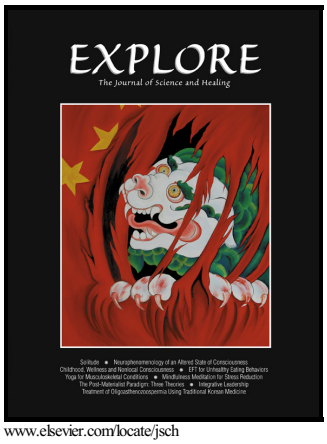

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EFFECTS OF ELECTROACUPUNCTURE ADMINISTERED 24HOURS PRIOR TO SURGERY ON POSTOPERATIVE NAUSEA AND VOMITING AND PAIN IN PATIENTS UNDERGOING GYNECOLOGIC LAPAROSCOPIC SURGERY: A FEASIBILITY STUDYPRE-OPERATIVE ELECTROACUPUNCTURE TO PREVENT PONV: A FEASIBILITY STUDY

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Effects of electroacupuncture administered 24 hours prior to surgery on postoperative nausea and vomiting and pain in patients undergoing gynecologic laparoscopic surgery: A feasibility study

Running title: pre-operative electroacupuncture to prevent PONV: a feasibility study

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Contribution

MZ and SL initiated the concept and developed the study protocol. JG , FBJ, ZZ contributed to the development of the detailed protocol. JG interviewed all participants. WZW delivered acupuncture. ZZ analysed the data, contributed to data interpretation. SL drafted the manuscript and all other authors commented on the drafts and approved the final version.

Key words: Electroacupuncture; Postoperative nausea and vomiting; post-operative pain, post-operative recovery, Gynecologic laparoscopic surgery

Abstract

Objective: Our study aimed to investigate the feasibility and effectiveness of preoperative electroacupuncture (EA), delivered 24 hours before surgery, on postoperative nausea and vomiting (PONV) and postoperative pain in patients undergoing gynecologic laparoscopic surgery.

Methods: In this randomized controlled trial, 40 patients scheduled for elective gynecologic laparoscopic surgery, were randomly assigned to the usual care (UC) group and the EA group (n=20 each). Both groups received the routine treatment consisting of intravenous Dexamethasone (5 mg) after induction of anesthesia and intravenous Tropisetron(5 mg) before the end of the operation. Those in the EA group received EA at bilateral Neiguan (PC6) and Zusanli (ST36) within 24 hours prior to the surgery. The incidence and severity of PONV and pain were recorded at 6hours, 12hours, and 24 hours after the operation. Time to first

flatus passage was also recorded. Bonferroni-corrected independent sample t-tests were used to analyse the data.

Results: In the first 6 hours after surgery, 15% and 20% of the patients experienced postoperative nausea in the EA and the UC groups, respectively. The incidences of postoperative vomiting were 5% for the EA group and 20% for the UC group. PONV reduced to zero over 12 hours in both groups and there was no statistically significant difference in PONV between the two groups at any time point. The EA group rated their postoperative pain statistically significantly lower than the UC group did at 6 hours postoperative (EA: 1.9 ± 0.8; UC: 2.9 ± 0.9, p = 0.001).The two groups did not differ in pain at 12 and 24 hours. The EA group had a shorter time to pass first flatus than the UC group did (EA: 20.3 hours ± 6.1; UC: 26.4 ± 5.2, p = 0.002). The common EA related adverse effects were minor, and did not require medical attention. The patients tolerated the EA treatment well.

Conclusion: It is feasible and safe to deliver one-session EA treatment within 24 hours preoperatively to preempt postoperative pain. One-session preoperative EA may also accelerate motility of the gastrointestinal track. Properly powered studies are needed to further test the effectiveness of preoperative EA on PONV.

Key words Electroacupuncture; Postoperative nausea and vomiting; Gynecologic laparoscopic surgery

Introduction

Postoperative nausea and vomiting (PONV) is one of the commonest complications after surgery under general anaesthesia. The incidence of PONV after inhalation anaesthetics is up to 30% when prophylaxis are not offerred.[1] The incidence reaches 70–80% in high-risk patients.[2] Women undergoing laparoscopic gynaecological surgery are at a high risk for PONV. Previous studies showed that in the absence of prophylactic antiemetics, the incidence of PONV in this cohort was 40% to 85%.[3,4,5]

Though self-limiting, PONV can cause significant morbidity including bleeding, aspiration pneumonia, electrolyte imbalance, suture tear, and psychological stress.[1,6,7] In addition, severe PONV often results in delayed recovery and increased costs to the individuals and to the health care system.[8,9] Although the management guidelines about PONV have been

established,[10] incidence of PONV is still high at 40% on average, largely due to inadequate PONV prevention and management. [7,11]

Classical treatments about PONV are mainly pharmaceutic, including 5-HT3 receptor antagonists, NK-1 receptor antagonists, corticosteroids, butyrophenones, antihistamines, anticholinergic and phenothiazines.[12] Antiemetic drugs, even in lower doses, may be associated with adverse effects such as affecting the QTc interval, visual disturbances, dry mouth, dizziness.[10,13] Furthermore they only have moderate effects on patients at high risk for PONV.[14] Women undergoing laparoscopic gynaecological surgery are at moderate to high risk for PONV, and the incidence is about 55% although preventative measures are applied.[3]

Increasing evidence supports the use of non-pharmacological techniques, such as acupuncture, in postoperative care.[14] Lee et al.[15] reported that PC6 acupoint stimulation was as effective as standard antiemetic drugs in reducing the incidence of nausea and vomiting. High quality systematic reviews conclude that acupuncture for PONV is effective, safe and of a low cost, and has been included in an international management guideline for PONV as the only non-pharmacological intervention.[10,16,17] However, optimal acupuncture for PONV as a prophylactic and as a treatment is not yet established. It is not clear when the best time for acupuncture is, that is preoperative, perioperative or postoperative.[16]

To prevent PONV, acupuncture should be administered preoperatively or intraoperatively. For the safety concern, it is ideal to provide acupuncture preoperatively on conscious patients as PC6 is directly on the medial nerve, and deep needling on un-conscious patients could damage the nerve. In many studies acupuncture was delivered 30 minutes before surgery.[14,18,19] This mode of delivery has its disadvantages due to limited time prior to surgery and patients could be nervous about the coming surgery. Delivering acupuncture the day before the surgery has its advantage as the patients are more relaxed, and are likely to benefit from acupuncture. A previous study showed that acupuncture one day prior to surgery produced better pain reduction than acupuncture given 30 min prior to the surgery. [20]It is not known whether acupuncture with standard prophylactic anti-emetics would provide additional benefits in reducing PONV when delivered the day before the surgery.

Our study aimed to: 1) investigate the feasibility of preoperative EA, delivered 24 hours before surgery, on PONV and postoperative pain in patients undergoing gynecologic

laparoscopic surgery. Specifically we looked at the acceptability of both the participants and the acupuncturist, when EA delivered 24 hours before surgery; 2) determine the effect size of the intervention to enable sample size calculation.

Materials and methods

Study design

This feasibility study was approved by the Human Research Ethics Committee of the Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, and conducted at the Affiliated Hospital of Nanjing University of Traditional Chinese Medicine between October 2015 and February 2016, Nanjing, Jiangsu Province, China（2016NL-019-02）.

The study procedure and method of EA were explained to the patients. Written informed consent was obtained from each patient prior to their participation in the study.

Selection Criteria

Inclusion criteria were: female patients (age 18–50 yr), ASA physical status class I or II, nonsmoking, undergoing elective gynaecological laparoscopic surgery under general anaesthesia, an operating time below 3 hours.

Exclusionary criteria were: pregnancy or breastfeeding; use of antiemetics, emetogenic drugs, opioids, or glucocorticoids within 3 days prior to surgery; known allergy to tropisetron or dexamethasone; nausea, vomiting, or both within 24 h before surgery; mental retardation, psychiatric, or neurological disease; wearing a cardiac pacemaker, cardioverter, or defibrillator; rash or local infection over the skin area of selected acupoints. We also excluded those who developed intraoperative drug allergy, converted to open procedures.

Randomization and blinded

An independent researcher used a random number table to generate

the randomization sequence. Each number was printed on a piece of paper, which was then put in an opaque sealed envelope. All envelopes were stored in a locked cabinet. Each eligible participant picked an envelope from the lot after baseline data collection was completed. Forty patients were randomly assigned to the following two groups: the usual care (UC) group and the EA group (n=20 each).

The patients, the surgeons, the anesthetist, and the investigator collecting the data were all blinded to the group allocation.

Description of Intervention

Electroacupuncture group

Participants in the EA group received EA at bilateral Neiguan (PC6) and Zusanli (ST36) within 24 hours prior to the surgery in the genecology ward. The acupuncture needles used in this study were stainless steel needles (Suzhou Medical Supplies Factory Co. Ltd,0.30x40 mm, China), and electrical stimulation was applied once for 30 minutes with the dense-disperse stimulation mode (20-100 HZ) using a stimulator (XS-998B, Nanjing Xiaosong Medical Instrument Research Institute, Nanjing , China). The intensity of stimulation was adjusted at strong but comfortable level as judged by the patients. The EA was delivered by a registered acupuncturist. The treatment was to be halted if participants reported discomfort or dizziness. No such adverse events occurred during the treatment, and none of the participants dropped out from the study. Data of all the participants were available for analysis.

Usual care group

UC was provided to both UC group and EA groups. Patients in the UC group received no EA. A standardized anaesthetic protocol was applied to all participants. One anaesthetist, who was blinded to the group allocation, provided the UC to all participants. All patients fasted for 8 h before anaesthesia. General anaesthesia was induced with midazolam 0.05 mg/kg i.v., propofol2–3 mg/kg i.v., sufentanil 0.2–0.4μg/kg i.v., vecuronium 0.1 mg/kg i.v., and lidocaine 1 mg/kg i.v. After induction, dexamethasone 5 mg i.v. was administered. Anaesthesia was maintained with intravenous infusion of propofol, sufentanil and vecuronium. Standard monitoring procedures were followed, including ECG, non-invasive blood pressure, pulse oximetry, end-tidal CO_2. Lactated Ringer's solution was given i.v. based on calculated preoperative deficits, surgical procedure, and estimated intraoperative blood loss. Laparoscopies were performed with CO_2 insufflation. All patients were placed in the Trendelenburg position. Patients' respiratory rate was adjusted to maintain normocapnia (end-tidal CO_2 between 4.3 and 5.1 kPa) as their lungs were mechanically ventilated. At the end of surgery, Parecoxib 40 mg i.v. was given for postoperative analgesia. Tropisetron 5 mg was administered i.v. at the end of skin closure for prophylaxis of PONV. Neostigmine 0–5 mg and atropine 0–2.5 mg were used to reverse the residual muscle relaxant effects.

Outcome Measures

The incidence and severity of PONV and pain were recorded at 6hours, 12hours, and 24 hours after the operation. The severity of PONV was rated using a validated four-point rating scale score(from 0= no nausea or vomiting to 3=the worst imaginable nausea or vomiting) [21] and pain was rated using a numerical rating scale with 0 indicating no pain and 10 the worst pain possible. Time to first flatus passage was also recorded. Recruitment rate and withdrawals were recorded. All the outcome measures were recorded by an independent research nurse, who was not involved in the management of patients and blinded to the group allocation. Adverse events of EA were recorded by the acupuncturist.

Statistical analysis

Statistical Package for Social Sciences for Windows (SPSS) V.19.0 was used to analyze the data. Bonferroni-corrected independent sample t-tests were employed to compare demographic data and baseline data between the two groups.

Results

A total of 43 patients were assessed for eligibility. Forty were admitted to the study and were randomized. All completed the study. None of the patients withdrew from the study. The study flow chart is depicted in Figure 1.

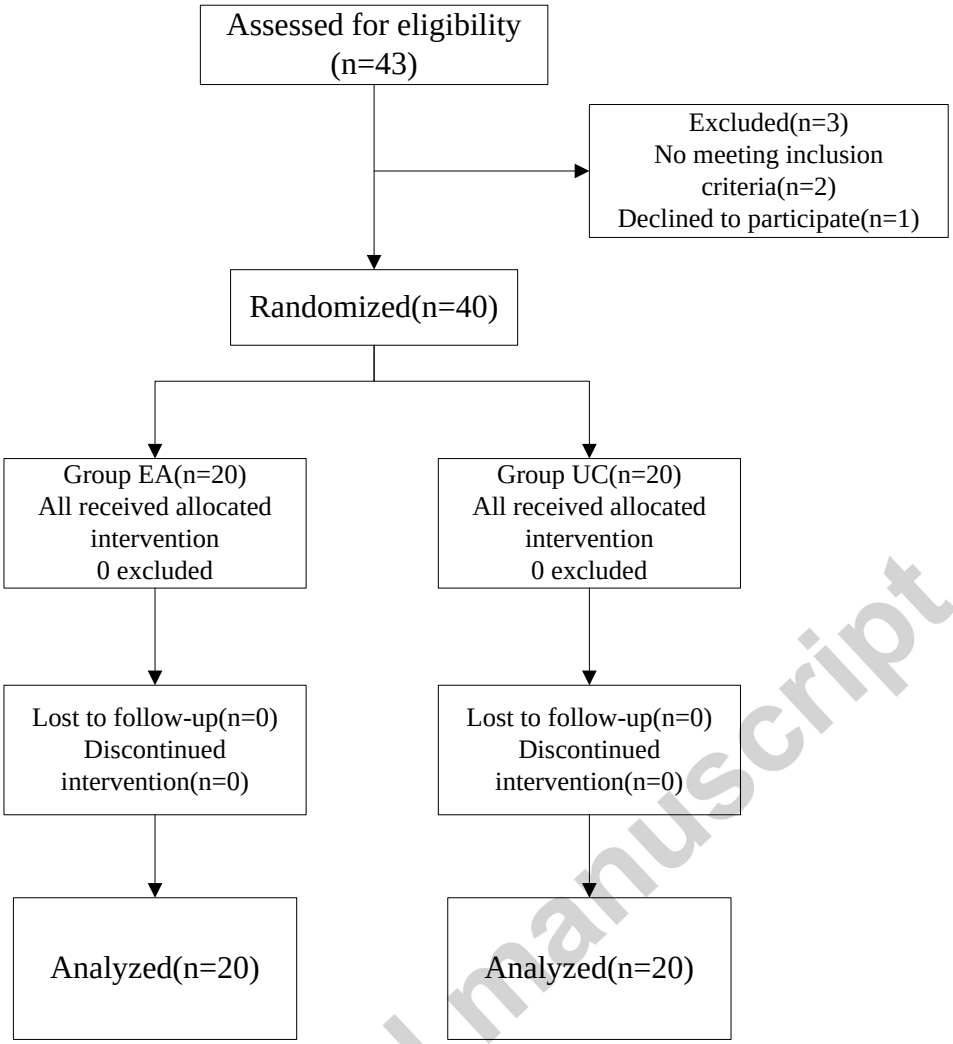

Figure 1 Flow chart of participants throughout the study. Three patients were excluded from the study because breastfeeding, use of antiemetics within 3 days prior to surgery, decided to open procedures before surgery.

The age and surgical and anaesthesia related information are presented in Table 1. The groups were comparable on demographic data, surgery- and anaesthesia-related profiles. (Table 1).

Table 1 Patient age and perioperative variables. (Mean（SD）orn(%).

Variable	Group EA(n=20)	Group UC(n=20)	P-value
Preoperative factors			
Age (yr)	35.2（6.1）	34.4（9.1）	0.745
Surgical and anaesthesia-related information			

Type of surgery			
Hysteromyomectomy (n(%))	12（60%）	10（50%）	0.537
Ovariocystectomy (n(%))	8（40%）	10（50%）	0.525
Duration of anaesthesia(min)	89.3（38.9）	95.5（32.8）	0.586
Duration of surgery (min)	75.5（38.4）	78.5（31.2）	0.788
Intraoperative sufentanil（μg）	36.5（6.7）	34.5（4.8）	0.286
I.V. fluid (ml)	1140（377.5）	1110（249.0）	0.768

EA: electroacupuncture; UC: usual care.

In the first 6 hours after surgery, 15% and 20% of the patients experienced postoperative nausea in the EA and the UC groups, respectively. The incidences of postoperative vomiting were 5% for the EA group and 20% for the UC group. PONV reduced to zero over 12 hours in both groups and there was no statistically significant difference between the two groups at any time point. There was no difference in the use of anti-emetics or pain medications between the two groups (Table 2).

Table 2 Postoperative nausea and vomiting scores, pain scores and time to first flatus passage after surgery. (mean (SD) .

Variable	Group EA (n=20)	Group UC(n=20)	P-value
0-6h after surgery			
Nausea [mean(SD)]	0.2（0.5）	0.4（0.9）	0.307
Vomiting [mean (SD)]	0.1（0.2）	0.3（0.8）	0.120
Nausea [incidence;n(%)]	3（15%）	4（20%）	0.677
Vomiting[incidence;n(%)]	1（5%）	4（20%）	0.151
Pain [mean (SD)]	1.9（0.8）	2.9（0.9）	0.001*
6-12h after surgery			
Nausea [mean(SD)]	0（0）	0.1（0.5）	0.324
Vomiting [mean (SD)]	0（0）	0.25（0.8）	0.163
Nausea [incidence;n(%)]	0(0)	1(5%)	0.311
Vomiting[incidence;n(%)]	0(0)	2(10%)	0.147
Pain [mean (SD)]	0.9（1.0）	1.75（1.6）	0.054
12-24h after surgery			

Nausea [mean(SD)]	0（0）	0（0）	
Vomiting [mean (SD)]	0（0）	0（0）	
Nausea [incidence;n(%)]	0（0）	0（0）	
Vomiting[incidence;n(%)]	0（0）	0（0）	
Pain [mean (SD)]	0.3（0.4）	0.4（0.6）	0.547
Time to first flatus passage [h; mean(SD)]	20.3（6.1）	26.4（5.2）	0.002*
Anti-emetics 0–48 h after surgery [n (%)]	0（0）	0（0）	
Analgesics 0–48 h after surgery [n (%)]	0（0）	0（0）	

EA: electroacupuncture; UC:usual care; PONV, postoperative nausea and vomiting.

*statistically significant difference between EA and UC

The EA group rated their postoperative pain statistically significantly lower than the UC group did at 6 hours post-surgery .The two groups did not differ in pain at 12 and 24 hours (Table 2). The EA group had a shorter time to pass first flatus than the UC group did.

Only one participant in the EA group reported pain at the needling sites and bruising. The incident was minor, and did not require medical attention. All patients tolerated the EA treatment well.

Discussion

The results of this study suggest that using the EA treatment in patients undergoing gynecologic laparoscopic surgery, delivered 24 hours before surgery, is not only feasible but also safe, and it has a multi-dimensional effect on postoperative recovery. One-session preoperative EA may reduce early pain after operation, reduce PONV, accelerate motility of the gastrointestinal track and shorten the time to pass first flatus after surgery. Due to the low PONV incidence in all participants, the group difference in PONV was not statistically significant.

The study shows it being feasible to provide preoperative acupuncture 24 hours prior to the surgery. Most of the participants (98%) we approached agreed to take part in the study, and there was no drop out at any stage of the study, indicating EA was well-accepted by all participants. Our verbal communication with participants indicated that both the acupuncturist and participants felt comfortable and not rushed when EA was delivered the day before the

surgery in the ward. EA related adverse effects were minor with only one participant reporting tolerable needling pain, reflecting EA provided in this study being safe to the patients.

It is also feasible to recruit participants. Eighty gynaecological laproscopic surgical procedures are conducted each month at our hospital, we recruited 12 participants permonth. Only one anaesthetist was involved in the study to ensure all the participants were managed consistently. It is possible to significantly enhance the enrollment rate if more anaesthetists take part in the study.

Since all participants in the current study were female and non-smokers, their PONV risk score were at 2 or above, putting them in the category of medium- to high-risk. [10] Guidelines recommend prophylactic treatment for those patients. Risk factors for PONV also include the patients' age, total length of surgery, type of anesthesia and opioid medication was employed. [10] In our study, the clinical characteristics for the two groups were similar in the risk level of PONV and profiles of surgery and anaesthesia.

In this study the incidence of postoperative nausea was 15% in the EA and 20% in the UC groups in the first 6 hours after surgery, respectively. 20% PONV in the UC group is lower than most of the previous reported incidences, [1,2,3,22,23] which was 55% in medication group among women with a moderate to high risk of PONV.[3] This could be due to the implementation of a few effective strategies that reduce PONV incidence. Our patients were admitted to the hospital at least one day before the surgery. They were well-hydrated, and felt relaxed before the surgery. Total intravenous anaesthesia including propofol was used, and prophylactic tropisetron and dexamethasone were administered intra-operatively. All of these were recommended by the guideline,[10] and could have contributed to the low PONV incidence in the UC group.

Although the incidence between the two groups was not statistically significantly different, EA decreased the absolute risk of nausea by 5%, which was 25% lower than the UC group. The data are consistent with the previous studies, where acupuncture consistently shows about 30% reduction from the medication alone group. [16,24,25,26] Using the data, we calculated the sample sizes needed are 906 in total to detect a 5% reduction in nausea with 80% power, and 76 to detect a 15% reduction in vomiting.

An important finding of this study was the multi-dimensional effect of one-session preoperative EA. It not only reduced the incidence of PONV, but also reduced postoperative pain, and shortened the time to pass first flatus. Based on the theory of traditional Chinese medicine (TCM), surgery may disturb the balanced state of the human body, and interrupts the movement of qi and blood. Consequently, stomach qi travels upwards, instead of downwards, causing nausea and vomiting and constipation.[27] PC6 free flows the adverse flow of qi, and regulates the digestive system. It has been shown to be an effective acupoint in preventing nausea and vomiting.[27] ST36 helps relax the gastrointestinal track , and enhance body recovery after surgery. [28] Concurrent stimulation of PC6 and ST36 could produce synergistic effect on regulating gastrointestinal function impacted by the surgery and anaesthetics to prevent PONV as well as accelerating motility of the gastrointestinal track.[28]

Some recent studies have suggested that acupuncture plays an important role in postoperative pain management, including a significant reduction in postoperative pain and use of opioids, leading to a reduced incidence of opioid-related adverse effects.[29,30] Animal and human studies show that preoperative EA could increase levels of enkephalins and β endorphin, which are benefit for relieving pain.[31-33] A recent study shows that acupuncture regulates serotonin and dopamine levels that are targeted by some common antiemetics. This might explain the PONV reduction effect of EA. [34]

Our study has several limitations. Firstly, when the participants were recruited, we did not assess their PONV or motion sickness history, therefore we were not able to calculate the Apfel score for PONV risk assessment. However, this could not have contributed to a lack of group difference. As mentioned above, the two groups were comparable in surgery and anesthesia-profile and many other aspects associated with PONV incidence. Secondly, we did not ask the patients whether they had any recent acupuncture treatment prior to the trial. The effect of acupuncture for post-operative pain or PONV often does not last more than 48 to 72 hours.[13]The chance of prior acupuncture treatment might impact on the results of the current study is very low. Nevertheless this could be taken into consideration in future studies. Thirdly, we did not have another group of patients who received EA delivered 30min before induction of anesthesia, which was usually used in previous studies;[16] therefore we could not assess if EA 24 hours prior to surgery is better than EA 30 min before surgery. Additionally, we did not

include a sham-acupunctue control group. The 2015 Cocohrane review of acupuncture for PONV[15] clearly states that evidence supports the use of PC6 acupoint stimulation over sham interventions. The review further recommends that further sham comparison trials will not change the conclusion. For this reason, a sham control group was not attempted in our study. Fourthly, we limited our study to a single type of short-duration surgery. It is unclear whether our findings could be extended to other surgical populations. Finally, we did not interview patients and the acupuncturist formally to ascertain their experience of EA 24 hours prior to surgery. Future studies should address those issues.

Conclusion

Our feasibility study demonstrates that one-session preoperative EA within 24 hours of the surgery is well-accepted by patients, easy to be administered by acupuncturists, is safe and has multi-dimensional effects on postoperative recovery. Future studies need to assess if this method is also safe and effective for complicated surgeries with extended surgical time. Properly powered studies are needed to further test the effectiveness of this form of EA on PONV.

References

1. Rüsch D, EberhartLH, Wallenborn J, et al. Nausea and vomiting after surgery under general anesthesia: an evidence-based review concerning risk assessment, prevention,and treatment. DtschArzteblInt. 2010; 107: 733–41.

2. Apfel CC, Korttila K, Abdalla M, et al. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med. 2004; 350: 2441–51.

3. Yuksek MS, Alici HA, Erdem AF, et al. Comparison of

prophylactic anti-emetic effects of ondansetron and dexamethasone in women undergoing day-case gynaecologicallaparoscopic surgery. J Int Med Res. 2003; 31: 481–8.

4. Boehler M, Mitterschiffthaler G, Schlager A. Korean hand acupressure reduces postoperative nausea and vomiting after gynecological laparoscopic surgery. AnesthAnalg. 2002; 94:872-5.

5. Lerman J. Surgical and patient factors involved in postoperative nausea and vomiting. Br J Anaesth. 1992; 69:24s-32s.

6. GanTJ. Risk factors for postoperative nausea and vomiting.AnesthAnalg. 2006; 102: 1884-98.

7. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology,treatment, and prevention. Anesthesiology. 1992;77:162–84.

8. Carroll NV, Miederhoff PA, Cox FM, et al. Costs incurred by outpatient surgical centers in managing postoperative nausea and vomiting. J ClinAnesth. 1994; 6: 364–9.

9. Watcha MF. The cost-effective management of

postoperativenausea and vomiting. Anesthesiology. 2000; 92: 931–3.

10. GanTJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. AnesthAnalg. 2014; 118:85-113.

11. Myklejord DJ, Yao L, Liang H, et al. Consensus guidelineadoption for managing postoperative nausea and vomiting.WMJ. 2012; 111(5): 207–13; quiz 214.

12. Shin HC, Kim JS, Lee SK, et al. The effect of acupuncture on postoperativenausea andvomiting after pediatric tonsillectomy:A meta-analysisand systematic review.Larynqoscope. 2016 Feb 10. doi: 10.1002/lary.25883.

13. Lee A, Fan LT. Stimulation of the wrist acupuncture point P6for preventing postoperative nausea and vomiting. CochranenDatabaseSyst Rev. 2009; 15:CD003281.

14. Yang XY, Xiao J, Chen Yh, et al. Dexamethasone alone vs in combination withtranscutaneous electrical acupointstimulationortropisetron for prevention of postoperative nausea andvomiting in gynaecological patients

undergoinglaparoscopic surgery. Br J Anaesth. 2015; 115:883-9.

15. Lee A, Chan SK, Fan LT. Stimulation of the wrist acupuncture point PC6 for preventing postoperative nausea and vomiting. Cocharane Database Syst Rev. 2015; 11:CD003281.

16. Cheonq KB, Zhang JP, Huang Y, et al. The Effectiveness of acupuncture in prevention and treatment of postoperative nausea and vomiting – a systematic review and meta-analysis. Plos One. 2013; 8:e82474.

17. Dune LS, ShiaoSY. Metaanalysis of acustimulation effects on postoperative nausea and vomiting in children. Explore (NY). 2006; 2:314-20.

18. al-Sadi M, Newman B, Julious SA. Acupuncture in the prevention of postoperative nausea and vomiting. Anaesthesia. 1997; 52:658-61.

19. Lv H. Observation of 50 clinical cases of Neiguanacupuncturefor the prevention of nausea and vomiting in general anaesthesia. NeiMongolJournal of Traditional Chinese Medicine. 2012; 31: 23.

(articleinChinese).

20. Coura LE, Manoel CH, Poffo R, et al. Randomised, controlled study of preoperative electroacupuncture for postoperative pain control after cardiac surgery. AcupuncMed. 2011; 29:16-20.

21. Lee S, Lee MS, Choi DH, et al. Electroacupuncture on PC6 prevents opioid-induced nausea and vomiting after laparoscopic surgery. Chin J Inteqr Med. 2013; 19:277-81.

22. Lerman J. Surgical and patient factors involved in postoperative nausea and vomiting. Br J Anaesth. 1992; 69: 24S–32S.

23. Kim YH, Kim KS, Lee HJ, et al. The efficacy ofseveral neuromuscular monitoring modes at the P6 acupuncture point in preventing postoperative nausea and vomiting.AnesthAnalg. 2011; 112: 819–23.

24. Amir SH, Bano S, Khan RM, et al. Electro-stimulation at P6 for prevention of PONV. J AnesthClin Pharmacology. 2007; 23:383-86.

25. Liu YY, Duan SE, Cai MX, et al. Evaluation of transcutaneous electroacupoint stimulation with the

train-of-four mode for preventing nausea and vomiting after laparoscopic cholecystectomy. Chin J Integr Med. 2008; 14:94-97.

26. Wang XQ, Yu JL, Du ZY, et al. Electroacupoint stimulation for postoperative nausea and vomiting in patients undergoing supratentorial craniotomy. J NeurosurgAnesthesiol. 2010; 22:128-31.

27. LvJQ, FengRZ, Li N. P6 acupoint stimulation for prevention ofpostoperative nausea and vomiting in patients undergoing craniotomy:study protocol for a randomized controlled trial. Trials.2013; 14: 153.

28. Alizadeh R, Esmaeili S, Shoar S, et al. Acupuncture in preventing postoperative nausea and vomitin g: efficacy of two acupuncture points versus asingle one. J Acupunct Meridian Stud. 2014; 7:71-5.

29. An LX, Chen X, RenXJ, et al. Electro-acupuncture decreases postoperative pain andimproves recovery in patients undergoing a supratentorial craniotomy. AmJ Chin Med. 2014; 42:1099–109.

30. SunY, GanTJ, DuboseJW, et al. Acupuncture and related

techniques for postoperative pain: A systematic review of randomized controlled trials. BrJAnaesth. 2008; 101: 151–60.

31. Jiang Y, He X, Yin X, et al. Anti-inflammatory and synovial-opioid system effects of electroacupuncture intervention on chronic pain in arthritic rats. Zhongguo Zhen Jiu. 2015; 35:917-21. (articleinChinese).

32. Wang Y, Gehringer R, Mousa SA, et al. CXCL 10 controls inflammatory pain via opioid peptide-containing macropahges in electroacupuncture. PLoS One. 2014; 9:e94696.

33. Hsieh YL, Honq CZ, Liu SY, et al. Acupuncture at distant myofascial trigger spots enhances endogenous opioids in rabbits: a possible mechanism for managing myofascial pain. Acupunct Med. 2016; pii: acupmed-2015-011026.

34. Zhang X, Jin HF, Fan YH, et al. Effects and mechanisms of transcutaneous electroacupuncture on chemotherapy-induced nausea and vomiting. Evid Based Complement Alternat Med. 2014;2014:860631.