

# Effectiveness of acupuncture-type interventions to prevent nausea and vomiting during and after cesarean delivery under spinal anesthesia : A systematic review

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## ABSTRACT

### Effectiveness of acupuncture-type interventions to prevent nausea and vomiting during and after cesarean delivery under spinal anesthesia : A systematic review

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**목 적:** 이 논문은 제왕절개 분만을 위한 척수마취로 인해 수술 중 또는 그 후에 발생할 수 있는 오심 및 구토에 대한 침관련 치료의 항구토 효과를 규명하기 위한 계통적 리뷰 논문이다.

**방 법:** 제왕절개 분만을 위한 척수마취로 인해 발생할 수 있는 오심 및 구토를 예방하기 위한 침관련 치료에 대한 randomized clinical trials(RCT's)를 검색하기 위해 2008년 3월까지 수록된 6개의 데이터베이스(MEDLINE, EMBASE, The Cochrane Library, CINAHL, AMED and PsycINFO)를 검색하였다. 논문의 선정 기준은 원저이며, 플라시보 대조군을 설정한 무작위 임상시험이고, 오심 또는 구토에 대한 결과가 실려 있는 것으로 하였다.

**결 과:** 총 5개의 논문을 선정하였으며 각 논문들의 연구방법은 일반적으로 좋은 편이었다. 5개의 논문들을 종합한 결과는 수술중 오심 발생률(OR=0.468, 95%CI:0.250-0.876, P=0.018), 수술 후 오심 발생률(OR=0.616, 95%CI:0.042-0.942, P=0.026), 수술 후 구토 발생률(OR=0.640, 95%CI:0.432-0.948, P=0.026)이 침관련 치료군이 대조군에 비해서 통계적으로 의미있게 적었다.

**결 론:** 본 문헌 고찰을 통해 제왕절개 수술을 위해 시행한 척수 마취로 인해 수술중 또는 수술후 발생한 오심 및 구토에 대해 침관련 치료가 예방효과가 있음을 밝힐 수 있었다.

**Key Words:** acupuncture, nausea, vomiting, cesarean delivery

## I . Introduction

Nausea and vomiting are major adverse effects during spinal anesthesia for cesarean delivery<sup>1)</sup>. The incidence of intraoperative emesis under spinal anesthesia is up to 50% to 80% of parturients who are not given prophylactic antiemetics<sup>1-3)</sup>. However, routine use of prophylactic antiemetics in this patient population is not recommended because of adverse effects<sup>1,4)</sup>.

Acupuncture is an important treatment modality of traditional Chinese medicine involving stimulation of specific points by manually inserting and manipulating fine needles with the aim of curing disease and/or promoting health. In addition to manual needling, several other methods are used for stimulation of acupuncture points, for example, electrical stimulation, acupressure<sup>5)</sup>.

Acupuncture-type interventions has been reported as a potential non-pharmacological method of preventing nausea and vomiting. Studies have shown that acupuncture-type intervention can decrease the nausea due to morning sickness<sup>6)</sup>, general anaesthesia<sup>7)</sup>, chemotherapy<sup>8)</sup> and motion sickness<sup>9)</sup>. Other studies of this technique which had unfavourable results include those by Yentis and Bissonnette<sup>10)</sup> and Lewis and colleagues<sup>11)</sup>.

Several studies suggest that acupuncture-type intervention is effective for prevention of nausea and vomiting during and after spinal anaesthesia for caesarean section, but the evidence is contradictory. Therefore,

this systematic review was conducted to critically evaluate and summarize all the evidence from randomized clinical trials(RCTs) of acupuncture-type intervention for prevention of nausea and vomiting during and after spinal anaesthesia for caesarean section.

## II . Methods

Systematic literature searches were conducted in the following electronic databases: MEDLINE, EMBASE, The Cochrane Library, CINAHL, AMED, PsycINFO(all from their inception to March 2008). The search terms were acupuncture, electroacupuncture, acupressure, nausea, vomiting, anesthesia and cesarean section. Combinations of these key words were used and no language restriction was imposed. The references lists of the literature found were searched and our department's own files on acupuncture were hand-searched for further relevant articles.

Studies were included if they were prospective, randomized, clinical studies of acupuncture, electroacupuncture, acupressure intervention during and after cesarean delivery under spinal anesthesia, and had outcomes of nausea or vomiting. The control interventions were usual care only or placebo acupuncture. Data extraction and validation were carried out by using a predefined, standardized form by 2 independent reviewers who

resolved differences by discussion. Quality of reporting was assessed on the 5-point Jadad scale<sup>12)</sup>. The Jadad scale was used for quality assessment of the included papers. It addressed 3 major aspects of research study quality:

(1) randomization;(2) blinding; and (3) withdrawal. The scale consisted of 5 questions:

1. Was the study randomized?
2. Was the randomization adequately described?
3. Was the study double-blinded?
4. Was the blindedness described adequately?
5. Was there a description of withdrawals?

One (1) point was assigned for each question that received a “yes” answer. Research studies that were assigned a total of 1 - points were regarded as low quality, while trials with a total of 3 points or more were considered to be high quality<sup>13)</sup>.

All statistical analysis was performed

with Comprehensive Meta-Analysis Version 2 software. If the heterogeneity was low, fixed effects model was used. And if not, random effects model was used to take into account the variation between the various studies. Furthermore, we calculated the pooled OR with the 95% CI of intraoperative or postoperative nausea and vomiting in the treatment group and the control group. And we analysed the heterogeneity between trials.

### III. Result

Our search identified 280 articles, of which we excluded 269 on the basis of the title and abstract and 6 studies on the basis of the full text(Fig. 1). In total 5 articles met the inclusion criteria and were included in our study. The trials were conducted between 1997 and 2006.

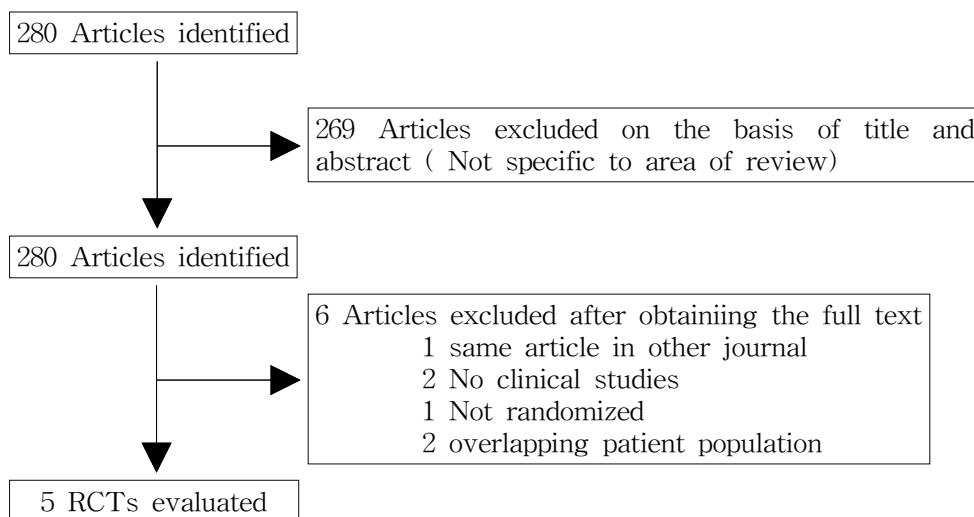


Fig. 1. Flow diagram of literature searching

The characteristics of the included studies are shown in Table 1 and the outcomes of the individual studies are summarized in Table 2. Five RCTs were included with 589 parturients undergoing elective cesarean section received spinal anesthesia. Spinal anesthesia was performed using only bupivacaine or

bupivacaine with fentanyl or morphine. Of the 589, 296 participants received acupuncture-type intervention in the treatment group and 293 participants acted as controls. In all studies participants in the treatment group received band at the P6 point<sup>14-18</sup>.

Table 1. Summary of main features of RCTs

	Year	N Tx. group	N control group	Tx. method	control method	Tx. time	anesthetic method	Jadad score
Ashraf <sup>14</sup>	2006	47	44	active ReliefBand at the P6 of the dominant hand	active ReliefBand at the dorsum of the wrist of the dominant hand	30-60min before ~ 24h after surgery	1.4 -1.6 mL of spinal bupivacaine 0.75% plus dextrose 8.25% with 20 g fentanyl and 200g preservative-free morphine	3
Chiu-Ming <sup>15</sup>	2006	55	55	SeaBand at the P6 bilaterally	placebo wrist band at the same point	more than 30min before anesthesia	0.5% hyperbaric bupivacaine (12-14mg)	4
Harmon <sup>16</sup>	2000	47	47	SeaBand at right P6	SeaBand at the dorsal side of the right forearm (2 'cun' proximal to the distal wrist crease)	5min before anesthesia - 6h after discharge to the ward	2.4 -21.6 mL of hyperbaric bupivacaine 0.5% preservative-free morphine 0.2mg	4
Duggal <sup>17</sup>	1998	122	122	SeaBand at the P6 bilaterally	placebo wrist band at the same point	before anesthesia - minimum of 10h of insertion of spinal	0.75% hyperbaric bupivacaine 10µg fentanyl and 250µg morphine	4
Deborah <sup>18</sup>	1997	25	25	SeaBand at the P6 bilaterally And 2ml of intravenous saline	placebo wrist band and 2ml of intravenous saline	15min before anesthesia	1.5 mL of spinal bupivacaine 0.75% plus dextrose 8.25% with 10 µg fentanyl	3

Tx, Treatment; N, number of patients

Table 2. Outcomes of the individual studies

Author(y)	N Tx. group	N control group	n			n			n			n		
			Intraoperative Tx.	nausea control	<i>P</i> value	Intraoperative Tx.	vomiting control	<i>P</i> value	postoperative Tx.	nausea control	<i>P</i> value	postoperative Tx.	vomiting control	<i>P</i> value
Ashraf <sup>14</sup>	47	44	14 (29.79%)	19 (43.18%)	0.186	6 (12.77%)	4 (9.09%)	0.577	11 (23.40%)	18 (40.91%)	0.076	12 (25.53%)	16 (36.36%)	0.265
Chiu-Ming <sup>15</sup>	55	55	35 (63.64%)	39 (70.91%)	0.417	12 (21.82%)	15 (27.27%)	0.507	-	-	-	-	-	-
Harmon <sup>16</sup>	47	47	7 (14.89%)	17 (36.17%)	<b>0.021</b>	4 (8.51%)	8 (17.02%)	0.225	4 (8.51%)	6 (12.77%)	0.506	13 (27.66%)	25 (53.19%)	<b>0.013</b>
Duggal <sup>17</sup>	122	122	33 (27.05%)	37 (30.33%)	0.571	8 (6.56%)	8 (6.56%)	1.000	69 (56.56%)	80 (65.57%)	0.149	50 (40.98%)	56 (45.90%)	0.439
Deborah <sup>18</sup>	25	25	6 (24.00%)	19 (76.00%)	<b>0.000</b>	3 (12.00%)	6 (24.00%)	0.278	-	-	-	-	-	-

Significant differences: *P*<0.05, in bold. Tx, Treatment; N, number of patients; n, number of patients with the event; -, not reported

One study used ReliefBand for transcutaneous acupoint electrical stimulation<sup>14</sup>. And four studies used SeaBand at the P6 point<sup>15-18</sup>. The SeaBand is a commercially available elastic wrist band with a small round plastic button on the inner side to pressure the acupoint. Two studies used active band at dorsum of the wrist or forearm in the control group<sup>14,16</sup>. And three studies used placebo wrist band at the same point of the treatment group in the control group<sup>15,17,18</sup>. All were conducted in a hospital setting. The methodologic quality was considered good: 3 points on the Jadad scale were given to 2 trials<sup>14,18</sup> and 4 points to 3 trials<sup>15-17</sup>. Ashraf et al<sup>14</sup> conducted a randomized, double-blind controlled trial in 94 parturients. The treatment group who received active ReliefBand at the P6 of the dominant hand (n=47) was compared with the control group who received active ReliefBand at the dorsum of the wrist of the dominant hand(n=44). The incidence of nausea and vomiting was recorded and severity of nausea was assessed using a VRS (0-10). There was a trend towards less intraoperative and postoperative nausea, postoperative vomiting rate in the treatment group, but these differences did not achieve statistical significance. As its sample size calculation was based on an expected decrease of 30%, statistically significant differences were not detected.

A randomized, double-blind controlled trial was performed by Chiu-Ming et al<sup>15</sup> in 110 parturients. Parturients were randomly assigned to either receive Seaband(n=55) or placebo wrist band (n=55) bilaterally at the P6 acupoint. Of the 55 parturients in the acupressure group, 1 received IV metoclopramide for intractable vomiting, whereas 2 of the 55 parturients in the control group required the same treatment (difference not statistically significant). The incidence of intraoperative nausea in the acupressure group was 64% compared with 71% in the control group(OR=0.718, 95%CI: 0.323-1.598, P=0.417); the incidence of intraoperative vomiting was 22% in the acupressure group and 27% in the control group(OR=0.744, 95%CI: 0.311-1.718, P=0.507). There were no statistically significant differences between two groups. No adverse effect was noted after the use of either SeaBand or placebo wrist band.

Harmon et al<sup>16</sup> conducted a prospective, randomized, double-blind study in 94 parturients. The treatment group(n=47) received SeaBand at right P6 acupoint. And the control group(n=47) received SeaBand at the dorsal side of the right forearm, 2 'cun' proximal to the distal wrist crease. There was a statistically significant reduction in intraoperative nausea (OR=0.309, 95%CI: 0.114-0.839, P=0.021) in the treatment group compared with control group. After operations there was a statistically

significant reduction in vomiting (OR=0.336, 95%CI: 0.143-0.794,  $P=0.013$ ) in the treatment group. 23 patients (50%) in the control group and 12 (25%) in the treatment group required rescue anti-emetic in the study period ( $P=0.01$ ). There was a statistically significant difference in anti-emetic requirement during and after operations. If patients who received an anti-emetic intra-operatively were excluded, the protective effect of acupressure remained. With this analysis the use of acupressure reduced the incidence of nausea and vomiting(95% CI 0.37-0.18,  $P=0.0002$ ) from 87%(35/40) to 50%(23/46), and antiemetic requirement (95% CI 0.21-0.20,  $P=0.03$ ) from 47%(19/40) to 26%(12/46) compared with placebo. The side effect of acupressure band was some localized discomfort in a small number of women.

A randomized, double-blind controlled trial was performed by Duggal et al<sup>17</sup> in 244parturients. Parturients were randomly assigned to either receive Seaband(n=122) or placebo wrist band(n=122) bilaterally at the P6 acupoint. Number of bouts of dizziness, vomiting were recorded, and horizontal 10cm Visual Analogue Scale(VAS) was used to indicate the severity of nausea. There was no statistically significant inter-group difference in the intraoperative incidence of nausea, vomiting, retching, or the amount of antiemetic medication administered. Thirty-seven patients in the control group and 33 in the

treatment group reported nausea intraoperatively (OR=0.852, 95%CI: 0.489-1.485,  $P=0.571$ ). Only eight patients in each group vomited or retched during surgery, and incidence of 6.6%(OR=1.000, 95%CI: 0.363-2.756,  $P=1.000$ ). The use of acupressure reduced the incidence of postoperative nausea(OR=0.683, 95%CI: 0.407-1.147,  $P=0.149$ ) and vomiting (OR=0.818, 95%CI: 0.493-1.359,  $P=0.439$ ) compared with placebo, but it is not statistically significant. However, postoperative nausea and vomiting were significantly reduced in a sub-group of patients who gave a history of previous PONV. Acupressure was associated with a statistically significant reduction in nausea postoperatively when compared with placebo (55.6% vs 85%,  $P<0.05$ ) in the patients who had experienced nausea or vomiting after previous surgery. Furthermore, in the same group of patients the incidence of postoperative vomiting/retching was lower in the acupressure group (41.7% vs 67.5%,  $P<0.025$ ). The most common side-effect reported(by 17.6% of patients overall) was swelling of the hands with prolonged wearing of the wristbands.

Deborah et al<sup>18</sup> conducted a prospective, randomized, double-blind study in 75 healthy parturients. Patients were randomized via an envelope system into one of three groups, 25patients per group. Group I patients received acupressure bands and 2mL IV saline, Group II Patients received placebo wrist bands

and 10mg IV metoclopramide, and Group III patients received placebo wrist bands and 2mL IV saline. In this review, we analysed only group I and group III. Because we limited the control interventions to usual care only or placebo acupuncture. Group I patients had much less intraoperative nausea than group III patients (OR=0.100, 95%CI: 0.027-0.365, P=0.000). Although group I patients had less intraoperative vomiting than group III patients (OR=0.432, 95%CI: 0.095-1.966, P=0.278), it is not statistically significant. However, when the analysis was restricted to hypotensive patients (systolic blood pressure <100mmHg), the proportion of patients with nausea was significantly less among group I patients than among

group III patients (37.5% vs 78.9%,  $P < 0.05$ ).

Table 3 and Fig. 2 - Fig. 5 show the comparisons of the available data and meta-analyses for the incidence of intraoperative or postoperative nausea and vomiting. Tests for significance and heterogeneity among trials are also presented. There is a statistically significant reduction in intraoperative nausea (OR = 0.468, 95%CI: 0.250-0.876), postoperative nausea (OR=0.616, 95%CI: 0.042-0.942, P=0.026) and postoperative vomiting (OR=0.640, 95%CI: 0.432-0.948, P=0.026) in the treatment group compared with control group. But there is no statistically significant differences between two groups in intraoperative vomiting (OR=0.768, 95%CI: 0.463-1.275, P=0.308).

Table 3. Comparisons and pooled outcomes for which there are data showing the effect size

comparison and outcome	No. of studies	No. of participants		Pt with the event(%)		statistical method	Effect size [95%CI]; (P value)	Heterogeneity between trials			
		Tx. (n/N)	con (n/N)	Tx. (%)	con (%)			Q-value	dif (Q)	P-value	I-squared
intraoperative nausea	5 <sup>14-18</sup>	95/296	131/293	32.09	44.71	random	OR=0.468[0.250-0.876] ( <b>0.018</b> )	10.704	4	0.030	62.630
intraoperative vomiting	5 <sup>14-18</sup>	33/296	41/293	11.15	13.99	fixed	OR=0.768[0.463-1.275] (0.308)	2.366	4	0.669	0.000
postoperative nausea	3 <sup>14,16,17</sup>	84/216	104/213	38.89	48.83	fixed	OR=0.616[0.042-0.942] ( <b>0.026</b> )	0.680	2	0.712	0.000
postoperative vomiting	3 <sup>14,16,17</sup>	75/216	97/213	34.72	45.54	fixed	OR=0.640[0.432-0.948] ( <b>0.026</b> )	3.079	2	0.214	35.054

Significant differences:  $P < 0.05$ , in bold. Tx, Treatment; N, number of patients; n, number of patients with the event

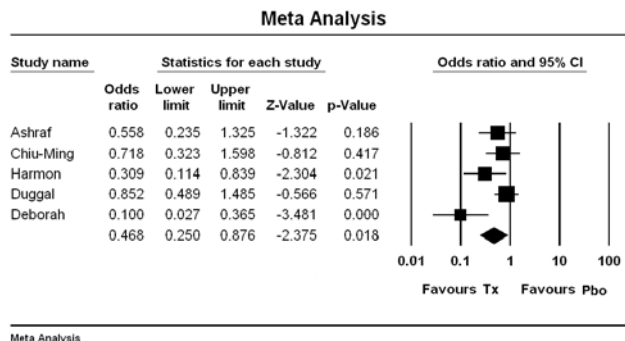


Fig. 2. Odds ratio and 95% confidence intervals of intraoperative nausea  
Odds ratio and 95% confidence intervals of intraoperative nausea for individual study and the pooled results. In this plot the symbol for each study is proportional in area to that study's weight in the analysis.

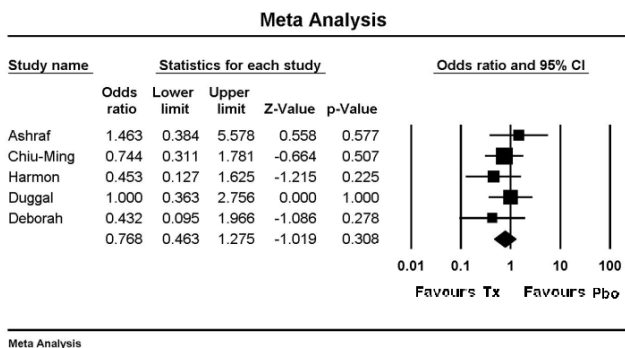


Fig. 3. Odds ratio and 95% confidence intervals of intraoperative vomiting  
Odds ratio and 95% confidence intervals of intraoperative vomiting for individual study and the pooled results. In this plot the symbol for each study is proportional in area to that study's weight in the analysis.

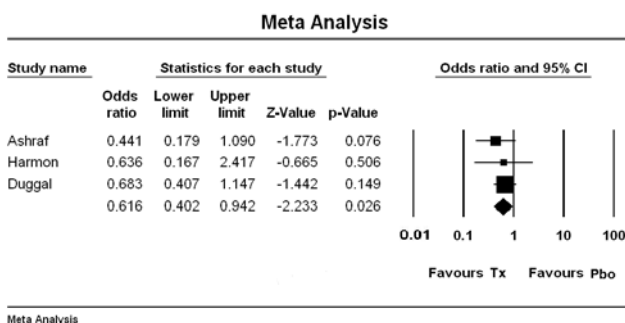


Fig. 4. Odds ratio and 95% confidence intervals of postoperative nausea  
Odds ratio and 95% confidence intervals of postoperative nausea for individual study and the pooled results. In this plot the symbol for each study is proportional in area to that study's weight in the analysis.



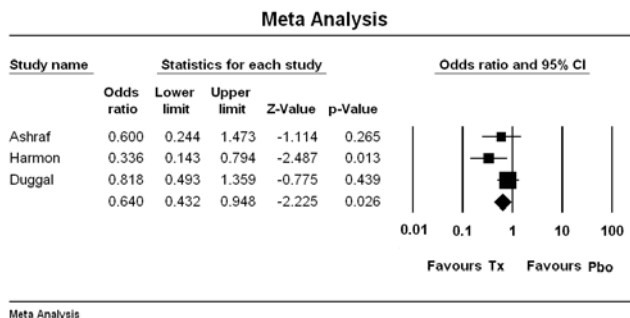


Fig. 5. Odds ratio and 95% confidence intervals of postoperative vomiting  
Odds ratio and 95% confidence intervals of postoperative vomiting for individual study and the pooled results. In this plot the symbol for each study is proportional in area to that study's weight in the analysis.

## IV. Discussion

Overall, the evidence of acupuncture for antiemetic is encouraging. The methodologic quality of the primary studies is generally good, and collectively these data suggest that acupuncture-type intervention prevents nausea and vomiting during and after spinal anaesthesia for caesarean section. Its antiemetic effect seems to be superior to placebo acupuncture, but data are limited.

Despite the increasing use of acupuncture<sup>19,20</sup>, the number of RCTs available for this systematic review is small.

In this systematic review data from five studies were extracted. In all studies, the point chosen for stimulation was Neiguan(P6) acupuncture points, located on the anterior surface of the wrists, threefingers breadth above the distal skin crease of the wrist joint between the tendons of the palmaris longus and flexor carpi radialis muscle<sup>21</sup>. The P6 acupuncture which serves as an

antiemetic remedy has been used in traditional Chinese medicine for a long time, although its mechanism is still unclear. Costello & Borison<sup>22</sup> suggested that the antiemetic effect of acupuncture may be mediated by the release of an endogenous morphine-like substance with antiemetic tone into the central nervous system. And Helms JM<sup>23</sup> suggested that acupuncture causes low-frequency electrical stimulation of the skin sensory receptors that may activate A- $\beta$  and A- $\delta$  fibers. These fibers all synapse within the dorsal horn and may in turn cause a release of endorphin from the hypothalamus. In addition, serotonergic and norepinephrinergic fibers may be activated. Although there is no clear explanation for the antiemetic effects of acupuncture and acupuncture, a possible explanation lies in this change in serotonin transmission<sup>18</sup>.

A limitation of our systematic review, as with other reviews, was that the possibility of publication bias can not be ruled out. We searched different

sources to identify all RCT's with controls of acupuncture-type intervention for the prevention of nausea and vomiting during and after cesarean delivery under spinal anesthesia, but were not able to retrieve any unpublished studies. If publication bias has prevented negative trials to be included in our review, our conclusions might be overoptimistic<sup>24)</sup>. Although the use of acupuncture is widespread in China, our literature search retrieved only one eligible trial from Taiwan. Databases only partially cover literature from china and it is possible that unidentified eligible trials from china exist.

Another limitation of our study was that the sample sizes of RCTs included were relatively small and among the included studies, a variety of spinal anesthesia drug was used. One trial<sup>15)</sup> used only bupivacaine, and four trials used bupivacaine with fentanyl<sup>18)</sup>, morphine<sup>16)</sup> or both<sup>14,17)</sup>. The usage of fentanyl and morphine may have affected the incidence of intraoperative emesis. Gastroduodenal motility was influenced early on approximately 30 minutes after intrathecal morphine administration<sup>25)</sup>. Thus the use of intrathecal morphine is associated with intraoperative nausea and vomiting. Inversely, intrathecal lipophilic opioids, such as fentanyl and sufentanil, have been found to decrease intraoperative nausea and vomiting under spinal anesthesia<sup>26)</sup>.

Furthermore, among the included studies, a variety of acupuncture-type interventions

(transcutaneous acupoint electrical stimulation with ReliefBand, acupressure with SeaBand/ bilateral, unilateral) were used. No studies have compared the efficacy of unilateral versus bilateral P6 point stimulation<sup>14)</sup>. Miller et al<sup>27)</sup> studied efficacy of acupressure and ReliefBand for the prevention of motion sickness. There is no differences between two groups in symptoms of motion sickness, gastric tachyarrhythmia and gastric myoelectric activity. The only difference was a potential delay in symptom onset for the ReliefBand compared with the acupressure. And a difficulty in P6 acupoint stimulation studies is the use of adequate sham treatment. There were different types of sham treatment but for the purposes of this systematic review, all were considered as one entity.

We tested possible statistical heterogeneity between trials. Statistical heterogeneity may be caused by known clinical or methodologic differences between trials, or may be related to unknown trial characteristics. In intraoperative nausea, the heterogeneity is substantial(P value =0.030, I<sup>2</sup>=62.63%). Therefore, we use a random effects approach to take into account this variability. And in other cases, the heterogeneity is low, so we use a fixed effects model. But nonsignificance of the test of heterogeneity can never be interpreted as evidence of homogeneity of the results of the included trials as tests of heterogeneity have low power and may fail to detect even a moderate degree of genuine heterogeneity as statistically

significant. For policy recommendations, a large number of acupuncture trials would be needed to investigate potential sources of heterogeneity<sup>28-31</sup>.

Safety issues of an intervention are important for estimating its risk-benefit profile. Routine use of anti-emetic drugs in patients during Caesarean section is not recommended by many because of adverse effects. Methoclopramide, which has been shown to have no deleterious effects on the neonate<sup>32</sup>, is most commonly used, but, it is associated with extrapyramidal symptoms<sup>33</sup> and peripartum supraventricular tachycardias<sup>34</sup>. Serious adverse events of acupuncture are on record<sup>35</sup> but infrequent, provided that it is practiced according to established safety rules in appropriate anatomic regions. Nonserious adverse effects such as mild pain or bleeding are reported in about 7% of all cases<sup>36,37</sup>. And no significant harmful effects of ReliefBand and SeaBand were reported in included studies in this review.

In conclusion, the collective data from RCTs suggest that acupuncture-type intervention reduces incidence of intraoperative nausea, postoperative nausea and postoperative vomiting. Mainly because of the paucity of primary studies in this area, the effectiveness of acupuncture-type intervention remains uncertain. Further research is required to establish the value of acupuncture as an adjunctive treatment for prevention of nausea and vomiting during and after cesarean section under

spinal anesthesia. Future studies are required to assess the optimal timing of P6 acupoint stimulation and whether bilateral stimulation at the P6 acupoint is more effective than unilateral stimulation. And also adequate target patients of P6 acupoint stimulation (ex: patients who had experienced PONV or hypotensive patients et al) must be studied.

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