

Acupressure and ondansetron for postoperative nausea and vomiting after laparoscopic cholecystectomy

[L'acupression et l'ondansétron contre les nausées et les vomissements suivant la cholécystectomie laparoscopique]

Anil Agarwal MD,* Neeta Bose MD,* Atul Gaur MD,* Uttam Singh PhD,† Mithlesh Kumar Gupta MD,* Dinesh Singh MD*

Purpose: To compare the efficacy of acupressure wrist bands and ondansetron for the prevention of postoperative nausea and vomiting (PONV).

Methods: One hundred and fifty ASA I–II, patients undergoing elective laparoscopic cholecystectomy were included in a randomized, prospective, double-blind and placebo-controlled study. Patients were divided into three groups of 50. Group I was the control; Group II received ondansetron 4 mg iv just prior to induction of anesthesia; in Group III acupressure wristbands were applied at the P6 points. Acupressure wrist bands were placed inappropriately in Groups I and II. The acupressure wrist bands were applied 30 min prior to induction of anesthesia and removed six hours following surgery. Anesthesia was standardized. PONV were evaluated separately as none, mild, moderate or severe within six hours of patients' arrival in the postanesthesia care unit and then at 24 hr after surgery by a blinded observer. If patients vomited more than once, they were given 4 mg ondansetron iv as the rescue antiemetic. Results were analyzed by Z test. A *P* value of < 0.05 was taken as significant.

Results: The incidence of PONV and the requirement of rescue medication were significantly lower in both the acupressure and ondansetron groups during the first six hours.

Conclusion: Acupressure at P6 causes a significant reduction in the incidence of PONV and the requirement for rescue medication in the first six hours following laparoscopic cholecystectomy, similar to that of ondansetron 4 mg iv.

Objectif: Comparer l'efficacité des bandes d'acupression et de l'ondansétron comme prévention des nausées et vomissements postopératoires (NVPO).

Méthode : Cent cinquante patients d'état physique ASA I–II devant subir une cholécystectomie laparoscopique ont été recrutés pour une étude prospective, randomisée et à double insu contre placebo. Ils ont été répartis en trois groupes de 50. Le groupe I a été le groupe témoin; les patients du groupe II ont reçu 4 mg iv d'ondansétron juste avant l'induction de l'anesthésie; chez les patients du groupe III, on a appliqué des bandes d'acupression aux point P6. Des bandes d'acupression ont été placées de façon inappropriée chez les patients des groupes I et II. Les bandes ont été appliquées 30 min avant l'induction et enlevées six heures après l'opération. L'anesthésie a été normalisée. Les NVPO ont été évalués séparément comme inexistantes, légers, modérés ou sévères pendant les six premières heures en salle de réveil, puis 24 h après l'opération par un observateur impartial. Si les patients vomissaient plus d'une fois, ils recevaient 4 mg d'ondansétron iv comme antiémétique de secours. Les résultats ont été analysés avec le test Z. Une valeur de *P* < 0,05 était considérée significative.

Résultats : L'incidence de NVPO et les besoins de médication de secours ont été significativement plus faibles autant avec l'acupression qu'avec l'ondansétron pendant les six premières heures.

Conclusion : L'acupression en P6 réduit de façon significative l'incidence de NVPO et la nécessité d'antiémétique de secours pendant les six premières heures suivant la cholécystectomie laparoscopique. Son effet est donc similaire à celui de 4 mg iv d'ondansétron.

From the Department of Anesthesia,* and Biostatistics,† Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India.

Address correspondence to: Dr. Anil Agarwal, Type IV / 48, S.G.P.G.I.M.S., Lucknow, 226 014, India. Phone: +91-522-440004-8, ext. 2473(O), 2474(R); Fax: +91-522-440017, 440047, 440078; E-mail: aagarwal@sgpgi.ac.in

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POSTOPERATIVE nausea and vomiting (PONV) is frequent in patients undergoing general anesthesia. This is a distressing experience for patients. When symptoms persist, they may lead to dehydration, electrolyte imbalance and delayed hospital discharge. This may have significant implications regarding cost of therapy especially in day stay surgery. More serious complications may ensue, including tension on suture lines, venous hypertension and increased bleeding under skin flaps affecting quality of surgical outcome. The patients are at increased risk of pulmonary aspiration of vomitus as the airway reflexes are depressed postoperatively.¹

The incidence of PONV may be as high as 60–70%, and is influenced by various patient related factors, type of surgery, anesthesia technique and drugs used and postoperative factors such as pain, dizziness, ambulation, usage of opioids etc.^{1,2-5} Laparoscopic cholecystectomy predisposes the patient to several stimuli which can induce vomiting. Various pharmacological means are available to alleviate PONV, but may cause side effects varying from lethargy, restlessness, tachycardia, extrapyramidal symptoms, dystonic reactions increasing the incidence of delayed discharge and unintended hospital re-admissions.

Acupuncture and acupressure are methods used by alternative medicine with varying results for the treatment of nausea and vomiting due to morning sickness,⁶ chemotherapy,⁷ general anesthesia,⁸ and postoperative morphine administration.⁹ Acupuncture and acupressure are based on the belief that an individual's well being depends on the balance of energy in the body. It is hypothesized that energy flows within the body along paths referred to as meridians and these techniques restore the balance of energy by manipulating these meridians.¹⁰ P6 (Nei-guan) a Chinese meridian point is used for the treatment of nausea and vomiting. The present study was aimed at comparing the effectiveness of acupressure wrist bands with ondansetron in preventing PONV in patients undergoing laparoscopic cholecystectomy.

Methods

Following approval from our institutional Research Committee and Ethical Clearance, informed consent was obtained from all patients included in this study. One hundred and fifty patients of either sex, aged between 18 and 60 yr, ASA grade I–II, undergoing laparoscopic cholecystectomy were included in this randomized, prospective, double-blind and placebo-controlled study. Patients were randomized into three groups of 50 each using a table of random numbers:

Group I – Control
Group II – Ondansetron
Group III – Acupressure

In Groups I and II, the spherical beads of the acupressure wrist bands were placed inappropriately on the posterior surface of both forearms 30 min prior to induction of anesthesia. Group II patients received ondansetron 4 mg *iv* just before induction. In Group III patients' acupressure bands were applied at the P6 point on both forearms 30 min before induction of anesthesia. Groups I and III patients received normal saline 1 mL *iv* just before induction of anesthesia to maintain blinding.

The acupressure wrist band has an adjustable strap 1.5 cm in width, a spherical plastic bead and a Velcro fastener to hold the bead in position (Figure 1). The treatment point P6 (Nei-Guan) is located on the anterior surface of the forearm approximately 1 cm deep to the skin, 2 *body inches* proximal to the distal crease of the wrist joint between the two tendons of flexor carpi radialis and palmaris longus. *One body inch* is equal to the width of the interphalangeal joint of the patient's thumb. The acupressure band was placed around the wrist, such that patient felt gentle pressure without discomfort. To confirm that compression was not excessive, a pulse oximeter was placed on the index finger to confirm adequate blood flow. Wrist bands were considered too loose and were tightened if a wedge of paper could fit between the pressure band and skin. Forearms were raised by 60° at the elbow and venous emptying occurred normally in all cases.

Exclusion criteria included patient's refusal to participate in the study, previous history of PONV and travel sickness, impaired renal function with increased urea and creatinine concentrations, diabetes mellitus, obesity, patients receiving antiemetic medication or a histamine H₂-receptor antagonist within 72 hr of surgery.

Anesthesia was standardized. No antiemetic medication was given before or during the operation. All patients received 2 mg lorazepam *po* the night before surgery and two hours prior to surgery with sips of water. Anesthesia was induced with 2 µg·kg⁻¹ fentanyl *iv* and 4–5 mg·kg⁻¹ thiopentone and maintained with isoflurane 0–1% and nitrous oxide 60% in oxygen. Neuromuscular block was provided by vecuronium. At the end of the surgical procedure patients were extubated in the operating room after reversal of the neuromuscular block with neostigmine and atropine. Postoperative analgesia was provided with 100 mg diclofenac *im* every eight hours. The acupressure wrist band was removed six hours postoperatively.

The incidence of PONV was evaluated within six hours of the patient's arrival in the postanesthesia care

TABLE I Demographic data and duration of surgery

Groups	Age (yr)	Sex (M/F)	Weight (kg)	Height (cm)	Duration of surgery (min)
I (Control)	40.2 ± 9.9	18/32	56 ± 11	159 ± 6	96 ± 30
II (Ondansetron)	41.4 ± 12.3	15/35	59 ± 10	157 ± 7	88 ± 33
III (Acupressure)	39.2 ± 10.4	16/34	63 ± 9	160 ± 5	90 ± 27

Values are mean ± SD; t test = three samples assuming equal variance.

TABLE II Incidence of nausea / vomiting / requirement of rescue antiemetics within six hours and between six to 24 hr following laparoscopic cholecystectomy

Groups (n = 50)	Nausea		Vomiting		Rescue antiemetics	
	6 hr	6-24 hr	6 hr	6-24 hr	6 hr	6-24 hr
I (Control)	12*	6	10*	3	4*	0
II (Ondansetron)	2	2	2	0	0	0
III (Acupressure)	3	2	2	0	0	0

* Denotes $P < 0.05$.

TABLE III Severity of nausea / vomiting within six hours following laparoscopic cholecystectomy

Groups (n = 50)	I (Control)	II (Ondansetron)	III (Acupressure)	Power of statistical test	
				Control vs ondansetron	Control vs acupressure
Nausea					
None	38	48	47		
Mild (A)	6	2	2		
Moderate (B)	4	0	1		
Severe (C)	2	0	0		
Nausea (A+B+C)	12*	2	3	87	75
Vomiting					
None	40	48	48		
Mild (A)	10	2	2		
Moderate (B)	0	0	0		
Severe (C)	0	0	0		
Vomiting (A+B+C)	10*	2	2	75	75
Antiemetic	4*	0	0	81	81

* Denotes $P < 0.05$.

unit and then at 24 hr after surgery by a blinded observer. The results were scored as none, nausea, retching/vomiting. Patients experiencing both nausea and vomiting were included in the vomiting group.¹¹ Nausea was graded by visual analogue scale from 1-10 (1 = none, 2-5 = mild, 6-7 = moderate and 8-10 = severe). Vomiting and retching were not distinguished and their severity was classified using the number of episodes over 24 hr i.e., none, mild (0-2), moderate (3-5), or severe (> 5).¹² If patients vomited more than once, they were given 4 mg ondansetron *iv* as the rescue antiemetic.

Patients' characteristics in the three groups were assessed using an unpaired Student's t test. PONV

data was analyzed using a Z test to compare the occurrence in all three groups. Comparisons between groups were performed for overall nausea and retching/vomiting. Nausea and retching/vomiting were then compared separately at various levels of severity. A P value of < 0.05 was considered significant.

Results

Patients were comparable in all three groups with regard to age, sex, height, weight and duration of surgery (Table I).

The incidence of PONV in the first six hours after laparoscopic cholecystectomy in the control group



FIGURE 1 Location of P6 meridian point and the proper application of the acupressure wristband (see methods for details)

was 44%. The acupressure and ondansetron groups had a significant decrease in the incidence of PONV during the same period (10% and 8% respectively). There was no significant difference in PONV in the six to 24 hr following laparoscopic cholecystectomy surgery in all three groups (Figure 2, Tables II and III). A significant decrease in the requirement for rescue medication in groups II and III was observed in the first six hours following surgery. Antiemetic requirements were similar in the three groups at 24 hr following surgery (Tables II and III). No side effects or complications were observed due to the placement of acupressure wrist bands.

Discussion

Laparoscopic cholecystectomy for the treatment of cholelithiasis is popular amongst surgeons as well as patients due to its associated advantages, which includes a short hospital stay. The latter advantage has been negated by PONV, which is turning out to be the leading cause of unexpected re-admission after day surgery.^{13,14} The incidence of PONV has been reported to be as high as 53–72%.¹⁵ After laparoscopic cholecystectomy up to 70% patients have PONV if they are not on any antiemetic prophylaxis.^{16–18}

The etiology of PONV after laparoscopic cholecystectomy is not wholly understood. Risk factors such as a prolonged CO₂ insufflation, gall bladder surgery, intraoperative use of isoflurane, fentanyl and glycopyrrolate, female sex and postoperative use of patient controlled analgesia with morphine may contribute to these episodes.^{1,15,17,19,20} CO₂ insufflation significantly

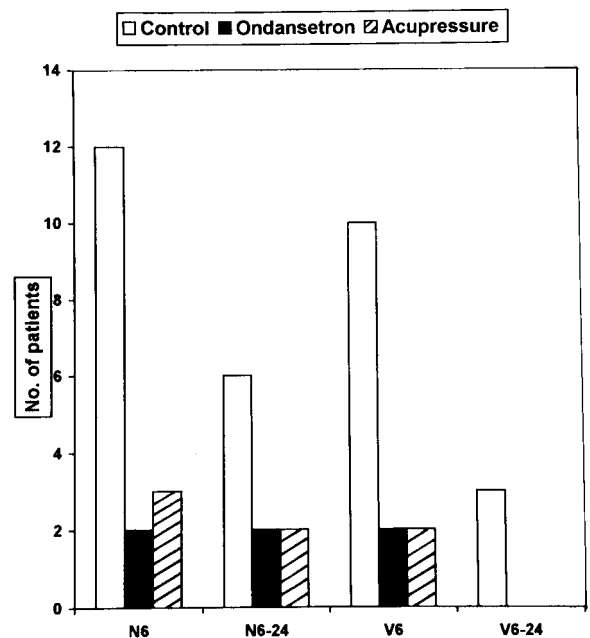


FIGURE 2 Number of patients presenting with nausea or vomiting during the first six hours (N6 and V6) and from 6-24 hr (N6-24 and V6-24) respectively after laparoscopic cholecystectomy.

increases peritoneal pressure, reduces intestinal blood flow and leads to intestinal ischemia and release of emetogenic substances.¹⁴ Also, the emetic centre is stimulated by the afferents from the gastro-intestinal track manipulated during surgery.¹ Intraoperative hypotension may cause brainstem hypoxia and thus trigger the vomiting centre to induce emesis.²¹ Further, the intestinal tissue is active metabolically and has a poor tolerance for even brief periods of hypoxia/ischemia. An important intestinal response to ischemia is the release of serotonin, a highly emetogenic substance.

There are various drug therapies for the prevention of PONV. Droperidol is an effective antiemetic, but is associated with side effects such as agitation, sedation, extra-pyramidal reactions and delayed awakening with large doses. Smaller doses of (0.625 mg) of droperidol are as effective as larger doses (1.25 mg) and 4 mg *iv* ondansetron. Lower doses of droperidol may also be associated with restlessness.¹⁸ Transdermal scopolamine decreases PONV after laparoscopic surgeries, but 91% of patients experience side effects.^{13,22} Phenothiazines and antihistamines can produce sedation and lethargy. Metoclopramide is also an effective antiemetic but not without side effects including dystonic reactions, rest-

lessness and tachycardia. Symptoms resembling parkinsonism have also been reported in children.²³ Antagonists at the NK₁ receptor represent a new class of antiemetics, which is still under investigation.²⁴

Ondansetron, a 5-hydroxy tryptamine subtype 3 (5HT₃) receptor antagonist, is an effective antiemetic for the prevention and treatment of PONV.^{1,13} It has been extremely useful in reducing PONV in women undergoing ambulatory gynecologic laparoscopic procedures. Despite its advantages, including minimal side effects, it is expensive compared with other antiemetics and may consume a major portion of an anesthetic pharmacy budget.^{18,25}

Non-pharmacological methods like acupuncture, acupressure and laser stimulation have shown comparable antiemetic efficacy.²⁶ The P6 (Nei-Guan) meridian point in acupuncture has been used to treat vomiting and other stomach ailments in traditional Chinese medical practice. In 1990, Dundee showed that acupuncture or acupressure at the P6 meridian point was as effective as a standard antiemetic in the treatment of nausea and vomiting.²⁷

The mechanism of action of acupressure is not clear. It is postulated that acupressure causes low frequency electrical stimulation of the skin sensory receptors which may activate A β and A δ fibres. These fibres synapse within the dorsal horn and may, in turn, cause release of endorphins from the hypothalamus. Increased levels of β -endorphin concentration have been reported in human cerebrospinal fluid after acupuncture stimulation.^{21,28} In addition, serotonergic and norepinephrinergic fibres may be activated and a possible change in serotonin levels has a role in prevention of PONV. It is also postulated that opioids may have antiemetic effects mediated by the action of β -endorphins on μ receptors. Acupressure has been shown to enhance gastric motility.²⁹ There is also a possible role of central dopaminergic receptors in acupuncture. The antiemetic effect of the P6 point may be mediated by an action opposing to that of central dopamine.³⁰

Acupuncture and acupressure at the P6 point is associated with mixed clinical results. Harmon,⁴ Stein,²¹ Fan,³¹ and Dundee^{27,32,33} have observed a decrease in the incidence of PONV after P6 stimulation. The important component of this treatment includes the timing of stimulation^{31,34} and correct point location.^{31,35} For acupressure to be effective, it has to be applied prior to the emetic stimulus. A meta analysis was conducted to assess the efficacy of non-pharmacological techniques such as acupuncture, electro-acupuncture, transcutaneous electrical nerve stimulation, acupoint stimulation and acupressure for

the prevention of PONV.³⁶ Non-pharmacological techniques were more effective in comparison to placebo for the prevention of PONV within six hours of surgery in adults.³⁶ However, P6 stimulation was ineffective in minimizing PONV in children following tonsillectomy and strabismus surgery.³⁷⁻³⁹ Similarly, acupressure has been ineffective in cases of urological endoscopic surgery and pregnancy.^{40,41}

In summary we compared acupressure with ondansetron and placebo for the prevention of PONV in adult patients undergoing laparoscopic cholecystectomy. We observed that the incidence of PONV and the requirement for rescue antiemetics were significantly lower in the acupressure and ondansetron groups in the first six hours following laparoscopic cholecystectomy. However, there was no significant difference in PONV and the antiemetics required at 24 hr following laparoscopic cholecystectomy in all three groups.

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Maison de l'Infante, St Jean de Luz (Pays Basque) - France