

SCIENTIFIC ARTICLE

Effect of acupuncture on the prevention of nausea and vomiting after laparoscopic cholecystectomy: a randomized clinical trial



Luiz Eduardo Miranda ^{a,*}, Luiz de França Maia e Silva Filho^b,
Ana Carolina Brainer de Siqueira^b, Ana Clara Miranda^b,
Bianca Rodrigues Castelo Branco Rocha^b, Ian Victor Paiva de Lima^b,
Victor Soares Gomes da Silva^b, Diego Laurentino de Lima ^c, Holmes Naspollini^a

^a Universidade de Pernambuco (UPE), Hospital Universitário Oswaldo Cruz, Divisão de Cirurgia Geral e Transplante de Fígado, Recife, PE, Brazil

^b Universidade de Pernambuco (UPE), Faculdade de Ciências Médicas, Recife, PE, Brazil

^c Universidade de Pernambuco (UPE), Hospital Universitário Oswaldo Cruz, Divisão de Cirurgia Geral e Transplante de Fígado, Programa de Pós-Graduação de Medicina, Recife, PE, Brazil

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Abstract

Background and objectives: Postoperative nausea and vomiting (PONV) is a common and undesirable complication observed after laparoscopic cholecystectomy (LC). We investigated the effects of auriculoacupuncture (AA) on the prevention of postoperative nausea and vomiting in the immediate postoperative period of uncomplicated laparoscopic cholecystectomy.

Methods: Sixty-eight patients were randomly divided into two groups, auriculoacupuncture (n = 35) and control (n = 33) and then they were evaluated prospectively. The needle was placed before anaesthesia induction and remained for 20 min. Nausea intensity was evaluated using an analogic visual scale and PONV events were registered immediately after anaesthesia care unit admission and in the second, fourth and sixth hours after the surgery.

Results: The auriculoacupuncture group had a significantly smaller incidence of nausea and vomiting than the control group throughout the whole postoperative period (16/35 vs. 27/33, $p=0.03$ and 4/35 vs. 15/33, $p=0.005$, respectively); the AA group had fewer nausea events 2 h ($p=0.03$) and 6 h ($p=0.001$) after surgery and fewer vomiting events 2 h ($p=0.01$) and 6 h ($p=0.02$) after surgery.

* Corresponding author.

E-mail: lecmiranda@gmail.com (L.E. Miranda).

PALAVRAS CHAVE

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Náuseas e vômitos
pós-operatórios;
Colecistectomia
laparoscópica

Conclusions: Auriculoacupuntura can partially prevent postoperative nausea and vomiting when compared to metoclopramide alone after uncomplicated laparoscopic cholecystectomy. Auriculoacupuntura can be recommended as an adjuvant therapy for postoperative nausea and vomiting prevention in selected patients.

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Efeitos da acupuntura para a prevenção de náuseas e vômitos após colecistectomia laparoscópica: um estudo clínico e randomizado

Resumo

Justificativa e objetivos: Náuseas e vômitos são complicações comuns e indesejáveis no pós-operatório de colecistectomia laparoscópica (CL). Nós investigamos os efeitos da auriculoacupuntura para a prevenção de náuseas e vômitos no período pós-operatório imediato da CL não complicada.

Métodos: 68 pacientes foram aleatoriamente divididos em dois grupos, auriculoacupuntura (n = 35) e controle (n = 33), e foram avaliados prospectivamente. A agulha foi aplicada antes da indução anestésica e permaneceu no lugar por 20 minutos. A intensidade da náusea foi avaliada mediante escala visual analógica e episódios de PONV foram registrados imediatamente após a admissão na unidade de recuperação anestésica e após duas, quatro e seis horas após a cirurgia.

Resultados: O grupo AA apresentou significativamente menos episódios PONV do que o grupo controle durante todo o período pós-operatório (16/35 vs. 27/33, $p=0.03$ e 4/35 vs. 15/33, $p=0,005$ respectivamente); O grupo auriculoacupuntura apresentou episódios de náuseas menos intensos 2 h ($p=0.03$) e 6 h ($p=0.001$) após a cirurgia e menos episódios de vômitos 2 h ($p=0.01$) e 6 h ($p=0.02$) após a cirurgia.

Conclusão: Auriculoacupuntura aliviou náuseas e vômitos no pós-operatório em número significativo de pacientes, mas não foi capaz de prevenir náuseas e vômitos no pós-operatório, em todos os pacientes. Auriculoacupuntura pode ser recomendada como terapia adjuvante para prevenção de náuseas e vômitos no pós-operatório de colecistectomia laparoscópica em pacientes selecionados.

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Introduction

Postoperative Nausea and Vomiting (PONV) is the most frequent complication after a surgical procedure and is reported by 20–70% of patients. PONV should be considered a relevant issue for postoperative management and pain control as it can cause clinical complications such as dehydration, electrolyte disturbances, aspiration of gastric contents, and upper gastrointestinal bleeding. Moreover, the longer hospital stay and medication used for treating PONV may increase treatment costs.¹ Psychological complications are also relevant, as PONV causes dissatisfaction and discomfort for the patient. There are a variety of factors related to the occurrence of PONV, which include the patient, surgical procedure, and anaesthesia. Laparoscopic Cholecystectomy (LC) is among the surgeries that have a high incidence of PONV.^{2–4}

There are several drugs and alternatives to treating PONV after laparoscopic surgeries. However, these drugs only address one part of the problem and are not free of side effects.^{5–8}

The use of complementary strategies without the unwanted side effects is necessary, and an example of such

strategies is acupuncture.^{9,10} Some studies analysed the use of Auriculoacupuntura (AA) for control of PONV after hysterectomies or open cholecystectomies.^{11,12} However, there are no adequate and conclusive studies to recommend the use of AA for the prevention of PONV after LC.

The purpose of this prospective, double-blind, placebo-controlled trial is to investigate AA efficacy in the prevention of PONV immediately after uncomplicated LC.

Materials and methods

Study design

This study is a clinical, single-centre, randomized, prospective, double-blind intervention study (Brazilian Registry of Clinical trial number RBR-7543ns, www.ensaiosclinicos.gov.br/rg/RBR-7543ns) with a sample of 68 patients who were randomly divided into control (n = 33) and AA (n = 35) groups. They underwent AA treatment and clinical parameters were observed.

This study employed auricular acupuncture therapy, which is a respected part of Traditional Chinese Medicine

and has been shown to be effective in treating postoperative PONV.^{11,12} Though it has been known and used for many centuries in China to diagnose and treat diseases, auricular acupuncture's popularity in China rose after the late 1950s with increasing interest from practitioners. It represents a kind of micro-needle system.

We used the CONSORT guidelines for adequate reporting of our randomized controlled trial.¹³

Ethical standards

All the patients invited to participate were properly informed about the study and affirmed their voluntary participation by signing a written informed consent form with the parameters recommended by the ethics committee of by ethics committee of Pernambuco University. The study does not have any conflict of interest and was registered under CAEE number 38462314.9.0000.5207 in the Brazilian National Ethic Research System. The results of this study were presented as an oral Podium Presentation at Society of American Gastrointestinal and Endoscopic Surgeons Meeting (SAGES 2018), but the full text has not been previously published.

Participants

Between December 2016 and September 2017, 68 non-consecutive patients who underwent LC were considered suitable for our study. We included patients who were adult women, aged between 18 and 70 years old with a Body Mass Index (BMI) under 35 kg.m^{-2} and had an American Society of Anesthesiology Physical Status Classification System classification of 1 or 2. The exclusion criteria included LC with surgical or anaesthetic complications, operation time longer than 90 min, pre-operative nausea and vomiting, patient classified as 3 or above, use of an anti-emetic 12 h before the procedure, continuous use of analgesics or corticoids, history of substance abuse or patients who declined the invitation to contribute to this trial. If the patient was excluded after cholecystectomy, a new randomization was performed using the remaining sample size.

Technical procedures

The patients who fit the criteria were instructed in the use of the analogic visual scale used to measure nausea intensity (Fig. 1). They were codified and randomly allocated into two groups using a random number generator in Microsoft Excel. The allocation sequence was generated by the coordinator of this trial (LEM). The acupuncturist responsible for the session enrolled the respective participant and assigned the participant to an intervention (HN, LM or V)

We based the auricular point selection on the same points previously reported as effective for PONV treatment^{11,12} and on the advice from the senior acupuncturist. After sedation, the skin was prepared with 70% alcohol, and disposable sterile stainless-steel needles ($0.18 \times 8 \text{ mm}$) made from steel 316 L (DongBang Medical Co, Korea) were inserted perpendicularly into the skin to a depth of 3 mm over the trigger point in patients in the AA group for 20 min in a

single session (Fig. 2). Manual stimulation was not applied. After 20 min, the needles were removed. Needles were not used in patients in the control group. The anaesthesiologist, patient, and surgeon were unaware of the study group to which the patient belonged. To handle the placebo effect and the double blinded status of the study, adhesive patches without pellet/seed were placed on the same ear acupoints as the experimental group. All patients in both groups were taped at the same auricular sites.

The auricular sites included in this study were: (1) Shen Men, located at the point of bifurcation of the superior and inferior parts of the antihelix crura and the lateral third of the triangular fossa; (2) kidney, located at the top of the cymba and below the antihelix bifurcation; (3) sympathetic, between the inferior branch of the antihelix and the helix; (4) stomach, which is where the root of the helix ends, and (5) occipital, located in the upper back corner of the lateral side of the antitragus (Fig. 2). There were no other components of treatment such as moxibustion, cupping, herbs, exercises or lifestyle advice.

A senior specialist in acupuncture, who was certified by the Brazilian Medical Association of Acupuncture (HN) and who had practised acupuncture for 20 years, trained and supervised the acupuncturists (LM and VB). All the acupuncturists were trained and licensed professionals.

Both groups underwent sedation with 5 mg midazolam 30 min before the surgery and were monitored through arterial oxygen saturation. Anaesthesia was induced and maintained with 2 mg.kg^{-1} of propofol, 5 mcg.kg^{-1} of fentanyl, 0.6 mg.kg^{-1} of the nondepolarizing neuromuscular blocker rocuronium, 2 g cefazolin, 2 g dipyron, 40 mg parecoxib, 10 mg metoclopramide, and continuous inhalation of sevoflurane. At the end of the surgery, atropine and prostigmine were applied for reversal of neuromuscular blockage. During surgery, blood pressure, arterial oxygen saturation, heart rate, and the capnography were continuously monitored. A multimodal protocol for pain management was used: a maximum of 150 mg of 0.75% ropivacaine was injected at all trocar puncture sites, 100 mg intravenous ketoprofen was given every 12 h and 2 g of intravenous dipyron was given every 8 h. The use of opioids was avoided. Four milligrams of intravenous ondansetron were given post-operatively when the patient reported intense nausea or vomiting. Gastric tube decompression was not used. The intra- and postoperative anaesthesia and the analgesia protocols were strictly followed.

Data collection

The primary endpoint was the incidence of PONV during the 6 h postoperative period. The patients were followed by a blinded researcher at time 0, which was immediately after orotracheal extubation, continuously until the second hour, and in the fourth and sixth hours. During these periods, the patients were evaluated using the analogic visual scale for nausea intensity, checked for the presence or absence of PONV episodes and were assessed if antiemetic use would be necessary. Nausea was defined as the unpleasant and imminent perception of the necessity to vomit. Furthermore, vomiting was defined as intense and involuntary abdominal contractions resulting in the elimination of gastric contents.

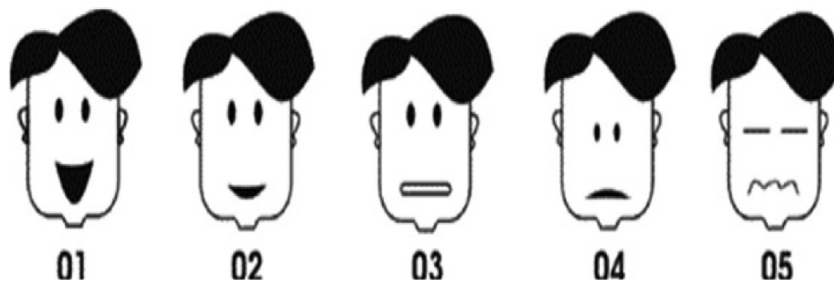


Figure 1 Analogic visual scale to measure nausea intensity. Grades of Nausea: (1) Absence of nausea; (2) tolerable nausea, with episodes that cannot be recalled by the patient or low intensity nausea that ceased with one episode of vomiting (there is no need for medication in either case); (3) nausea, with episodes that cannot be recalled and needs medications; (4) unforgettable nausea where anti-emetic drugs are necessary to control symptoms; and (5) persistent nausea, with no significant improvement even with the use of anti-emetic drugs.

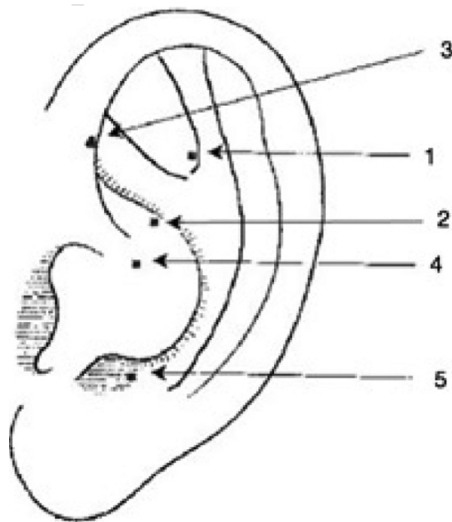


Figure 2 Auricular sites chosen for needle placement: (1) Shen Men, located at the point of bifurcation of the superior and inferior parts of the antihelix crura and the lateral third of the triangular fossa; (2) kidney, located at the top of the cymba and below the antihelix bifurcation; (3) sympathetic, between the inferior branch of the antihelix and the helix; (4) stomach, which is where the root of the helix ends; and (5) occipital, located in the upper back corner of the lateral side of the antitragus.

The patients were discharged from the post-anaesthesia care unit when their vital signs became stable and they awoke from the effects of anaesthesia.

Sample size determination

A sample size power analysis was performed using Stata 12.1 SE, StataCorp, USA. The sample size calculation was based on a preliminary survey conducted in our institution, which showed 40% incidence of vomiting in the control group compared to 2% incidence in the treatment group after laparoscopic cholecystectomy.⁶ Assuming the same difference in PONV in our study, with a power of 90% ($\beta = 0.1$) and significance level of 5% ($\alpha = 0.05$), our sample size required 27 patients in each group.

Statistical analyses

The demographic data and observed results were plotted using Excel 2013 spreadsheets and were expressed as the mean values \pm standard deviation or median \pm maximum and minimum values when appropriate. Fisher's exact test was used to assess differences between proportions and Student's *t*-test or Mann-Whitney *U* test were used to evaluate parametric or nonparametric data, respectively. A significance level of 5% was considered for all analyses. For the statistical analysis, PRISM 5.0 and GraphPad software, Inc, CA, USA, were used by a blinded researcher.

Results

From December 2014 to November 2015, a total of 68 patients ($n = 68$) participated in our study, in which 33 (48.5%) patients were in the control group and 35 (51.5%) patients who underwent LC at Oswaldo Cruz University Hospital were in the AA group. There were no significant differences between patients in terms of age, race, BMI, marital status, PONV history, smoking habits, or duration of surgery (Table 1). All patients were discharged from the hospital 24 h after the procedure. There were no recorded surgical complications, such as intra-operative bleeding, hypotension, or organ perforation, nor exclusion after randomization to any of the groups. There were no harms or unintended effects of acupuncture treatment in any of the groups.

The AA group had significantly less nausea and vomiting than the control group throughout the whole postoperative period (16/35 vs. 27/33, $p = 0.03$ and 4/35 vs. 15/33, $p = 0.005$, Fisher's exact test, respectively).

Through the comparison of postoperative nausea intensity between the two groups using the analogic visual scale, it was observed that nausea intensity significantly differed between groups at the second ($p = 0.005$) and 4 h ($p = 0.001$). Moreover, as illustrated in Table 2, the AA group had lower nausea intensity two and four hours after surgery compared to the control group.

Two and six hours after surgery, as presented in Table 3, the AA group had significantly less nausea ($p = 0.03$ vs. $p = 0.001$) and vomiting ($p = 0.01$ and $p = 0.00$) than the control group.

Table 1 Frequency distribution of patient characteristics and previous history of PONV.

	Control group (n = 33)	Intervention group (n = 35)	p
Age (years) ^a	41 (±2.5)	41.3 (±2.3)	0.91
Race (white/non-white) ^c	17/16	14/21	0.98
BMI ^b	28 (19–35)	29 (17–35)	0.19
Married (yes/no) ^c	19/14	25/10	0.96
Surgery time (minutes) ^a	55.9 (±3.7)	56 (±3.9)	0.9
HPONV (yes/no) ^c	05/28	04/31	0.99
Smoking (yes/no) ^c	04/29	02/33	0.99

Values are expressed as ^a Mean ± Standard Deviation; ^b Number of patients or; ^c Max–min range; p-value represents the comparison between AA and control groups, and it is considered significant if $p < 0.05$.
BMI, Body Mass Index; HPONV, Previous History of PONV.

Table 2 Postoperative nausea intensity in study groups.

Postoperative time (hours)	Nausea intensity	Control (n = 33)	AA (n = 35)	p
0	1	24	26	NS
	2	2	6	
	3	2	2	
	4	1	0	
	5	4	1	
2	1	19	30	0.005
	2	6	5	
	3	1	0	
	4	0	0	
4	1	24	29	NS
	2	5	3	
	3	1	0	
	4	0	0	
	5	3	3	
6	1	22	34	0.001
	2	3	0	
	3	1	0	
	4	0	0	
	5	7	1	

Values are expressed as number of patients at each postoperative time according to nausea intensity (VAS score). The Mann-Whitney test was significant if $p < 0.05$.
NS, Not statistically significant.

Discussion

LC is one of the most performed surgeries worldwide due to high prevalence of stone formation in the gallbladder. PONV frequently complicates the postoperative period of LC. It is frequent in 30% of cases, and it can create severe distress for patients that lead to the postponement of hospital discharge. For this reason, PONV remains a significant postoperative issue despite implementation of risk factor-based guidelines and availability of new drugs.^{14,15}

As PONV is a multifaceted disorder with numerous aetiologies, such as anaesthetic, surgical, clinical risk factors, and different pathophysiologic pathways, it is expected that treating PONV cannot be reduced to a single drug or clinical measure.¹⁶ Clinical alternatives that can be associated with drugs used in treating PONV are interesting options to decrease PONV symptoms.¹⁷ Acupuncture is an appropriate alternative as it is cheap, demands little skill, has few clin-

ical complications and has been demonstrated to be useful in PONV prevention.^{17–20}

The biological basis of acupuncture remains unclear. However, a considerable amount of evidence has established that acupuncture contributes to the equilibrium of neurochemicals in the central nervous system and to the recovery or maintenance of homeostasis via low-frequency electrical stimulation of the skin, which subsequently stimulates nerve activity and consequently affects nerve transmission in the dorsal horn and upper neurons.^{21,22} Manipulation of acupuncture needles is still the most practicable clinical procedure used to enhance stimulation intensity to improve therapeutic effects. In Chinese medicine, acupuncture causes the flow of an energy force known as ‘‘Qi’’, which maintains the equilibrium between Yin (negative-dark water) and Yang (positive-bright fire). For AA, all the points in the ears may be stimulated to correct Qi imbalance.²³ Distance from the surgical site, decreased patient exposure and no interfer-

Table 3 PONV incidence in study groups.

Postoperative time	Nausea		
	AA Group	Control	<i>p</i>
0 h	9 (27%)	9 (25%)	NS
2 h	5 (14%)	14 (42%)	0.03
4 h	6 (17%)	9 (27%)	NS
6 h	1 (2%)	7 (21%)	0.001
Postoperative time	Vomiting		
	AA Group	Control	<i>p</i>
0 h	1 (2%)	2 (6%)	NS
2 h	0	6 (18%)	0.01
4 h	3 (8%)	3 (9%)	NS
6 h	1 (2%)	7 (21%)	0.02

Values are expressed as number (%) of patients at each postoperative time according to presence of nausea and vomiting events. The Fisher's exact test was significant if $p < 0.05$.

ence with electrical energy are clear advantages of AA over body acupuncture.

Few studies have investigated the effects of AA on postoperative PONV. Kim and colleagues²⁴ examined the effects of AA on PONV after abdominal surgery, and they concluded that AA is effective at reducing the incidence of vomiting after transabdominal hysterectomy. Zhang and colleagues studied the influence of AA on the incidence of PONV and the analgesic effect of AA after gynaecological laparoscopy.¹¹ They concluded that AA could significantly decrease the incidence of PONV in patients who underwent gynaecological laparoscopy and they reported that AA had a positive analgesic effect as well. In a retrospective cohort study on database entries of patients treated with either the conventional approach or AA for PONV prophylaxis, Moore and colleagues revealed that the incidence of PONV was comparable between the two groups, with 25 patients receiving AA and 185 patients receiving the conventional approach.²⁵

We were not able to find any study that investigated the effects of AA on PONV after LC. The objective of our study was to investigate the effects of AA on PONV in common surgical practices. In line with this aim, we included women who underwent uncomplicated LC as they represent the majority of surgical cases. To avoid including complicated cases, we excluded patients with long surgery duration, classified as ASA 3 and above, and those with surgical or anaesthetic intraoperative complications, such as bleeding, hypotension, cardiac arrhythmias, or gallbladder empyema. Furthermore, we excluded patients with habits or symptoms that could cause nausea and vomiting, which could consequently interfere with the observation. In addition, we avoided the use of opioids in treating postoperative pain. Therefore, we investigated the effects of AA in females with few PONV risk factors who underwent simple LC. The results showed rates of nausea and vomiting of 63% and 28%, respectively. The results of our study were similar with that of previously published studies. Both groups received metoclopramide as PONV prophylaxis for ethical reasons. As the patients in our study had few PONV risk factors, conventional postoperative drugs were only dispensed upon the patient's

request to decrease its interference on the postoperative results. AA reduced the incidence and intensity of nausea in the second and sixth hours after surgery. However, it was unable to provide satisfactory comfort to patients, and anti-emetic medications were still distributed. There were no recorded AA complications. As more patients in the control group had intense nausea in the second hour after surgery and were consequently provided ondansetron, it is possible that the results observed in the fourth hour post-operation were altered by the effects of the anti-emetic medication. However, there was no difference in the type of medications distributed to patients 4 h after surgery. Moreover, the difference in nausea intensity and number of patients with referred PONV was observed again 6 h post-operation, and it was found that AA was effective up to 6 h post-operation.

Our study had limitations. First, this study was a single-centre study. Therefore, the characteristics of the local population and issues related to the hospital and the surgical and anaesthesiology team can influence the conclusions. Involvement of other hospitals and professionals at different medical centres would reduce this limitation. We included only females with few PONV risk factors who underwent uncomplicated LC in our study. We excluded the interference of other factors that could cause PONV and investigated a population that represents the majority of surgery cases. However, we were not able to observe higher risk cases or longer and complicated LC or surgery in men. The population size included in our study was small, but as we were able to demonstrate a significant difference between the groups, we considered it adequate. We evaluated nausea intensity using the visual analogic scale, which demands some level of understanding from the subject. Although they were instructed by the researchers and VAT is easy to comprehend, nausea is a peculiar symptom and its interpretation is subjective. Thus, we can expect a level of inconsistency or idiosyncrasy in the interpretation of this symptom. We observed only the initial 6 h of the postoperative period and no further observations were made after this period. Finally, we did not use any validated risk factors to determine which patients are at highest risk of developing PONV before being discharged from the postoperative care unit. As a consequence, no comparison between our study and previous research was made.

In conclusion, by considering the employed methodology, the results gathered, and the limitations of the study, AA can partially prevent PONV when compared to metoclopramide alone after uncomplicated LC. AA may be recommended as an adjuvant therapy in selected patients. Subsequent studies that include more patients and research centres can help to elucidate the effect of AA in this clinical context.

Conflicts of interest

The authors declare no conflicts of interest.

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