



# The Effect of Preoperative Zintoma Capsule on Postoperative Nausea and Vomiting After Laparoscopic Cholecystectomy

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## Abstract

**Background:** Postoperative nausea and vomiting (PONV), as one of the complications after laparoscopic cholecystectomy, occurs in over 40% - 77% of cases. Considering the numerous complications of synthetic drugs, there is a growing tendency towards the use of herbal medicines due to their unique features. Ginger root is one of the herbal compounds effective on nausea and vomiting.

**Objectives:** The aim of this study was to evaluate the effect of preoperative Zintoma capsules on PONV after laparoscopic cholecystectomy.

**Methods:** In this quasi-experimental study, 130 eligible patients were randomly assigned to intervention (n = 65) and control (n = 65) groups using the four-block method. The intervention group received two capsules of 500 mg and one of 250 mg Zintoma. The control group received three placebo capsules. The severity of patients' PONV was recorded at 0, 2, 6, 12, and 24 hours after surgery using a checklist and a standard VAS instrument. Data were analyzed using t-test, Chi-square test, and LSD Post Hoc test (ANOVA) in SPSS 19.

**Results:** The severity of PONV and vomiting was significantly different between the two groups (P = 0.001) at the above time points. The mean severity of nausea (by VAS) changed in the intervention group from  $7.92 \pm 1.28$  to  $0.33 \pm 0.67$  and in the control group from  $8.00 \pm 1.20$  to  $2.11 \pm 1.55$ . The postoperative vomiting was less frequent in the group receiving the Zintoma capsules. The postoperative use of chemical anti-vomiting and nausea drugs was significantly lower in the intervention group than in the placebo group (P = 0.001).

**Conclusions:** Zintoma capsules can be used as a supportive treatment in the prevention of nausea and vomiting by reducing the incidence rate of PONV.

**Keywords:** Ginger, Preoperative Period, Postoperative Nausea and Vomiting, Laparoscopic Cholecystectomy

## 1. Background

Postoperative nausea and vomiting (PONV), as one of the most common and most annoying complications after laparoscopic cholecystectomy, occurs in more than 40% - 77% of the cases (1). PONV causes aspiration, hypoxia, bleeding, suture rupture, patient discomfort, increased hospital stay, and increased hospital costs (2). Preoperative drugs that are used intravenously to prevent PONV include endostenone, troposterone, granistorone, dilustran,

metoclopramide, and perphenazine. The problems associated with preventive anti-vomiting prescriptions typically include increased costs, especially if serotonin antagonists are prescribed, orthostatic hypotension, and vomiting with or without prophylaxis of vomiting (3-6). However, it should be noted the use of anti-nausea and vomiting drugs is not merely suitable for patients, but the routine use of these drugs causes complications leading to more required drug interference and prolonged length of stay (6-8). Restlessness, dry mouth, drowsiness, tachycar-

dia, hypotension, and fatigue are among the other complications of the drug therapy (6, 7). Considering the numerous complications of synthetic drugs, there is a growing tendency towards the use of herbal medicines due to their unique features such as variety and flexibility, easy access, worldwide availability, high acceptance among the majority of people in developing countries, relatively cheap price, less technology-dependence nature, and increasing economic importance (4, 9). Herbal medicine, as one of the complementary methods, has been used by various communities thousands of years ago. According to the World Health Organization (WHO) statistics, currently, around 80% of the world population uses herbal compounds for treatment purposes, which is higher in the non-developed countries than in developed countries (7). The Ginger root is one of the herbal compounds with an effect on nausea and vomiting that does not cause any specific complications (4, 9, 10). Ginger products exert their anti-vomiting effects through several mechanisms; for example, Ginjervel and Chagall reduce stomach contractions but increase the activity of the gastrointestinal tract. These compounds also have anti-serotonergic effects and exert a dust effect on the free radicals causing the vomiting (10). Apariman et al. showed that the severity of PONV significantly reduced in a ginger-treated group compared to a placebo group (11). It has been shown in a study that the daily consumption of 1 gram of ginger significantly reduces the vomiting of pregnancy (12); however, Willetts stated that 1.5 grams of ginger did not affect vomiting (13). Considering the frequent surgical operations at hospitals and the PONV as the most common post-surgical and general anesthetic complication, as well as the complications caused by drugs used to prevent PONV, and in spite of various studies so far conducted to evaluate the effectiveness of ginger capsules in various conditions of nausea and vomiting, such as motion sickness (14), chemotherapy-induced vomiting (15), nausea (16), vomiting (9), its effectiveness is still controversial (17).

## 2. Objectives

This study aimed at evaluating the effect of preoperative Zintoma capsule on postoperative nausea and vomiting in patients who had laparoscopic indications.

## 3. Methods

This is a quasi-experimental study with two groups (intervention and control). After obtaining an approval from the Vice Chancellor for Research of Ahvaz Jundishapur University of Medical Sciences and receiving an Ethical Code from the relevant Ethics Committee (Code:

ajums.REC.1392.316), a total of 130 patients who were willing to participate in the study (after obtaining their informed consent) and met the inclusion criteria were randomly selected to be examined from among those who referred to Razi Hospital in Ahvaz for the Laparoscopic Cholecystectomy operation in 2015 - 2016. The inclusion criteria included ASA class I/II, maximum surgery duration of 60 to 90 minutes, lack of motion sickness, age of 18 to 65 years, BMI of 19 - 25, ability to swallow capsules used in the study, platelet count more than 100,000, lack of intestinal obstruction and hepatitis, lack of pregnancy and use of anti-nausea and vomiting drugs, the lack of long-term treatment with corticosteroid drugs, lack of a history of allergy to ginger and other diseases that affect the digestive system, heart and kidneys, nerves, and so on, such as, diabetes, heart disease, nervous and muscular disorders, etc. It should be noted that all patients had NPO time between 8 and 12 hours. The exclusion criteria included severe PONV and a statement of the lack of interested in continuing the study. All eligible patients were randomly assigned to either (A) intervention group (n = 65) or (B) control group (n = 65) using the four-block method. Individuals in the intervention group received three capsules (two of 500 mg and one of 250 mg ginger), made by Goldaru Pharmaceutical Co. The individuals in the control group received three placebo capsules, which were similar to the ginger capsules and were made using the same method by the Faculty of Pharmacy, Ahvaz Jundishapur University of Medical Sciences. Patients took A or B regimens (ginger or placebo capsules) with 30 mL of water one hour before the surgery. The type of anesthetic drug, the use of anesthetic drugs, duration of anesthesia, and the intra-operative administration of opioid drugs were determined according to the anesthetist's decision and were identical for all patients. For all the patients, the way of induction of anesthesia included midazolam 2 mg, fentanyl 2  $\mu$ g/Kg, thiopental 5 mg/kg, atracurium 0.5 mg/kg, and morphin 0.1 mg/kg. For the maintenance of anesthesia, 50% oxygen, 50% N<sub>2</sub>O, 1 mg/kg propofol and 1  $\mu$ g/kg/min remifentanil were used. The anesthesia technique and the used amount of long-acting opioids during the anesthesia were identical and the surgery was performed by the same surgeon.

Analgesics (100 mg of diclofenac suppository, which is not associated with nausea and vomiting, unlike other intravenous opioids) were prescribed postoperatively based on the patients' request and anti-vomiting drugs (metoclopramide 10 mg IV PRN) were prescribed for each patient when more than two vomiting episodes occurred (regardless of the grouping and placement of patients in the study). All patients were trained how to strongly score their nausea based on the VAS criterion. This tool consists of a 10-cm line (ranging from 0 to 10), with 0 and 10 of

the instrument being equal to the absent and severe nausea, respectively. The instrument is rated as follows: scores 0, 1-3, 4-6, 7-9, and 10 respectively assigned to no nausea, mild, moderate, severe, and very severe nausea. Vomiting was defined as a severe gastrointestinal stimulation, which caused the expulsion of the contents of the digestive tract from the mouth, and its frequency was recorded by one nurse who was unaware of the type of intervention. The demographic questionnaire included age, gender, level of education, underlying disease, duration of NPO, history of surgery, history of PONV, and history of using anti-vomiting and nausea drugs. The duration of surgery, demand for opioids, the demand for postoperative anti-vomiting drugs, the duration of anesthesia, the score obtained from the VAS scale, and the frequency of bloating and vomiting were also recorded in the postoperative checklist. The severity of PONV was assessed using a checklist and a standard tool by one nurse who was not aware of the type of (A) or (B) treatments at 0, 2, 6, 12, and 24 hours after the operation. It is necessary to explain that all subjects participated in the study were asked about possible complications such as abdominal pain, heartburn, shortness of breath, and insomnia. After being collected, the data were analyzed using central and dispersion index table for describing the samples in SPSS ver. 19. A *t*-test was used to analyze quantitative variables and Chi-square test and LSD test to compare the severity of nausea at the above different time points.

#### 4. Results

The statistical analysis of the data showed that there was no significant difference between the two groups in terms of individual characteristics (age, height, and weight) according to the independent *t*-test ( $P > 0.05$ ) (Table 1). There was no significant difference between the two groups in terms of other demographic characteristics (gender, occupation, education, marital status, and ethnicity) according to the Chi-square test. Thus, the two groups were homogenous in this regard. The LSD test was used to compare the mean severity of nausea in the two groups, which showed a significant difference ( $P = 0.001$ ).

The LSD test was used to compare the mean severity of nausea in the two groups, which showed a significant difference ( $P = 0.001$ ) (Table 2).

The Chi-square test was used to compare the frequency of vomiting in the two groups. The results showed that there was a significant difference between the two groups in terms of the incidence of vomiting immediately after the surgery and anesthesia up to 6 hours later ( $P < 0.05$ ) in such a way that the vomiting occurred in four and three patients receiving the Zintoma capsules immediately and

two hours after the operation, respectively. However, 33, 24, and 14 patients who received placebo capsules immediately, 2, and 6 hours after the operation experienced the vomiting, respectively. No vomiting was reported in the two groups 12 and 24 hours after the operation (Table 3).

The Chi-square test was used to compare the percentage of anti-vomiting/anti-nausea drugs use between the two groups and the results showed that these drugs were used at a significantly lower level in the intervention group than in the control group ( $P = 0.001$ ) (Table 4).

#### 5. Discussion

Considering the main goal of the study, i.e. investigating the effect of Zintoma capsules on the severity of PONV after laparoscopic cholecystectomy, the results indicated that the placebo capsules in the control group did not show a significant effect on reducing the severity of postoperative nausea and frequency of vomiting, while the severity of nausea and frequency of vomiting significantly reduced in the intervention group following the use of Zintoma capsules.

The results of many studies are similar to those of our study (12, 18-21), but a few studies reported contradictory results (22-24). As Montazeri et al. showed, taking 1000 mg of ginger capsules one hour before surgery could not have any effect on nausea and vomiting at four and six hours after surgery (25). In addition, the results of a meta-analysis study that evaluated six clinical trials showed that ginger had no effect on postoperative nausea and vomiting (22).

In addition, in the study of Arfeen et al. there was no significant difference in the reduction of postoperative nausea and vomiting in 108 women receiving 0.5 g of ginger and 1 g of ginger and placebo (23).

Furthermore, Eberhart et al. indicated no advantage for ginger over the placebo in the prevention of PONV after laparoscopic surgery (24).

These opposite results can be attributed to single-woman samples in these studies or different types of laparoscopic surgery and the different anesthetic drugs or different doses of ginger capsules (500 mg, 750 mg, 1 g, 1.250 g, 1.5 g, and 2 g) (12, 18, 20, 21, 25).

In addition, in our study, we compared the use of ginger capsules and placebo to control postoperative nausea, but in other studies, ginger was compared with other anti-emetic agents such as ondansetron. Differences in the methodology, the study samples, and the time to evaluate PONV and using various doses are the other causes of inconsistency between our results and other study results (1, 11, 18, 26-28).

From comparing similar studies, such as Nanthakomon et al. study, with our study, we can conclude

**Table 1.** Comparison of Age, Height, and Weight of the Participants in the Intervention and Control Groups<sup>a</sup>

Variable	Group		P Value
	Control, N = 65	Intervention, N = 65	
Age, y	41.67 ± 12.05	40.93 ± 12.1	0.82
Height, cm	167.07 ± 8.21	163.85 ± 7.92	0.14
Weight, kg	81.59 ± 11.14	79.56 ± 19.12	0.63

<sup>a</sup>Values are expressed as mean ± SD.

**Table 2.** Comparison of Mean Nausea Severity During the Study in Intervention and Control Groups<sup>a</sup>

Time	Nausea		P Value
	Control, N = 65	Intervention, N = 65	
Immediately after surgery	8.00 ± 1.20	7.92 ± 1.28	
2 hours after intervention	7.67 ± 1.59	4.81 ± 1.07	
6 hours after intervention	6.81 ± 1.71	2.81 ± 1.36	0.001
12 hours after intervention	4.93 ± 1.70	0.74 ± 1.13	
24 hours after intervention	2.11 ± 1.55	0.33 ± 0.67	

<sup>a</sup>Values are expressed as mean ± SD.

**Table 3.** Comparison of Vomiting During the Study in Both Groups Before and After Intervention<sup>a</sup>

Vomiting	Group		P Value
	Control, N = 65	Intervention, N = 65	
Immediately after surgery	33 (50.76)	4 (6.15)	0.0001
2 hours after intervention	24 (36.92)	3 (4.61)	0.0001
6 hours after intervention	13 (23.07)	0 (0)	0.0001
12 hours after intervention	0 (0)	0 (0)	0.999
24 hours after intervention	0 (0)	0 (0)	0.999

<sup>a</sup>Values are expressed as No. (%).

**Table 4.** Comparison of the Use of Antiemetic Drugs in Intervention and Control Groups<sup>a</sup>

Used Drug	Response	Group		P Value
		Control, N = 65	Intervention, N = 65	
Antiemetic: Metoclopramide	Yes	30 (46.15)	2 (3.07)	0.001
	No	35 (53.58)	63 (96.93)	

<sup>a</sup>Values are expressed as No. (%).

that Ginger can reduce postoperative nausea and vomiting at two and six hours after gynecologic surgery (29).

Kalava et al., Apariman et al. and Phillips et al. also showed that ginger could be effective in reducing the PONV at 1 g and 1.5 g, as compared to the placebo (11, 30).

In addition, Hosseini et al. showed that using ginger drops in open or laparoscopic surgery could reduce postoperative nausea and vomiting (19), which is similar to the results of our study.

One of the most important strengths of this study was that the intervention was performed on two male and female sex groups. One of the limitations of our study was the presence of three pills that were eaten by the patients who were often reluctant to eat three pills before surgery (it should be noted that all patients had NPO time between 8 and 12 hours).

### 5.1. Conclusion

The results of the present study showed that the use of 1.250 g of Zintoma capsules before laparoscopic cholecystectomy could significantly reduce the amount of PONV and thus, they are recommended to use prior to the surgeries associated with severe PONV.

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### Footnotes

**Authors' Contribution:** Study concept and design: Masoomeh Albooghobeish; analysis and interpretation of data: Abdolkazem Neisi, Saba Arya Nasab, and Sara Adarvishi; manuscript preparation: Kamran Mahmoodi and Masoomeh Asadi; collection of data: Fereshteh Amiri and Nasrin Khajeh Ali; critical revision: Maryam Kouchak and Sara Adarvishi.

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