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Effects of preoperative administration of ginger (*Zingiber officinale* Roscoe) on postoperative nausea and vomiting after laparoscopic cholecystectomy

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ABSTRACT

One of the most common postoperative problems is nausea and vomiting. Although using some anesthetic materials has been considered as the mainstay of this phenomenon, the exact factors are not known. Because of several morbidities associated with postoperative nausea and vomiting (PONV), its prevention and treatment has been a challenge for physicians, so several drugs have been recommended for this purpose. Based on the documented antiemetic specificity of ginger, we evaluated and compared the effects of preoperative administration of ginger on PONV with ondansetron administration as the standard medication. The participants included 100 patients with cholelithiasis who were candidate for laparoscopic cholecystectomy. Patients were divided into two groups: group A comprised 50 patients who received 500 mg oral ginger 1 h before surgery, and group B included 50 patients who received 4 mg intravenous ondansetron before completion of surgery. Antiemetic efficacy was assessed by visual analogue scale scores of nausea intensity at 0, 4, 8, 16, and 24 h after surgery and frequency of vomiting during the evaluation period. Although multifactor analysis showed that nausea severity was significantly lower in the ginger group, the data indicated that except 16 h after operation, the differences between two groups in the frequency of vomiting was not significant. In conclusion, though complementary studies are needed to have a strong suggestion, based on this study, we recommend administration of oral ginger 1 h before operation to control the severity of PONV in patients undergoing laparoscopic cholecystectomy.

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1. Introduction

Postoperative nausea and vomiting (PONV) with an incidence between 1–43% is one of the most common morbidities associated with surgical operations.^{1–6} Although some believe that the main causative factor for PONV is the anesthetic materials, several studies demonstrated effect of a wide range of factors such as age,

sex, the time between last meal and operation, the history of PONV, the anesthetic methods and the type of surgical procedures on PONV.^{2,4,5} Since long hospital stay, poor patient satisfaction from the medical team and increased treatment cost are the most morbidities associated with postoperative nausea and vomiting, its prevention and treatment pose a significant challenge in the modern medicine.^{2,5–7} Other complications of PONV include electrolyte disorders, increased pain, hypertension and probably elevated risk of pulmonary aspiration.^{2–4}

Although several agents such as Metoclopramid, Droperidol, Dexamethasone and Diphenhydramine have been used for this purpose, and finally intravenous administration of ondansetron has been suggested as the standard medication, efforts in presenting a gold standard drug is still under progress.^{4,8,9}

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Based on the historical usage of ginger (*Zingiber officinale* Roscoe) as an antiemetic agent in the east traditional medicine, using ginger in the treatment of pregnancy-induced nausea and vomiting has been evaluated and well accepted by a number of studies.^{10–18} However, ginger effects in preventing chemotherapy induced nausea and vomiting faced with some agreements and oppositions.^{19–24} Recently, prevention of PONV by administration of ginger has been evaluated by some studies, although the exact mechanism has been uncertain. In addition, most of these studies performed in gynecologic field and open surgery.^{6,7,9,25–29}

In comparison to open surgery, PONV in laparoscopic operations is noisier and the purpose of this study was to evaluate and compare the effects of preoperative oral administration of a single dose of ginger on PONV with ondansetron administration as the standard medication in laparoscopic cholecystectomy.

2. Material and methods

This is a simple randomized, double blind, single-dose, parallel group clinical trial study which was conducted on patients underwent laparoscopic cholecystectomy from March 2013 to February 2014. The study was approved by the ethics committee of Mashhad University of Medical Sciences, Iran. The participants included 100 patients (Age ranged from 20 to 60 years) with cholelithiasis who were candidate for laparoscopic cholecystectomy. Patients with a history of lung disease, probable gastroparesia (such as diabetic patients), any co-morbidities (such as diabetes mellitus, renal failure and heart failure), gastrointestinal bleeding, inflammatory bowel disease or bowel obstruction, allergy to ginger, patients with a history of using any antiemetic or prokinetic drugs during the last month before surgery, any drug with the side effect of nausea and also patients with a history of general anesthesia during the last week before surgery, aspirin or anticoagulation agents consumption, patients with $18 > \text{BMI} > 30$ and pregnant patients were excluded from the study. The patients with operative time more than 1 h were also excluded from the study. Written informed consent was obtained from all participants.

Using SPSS (version 16.0), patients were divided into two groups: group A comprised 50 patients who received 500 mg oral ginger [Cap Zintoma 500 mg, Isfahan, *Gol Daru* Company – each capsule has 0.5 gr essential oils (volatile oils) of Ginger root] 1 h before surgery, and group B included 50 patients who received 4 mg intravenous ondansetron - to have a standard control in our study, ondansetron was selected - before completion of surgery. Since ginger T_{max} is approximately 45–60 min, it has enough time to reach the maximum serum concentration if it is administered 1 h before the operation. Because of the importance of the blindness of the study, the prescription of Zintoma or Ondansetron was performed by one of the researchers who were not involved in patients' evaluation.

All patients underwent general anesthesia with the same anesthetic protocol (induction with midazolam, fentanyl, atracurium and thiopental sodium, and maintenance with propofol and N2O). Laparoscopic cholecystectomy was performed by a standard technique. The range of operative time was 15–45 min and the anesthesia time was 25–60 min. To treat PONV and based on patients' request, intramuscular metoclopramide (10 mg per dose) was administered.

All parameters such as age range, sex match, unique anesthesia and operation technique and also study exclusion criteria were designed in the study to having acceptable matching in two study groups.

Clinically, maximum nausea and vomiting appears in the first 24 h after completion of surgery, so we assigned this period of time to evaluate the participants. All assessments were performed by an

independent, blind nurse who was unaware of the patients' group allocation. Antiemetic efficacy was assessed based on two criteria: 1) Visual analogue scale (VAS) scores of nausea intensity at 0, 4, 8, 16, and 24 h after surgery and 2) frequency of vomiting during the evaluation period. The visual analog scale of nausea intensity consists of a 10 cm line with two end-points representing 'no nausea' and 'worst nausea'. Patients were asked to rate their nausea by placing a mark on the line corresponding to their level of nausea on the given time. Patients were not awakened for the assessments if they were asleep. During their hospital stay, all patients were evaluated concerning induced complications of oral ginger administration (i.e. abnormal intra-operative bleeding, airway aspiration in the operating room, allergic reaction and upper gastrointestinal bleeding).

After data collection, statistical analysis was performed using SPSS (Version 16.0), by means of student t-test, regression logistic and chi square tests with mean \pm 2 SE for determination of confidence interval of 95%. The generalized estimating equation (GEE) test was used to evaluate the rate and severity of nausea.

3. Results

Among the 100 patients enrolled in this study, 71 (71%) were female and the remaining 29 patients were male. The mean age of the patients was 43.97 ± 16.19 and 38.97 ± 16.8 years for ginger and ondansetron group, respectively (Table 1). The parallel groups were well matched in terms of age and sex.

The severity of nausea which was checked by VAS technique, was significantly lower in group A (ginger) at 0, 2 and 4 h after the operation (Fig. 1). Although at 8 and 24 h after surgery, ginger group showed more reduction in nausea severity, likewise 16 h after surgery that ondansetron group demonstrated a better condition in this regard; the differences were not statistically significant (Table 2). Multifactor analysis by "regression logistic" and "regression negative binominal" methods showed that nausea severity

Table 1
Baseline characteristics of the study population.

Variable	Study Group				Statistic ^a	P-value
	Ginger Group		Ondansetron Group			
	Male (%)	Female (%)	Male (%)	Female (%)		
Sex	32 (35.5)	58 (64.5)	27 (30)	63 (70)	2.6	0.10
Age	43.97 ± 16.19		38.97 ± 16.8		1.06	0.10

^a Student t-test, chi square test.

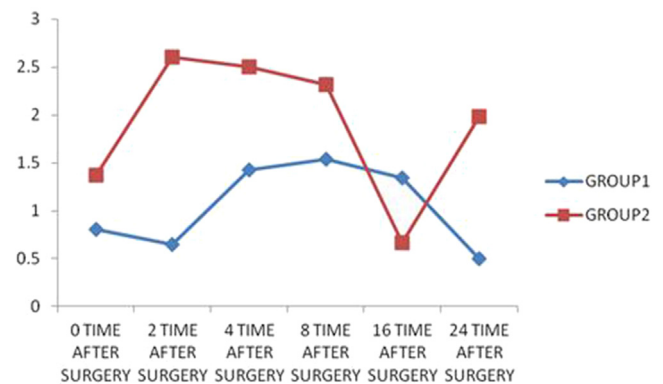


Fig. 1. The differences of severity of nausea between the studied groups (1: Ginger – 2: Ondansetron) based on the visual analogue scale assessment (vertical axis) during 24 h (horizontal axis) after surgery.

Table 2

The differences of severity of nausea between the studied groups based on the VAS evaluation 24 h after surgery.

Time from operation (hour)	Study Group		Statistic ^a	P-value
	Ginger Group	Ondansetron Group		
	Mean ± SD	Mean ± SD		
0	0.81 ± 2.6	1.37 ± 2.4	3.01	0.002
2	0.65 ± 2.3	2.6 ± 3.04	4.44	0.0001
4	1.43 ± 3.2	2.5 ± 3.05	2.6	0.008
8	1.54 ± 3.1	2.32 ± 2.7	2.04	0.41
16	1.34 ± 2.9	0.67 ± 1.69	0.18	0.4
24	0.5 ± 0.1	1.98 ± 0.56	0.79	0.4

^a Mann–Whitney U test.**Table 3**

The differences of vomiting frequency between the studied groups 24 h after surgery.

Time from operation (hour)	Study Group		Statistic ^a	P-value
	Ginger Group	Ondansetron Group		
	Mean ± SD	Mean ± SD		
0	0.3 ± 1.41	0.23 ± 1.36	1.07	0.28
2	0.45 ± 2.00	0.58 ± 1.46	2.9	0.004
4	0.39 ± 1.43	0.39 ± 0.82	0.95	0.34
8	0.47 ± 1.62	0.32 ± 0.5	0.98	0.34
16	0.27 ± 1.5	0.89 ± 0.28	0.98	0.32
24	0.11 ± 0.49	0.02 ± 0.13	0.34	0.72

^a Mann–Whitney U test.

was significantly lower in the ginger group. Although the severity of nausea was significantly decreased over time in this group, the effect of ginger on nausea severity was not consistent and over time the effect of ginger was similar to that of the ondansetron.

Concerning the frequency of vomiting, data analysis indicated that except at 16 h after operation, differences between two groups were not significant (Table 3).

No significant intraoperative hemorrhage, airway aspiration or other complications were noted in these patients.

4. Discussion

Evaluating the data, we realized that the incidence of post-operative nausea in the ginger group was significantly lower than ondansetron group and it remained constant over time. Although the rate of vomiting had not significant difference between the two groups, this similar rate could approve the efficacy of ginger in prevention of postoperative vomiting.

Although oral administration of ginger violates the non per os status before surgery, in consistent with other studies, our results showed no elevated risk of aspiration.^{6,7,17,30}

The antiemetic effect of ginger has been known as a treatment method in traditional medicine specially the Chinese and Iranian medicine.³¹ Several studies have been described the antiemetic mechanisms of ginger. For example, some in vitro studies have demonstrated that ginger extract anti-serotonergic, cholinergic M3 and serotonergic 5-HT3 and 5-HT4 receptors antagonisms, play an important role in prevention of PONV. It seems that the efficacy of ginger on reducing nausea and vomiting may be based on a weak inhibitory effect of gingerols and shogaols (the most important major chemical constituents of ginger) at M3 and 5-HT3 receptors. The 5-HT4 receptors, which play a role in gastroduodenal motility, appear not to be involved in this compounds' action.^{32–35}

Because ginger is an herbal, easily available, low price medication which is associated with low risk can be substituted for a chemical, scarce and expensive drug such as ondansetron. Based on our findings, we conclude that prescription ≥ 500 mg oral ginger

(based on the patient's weight) 1 h before the operation may significantly reduce the incidence of 24-hour PONV in patients undergoing laparoscopic cholecystectomy.

In conclusion, we recommend administration of 500 mg oral ginger 1 h before laparoscopic cholecystectomy, which is safe and tolerable. To generalize our finding, further studies are needed to evaluate ginger's effect on PONV in other laparoscopic surgeries such as bariatric surgery, colectomy and splenectomy.

Author contribution

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Conflict of interest

None declared.

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