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Original Research Article

The effect of chamomile on flatulence after the laparoscopic cholecystectomy: A randomized triple-blind placebo-controlled clinical trial

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ABSTRACT

Objective: Flatulence is one of the main post-operative Ileus-related complications, especially in abdominal surgeries, which can be largely due to the effects of anesthesia. There are various kinds of therapeutic methods used for their treatment though sometimes their effects are limited. Thus, it is essential to find alternative treatments to decrease the implications of the disease. The present study is aimed to investigate the effect of *Chamomilla recutita* on flatulence after Laparoscopic cholecystectomy.
Methods: This randomized controlled trial was carried out in 2020 at Isfahan in Iran. Patients randomly fell into either chamomile (n = 32) or placebo groups (n = 32). The intervention was performed 1 h before the operation. The severity and the frequency of flatulence were recorded using a visual analog scale in both groups in three stages before the operation, after the operation in recovery, and 2 h after the operation.
Results: The flatulence was not observed before the operation and on arrival in the recovery room. Before leaving the recovery room, the frequency of flatulence was the same in both the groups. However, in the surgical ward, the frequency of flatulence in the chamomile group was significantly lower than in the placebo group. The mean of flatulence severity has significantly increased in both groups over time but in the chamomile group, this increase was significantly lower than in the placebo group.
Conclusion: These results suggest that chamomile has a potential therapeutic effect on the gastrointestinal and can reduce flatulence. In laparoscopic surgeries, using chamomile drops as a preventive drug seems to be effective in reducing the incidence of postoperative flatulence.
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1. Introduction

1.1. Background

Flatulence is one of the main post-operative Ileus-related complications, especially in abdominal surgeries, characterized by nausea and vomiting, anorexia, abdominal pain, and distention [1,2] which can be largely due to the effects of anesthesia [3]. Flatulence is a feeling of fullness, tightness, and swollen (flow of gas) in the abdomen, which is a very uncomfortable condition [4]. It is a mental symptom and is often measured by the patient himself [5]. Severe abdominal distension can impair respiratory function, strain the stitches, and affect blood pressure [2,6]. Flatulence causes painful colic, increases bowel sounding [3,7], and pain [1,6,8]. The more severe the pains after the operation are, the more unfavorable hemodynamic and metabolic responses will be [9]. However, improving gastrointestinal function after the operation causes a rapid recovery [10].

Laparoscopic cholecystectomy is a standard surgical procedure for patients with symptomatic gallstone disease [11]. Although the advantages of this method are identified compared to open cholecystectomy, it is not complication-free [12]. For example,

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flatulence is one of the complications appearing after laparoscopic cholecystectomy surgery. The use of CO2 in laparoscopic surgery causes some of the CO2 gas to be absorbed into the intestines and causes flatulence. Also, due to intra-abdominal visceral manipulations and parasympathetic dysfunction, ileus (Intestinal dysfunction) complications occur. Ileus causes complications such as abdominal flatulence. The results of the study by O'Rourke and Van Rensburg (2018) depicted that flatulence appears in 26–62% of cases after this type of operation [13].

Prokinetic and Antispasmodics drugs, antibiotics, probiotics, abdominal gas reducers such as simethicone, and antidepressants have been introduced as flatulence treatment [14]. However, using conventional medicines to relieve this complication may be ineffective or may have unpleasant side effects [6,8,15].

Various methods have been recommended for controlling flatulence, however, the effectiveness of these methods is limited [1,6,16,17]. Therefore, it is necessary to find alternative therapies to reduce the patients' complications and the burden of hospitalization costs [17]. At present, the use of traditional medicine can be very appropriate due to the global interest in complementary and integrative medicine [5,18–20].

Chamomilla recutita (L.) is one of the most prominent dark plants of chicory in traditional medicine and has been used as a sedative in cases such as gastrointestinal disorders, colic, flatulence, and irritable bowel syndrome [18–24]. This may be caused by the flavonoid compounds, chamazulene, and bisabolol in chamomile having antispasmodic and anti-inflammatory effects [22,28,29].

According to some studies, chamomile seems to be safe and may only cause minor allergic reactions in people who are allergic to the medicinal plants of the chamomile family [18,20,25].

The study of Khadem et al. (2018) showed that chamomile effect on gastrointestinal motility disorders [17]. Agah et al.'s (2015) study showed that chamomile decreased the symptoms of irritable bowel syndrome significantly [26]. Ghorat et al. (2017) showed that chamomile oil can be considered as a complementary method to reduce colic symptoms in children [27]. Concerning animal samples, Masoumi et al. (2010) showed that an aqueous extract of chamomile significantly reduced inflammatory and wound indices of ulcerative colitis in rats [28].

1.2. Objectives

Considering the increasing number of laparoscopic surgeries the present study aimed to evaluate the effect of chamomile on the severity and frequency of flatulence after laparoscopic cholecystectomy before being discharged from recovery and 2 h after the operation.

2. Materials and methods

This study was designed with trial registration code IRCT20200612047737N1 and ethics code IR. MUI.RESEARCH.REC.1398.745 from Isfahan University of Medical Sciences in Iran. Patients that underwent laparoscopic cholecystectomy with general anesthesia and were referred to selected training hospitals in Isfahan in June, July and August 2020.

2.1. Trial design

The trial was designed as a randomized, triple-blind, placebo-controlled, parallel clinical trial. After obtaining approval from the University Ethics Committee and the Research Center, the researcher explained the objectives of the study to the participants. Post taking the written informed consent from the participants, they were divided into chamomile and placebo group using a random number table. There were 32 patients in each group. On the patients' arrival into the operating room and 1 h before the operation, the intervention group received 20 drops of chamomile extracts produced by Zardband Tehran Pharmaceutical Company (containing 17% Chamazulene, 45% Bizabolol and DER; 80kg/0/4 kg = 200 solutions in 20 cc water) with glass and a placebo group received distilled water. The severity and frequency of flatulence were recorded using a visual analog scale in three stages (before the intervention, before being discharged from recovery and 2 h after the ward).

2.2. Participants

The patients who were referred to Al-Zahra, Amin and Ayatollah Kashani hospitals in Isfahan for laparoscopic cholecystectomy were identified. After explaining the purpose of the study and obtaining written informed consent, they agreed to participate in the study. After random allocation, they were placed in 2 intervention or control groups. The study sample consisted of 64 patients in the 18–65 age range, and with a body mass index of 18–28.

2.3. Sample size

In this study, using the following formula with a 95% confidence interval and 80% test power, the number of samples for each group of 32 people in the study population was calculated.

$$n = \frac{(Z1 + Z2)2(2S)2}{d\,2}$$

2.4. Inclusion and exclusion

Inclusion criteria included insensitivity to herbal medicine, absence of known gastrointestinal diseases such as stomach ulcers, gastritis, colitis, etc, consciousness, non-pregnancy, ASA[1] class 1 and 2(Class 1 ASA refers to patients without any systemic problems and Class 2 are patients with mild systemic problems but whose disease is under control), and willing to participate in the study. Exclusion criteria included the patient's cooperation discontinuance, the patient's inability to determine the severity of flatulence despite the instructions, taking any type of analgesic and anti-flatulence drugs such as prophylaxis and blood transfusion, and changing the method of anesthesia during the operation.

2.5. Method of administration

The severity of flatulence was recorded using a visual analog scale being scored ranging from 0 to 10 according to the patient's self-declaration in three stages (before the intervention, before being discharged from recovery, and 2 h after the operation). This scale consists of a 10 cm ruler (range between 0 and 10). The number zero of the tool indicates the absence of flatulence and the number 10 indicates severe flatulence. The score 1 to 3 in this tool indicates the severity of mild flatulence, the score 4 to 7 indicates the severity of moderate flatulence, and score 8 to 10 indicates the severity of severe flatulence. To prevent the psychological effect of the type of intervention on the results, patients were asked to drink the harmless substance to help conduct a study aiming at caring for patients undergoing cholecystectomy, then the type of substance and its effect on patients were not described (one blind). All clinical and demographic information was recorded by the researcher

[1] - American Society of Anesthesiologists.

before intervention and during the intervention (giving chamomile drops and distilled water) and then they were recorded by a trained researcher assistant (Doubleblind).

2.6. Statistical methods

Mean, standard deviation, and frequency indices were used to report the results of the descriptive statistics. Fisher's exact test and independent t-test were used to analyze baseline and demographic information between groups. To analyze the data, analysis of variance with repeated measurement and the Chi-square tests were used. Data analysis was performed using SPSS 20 and a statistical consultant who did not know the type of groups (triple_blind).

The study adheres to CONSORT guidelines.

3. Results

3.1. Participant flow

The participants of the present study included 69 patients (n = 32, chamomile group; n = 32, placebo group). Of the 96 screened patients, 27 were excluded before randomization [Not meeting inclusion criteria (n = 16)/Declined to participate (n = 6)]. The patient flow is detailed in the CONSORT diagram [Fig. 1]. 69 patients were randomly assigned and 5 patients were excluded from the study due to lack of consciousness in the recovery ward.

3.2. Baseline data

The results of the independent t-test showed that the mean age and body mass index did not differ significantly between both groups ($P > 0.05$) (Table 1). The frequency distribution of sex and ASA class was not significantly different between these groups ($P > 0.05$) (Table 2).

3.3. Outcomes

No flatulence was not observed in either group before the operation and on patients' arrival patients in the recovery room. The frequency of flatulence before leaving recovery was the same in both groups, but the Chi-square test showed that the frequency of flatulence in the operation ward was significantly low in the chamomile group compared to the placebo group ($P < 0.05$) (Table 3).

Analysis of variance with repeated observations showed that the effect of time, as well as the effect of group on the severity of flatulence, was significant ($P < 0.001$). The mean of flatulence severity increased significantly over time in both groups, but this increase was significantly lower in the chamomile group than in the placebo group (Table 3).

Independent t-test showed that the mean dose of received fentanyl and morphine, duration of operation, the volume of gas used, and gas pressure were not significantly different between both groups ($p > 0.05$). Accordingly, it shows that both groups were in the same condition regarding anesthesia and the operation (Table 4).

In this study, because only one dose of chamomile was given to the patients, no complications were seen in any of the patients.

3.4. Harms

During the study, no complications were observed in any of the participants.

4. Discussion

This study aimed to evaluate the effect of chamomile on abdominal flatulence after laparoscopic cholecystectomy. The evaluation of the present study on 64 patients showed that chamomile drops affect the severity of flatulence after the operation and had decreased significantly in the chamomile group compared to the placebo group. Data analysis showed that the severity of flatulence increased significantly over time in both groups but the extent of increase in the intervention group was significantly lower than that in the control group.

In the present study, the effect size of chamomile on the severity of flatulence was 4.8% in the recovery ward and 36.3% in the surgical ward (that means 36.3% performed better). Also, the effect of chamomile on the frequency of flatulence in recovery was 0% and in the surgical ward was 23%.

No study examining the effect of chamomile on flatulence after the operation was not found, but some studies were done on the effect of chamomile on gastrointestinal disorders, for example, in the study of Agah et al. (2015) on 45 patients with Irritability intestinal syndrome, patients were asked to take 20 drops of chamomile daily for 4 weeks; and symptoms were checked on the first day, the second and fourth weeks at the beginning of treatment and the second and fourth weeks after completing the intervention. The results showed that the symptoms of irritable bowel syndrome including flatulence, abdominal pain, defecation problems, and stool consistency significantly decreased after the consumption of chamomile in the second and fourth weeks, and symptoms continued to relieve until 4 weeks after the intervention [26]. The effect size of chamomile on reducing severe flatulence was 75% (4 weeks after treatment compared to the first visit). These results are consistent with those of the present study due to the use of the same amount of chamomile (20 drops) in both studies. The greater effect of chamomile on flatulence in this study can be attributed to the daily and frequent use of chamomile for 4 weeks. Unlike the present study, which evaluated only 2 h after the patients were transferred to the surgical ward.

Besides, the case study of Ghorat et al. (2017) on a 2-month-old baby with severe abdominal pain showed that in addition to previous treatments, topical chamomile oil was rubbed three times a day on the baby's entire abdomen. At the end of the first day of treatment, the duration of the baby's crying was reduced to about 30 min compared to the day before treatment. In addition to reducing infant crying, there was an increase in sleeping time at the end of the seventh day [27]. Further, a study by Masoumi et al. (2010) on 35 adult male rats showed that the aqueous extract of chamomile was effective in the treatment of ulcerative colitis in this model and significantly reduced the inflammatory and ulcerative indices of ulcerative colitis [28].

Moreover, the study of Khadem et al. (2018) on 150 patients regarding the effect of topical application of chamomile oil on gastrointestinal motility after cesarean section, showed that chamomile has a potential therapeutic effect on gastrointestinal motility and can reduce the duration of postoperative ileus [17]. The effect size of chamomile at the time of first bowel sound was 39.9%, abdominal pain was 80% and abdominal distention was 0%. Although the results of this study showed that chamomile affects some digestive disorders, but the present study showed that it does not affect flatulence and abdominal distention. In this respect, the results are inconsistent with the present study.

The results of these studies are consistent with those of the present study and indicate the effect of different forms of chamomile (drops, topical oils, etc.) on gastrointestinal disorders. This may be caused by the flavonoid compounds, chamazulene, and

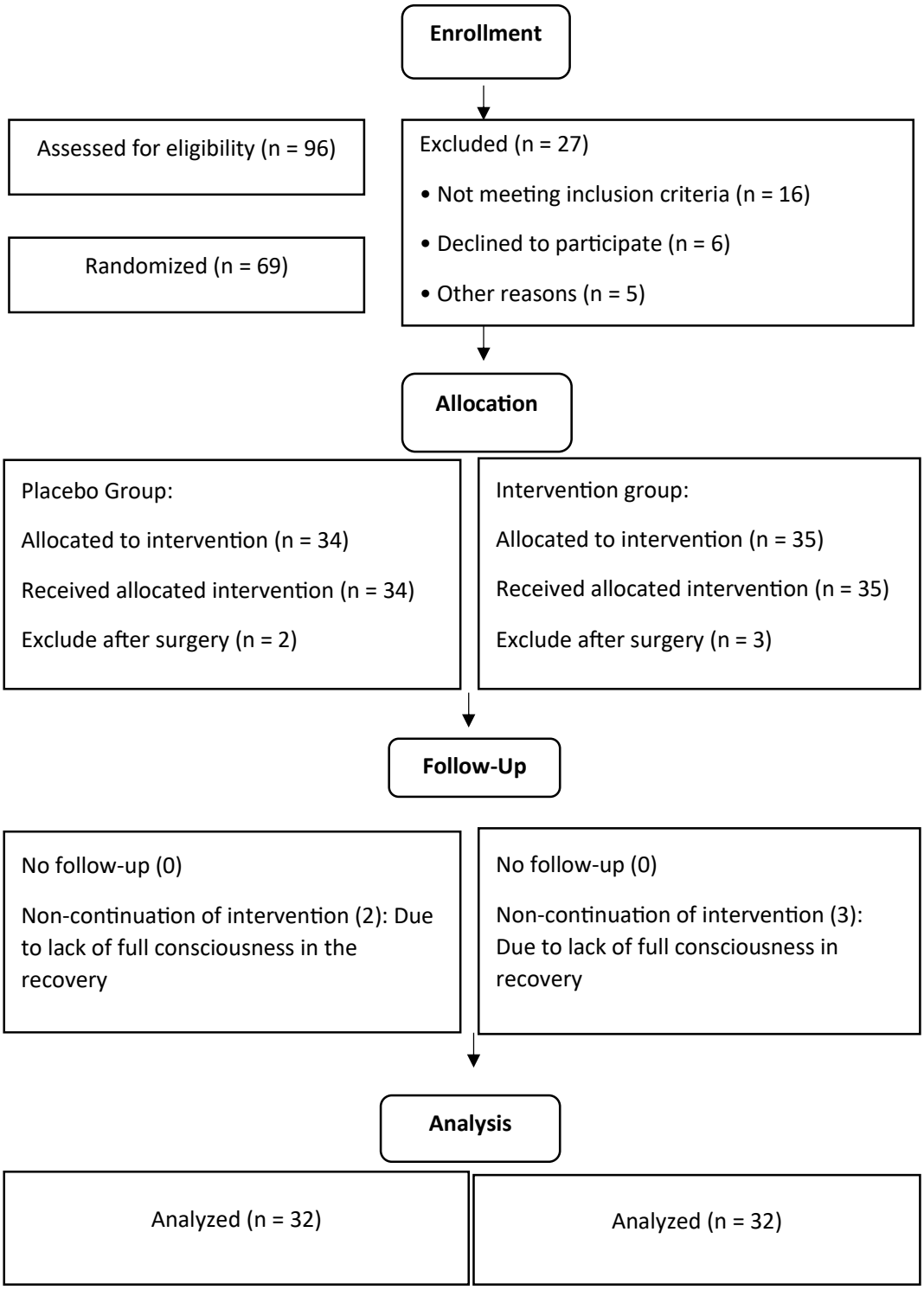

Fig. 1. CONSORT diagram (Flow chart)of study.

bisabolol in chamomile having antispasmodic and anti-inflammatory effects. Besides, the gastrointestinal protective effects of chamomile hydroalcoholic extract have been attributed to the antioxidant effects of this plant. Because antioxidants have antibacterial effects and are effective in relieving inflammation of the digestive system. Prostaglandin causes the muscles of the digestive system to contract. By inhibiting the release of prostaglandin, chamomile relaxes the smooth muscle of the digestive tract and reduces abdominal flatulence [19,27,29,30].

The present study was performed on patients undergoing laparoscopic cholecystectomy and evaluated up to 2 h after the operation. Using chamomile as a suitable alternative to chemical drugs relieving the severity of flatulence and patients' pain is beneficial, but there are some limitations.

Table 1
Mean age, weight, height, and body mass index in the intervention and placebo groups.

Variable	Chamomile Group	Placebo Group	Independent t-test		
	Mean ± SD	Mean ± SD	t	Df	P-value
Age (year)	43.66 ± 13.70	44.37 ± 12.43	0.22	62	0.83
Weight (kg)	69.89 ± 11.79	70.56 ± 10.47	0.24	62	0.81
Height (cm)	166.37 ± 9.42	165.81 ± 8.27	0.25	62	0.80
Body Mass Index (BMI)	25.05 ± 2.28	25.55 ± 2.22	0.89	62	0.38

Table 2
Frequency distribution of gender and ASA class in the intervention and placebo groups.

Variable		Chamomile Group		Placebo Group		Chi-square Test		
		No.	%	No.	%	χ^2	df	P
Gender	Males	15	46.9	11	34.4	1.04	1	0.34
	Females	17	53.1	21	65.6			
Class ASA	Class 1	27	84.37	25	78.12	_	_	0.50
	Class 2	5	15.63	7	21.88			

Table 3
The frequency distribution of flatulence and mean of flatulence severity in different periods in the intervention and placebo groups.

Time	Chamomile Group		Placebo Group				
Frequency distribution of flatulence							
	No.	%	No.	%	Chi-square Test		
					χ^2	df	P
Before the operation	0	0	0	0	–	–	1
Before leaving recovery	12	37.5	12	37.5	–	1	1
At ward	21	65.6	27	84.4	3	1	0.04
Mean of flatulence severity							
	Mean ± SD		**Mean ± SD**		P-value 1 (effect of time)		P-value2 (effect of group
Before the operation	0 ± 0		0 ± 0				
Before leaving recovery	1.19 ± 0.29		1.25 ± 0.33		<0.001		0.047
At ward	2.97 ± 0.48		4.66 ± 0.54				

Table 4
A dose of anesthesia drugs, duration of operation, gas volume, and gas pressure in the intervention and placebo groups.

Variable	Chamomile Group	Placebo Group	Independent t-test		
	Mean ± SD	Mean ± SD	T	df	P
The dose of received fentanyl	119.37 ± 15.76	132.81 ± 18.54	1.03	62	0.31
The dose of received Morphine	9.50 ± 1.83	9.84 ± 1.55	0.81	62	0.42
Operation period	82.8 ± 29.4	81 ± 27	0.25	62	0.80
Gas volume	97.59 ± 10.75	93.83 ± 8.70	0.27	62	0.79
Gas pressure	14.12 ± 1.07	14.47 ± 0.88	1.40	62	0.16

5. Limitation and generalisability

Research limitations include prolonged sampling time due to a reduced number of hospitalized patients due to the prevalence of coronary heart disease, Short-term evaluation of patients only up to 2 h after surgery, Lack of cooperation of some anesthesiologists to give chamomile drops to patients before surgery, Since the method of determining the severity of flatulence and is based on patients' self-declaration, in the present study, patients may have made an individual error in determining the severity of flatulence.

We may not be able to generalize the results to other types of laparoscopies and surgeries. It is suggested that further studies be performed on the effect of chamomile on the severity of flatulence in patients after various types of operations, and a longer evaluation to obtain more accurate information about the effect of this medicinal plant.

6. Conclusion

These results suggest that chamomile may have potential therapeutic effect on the gastro bowel disease and can reduce flatulence. However, further studies with a longer-term evaluation to investigate the effectiveness of Chamomile in reducing flatulence need to be done.

Ethical approval

The study complies with the guidelines for human studies and is performed ethically based on the World Medical Association Declaration of Helsinki. Subjects have given their written informed consent. The Ethics Committee of Isfahan University of Medical Sciences approved the study (IR.MUI.RESEARCH.REC.1398.745).

This triple-blind randomized clinical trial was registered in the Iranian clinical trial database with the code IRCT20200612047737N1.

Author contributions

SB and RSZ contributed to the study design and concept; GK and RSZ: performed the study and conducted data collection; RSZ, SB, GK and MM: reviewed the literature and made the drafts; All authors approved the study.

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Declaration of competing interest

The authors have no conflicts of interest to declare.

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