

Randomized Controlled Trial Study for Evaluation of Herbal Lozenge Compared with Standard Postoperative Care to Enhance Postoperative Bowel Function Recovery Following Elective Open Abdominal Surgery

Sarinda Lertbannaphong MD¹, Weerapat Suwanthanma MD¹, Youwanush Kongdan MD¹, Chakrapan Euanorasetr MD¹

¹ Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background: Early return of bowel function after surgery is essential for successful patient recovery from abdominal surgery.

Objective: To compare the effect of Tamarind lozenge with standard postoperative care on the postoperative bowel function recovery following elective open abdominal surgery.

Materials and Methods: In this prospective trial, 98 eligible patients, aged between 31 and 91 years, who underwent elective open abdominal surgery at Ramathibodi Hospital between January and December 2016 were randomized into two groups. The first group received Tamarind lozenge together with standard postoperative care (treatment group, n = 49) and the second group received standard postoperative care (control group, n = 49). The primary outcome was the return of bowel function. The secondary outcome was the patient's length of hospital stay and discomfort from bowel ileus.

Results: There was no significant difference between the two groups for the return of bowel function regarding to flatus time ($p = 0.24$). In addition, the time to tolerate solid food and length of hospital stay were similar with no significant difference ($p = 0.32$ and 0.69 , respectively).

Conclusion: The addition of Tamarind lozenge to standard postoperative care did not reduce the period of postoperative bowel ileus or shorten the length of hospital stay following elective open abdominal surgery.

Keywords: Tamarind lozenge, Postoperative care, Bowel function recovery

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Postoperative hospital stay is needed for most patients who undergo elective open abdominal surgery. Bowel Ileus, a delay in the return of postoperative bowel function, results from ineffective transit of intestinal contents and/or tolerance of intake, is one of the factors that can significantly affect or extend the period of postoperative patient's stay after having an operation⁽¹⁾.

Although postoperative bowel ileus is not a life-threatening condition, a patient may experience overall discomfort, abdominal pain, abdominal distention, nausea and vomiting, delayed return of normal enteral nutrition, and prolonged hospital stay. The prolonged hospital stay may lead to hospital-acquired infection,

deep vein thrombosis, pulmonary compromise, and other postoperative complications. Moreover, resources such as medical equipment could be subjected to overuse instead of being stored and prepared to assist other patients in potentially life-threatening emergency cases. In addition, the higher the number of patients who spend extended periods in hospital after an operation, the higher the total health care cost of the country⁽²⁾.

There are several arrangements to minimize postoperative ileus, such as minimal use of nasogastric tubes, early enteral intake, early ambulation, and adequate pain control. However, it could take many days to complete these standard managements.

Herbal (Tamarind) lozenge, a small tablet made from herbs, can stimulate bowel function by activating the cephalic vagal reflex, which can be enhanced by the theory of sham feeding⁽¹¹⁾. In animal experiment, Tamarind has been found to increase colonic

Correspondence to:

Suwanthanma W. Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, 270 Rama VI Road, Ratchathewi, Bangkok 10400, Thailand.

Phone & Fax: +66-2-2011527

Email: weerapat.suw@mahidol.ac.th

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contractility in guinea pig and some components such as malic acid and tartaric acid were found to be the active compound to stimulate the colonic function, so this could be used traditionally as laxative^(17,18). Then, when the bowel movement is stimulated by the Tamarind lozenge and hormones, nausea, vomiting, and the associated risk of aspiration will be reduced⁽⁹⁾.

Therefore, the use of tamarind lozenges is an interesting and potential alternative as a new way to shorten the period of recovery for postoperative bowel function. Thus, we aimed to determine whether the introduction of tamarind lozenges in the immediate postoperative period could facilitate recovery from bowel ileus following elective open abdominal surgery.

Materials and Methods

Study design, population, and sample size calculation

This was a prospective, open-label, randomized controlled trial study to compare the use of tamarind lozenges and standard postoperative care for patients undergoing elective abdominal surgery. This study was approved by the Institutional Review Board of Ramathibodi Hospital. The study included both men and women, at least 18 years of age, who underwent scheduled elective open abdominal surgery. Patients who had any alteration of consciousness, underlying neurologic disease, mental retardation, or swallowing defect were excluded. Patients who were unable to complete simple daily activities, unable to have oral intake or refused to sign informed consent were excluded as well. For cancer patients, we excluded the patients with poor performance status and had received preoperative chemoradiation. The study was conducted at the Department of Surgery, Ramathibodi Hospital, Bangkok, Thailand, between January and December 2016.

Randomization and clinical procedures

All eligible patients were randomly assigned by block randomization to ingest tamarind lozenges or receive standard postoperative care at an inpatient clinic. The patients in the treatment group received tamarind lozenges on the operative day after becoming fully conscious and ready to cooperate. The patients ingested two tamarind lozenges at meal times (3 times/day) until the first flatus passed. The patients in the control group received routine postoperative care. Medical history and all baseline characteristics, peri-operative data and operative procedures were obtained. The patients were reassessed every eight hours by the same physician to detect the first passage of flatus,

first bowel sound, and first bowel movement using the protocol yes/no question. The time to tolerate solid food and length of hospital stay were recorded.

Study endpoint

The primary objective of the present study was to assess the return of bowel function including time to pass the first flatus, time to hear the first bowel sound, and time to pass the first stool. The secondary objective was to identify the length of hospital stay and discomfort symptoms related to ileus, including nausea, vomiting, and abdominal distention.

Statistical analysis

The data was verified and recorded by Stata program version II, followed by intention-to-treat analysis. Continuous variables were reported as mean \pm SD and categorical variables were reported as percentages. The Fisher's exact test and Chi-square test were used to compare the categorical data variables. The t-test was used to compare the continuous data

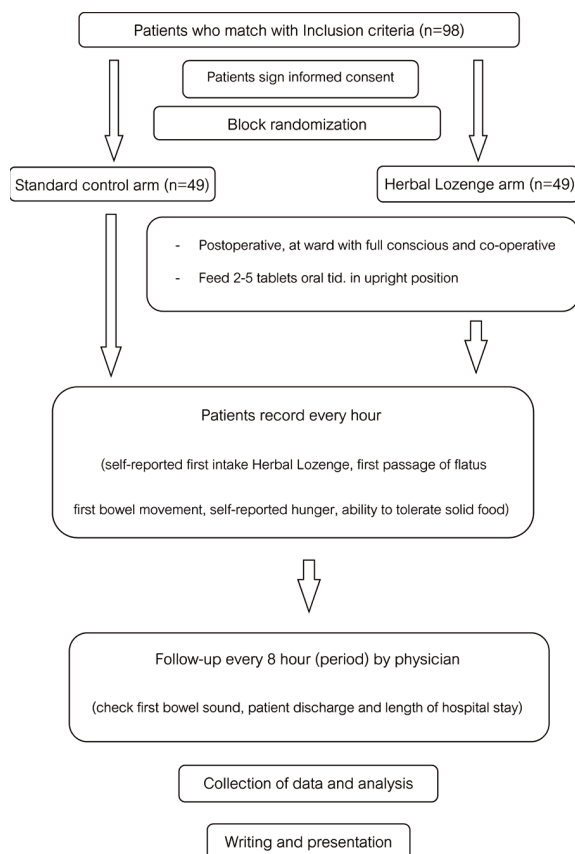


Figure 1. Study protocol.

variables. The Mann-Whitney test was used to compare the outcome variables. A *p*-value less than 0.05 was considered statistically significant.

Results

Baseline characteristics

Ninety-eight consecutive patients (55 males and 43 females) who underwent open abdominal surgery at our institution were eligible for the study. The mean age of each patient in the tamarind lozenge group (*n* = 49) and control group (*n* = 49) were 62.3 years and 60.3 years, respectively. For the tamarind lozenge group, 37 (72.6%) had underlying diseases, while in the control group, 29 (61.7%) had an underlying disease. Most patients in both groups had undergone abdominal operation due to colonic disease (54.9% in

the tamarind lozenge group and 53.2% in the control group). Moreover, the most common indication for surgery in both groups was diagnosis of cancer (74.5% in tamarind lozenge group and 80.9% in control group). All demographic data did not vary significantly among study groups (Table 1).

Perioperative data

All patients underwent abdominal surgery with general anesthesia. Twenty-nine patients (56.9%) in the tamarind lozenge group and twenty-three (48.9%) in the control group had operations with anastomosis of bowel. Operative blood loss was similar between the two groups (median 100 ml). Operative time in the control group (median 95 minutes, range 25 to 250 minutes) was less than in the tamarind lozenge group (median 105 minutes, range 30 to 215 minutes). In the tamarind lozenge group, 32 patients (62.8%) had postoperative pain control by opioids, compared to 28 patients (59.6%) in the control group. Of note, injury to the urinary bladder occurred in 2% of the tamarind lozenge group and 2.1% in the control group (Table 2).

Return of postoperative bowel function

All parameters regarding postoperative bowel function and postoperative complications are shown in Table 3. All parameters were counted as positive at every consecutive 8-hour period. The control group had rapid return of first bowel sound (5 periods)

Table 1. Demographic data

Characteristics	Lozenge n (%)	Control n (%)	<i>p</i> -value
Male	31 (60.8)	24 (51.1)	0.333
Age (years), mean ± SD	62.3±11.5	60.3±11.6	0.395
Known underlying disease	37 (72.6)	29 (61.7)	0.253
Disease			0.420
Colon	28 (54.9)	25 (53.2)	
Rectum	15 (29.4)	17 (36.2)	
Small bowel	5 (9.8)	1 (2.1)	
Other	3 (5.9)	4 (8.5)	
Diagnosis			0.452
Cancer	38 (74.5)	38 (80.9)	
Benign	13 (25.5)	9 (19.2)	

Table 2. Perioperative data

	Lozenge, n (%)	Control, n (%)	<i>p</i> -value
General anesthesia	51 (100)	47 (100)	
Postoperative pain control by opioids			0.591
IV	32 (62.8)	28 (59.6)	
IV patient controlled analgesia	8 (15.7)	11 (23.4)	
Epidural block	11 (21.6)	8 (17.0)	
Postoperative pain control by NSAIDs (IV)	14 (27.5)	18 (38.3)	0.253
Retain NG tube	8 (15.7)	3 (6.4)	0.145
Operations			0.267
Anastomosis	29 (56.9)	23 (48.9)	
Anastomosis with proximal diversion	7 (13.7)	8 (17.0)	
Proximal end colostomy with distal end stump	9 (17.7)	6 (12.8)	
Loop enterostomy	3 (5.9)	9 (19.2)	
Others	3 (5.9)	1 (2.1)	
Blood loss (ml), median (range)	100 (5 to 2,200)	100 (10 to 3,200)	0.642
Operative time (minutes), median (range)	105 (30 to 215)	95 (25 to 250)	0.859
Intraoperative complication			0.610
Tear bowel	0 (0.0)	1 (2.1)	
Tear vessel	0 (0.0)	1 (2.1)	
Tear urinary bladder	1 (2.0)	1 (2.1)	

IV = intravenous; NG = nasogastric; NSAIDs = nonsteroid anti-inflammatory drugs

Table 3. Outcomes

Outcomes	Lozenge, median (range)	Control, median (range)	p-value
Bowel sound time	5 (1 to 26)	3 (1 to 26)	0.201
Flatus time	8 (3 to 31)	8 (3 to 29)	0.249
Feces time	14 (6 to 60)	14 (5 to 35)	0.800
Self-report hunger time	11 (4 to 34)	11 (3 to 32)	0.358
Tolerate solid food	14 (6 to 63)	14 (4 to 38)	0.321
Discharge from hospital	18 (9 to 100)	18 (5 to 54)	0.690
Postoperative complication, n (%)			
Wound infection	3 (5.9)	3 (6.4)	1.000
Anastomosis leakage	1 (2.0)	1 (2.1)	1.000
Bowel ileus	6 (11.8)	4 (8.5)	0.743
Diarrhea	0 (0.0)	1 (2.1)	0.480
Obstruction	1 (2.0)	0 (0.0)	1.000
Others	2 (3.9)	1 (2.1)	1.000
Re-operation, n (%)	2 (3.9)	1 (2.1)	1.000

compared to the tamarind lozenge group (3 periods), with no significant group differences ($p = 0.201$). There was no significant difference in time to first passage of flatus between the two groups (eight periods in both groups, $p = 0.249$). In addition, the first bowel movement in the tamarind lozenge group and control group was similar (14 periods in both groups, $p = 0.800$). Patients in both groups started to feel hungry at 11 periods and could tolerate solid foods in 18 periods ($p = 0.358$ and 0.321 , respectively). Length of hospital stay was 18 periods in both groups (9 to 100 in the tamarind lozenge group and 5 to 54 in the control group), without any statistical difference ($p = 0.690$).

Postoperative adverse events

Six patients (11.8%) in the tamarind lozenge group and four patients (8.5%) in the control group had anastomosis leakage. One patient in each group (2% in the tamarind lozenge group and 2.1% in the control group) experienced wound infection. There were no differences of anastomosis leakage between the two groups. The patient in tamarind lozenge group (six patients, 11.8%) had more bowel ileus compared to control group (four patients, 8.5%). Patients in the tamarind lozenge group (two patients, 3.9%) experienced more postoperative gut obstruction compared to the control group (one patient, 2.1%). The rate of reoperation was higher in the tamarind lozenge group (two patients, 3.9%) than in the control group (one patient, 2.1%).

Discussion

For more than a century, postoperative bowel ileus has been a challenging problem for surgeons. Clinical burdens include abdominal discomfort,

nausea, vomiting, and increased hospital-acquired infections. Major economic influence is related to prolonged duration of hospitalization⁽²⁾. The pathogenesis of bowel ileus was described as a biphasic pathologic reaction of the affected bowel. The initial phase, operative maneuvers, and tissue handling causes the activation of sympathetic reflexes suppressing the bowel motility⁽⁴⁾. The second phase was related to the release of corticotrophin-releasing factors, resulting in secondary inflammatory response⁽⁵⁾.

The postoperative bowel ileus occurs most often after intra-abdominal surgery. It can also occur with retroperitoneum or even thoracic surgery. Usually, gastrointestinal tract needs several days to return to its normal function; several hours for small intestine, 24 to 48 hours for stomach, and 3 to 5 days for colon^(6,7).

Early feeding may stimulate bowel motility, especially in the stomach and duodenum. Gum chewing can be used to stimulate bowel function since it mimics food intake. This is known as “Sham feeding”⁽⁸⁾. Gum chewing directly stimulates cephalovagal axis^(9,10), which then triggers the secretion of gastrointestinal hormones, saliva, and pancreatic enzymes⁽¹¹⁾. Several trials and meta-analyses showed that gum chewing resulted in the earlier return of postoperative bowel function following abdominal surgery compared to control⁽¹²⁻¹⁶⁾.

Chewing gum is not a popular snack or pastime in Thai culture. On the other hand, tamarind lozenges are commercially available in most supermarkets in Thailand. According to a previous study, the aqueous extract of *Tamarindus indica* can increase spontaneous contractile activity of guinea-pig taenia coli in a dose-dependent manner⁽¹⁷⁾. The present study described the phytochemical investigations carried out on *T. indica*

and revealed the presence of many active constituents such as phenolic compounds, cardiac glycosides, malic acid, tartaric acid, pectin, and mucilage. Based on these chemical compounds, *T. indica* has been reported to stimulate isolated tissue of duodenum and ileum. A recent study by Kuru P revealed that *T. indica*, known as the tamarind tree, contains many health related components⁽¹⁸⁾. *T. indica* fruit is used in traditional medicine as a laxative because of high content of malic acid and tartaric acid, which are the active compound for stimulation of colonic contraction⁽¹⁸⁾. Further, these stimulating effects on the gastrointestinal tract should be studied, whether tamarind lozenges could reduce postoperative ileus in patients undergoing open abdominal surgery.

From a clinical perspective, the use of tamarind lozenges to help decrease postoperative ileus is promising. It is a simple and inexpensive method with no known adverse effects, as evidenced by previous studies reviewed. However, questions about the use of tamarind lozenges persist, such as the exact timing and dosing regimen for administration. The limitation of this trial was the small number of sample size that could result in no positive outcome. Finally, even though positive results could be achieved by our study, further research into whether positive clinical outcomes could significantly reduce of the length of hospital stay is still required.

Conclusion

The evidence from our study suggests that the addition of herbal lozenges to standard postoperative care did not significantly reduce the period of postoperative bowel ileus or shorten the length of hospital stay following elective open abdominal surgery. Further prospective randomized controlled clinical trials with larger samples of subjects or larger dose of Tamarind lozenges are required to determine the true efficacy of tamarind lozenges in shortening postoperative bowel ileus exists.

What is already known on this topic?

Recovery from postoperative ileus depends on many factors. There are many measures and drugs that are on the experimental study. Shortening of postoperative ileus can theoretically reduce patient's discomfort and length of hospital stay.

What this study adds?

Study dosage of Tamarind lozenge did not show the positive effect for reducing postoperative bowel

ileus compared to standard postoperative care. Study of higher dose of Tamarind lozenge or larger samples of subjects are required to answer the question.

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Potential conflicts of interest

None.

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การศึกษาแบบทดลองสุ่มเปรียบเทียบการใช้ herbal lozenge กับการดูแลมาตรฐานหลังผ่าตัด เพื่อเร่งการกลับมาทำงานของลำไส้หลังผ่าตัดช่องท้องแบบเปิด

สรีนดา เลิศบรรณพงษ์, วีรพัฒน์ สุวรรณธรรม, เขาวนุช คงदान, จักรพันธ์ เอื้อนรเศรษฐ์

ภูมิหลัง: การกลับมาทำงานหลังผ่าตัดของลำไส้มีความสำคัญสำหรับการฟื้นตัวของผู้ป่วยที่ได้รับการผ่าตัดช่องท้อง

วัตถุประสงค์: เพื่อประเมินผลของการใช้ herbal lozenge เทียบกับการดูแลมาตรฐานหลังผ่าตัดในการกลับมาทำงานของลำไส้หลังการผ่าตัดช่องท้องแบบเปิด

วัสดุและวิธีการ: ทำการศึกษาแบบทดลองสุ่มโดยเก็บข้อมูลไปข้างหน้า ผู้ป่วยจำนวน 98 ราย ที่ได้รับคัดเลือกเข้าร่วมการศึกษานี้ ซึ่งมีอายุระหว่าง 31 ถึง 91 ปี และมาผ่าตัดช่องท้องแบบเปิดที่โรงพยาบาลรามธิบดี ในระหว่าง เดือนมกราคม ถึง ธันวาคม พ.ศ. 2559 ถูกแบ่งออกเป็น 2 กลุ่ม กลุ่มแรกใช้ herbal lozenge ร่วมกับการดูแลมาตรฐานหลังผ่าตัด (กลุ่มที่ได้รับการรักษาจำนวน 49 ราย) กลุ่มที่สองได้รับการดูแลมาตรฐานหลังผ่าตัด (กลุ่มควบคุมจำนวน 49 ราย) ผลการประเมินลำดับแรก คือ การกลับมาทำงานของลำไส้ ส่วนผลการประเมินลำดับสอง คือ ระยะเวลาการพักในโรงพยาบาล และความไม่สบายจากผลของการหยุดทำงานของลำไส้

ผลการศึกษา: พบว่าไม่มีการแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างผู้ป่วยสองกลุ่ม สำหรับการกลับมาทำงานของลำไส้โดยดูจากการผายลม ($p = 0.24$) นอกจากนี้ระยะเวลาที่ผู้ป่วยเริ่มรับประทานอาหารแข็งได้และระยะเวลาการพักในโรงพยาบาลไม่มีความแตกต่างกันทางสถิติ ($p = 0.32$ และ 0.69 ตามลำดับ)

สรุป: จากข้อมูลของการศึกษานี้พบว่าการใช้ herbal lozenge ร่วมกับการดูแลมาตรฐานหลังผ่าตัด ไม่ได้ลดระยะเวลาของการกลับมาทำงานของลำไส้หลังผ่าตัด และไม่ได้ลดระยะเวลาการพักในโรงพยาบาลหลังการผ่าตัดช่องท้องแบบเปิด
