Effect of sham feeding on postoperative ileus

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Abstract

Background: To evaluate the effects of different sham feeding methods on postoperative ileus after low anterior resection and diverting ileostomy for rectal cancer.

Methods: 72 patients who underwent low anterior resection with a diverting ileostomy were randomized into 4 groups as: control (n = 16), ice cream (n = 18), gum (n = 17) and nicotine gum (n = 17). Four patients were excluded due to a lack of data. Patients' demographics, constipation scores, neoadjuvant treatment, amount of perioperative bleeding, fluid administration, drain placement, time of intestinal movement, ileostomy discharge, and return of appetite were compared.

Results: Patients' demographics, constipation scores, neoadjuvant treatment existence, amount of perioperative bleeding, fluid administration, drain placement were similar between groups ($p > 0,05$). The first sense of intestinal movement was shorter in the nicotine group than control and gum groups ($p=0,004$ and $0,046$, respectively). The average time to first ileostomy discharge and first appetite was shortest in the nicotine gum group. Diverting ileostomy discharge time was significantly shorter in the nicotine gum group than the control group ($p=0,011$). Return of appetite time was shorter in the nicotine gum group when compared to the gum group ($p=0.036$).

Conclusions: Nicotine gum chewing is an effective method to resolve postoperative ileus after rectal surgery. Other methods such as ice-cream feeding and gum chewing showed no benefit compared to control.

Background

Postoperative ileus (POI) is one of the main predictors of hospital stay, delayed oral nutrition, and hospital cost among colorectal surgery patients [1]. POI pathogenesis was shown to be multifactorial and the main causes were defined as surgical trauma, manipulation of bowels, length of surgery which all trigger a local inflammatory response at bowel wall resulting in hypo-motility of the gastrointestinal tract [2].

Several methods were described to solve POI including different medications and sham feeding. Different sham feeding materials have been used in daily practice and several studies showed significant benefits among colorectal surgery patients [3, 4]. But publications about sham feeding are still controversial [5]. Nicotine is a potent parasympathomimetic and anti-inflammatory mediator. There are very few studies investigating the effect of nicotine gums in the treatment of POI. Nicotine gum has the potential to resolve POI at multiple levels of pathophysiology [6]. In this study, we aimed to evaluate the effect of different sham feeding methods including nicotine gum on POI after colorectal surgery.

Methods

The study consisted of 72 consecutive patients who underwent low anterior resection and diverting ileostomy for rectal cancer at Istanbul University, Istanbul Faculty of Medicine, Department of General Surgery between November 2013 and May 2014. Informed consent was obtained and patients were randomized via a web-based program into 4 groups according to their sham feeding. All patients were given a protocol number, starting at 1 and ending at 72. Patients were included in groups according to their protocol numbers.

Group I patients were given only intravenous (iv) fluid for the first 24 hours at postoperative day 1 and then they were given only clear fluid until the first bowel movement. After ileostomy discharge, all patients were given a full liquid diet followed by a low residue diet if tolerated. Group II patients were given 100 ml oral ice cream with an interval of 8 hours, beginning 6 hours after the surgery in addition to iv fluids until the first discharge from an ileostomy. Group III patients chewed gum for 30 minutes with 8 hours of interval beginning 6 hours after surgery until the first discharge from an ileostomy. Group IV patients chewed nicotine gum (Nicotinell Gum; Novartis Consumer Health S.A., Nyon, Switzerland) including 2 milligrams of nicotine at the same frequency and duration of Group III.

Patients' demographics, preoperative constipation scores (7), intraoperative bleeding amounts (milliliter/ml), operative time, intraoperative fluid administration amounts (ml), number of abdominal drains, first bowel movement, ileostomy discharge and first feel of appetite times were recorded. Bowel movements were assessed by clinical nurses who were blinded to study protocol and trained before the study by a colorectal surgeon in terms of auscultation, appetite, and stoma discharge.

Patients with severe hypertension, cardiac arrhythmia, history of coronary artery disease, and hypersensitivity to the nicotine gum were excluded from the study.

Study ethics committee approval was taken from Sağlık Bilimleri University, Istanbul Fatih Sultan Mehmet Training and Research Hospital.

The Number Cruncher Statistical System (NCSS) 2007 & PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program was used for statistical analysis. Mann Whitney U test was used to compare the two statistical methods (Mean, Standard Deviation, Median, Frequency, and Ratio) as well as the two groups of parameters that did not show the normal distribution in the comparison of the quantitative data. OnewayAnova Test in three and over groups with normal distribution; the Kruskal Wallis test was used in three groups with no normal distribution and the comparison of the above groups. Pearson Chi-square test and Fisher-Freeman-Halton test were used for comparison of qualitative data. Significance was assessed at $p < 0.01$ and $p < 0.05$ levels.

Results

The study group consisted of 72 patients. Two patients from the control group, 1 from the gum group and 1 from the nicotine gum group were excluded due to lack or doubt of their data. Finally, groups were formed as the group I (iv fluid only, control; $n = 16$, 23.5%), group II (ice-cream; $n = 18$, 26.5%), group III

(chewing gum; n = 17, 25%), and group IV (nicotine chewing gum; n = 17, 25%). Out of 68 patients, 33 (48.5%) were female and 35 (51.5%) were male. The average age was 59.6 ± 12.7 (24–82) years. The mean operative time was 108.09 ± 40.24 (45 to 250) min. The surgical approach was laparoscopic in 57 (83.8%) patients and 11 (16.2%) surgeries were open. Thirty-five patients (51.5%) received neoadjuvant treatment (Table 1). The groups had similar mean age, gender distribution, body mass index, and body surface area measurements ($p > 0.05$). There was no statistically significant difference ($p > 0.05$) between the groups in terms of operation time (Table 2).

Table 1
Patients' demographics

		Min-Max	Mean $\pm$ SD
Age (year)		24–82	59.57 ± 12.69
Body Mass Index (BMI) (kg/m ²)		17–37	26.29 ± 4.19
Body Surface Area (BSA) (m ²)		1.4–2.2	1.76 ± 0.17
Duration of Surgery (minutes)		45–250	108.09 ± 40.24
		n	%
Sex	Female	33	48.5
	Male	35	51.5
Previous Abdominal Surgery	No	46	67.6
	Yes	22	32.4
Drain	No	9	13.2
	Yes	59	86.8
Operation	Laparoscopy	57	83.8
	Open	11	16.2
Neoadjuvant Treatment	No	33	48.5
	Yes	35	51.5

Table 2
Groups Descriptive

		Control	Ice-cream	Gum	Nicotine Gum	<i>p</i>
Age (years)		62.5 ± 12.7	56.8 ± 12.4	58.0 ± 14.2	61.2 ± 11.4	^d 0.548
Sex (n,%)	Female	8 (50.0)	9 (52.9)	9 (50.0)	7 (41.2)	^b 0.912
	Male	8 (50.0)	8 (47.1)	9 (50.0)	10 (58.8)	
BMI (kg/m ²)		24.9 ± 3.2	28.0 ± 4.7	26.4 ± 4.3	25.8 ± 4.1	^d 0.175
BSA (m ²)		1.71 ± 0.19	1.80 ± 0.16	1.74 ± 0.15	1.80 ± 0.18	^d 0.373
Surgery time (min) (median)		103.1 ± 27 (110)	92.9 ± 27.5 (90)	132.7 ± 58.4 (132.5)	101.7 ± 26.69 (100)	^e 0.099
Bleeding (ml) (median)		115.31 ± 110.6 ((72.5)	107.06 ± 69.1 (100)	164.44 ± 125.2 (120)	98.53 ± 87.7 (60)	0.222
Intravenous fluid (ml)		2025 ± 840	1847.06 ± 855	2494.44 ± 911	2064.12 ± 744	0.142
Drain	No	3 (18.8)	1 (5.9)	4 (22.2)	1 (5.9)	^c 0.377
	Yes	13 (81.3)	16 (94.1)	14 (77.8)	16 (94.1)	
Neoadjuvant Treatment	No	7 (43.8)	7 (41.2)	11 (61.1)	8 (47.1)	^b 0.644
	Yes	9 (56.3)	10 (58.8)	7 (38.9)	9 (52.9)	
Previous Abdominal Surgery	No	13 (81.3)	11 (64.7)	12 (66.7)	10 (58.8)	^b 0.566
	Yes	3 (18.8)	6 (35.3)	6 (33.3)	7 (41.2)	
Surgical approach	Laparoscopy	13 (81.3)	12 (70.6)	17 (94.4)	15 (88.2)	^c 0.256
	Open	3 (18.8)	5 (29.4)	1 (5.6)	2 (11.8)	
^b Pearson x ² Test, ^c Fisher-Freeman-Halton Test, ^d OnewayAnova Test, ^e Kruskal Wallis Test						

Evaluations of initial intestinal movement

The mean initial intestinal movement measurements of the control group were 34.00 ± 16.57 hours; the average of the group using ice cream was 28.00 ± 17.97; the group using gum is 30.89 ± 17.83 and the group using nicotine is 18.35 ± 9.12 hours (Table 3). In paired comparisons; the initial bowel movement

time of the group using nicotine gum was significantly lower than the control and gum using groups ($p = 0.004$, $p = 0.046$, respectively).

Table 3

Intergroup comparison of intestinal movement, first appetite, ileostomy discharge, and constipation scores.

	Initial Intestinal Movement (hour)	First Appetite (hour)	First Ileostomy Discharge (hour)	Constipation Score
	Mean $\pm$ SD (Median)	Mean $\pm$ SD (Median)	Mean $\pm$ SD (Median)	Mean $\pm$ SD (Median)
Control (n = 16)	34.00 $\pm$ 16.57 (32.5)	41.13 $\pm$ 21.80 (39.0)	43.56 $\pm$ 17.33 (46.5)	2.94 $\pm$ 2.21 (3.0)
Ice cream (n = 17)	28.00 $\pm$ 17.97 (26.0)	39.47 $\pm$ 24.16 (30.0)	40.24 $\pm$ 21.24 (36.0)	3.47 $\pm$ 2.48 (3.0)
Gum (n = 18)	30.89 $\pm$ 17.83 (22.0)	37.56 $\pm$ 14.70 (38.0)	41.72 $\pm$ 23.19 (33.5)	5.17 $\pm$ 3.87 (4.5)
Nicotine Gum (n = 17)	18.35 $\pm$ 9.12 (16.0)	27.06 $\pm$ 11.39 (28.0)	30.82 $\pm$ 15.09 (30.0)	5.47 $\pm$ 4.09 (4.0)
<i>Paired Comparisons; ^ap</i>				
Control*Ice cream	0.288	0.843	0.504	0.812
Control*Gum	0.557	0.756	0.629	0.102
Control*Nicotine Gum	0.004**	0.056	0.011*	0.069
Ice-cream*Gum	0.597	0.843	0.974	0.205
Ice-cream*Nicotine Gum	0.113	0.248	0.078	0.118
Gum*Nicotine Gum	0.046*	0.036*	0.190	0.842
^a Mann Whitney U Test **p < 0.01 *p < 0.05				

Evaluations of the first feel of appetite

The first feel of appetite time of the group using nicotine gum was 27.06 $\pm$ 11.39 hours. In paired comparisons; the first appetite time of the group using nicotine gum was significantly lower than the group using the gum ($p = 0.036$). Although there was no difference between the nicotine gum and the control group, it was close to statistical significance ($p = 0.056$).

Evaluations of initial ileostomy discharge

The mean initial ileostomy discharge time measurements of the control group, gum, and nicotine gum groups were 43.56 ± 17.33 hours; 40.24 ± 21.24 hours; 41.72 ± 23.19 hours and 30.82 ± 15.09 hours, respectively. Time to first ileostomy discharge of the nicotine gum group was significantly lower than the control group ($p = 0.011$).

Evaluations of constipation scores

The constipation scores mean of the control group was 2.94 ± 2.21 , the ice-cream consuming group was 3.47 ± 2.48 , the gum-using group was 5.17 ± 3.87 , and the nicotine-using group was 5.47 ± 4.09 . The constipation scores of the nicotine gum group were higher than the control group but it was not statistically significant ($p = 0.069$). There was no statistically significant difference between the constipation scores of the other groups ($p > 0.05$).

Discussion

Despite no consensus on the definition of POI, transient impairment of bowel motility is widely accepted [8]. Postoperative ileus is defined as transient and functional bowel movement defect following surgery [8]. Ileus commonly occurs after colorectal surgery and may cause serious complications and prolonged hospital stay. According to the United States data, POI leads to an increase in the length of the hospital stay and readmissions which result in an increase of US \$ 1.5 billion per year in cost [9]. POI is considered to be multifactorial as many factors influence postoperative surgical stress response that yields to prolongation of bowel movement and development [10]. Several risk factors were defined including age, BMI, operation time, degree of bowel manipulation, surgical trauma level, postoperative opiate utility in pain management, prolonged anesthesia, intraoperative bleeding, limited iv fluid administration, and early postoperative feeding. Similarly, several preventive methods have been investigated like gum chewing [11–13], acupuncture [14], early feeding [15] early mobilization [16]. Some of these were argued to be included in ERAS protocols [17]. According to our knowledge, this study is the first one to compare only iv fluid administered control group to gum, nicotine gum, and sham feeding (ice-cream) groups for the treatment of POI in colorectal surgery. The para-symphathomimetic nicotine-containing gum chewing was found to be effective in the treatment of POI after rectum resection. This result is encouraging to plan further trials including more patients and different doses of nicotine.

In the pathophysiology of postoperative ileus, early neurogenic pathway and late inflammation in the intestinal wall are accused [18]. The mechanism of sham nutrition is the induction of complex cephalic vagal response by chewing. The response leads to both humoral and nervous stimulation of bowel motility. Sham nutrition is widely used in the treatment of postoperative ileus, but its effect is still controversial. The most commonly used agent in this regard is gum chewing. Studies on gum chewing after abdominal surgery reported good results, but there are clinical studies that do not support these findings. Vasquez et al. reported in their meta-analyses involving 6 studies chewing gum after colorectal surgery was effective in the treatment of postoperative ileus [3]. Ho et al. evaluated 10 studies on gum chewing after colorectal surgery and found that the method was safe and shortened the length of

hospitalization, but they also mentioned the data they used were heterogeneous [16]. In another study, when compared with the control group, the positive effects of gum chewing on paralytic ileus were not shown in left colon resections [19]. Cochrane analysis indicated that gum chewing may have positive effects on the recovery of the gastrointestinal system postoperatively, but further studies are needed due to the poor quality of the studies [20].

The amount of intravenous fluid given during abdominal surgery may have effects on the paralytic ileus. Studies have shown that restricted fluid infusion may reduce the frequency of the impaired bowel movement [21, 22]. Lee et al. compared the characteristics of patients who developed and did not develop postoperative ileus and found a history of severe constipation and higher amounts of operative bleeding which were related to POI development [23]. Amount of operative intravenous fluid infusion, amount of perioperative bleeding, and preoperative constipation scores were examined in our study, and no difference was found between the groups. We also evaluated patients in terms of demographic specifications, previous abdominal surgery, type of surgery (open or laparoscopic), duration of the procedure, drain usage, etiology, and neoadjuvant treatment to eliminate other factors that might compromise the results.

Early postoperative feeding is recommended after colorectal surgery, and many have demonstrated efficacy in the Enhanced Recovery After Surgery (ERAS) protocols. Ice cream is used in many protocols and is recommended for early feeding after colorectal surgery [24]. In our study, we could not detect a positive effect of early enteral feeding with ice cream on POI.

Nicotine, a strong para-sympathomimetic included gum chewing may shorten the postoperative ileus by acting on early neurogenic pathway and late inflammation in the intestinal wall [18]. The study demonstrated positive effect of nicotine gum in postoperative ileus management when compared to the control and sham feeding groups. The main goal of nicotine gum utility in the study was the strong para-sympathomimetic effect of nicotine. Leuzinger et al. [25] reported using a nicotine patch as an alternative treatment for a patient with Ogilvie syndrome in 1996. Several years later, Wu and colleagues hypothesize that chewing gum containing nicotine may be an effective method of postoperative ileus treatment. In this study, it was emphasized that the cholinergic anti-inflammatory effect of both the cephalic vagal route and nicotine could be used with this method [6]. Lambrichts et al reported that nicotine gum was safe but ineffective in the treatment of prolonged postoperative ileus in a multicenter randomized study [26].

In the pathophysiology of postoperative ileus, the neurogenic pathway is responsible early in the event, while the inflammatory pathway is active in the late period [18]. The cause of impaired bowel activity is the inflammatory cells that infiltrate the gut muscular layer during the late period. Nicotine may suppress this second mechanism by the cholinergic anti-inflammatory effect [27].

Nicotine also has some potential positive effects. It reduces the need for opioids, which are one of the causes of prolonged paralytic ileus in the postoperative period [28]. In experimental studies, nicotine stimulated angiogenesis by stimulating endothelial nicotinic acetylcholine receptors, thereby increasing

wound healing [29, 30]. Side effects of nicotine chewing gum have been well studied since they are used for smoking cessation for a very long time. In Cochrane analysis conducted in 2012, the most significant side effect of nicotine chewing gum was found to be irritation in the mouth and throat, and no evidence was found that nicotine replacement treatments increased the risk of heart attack [31].

This study has restrictions due to the low number of patients. Obtained favorable results in the management of POI may encourage further studies including a larger number of patients and comparing different doses of nicotine.

Conclusion

The nicotine gum chewing resulted in shorter duration recovery of bowel movements, appetite and ileostomy discharge when compared to the control group. Nicotine gum chewing seems to be an effective method for resolution of postoperative ileus after rectal cancer surgery.

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Declarations

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Compliance with ethical standards: This article was written in accordance with the ethical standards of the institutional review board and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Analysis and interpretation of data: I.Ozgur, B. Karip

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