Original Article

The Efficacy and Results of Medical Treatment in Postoperative Ileus

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Abstract

Background: Postoperative paralytic ileus refers to the disruption of the normal coordinated propulsive motor activity of the gastrointestinal system following surgery. Surgery causes inflammation in the muscle walls of organs with an intestinal lumen that, in turn, leads to a decrease in intestinal motility. **Aim:** The aim of this study was to investigate the efficacy of gastrografin, neostigmine, and their combined administration in patients diagnosed with paralytic ileus in the postoperative period. **Patients and Methods:** One-hundred twelve patients were included from January 2017 and November 2019. The retrospective study is involving prolonged postoperative ileus cases following colorectal surgery. The effect of gastrografin, neostigmine, and gastrografin neostigmine combination was compared retrospectively in the treatment of prolonged ileus after surgery. **Results:** The study covered 112 patients. Gastrografin was administered to 63 patients; neostigmine was administered to 29, while 20 patients received the combination of the two. Data pertaining to the comparison of the two groups revealed that patients in the gastrografin group were discharged earlier than those in the neostigmine group. Further, patients in the combined group had earlier gas and/or stool discharge and were also discharged from the hospital earlier than those in the neostigmine group. **Conclusion:** Gastrografin and combined use of gastrografin and neostigmine are effective and viable methods for postoperative ileus cases. Gastrografin can safely be used in patients with anastomoses.

Keywords: *Gastrografin, neostigmine, postoperative ileus*

Introduction

Postoperative paralytic ileus refers to the disruption of the normal coordinated propulsive motor activity of the gastrointestinal system following abdominal or extra-abdominal surgery and to non-mechanical intestinal obstruction preventing oral intake.[1]

Disruption of intestinal motility for a specific period of time after surgery is a normal process.[2] This is a benign and self-limited condition. Normal period lasts for 0-24 hours in the small intestines, 24-48 hours in the stomach, and 48-72 hours in the colon.[3] It is known that gastric and small intestine activity usually returns within hours after surgery, while colonic activity comes back on the second or third postoperative day.[4] If this period is prolonged the patient develops a sensation of discomfort and dissatisfaction. This condition is called postoperative paralytic ileus. Postoperative paralytic ileus is diagnosed when two or more of the signs and symptoms such as nausea and vomiting, oral intake intolerance, inability to pass gas, abdominal distension, and radiological air fluid level are present after the 3rd postoperative day.[5] Surgical manipulation causes inflammation in the colonic wall muscles and this in turn decreases intestinal motility. Yet, studies that investigated experimental cases reported that inflammation was observed in intact intestinal parts as well.[6,7]

The aim of this study was to investigate the efficacy of gastrografin, neostigmine, and their combined administration in patients diagnosed with paralytic

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ileus in the postoperative period and to compare their respective results.

Patients and Methods

The study was carried out upon the approval of Necmettin Erbakan University Meram Medicine Faculty Ethics Board which number is 2019/2177. This study was conducted by retrospectively examining the files of patients who were treated with the diagnosis of prolonged postoperative paralytic ileus cases following major colorectal surgery (colectomy, proctectomy, Hartmann's colostomy closure) between January 2017 and November 2019.

In our clinic, "enhanced recovery after surgery" (ERAS) protocol is applied to all patients after major colorectal surgery in the postoperative period routine practice. Patients are mobilized in the early postoperative period and oral intake is initiated as soon as possible while achieving multimodal pain management. Oral fluid intake is resumed when there is no risk of postoperative aspiration. Parenteral fluid treatment is stopped in patients who tolerate oral ingestion. Semi-solid food intake is started on the first postoperative day. Patients are discharged on the second or third postoperative day.

Postoperative paralytic ileus is diagnosed when two or more of the signs and symptoms such as nausea and vomiting, oral intake intolerance, inability to pass gas, abdominal distension, and radiological air fluid level are present after the 3rd postoperative day.[5] This is how we are doing same in our own practice. All patients included in the study were diagnosed and treated with postoperative paralytic ileus.

Efficacy of treatment: Patients who had gas or stool discharge, no distension, tolerated oral intake, and were discharged from the hospital after 24 hours of well-being were accepted as the success criteria in the treatment.

Exclusion criteria for the study included anastomotic leak, intraabdominal infection and abscess formation, previous history of abdominal and pelvic surgery, patients with serious cardiac and renal pathologies, patients with a history of previous operation other than colorectal surgery, pregnancy, and lactation. Patients who developed allergy to gastrografin or neostigmine during treatment were also excluded from the study.

Patients were divided into three groups according to the treatment applied: neostigmine treatment, gastrografin treatment, and the combination group, both of which were given. The patients in the first group who were given neostigmine treatment were those who received 2.0 mg neostigmine intravenous treatment over 30 minutes. In this group of patients, once-daily dosing was continued until peristalsis began. In the second group, the patients received 100 ml orally gastrografin treatment once. In the third group, the combined treatment group, the patients received 2.0 mg of neostigmine intravenously every day for 30 minutes and 100 ml of gastrografin once by mouth until peristalsis began. All patient groups had standing direct abdominal radiographs every 24 hours.

The files of the patients in all three groups were scanned backwards for smoking, neoadjuvant chemotherapy status, diabetes mellitus, use of nasogastric catheter in the postoperative period, oral intake restriction, nausea and vomiting, CT scans, complications, defense and rebound status in abdominal examination, complete blood count, BMI, blood electrolyte panel (including magnesium), urea, creatine, liver panel, amylase and lipase values, air-fluid level in erect direct abdominal X-ray, day of discharge from hospital, day of gas, and stool discharge, was recorded.

Statistical analysis: The Kolmogorov–Smirnov and Shapiro–Wilk tests were used to control the distribution of the parameters. Mann–Whitney U test was used for the comparison of independent groups. In categorical data, Chi-square tests were used in cross tables. In the interpretation of statistical hypothesis tests, the type 1 error was accepted as 0.05. The collected data were analyzed by the SPSS program.

Results

The study covered 112 patients [Table 1]. 63 patients (56.3%) received gastrografin, 29 patients (25.9%) received neostigmine, while 20 patients (17.9%) received the combination of the two. 39 (34.8%) of the patients were female, while 73 (65.2%) were male and their mean age was 53.9 (19-84).

The intergroup comparison revealed no differences among the groups as per smoking, neoadjuvant

Table 1: Patient data with no statistical significance

Parameters	Yes (*n*/%)	No (*n*/%)
Smoking	51 (45.5)	61 (54.5)
Neoadjuvant chemoradiotherapy	18 (16.1)	94 (83.9)
DM	16 (14.3)	96 (85.7)
NG placement	52 (46.4)	60 (53.6)
Nausea vomiting	66 (58.9)	46 (41.1)
Oral stop	78 (69.6)	34 (30.4)
Distension	93 (83.0)	19 (17.0)
Rebound –defense	0	112 (%100)
Electrolyte deficit	30 (26.8)	82 (73.2)
Air-fluid level	108 (96.4)	4 (3.6)
CT scan	28 (25)	84 (75)
Complication	2 (1.8)	110 (98.2)

Table 2: Patient data with statistical significance

Parameters	Gastrografin (*n*:63)[a]	Neostigmine (*n*:29)[b]	Combined (*n*:20)[c]	*P*
Day of discharge from hospital	8.6±4.0	9.2±1.7	8.1±2.5	0.02[a-b, c-b]
Day of discharge (gas and stool)	4.6±2.1	5.9±2.5	4.3±2.4	0.06[c-b]
BMI	27.4±4.3	24.9±3.7	27.8±3.7	0.02[a-b, c-b]

Day of discharge from the hospital— Significantly higher in groups a and c than group b. Day of gas and/or stool discharge— Significantly higher in group c than group b. BMI— Significantly higher in groups a and c than group b

chemoradiotherapy, DM, NG placement, nausea and vomiting, oral stop, distension, rebound-defense, electrolyte deficit, air-fluid level, CT scan, and complications [Table 1]. 51 patients were smokers, 18 had received chemoradiotherapy and 16 were diabetic. While nausea-vomiting was observed in 58.9% of the cases during the treatment, nasogastric tubes were placed in 46.4%. Oral liquid intake was not restricted in patients with no nausea and vomiting (34%). 12.5% of the patients diagnosed with postoperative ileus gas discharge held out. Distension was observed in a great majority of the patients. None of our patients developed acute abdomen examination symptoms during the follow-ups. Yet, 30 patients had electrolyte deficit. Low sodium levels were most commonly observed in such cases. Erect direct abdominal radiography did not reveal any levels in 3.6% of the cases. Contrast abdominal CT was performed for 28 cases with non-definitive diagnoses. 36.6% (41) of the cases received transfusion before postoperative ileus diagnoses. No serious complications were seen in patients during the follow-ups other than two that had wound site dehiscence. Laparoscopic surgery was performed for only 10 cases. Among all the patients with laparoscopic colorectal procedures, 2% developed postoperative prolonged ileus. 12% of the laparotomy cases developed postoperative ileus. Postoperative gas-stool discharge day was significantly lower in laparoscopic surgery compared to conventional surgery ($P < 0.001$). No significant difference was observed between the groups in terms of discharge day ($P = 0.42$). No significant difference was observed when the three groups were compared together in terms of gas stool discharge ($P = 0.06$). In the pairwise comparison of the groups, gas stool discharge was found to be significantly delayed in the neostigmine group compared to the combined group ($P = 0.02$ [Table 2].

When the neostigmine only group was compared with the gastrografin or combined treatment group, hospital discharge time was significantly lower in both groups compared to the neostigmine administered group ($P = 0.02$) [Table 2]. The most important disadvantage of neostigmine was that it was not a viable treatment modality for patients with cardiac problems and, therefore, there were fewer cases in this group. Body mass index figures were higher, while leukocyte was significantly higher in the neostigmine group. The C-reactive protein value was found to be significantly low in the gastrografin group. Gas discharge happened on an average of 4.9 (1-12) days.

Gastrografin was administered in patients with anastomoses as well. Anastomotic leak was not seen in any of the cases. Its disadvantage was that it caused vomiting in some patients because of its foul taste. We observed that discharge began in patients when the contrast material reached the left colon. It was observed that the combined use only had minimal contribution to treatment and this contribution did not bear any statistical significance. One case developed tachycardia which got better rapidly without having to resort to any intervention.

Discussion

Pathological postoperative ileus has not been definitively defined yet. The onset of intestinal peristalsis is usually taken into account for the definition of postoperative ileus. Absence of the return of intestinal motility after the fourth day is commonly held to be postoperative ileus. Nausea and vomiting after the fourth postoperative day, oral intake intolerance, inability to pass gas, abdominal distension, and radiological confirmation constitute the diagnosis of postoperative ileus.[5] Yet, the primary criterion within this scope is time. Patients' symptoms should be taken into account after the time is up. Radiological confirmation proves to be important in symptomatic patients. We did, however, take into account not only the onset of symptoms but also the symptoms themselves. Nevertheless we diagnosed patients according to the symptoms they developed after the fourth day. Erect direct abdominal radiography was performed for all patients, while abdominal CT was performed for cases suspected of having complications that might require surgery in the postoperative period. We rather used radiology to investigate treatment response as well.

Numerous theories have been put forth to clarify the etiology of postoperative ileus. Researchers have attempted to explain the formation of postoperative ileus through neuronal reflex and neurohumoral peptidase mechanisms. The most effective factor impacting

the inhibition of gastrointestinal motility is the interaction among the inflammatory and neurohumoral pathways.[8] Studies have shown that such activation was associated with the increase in inflammatory cell secretion and inflammatory cell activation (cytokines, cyclooxygenase-2 -COX-2- and leukocyte-derived inducible nitric oxide synthase).[8,9] Inflammation occurs after intestinal manipulation and trauma. An experimental study reported that intestinal dysmotility developed as a result of leukocyte infiltration formed on the muscular layer following operative intestinal trauma.[8] This inflammation, however, was not merely limited to the manipulated segments. Further, intestinal inflammation can also be seen in nonabdominal procedures[9] and its mechanism has not been entirely known yet. It has, nonetheless, been assumed that reduced intestinal blood perfusion (ischemia) arises through the translocation of endogenic cellular molecules and cytokines to the distant surgical trauma area. It has been suggested that inhibitor neural reflexes were set off locally through spinal afferent signals that increased inhibitor sympathetic activity within the gastrointestinal system.[10] It has also been suggested that neurohumoral peptides acted as inhibitor neurotransmitters in the intestines that slowed down the intestinal motility of nitric oxide, vasoactive intestinal polypeptide and substance P.[1,11] All our cases had intestinal trauma. We believe that peristalsis was lost due to events associated with intestinal manipulation which led us to identify it as the reason why less postoperative ileus cases were seen in laparoscopic surgery. Accurate information about epidemiology and the risk factors has not been available either. Its incidence depends on the modality of surgery performed. Lower abdominal surgery, large incisions and intestinal manipulation prove to be the most important risk factors. Although the ERAS protocol decreases its incidence, it failed to eliminate it in its entirety.[12] It has been reported that postoperative ileus was seen in 17.4% of the cases following colectomy, the rate was found to be 12.7% following elective colectomy and 15% following ileocolic anastomosis.[13] Anastomotic leak and intraabdominal infection increases the risk, while laparoscopic surgery and intestinal preparation with oral antibiotics reduces it.[14] Intestinal trauma should be avoided as much as possible. In our study, postoperative gas stool discharge was significantly lower in laparoscopic surgery compared to conventional surgery. The rate of postoperative ileus in our cases was less than 10%. The most important reason bringing about such a rate was the fact that laparoscopic surgery was quite often preferred. The results of our study, however, did not reveal a distinctive risk factor for postoperative ileus. Yet, it is seen way less in laparoscopic procedures that lead to less intestinal trauma. A more standard patient group was formed within the scope of our study since it analyzed the cases of colorectal surgery patients.

Clinical responses included abdominal distension, swelling, inability to pass gas, diffuse persistent abdominal pain, nausea, and vomiting, delayed passage or insufficient gas passage and oral intake intolerance. Treatment was rather in the form of palliative care which aimed to compensate electrolyte and liquid deficits, achieve pain control and prevent aspiration. The treatment used to increase intestinal peristalsis was the administration of gastrografin and neostigmine.[15] Gastrografin is an orally administered hyperosmolar water-soluble contrast medium. Gastrografin brings about a decrease in the edema on the intestinal wall through its hyperosmolar impact and initiates peristalsis.[16,17] Neostigmine, on the other hand, is an acetylcholinesterase inhibitor that is believed to stimulate colonic motility by causing an increase in cholinergic (parasympathetic) activity on the intestinal wall.[18] Some studies reported that neostigmine had a moderate effect on the alleviation of acute colonic pseudo obstruction but its clinical benefits in postoperative patients might have been limited to adverse effects like abdominal cramping, excess saliva, vomiting, and bradycardia.[19] Its use and efficacy in postoperative ileus cases are a matter of controversy. We compared gastrografin, neostigmine, and their combined use in postoperative ileus cases within the scope of our study. In a study by Vather *et al*.,[16] gastrografin alone was not found to be effective in the treatment of prolonged postoperative ileus. In our study, there was a significant difference in gas-stool discharge and discharge time from the hospital in the group given gatrografin or combined treatment compared to the neostigmine group.

Another study by Tony G E Milne *et al*.,[20] it was revealed that gastrografin had an effect on tolerating early oral intake in patients with postoperative ileus, but had no effect on the duration of ileus. In our study, positive effects on early oral intake and early treatment of ileus were observed in both the gastrografin and combined groups.

There are resources in the literature on neostigmine showing its use for the treatment of acute colonic pseudoobstruction. However, there is no clear evidence to support its use in the treatment of paralytic ileus. In addition, it should be used with caution, considering its serious side effects and short duration of action. İlban Ö. *et al*.,[21] in their study, showed that the use of neostigmine was effective in 60% of colonic ileus cases. In our study, the efficacy of neostigmine was found to be more limited in the group in which neostigmine was

used alone compared to the gastrografin and combined group. Although the best results were achieved by their combined use among these methods, gastrografin is a method that can also be used on its own.

We did not observe any anastomotic leaks in any of the cases that received gastrografin. We placed nasogastric tubes in patients with distinctive vomiting or in those that risked aspiration. We did not impose a marked restriction on oral intake. We did not observe any significant side effects in cases that received neostigmine. One of the reasons for this might be the fact that we did not use it in patients with cardiac risks.

Conclusion

In conclusion, gastrografin and the combined use of gastrografin and neostigmine are efficient and viable methods for postoperative ileus cases. The efficacy of neostigmine is low and physicians should be careful about the cardiac functions of patients on neostigmine. Gastrografin can also be safely used in patients with anastomoses.

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Conflicts of interest

There are no conflicts of interest.

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