

Original Research Article

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Influence of combined mechanical-chemical versus mechanical bowel preparation on anastomotic leak and surgical site infections after elective resection of left colon cancer

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ABSTRACT

Background: Mechanical bowel preparation (MBP) before elective resection of left colon cancer remains controversial. We propose that the protective effect of MBP is dependent on its combination with chemical preparation by oral antibiotics.

Methods: Medical data of adult patients with left colon cancer who underwent elective resection at Sohag University Hospital (August 2016-March 2019) were reviewed. Anastomotic leak (AL), surgical site infections (SSI), postoperative morbidity and mortality were compared among patients who preoperatively received MBP followed by chemical preparation with oral antibiotics (MBP and OABx group) versus another group of preoperative MPB alone (MBP group).

Results: Forty-two patients with left colon adenocarcinoma were enrolled, 21 per group. Overall, sigmoid colon was the most common site of left sided colon cancer (76%). Malignant lesions were found in proximal sigmoid in 19 (45%), rectosigmoid in 13 (31%), descending colon in 8 (19%) and splenic flexure in 2 (5%) patients. Dukes' classification was A in 6 (14%), B in 19 (45%) and C in 17 (41%) patients. Compared with MBP, MBP and OABx group showed significantly lower rates of anastomotic leak (3 patients (14%) versus 1 (5%) respectively, $p<0.05$) and surgical site and intraabdominal infections (7 patients (33%) versus 2 (10%), $p<0.05$). MBP and OABx group exhibited lesser grades of postoperative complications ($p<0.05$) and shorter hospital stay ($p<0.05$). Postoperative mortality occurred only in the MBP group.

Conclusions: Combined mechanical-chemical bowel preparation prior to elective resection of left colon cancer confers superior clinical outcome regarding anastomotic leak, surgical site infections and overall postoperative complications.

Keywords: Bowel preparation, Oral antibiotics, Colon cancer, Colectomy

INTRODUCTION

Cancer of the colon and rectum ranks third among commonest cancers worldwide and fourth cause of cancer-related death.¹ Incidence of colorectal cancer in adults younger than 50 years is continuously increasing.^{2,3} In Egypt, data from cancer registry shows progressive increase in the incidence of colon cancer.⁴ While surgery remains as the sole potentially curative treatment option,

the optimal approach of bowel preparation before elective left colon resection remains unsettled.⁵

Until the early seventies of the last century, standard preoperative measures prior to left colectomy entailed mechanical bowel preparation (MBP) with vigorous purgatives.⁶ Advocates of this strategy propose that anastomotic leak (AL) is directly related to the contact between colonic fecal material in the unprepared colon and

the newly sewn anastomosis. For further elimination of this risk, defunctioning stomas were recommended proximal to colonic anastomosis in conjunction with MBP preoperatively.⁶

On the other hand, opponents of MBP argue that this policy provokes preoperative dehydration, electrolyte imbalance and bowel mucosal changes with opportunity for bacterial translocation. Furthermore, MBP was described as unpleasant inducer of abdominal pain, gas bloating and exhaustion.⁷

Several clinical trials comparing the incidence of AL and surgical site infections (SSI) following elective colon resection and re-anastomosis in patients with left colon cancer have emerged. The results were unfortunately contradictory and might have contributed to further confusion.^{5,8,9}

For instance, recent systematic review and meta-analysis showed that MBP do not diminish the incidence neither of AL nor SSI after colorectal resections.¹⁰ In sharp contrast, other studies have demonstrated clear advantage of MBP in reducing both AL and SSI.¹¹

It appears that a key factor explaining the divergent results from the currently available literature is the lack of consideration of the influence of oral antibiotics (OABx) on adequacy of preoperative bowel preparation.¹² In this context, MBP is supposed to enhance the uptake of OABx by colonic mucosa.¹³ This concept was supported by the documented advantage of oral over intravenous antibiotics when administered after MBP as preparatory measure before colon and rectal resections.¹⁴ Thus, the mitigation of AL and SSI rates in patients who received MBP prior to elective left colectomy could be attributed to the synergistic effect induced by combining MBP and OABx.¹³

Therefore, in this study we will address, for the first time from South Egypt cancer surgery programs, the influence of dual bowel preparation (MBP and OABx) versus MBP alone before elective resection of left colon cancer on the incidence of AL, SSI and overall complications.

METHODS

Data records of adult patients with histologically proven primary left colon cancer (Dukes' A-C), who had undergone open elective resection and primary re-anastomosis at Sohag University Hospital (August 2016–March 2019), were retrospectively analyzed. Left colon cancer was defined as adenocarcinoma of the splenic flexure, descending colon, sigmoid colon and rectosigmoid junction. Exclusion criteria were primary cancer in other segments of the colon, proven distant metastasis (Dukes' D), locally advanced, recurrent and multifocal cancers, previous chemotherapy, unfit patients and refusal to sign an informed consent.

Before elective resection of left colon cancer, patients who received a combination of MBP followed by OABx (MBP and OABx group) were compared to those who were treated with MBP alone (MBP group). The study was conducted in accordance with the guidelines of Medical Research Ethics Committee at Sohag University.

Preoperative evaluation, bowel preparation and surgical procedures

Thorough clinical evaluation including abdominal imaging studies, routine laboratory tests, metastatic workup and measurements of carcinoembryonic antigen levels were carried out for all patients prior to surgical intervention.

Mechanical bowel preparation entailed ingestion of fluid diet, avoidance of solid food, oral purgatives (picolax) and repeated enemas 3 days preoperatively. During the last day before surgery, patients received 3 doses of neomycin and metronidazole 3 times orally to achieve adequate chemical preparation of the mechanically cleansed bowel. Both techniques were sequentially applied on patients of the MBP and OABx group. MBP group was prepared only with the same regimen of purgatives and enemas.

Types of colectomy procedures were carried on the basis of tumor location. These procedures comprise left hemicolectomy, including sigmoidectomy, for descending and proximal sigmoid colon cancer, extended left hemicolectomy for cancers involving the splenic flexure and anterior resection for cancers of the rectosigmoid junction. End-to-end anastomosis was carried out in all cases.

Postoperative assessment

The severity of postoperative complications was objectively assessed by Clavien-Dindo classification.¹⁵ The seven grades of complications include any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions (allowed therapeutic regimens include antiemetics, antipyretics, analgetics, diuretics, electrolytes, physiotherapy and bedside opening of wound infections (grade I), use of other drugs, blood transfusions and total parenteral nutrition (grade II), intervention not under local anesthesia (grade IIIa), intervention under general anesthesia (grade IIIb), single organ dysfunction requiring intermediate care (grade IVa), multiple organ dysfunction requiring intensive care (grade IVb) and death (grade V).¹⁵

These seven grades were allocated number of points from 1 to 7 in ascending order (grade I: one point, grade II: two points, grade IIIa: three points, grade IIIb: four points, grade IVa: five points, grade IVb: six points and grade V: seven points).^{16,17} Statistical analysis was conducted using GraphPad Prism 6.0 software.

RESULTS

Forty-two patients were enrolled according to the study protocol. The patients were distributed equally between MBP and OABx and MBP groups (21 per group). Differences regarding gender and age distribution, smoking, tumor location in the four anatomical segments within the left side of the colon (splenic flexure, descending colon, sigmoid colon and rectosigmoid junction) and Dukes' class were not remarkable. Preoperative data were shown in Tables 1 and 2.

Table 1: Demographic data and medical history.

Characteristics	MBP and OABx	MBP
Age, median (range)	52 (40-76)	49 (38-79)
Male gender (n)	13	11
Family history (n)	1	0
Smoking (n)	8	6

Table 2: Clinical presentation.

Symptoms	Percentage (%)
Constipation	23 (55)
Anorexia	20 (48)
Bleeding per rectum	17 (41)
Wight loss	14 (33)
Altered bowel habits	13 (31)
Abdominal pain	11 (26)
Tenesmus	8 (19)
Abdominal mass	7 (17)
Constipation	23 (55)

Table 3: Preoperative endoscopic data and tumor Dukes' classification.

Variables	MBP and OABx	MBP
Tumor location within the left colon		
Proximal sigmoid (%)*	8 (38)	11 (52)
Recto-sigmoid (%)*	7 (33)	6 (29)
Descending (%)*	5 (24)	3 (14)
Splenic Flexure (%)*	1 (5)	1 (5)
Dukes' class		
Dukes' A (%)*	3 (14)	3 (3)
Dukes' B (%)*	10 (48)	9 (43)
Dukes' C (%)*	8 (38)	9 (43)

(*) indicates percentage within the related group.

Operative data

Left hemicolectomy was the most common procedure in both groups. Almost two thirds of patients have undergone left hemicolectomy due to carcinoma of the descending or proximal sigmoid colon. Rectosigmoid tumors requiring anterior resection was carried out in 13 patients. Only 2 patients had extended hemicolectomy for carcinoma of the

splenic flexure. There was no significant difference with regard to the operative time between both groups. Likewise, the amount of blood loss and intraoperative transfusions were almost similar. The types of surgical procedures and operative data are summarized in Tables 3-5.

Table 4: Types of surgical procedures.

Types	MBP and OABx	MBP
Left hemicolectomy	13	14
Anterior resection	7	6
Extended left hemicolectomy	1	1

Table 5: Operative data.

Variables	MBP and OABx	MBP	P value
Operative time (minute)*	140(100-240)	130(110-210)	ns
Blood loss (ml)*	300(80-650)	320(100-550)	ns
Units of RBCs transfusion*	1 (0-3)	2 (1-3)	ns
Plasma transfusion(units)*	2 (0-4)	2 (1-3)	ns

*median (range)

Incidence of anastomotic leak, surgical infections and ileus

Overall, patients in MBP and OABx group exhibited better postoperative course than MBP group. Considering the whole study population, anastomotic leak occurred in 4 patients, among them 3 were in MBP versus 1 in MBP and OABx group.

Surgical site infections including wound sepsis and intra-abdominal abscess occurred in 9 patients (21%), the majority of them were in the MPB group (7 patients) compared with only 2 patients in the MBP and OABx group. Of note, abdominal abscess occurred exclusively in the MBP group in 3 patients.

Infectious complications were associated with significant delays in restoration of bowel sounds and commencement of oral feeding in patients enrolled in the MPB compared with MBP and OABx group. Likewise, the time required before removal of abdominal drains postoperatively was significantly longer in MBP than MBP and OABx group.

Postoperative complication score, length of hospital stays, postoperative mortality

Overall, postoperative complications were more common in MBP (16/21 patients) compared with MBP and OABx

(9/21 patients) group. Incidence of major complications (grade III and above) was remarkably increased in MBP (9 patients, 43%) than MBP and OABx (2 patients, 10%) group. Complication scores were significantly higher in the MBP than the MBP and OABx group. In line with increased complications among patients who received MBP without oral antibiotics, patients within this group required significantly longer periods of hospital stays

compared with those in the MBP and OABx group. Post-operative mortality occurred only in the MBP group (one patient dies due to sepsis following relaparotomy for anastomotic leakage), while there was no postoperative death among MBP and OABx patients. Post-operative data and details of post-operative complications are shown in the tables below (Tables 6-8).

Table 6: Postoperative data.

Variables	MBP and OABx	MBP	P value
Number of days required to			
Tolerance of oral feeding* [§]	3 (4-6)	5 (3-8)	<0.05**
Removal of abdominal drains* [§]	5 (4-7)	7 (4-10)	<0.05**
Complication score [§]	2 (1-4)	3 (1-7)	<0.05**
Length of hospital stay [§]	8 (7-28)	12 (9-35)	<0.05**

*in patients who have not developed AL, [§] median (range), **significant difference

Table 7: Postoperative complications in MBP and OABx group (9 patients*).

Patient number	Type of complication, treatment and intervention	Complication grade	Complication score
1	Anastomotic leak (laparotomy and re-anastomosis)	IIIb [§]	4
2	Intra-abdominal abscess (drainage under local anesthesia)	IIIa [§]	3
3	Wound infection (antibiotics and opening at bedside)	II ⁺	2
4	Anemia (transfusion of packed RBCs)	II ⁺	2
5	Hypoalbuminemia (transfusion of fresh frozen plasma)	II ⁺	2
6	Hypoalbuminemia (transfusion of fresh frozen plasma)	II ⁺	2
7	Deep venous thrombosis (medical treatment)	II ⁺	2
8	Respiratory tract infection (antibiotics)	II ⁺	2
9	Prolonged ileus (medical treatment)	I ⁺	1

*highest complication per patient, [§]complication grade IIIa and higher grades are considered major complications, +complication grade I and II are considered minor complications

Table 8: Postoperative complications in MBP group (16 patients*).

Patient number	Type of complication, treatment and intervention	Complication grade	Complication score
1	Death (relaparotomy for anastomotic leak, sepsis)	V [§]	7
2	Renal impairment (managed in intermediate care unit after relaparotomy for anastomotic leak)	IVa [§]	5
3	Pneumonia ((managed in intermediate care unit)	IVa [§]	5
4	Anastomotic leak (laparotomy and re-anastomosis)	IIIb [§]	4
5	Intra-abdominal abscess (laparotomy and drainage under general anesthesia)	IIIb [§]	4
6	Intra-abdominal abscess (drainage under local anesthesia)	IIIa [§]	3
7	Intra-abdominal abscess (drainage under local anesthesia)	IIIa [§]	3
8	Wound infection (drainage of abscess under local anesthesia)	IIIa [§]	3
9	Wound infection (drainage of abscess under local anesthesia)	IIIa [§]	3
10	Wound infection (antibiotics and opening at bedside)	II ⁺	2
11	Wound infection (antibiotics and opening at bedside)	II ⁺	2
12	Anemia (transfusion of packed RBCs)	II ⁺	2
13	Hypoalbuminemia (transfusion of fresh frozen plasma)	II ⁺	2
14	Respiratory tract infection (antibiotics)	II ⁺	2
15	Prolonged ileus (medical treatment)	I ⁺	1
16	Prolonged ileus (medical treatment)	I ⁺	1

*highest complication per patient, [§]complication grade IIIa and higher grades are considered major complications, +complication grade I and II are considered minor complications

DISCUSSION

In this study we demonstrated that, in the setting of elective resection of left colon cancer, the combined strategy of MBP and OABx was remarkably superior to preoperative MBP alone. The combined strategy was associated with lower rates of postoperative anastomotic leaks, infectious and overall complications and mortality.

A debate on the influence of bowel preparation on the clinical outcome of colon resection dates back to several decades. Mechanical bowel cleansing combined with oral antibiotics was standard practice prior to elective colonic resections. This strategy was challenged by the evidence that omission of mechanical bowel preparation is not only welcomed by patients and nursing staff but also carried no risk on the postoperative outcome. Moreover, bowel preparation was reported as aggressive and time-consuming procedure that might trigger the risky consequences of dehydration and electrolyte imbalances.^{6,7}

Nonetheless, most of these studies were hampered by the lack of consideration 2 key factors. The first is the potential synergistic effect of chemical bowel preparation by preoperative antibiotics when combined with MBP.¹⁸ The second was the inclusion of resectional procedures of the right and left colon in the same analysis.^{10,19}

For instance, in a study on 234 patients with cancers located at different sites of the right colon, left colon or rectum, preoperative bowel preparation prior to colectomy procedures was reported to be unnecessary and could be harmful. However, the discrepancy in healing power in different colonic segments in relation to presence of peritoneal coverage and the nature of colonic contents was not considered. In addition, the potential beneficial influence of preoperative oral antibiotics with MBP was not addressed.⁹

To avoid both major limitations, we compared two homogenous groups of patients who underwent elective resections of left colon cancers. We compared that influence of combined mechanical and chemical bowel preparation (MBP and OABx) versus MBP without oral antibiotics (MBP group). We found that MBP and OABx resulted in significant improvement in the rates of anastomotic leaks. This finding accords with the results large multicenter European study on 3676 patients with left sided colon cancer, which showed a strong evidence on prevention of anastomotic leaks by preoperative MBP and OABx.²⁰

Similar results were recently reported in the setting of open or even minimally invasive colon resections.^{13,21,22} We have also found decreased rates of infectious complications, including wound infections and intraabdominal abscesses, and ileus among patients in MBP and OABx. These observations are in agreement with Kiran and coworkers who demonstrated that

preoperative antibiotics in combination with mechanical bowel preparation resulted in almost 50% reduction in postoperative infectious complications and ileus.²³ Similar decrease of infectious complications was reported by several other studies.^{11,24,25} An added advantage of MBP and OABx was the remarkable cost saving in association with diminished incidence of surgical site infection.²⁶

We also found that bowel preparation in MBP and OABx was associated with reduction of postoperative complications, including mortality, and concomitant shortening of the length of hospital stay. These findings are in agreement with the reported significant improvement in overall complications and reduction of the length of hospital stay after left-sided colon resections for left sided colon cancer among patients who received preoperative combination of mechanical and chemical bowel preparation.²⁷

CONCLUSION

The results of this study strongly support the applications of dual bowel preparation by mechanical cleansing followed by oral antibiotics to improve the clinical outcome of elective resections for left colon cancer.

The study is limited by the relatively small number of patients and the inherent defects of the retrospective analysis.

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Ethical approval: Not required

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