Mechanical and oral antibiotic bowel preparation versus no bowel preparation in right and left colectomy: subgroup analysis of MOBILE trial

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Abstract

Background: In retrospective series, mechanical and oral antibiotic bowel preparation (MOABP) has been reported to reduce surgical-site infections (SSIs) after colectomy compared with no bowel preparation (NBP).

Method: This was a subgroup analysis of a multicentre randomized trial that included patients scheduled for elective colectomy. The MOABP group underwent mechanical bowel preparation, and took 2 g neomycin and 2 g metronidazole orally during the day before surgery. The NBP group did not undergo bowel preparation. Patients were categorized according to the side of resection (right versus left colectomy), and these subgroups compared for postoperative outcomes.

Results: Among 217 patients undergoing right colectomy (106 in MOABP and 111 in NBP group), SSI was detected in seven (7 per cent) and 10 (9 per cent) patients (odds ratio (OR) 0.71, 95 per cent c.i. 0.26 to 1.95; P = 0.510), anastomotic dehiscence in two (2 per cent) and two (2 per cent) patients (OR 1.05, 0.15 to 7.58; P = 1.000), and the mean(s.d.) Comprehensive Complication Index (CCI) score was 9.4(12.9) and 10.5(18.0) (mean difference –1.09; 95 per cent c.i. –5.29 to 3.11; P = 0.608) in the MOABP and NBP groups respectively. Among 164 patients undergoing left colectomy (84 in MOABP and 80 in NBP group), SSI was detected in five (6 per cent) and eight (10 per cent) patients (OR 0.57, 0.18 to 1.82; P = 0.510), anastomotic dehiscence in two (2 per cent) and three (4 per cent) patients (OR 0.75, 0.19 to 2.90; P = 0.742), and the CCI score was 10.2(13.1) and 6.5(11.0) (mean difference 3.68, –0.06 to 7.42; P = 0.053) in the MOABP and NBP groups respectively.

Conclusions: MOABP did not decrease the rate of SSI or complications in patients undergoing either right or left colectomy compared with NBP.

Introduction

Surgical-site infection (SSI), including anastomotic dehiscence, is still a major problem after colorectal surgery. Mechanical and oral antibiotic bowel preparation (MOABP) has emerged for debate as several recent large retrospective studies 1–6 using data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) and a prospective cohort study from the European Society of Coloproctology (ESCP) have suggested a beneficial effect on SSIs after colorectal surgery. Based on these non-randomized data, the American Society of Colon and Rectal Surgeons, American Society of Enhanced Recovery, and Society of American Gastrointestinal and Endoscopic Surgeons have updated their guidelines to recommend MOABP 7–9. These studies and changes in the recommendation have sparked a lively debate about whether MOABP should be performed in every patient undergoing colorectal surgery. 10–12 Advocates of no bowel preparation (NBP) have pointed out that, although there are RCTs comparing MOABP with mechanical bowel preparation alone showing the benefit of MOABP in colorectal surgery 13–16, until very recently there have been no data from an RCT comparing MOABP with NBP directly. The MOBILE (Mechanical and Oral Antibiotic Bowel Preparation Versus no Bowel preparation for eLective Colectomy) trial (NCT02652637) 17 was the first RCT to directly compare MOABP with NBP in patients undergoing colectomy. The main finding of the trial was that MOABP did not reduce the rate or severity of SSIs, or overall postoperative complications. The trial was rightly criticized for including low-risk right colectomies, and not reporting right- and left-sided colectomies separately 18–20. Indeed, right- and left-sided procedures may have different complication and SSI profiles, and may be affected differently by...
The variation in complication profile between right- and left colectomies might stem from differences in anastomoses (ileocolonic versus colocolonic) and microbiome.

To address this shortcoming of the MOBILE trial\textsuperscript{17}, in the present post hoc subgroup study, the outcomes of patients randomized to either MOABP or NBP were analysed separately according to the location of the colectomy (right or left side).

Methods

The MOBILE trial was a national, multicentre, single-blinded, parallel-group, randomized superiority trial comparing MOABP with NBP in patients undergoing elective colonic surgery\textsuperscript{17}. Briefly, the trial was carried out in four Finnish hospitals: two university hospitals (Helsinki University Hospital and Oulu University Hospital) and two community hospitals (Central Finland Central Hospital and Seinäjoki Central Hospital). Patients who were scheduled for colorectal resection in participating centres were assessed for eligibility. Exclusion criteria were: emergency surgery; bowel obstruction; colonoscopy planned to be undertaken during surgery; other indication for, or contraindication to, mechanical preparation; allergy to drugs used in the trial (polyethylene glycol, neomycin, metronidazole); and age under 18 years or over 95 years. Patients were allocated randomly to either MOABP or NBP. The patients could not be masked to mechanical bowel preparation, but the recruiters, treating physicians, operating surgeons, data collectors, and analysts were blinded to the allocation group. Patients allocated to MOABP were instructed to undertake bowel preparation with 2 litres of polyethylene glycol (Moviprep\textsuperscript{26}; Norgine, Amsterdam, the Netherlands) and 1 litre of clear fluids the day before surgery, and after bowel preparation to take 2 g neomycin orally at 19.00 hours and 2 g metronidazole orally at 23.00 hours the evening before surgery. Patients in NBP group were instructed not to prepare the bowel. Prophylactic intravenous antibiotics (1500 mg cefuroxime and 500 mg metronidazole) were administered at the induction of anaesthesia and readministered if the operation lasted more than 3 h from the first antibiotic dose or if blood loss exceeded 1.5 litres.

In this subgroup study, all outcomes were analysed separately for right and left colectomies. Right colectomies were those with ileocolic anastomoses; all colocolic anastomoses were included in the left colectomy group. The primary and secondary outcome measures were the same as those in the original trial. The primary outcome was the rate of SSI within 30 days after surgery as well as subcategories of SSI (superficial incisional, deep incisional, or organ/space), as defined by Centers for Disease Control and Prevention\textsuperscript{22}. Secondary outcomes included overall morbidity measured using the Comprehensive Complication Index (CCI) score\textsuperscript{23}, anastomotic dehiscence rate, reoperations, readmission, mortality, and adverse effects of antibiotics, all within 30 days after surgery, as well as duration of hospital stay and the rate of adjuvant therapy (number of patients receiving adjuvant therapy divided by number needing adjuvant therapy). The trial was approved by the Finnish National Committee on Medical Research Ethics and Finnish Medicines Agency, and further approved by the local ethics committee of Helsinki University Hospital and by each participating centre’s institutional review board (Helsinki University Hospital, Oulu University Hospital, Central Finland Central Hospital, and Seinäjoki Central Hospital).

Results

There were 381 patients in the intention-to-treat analysis: 217 patients (106 in MOABP group and 111 NBP group) who underwent right colectomy, and 164 (84 in MOABP group and 80 in NBP group) who underwent left colectomy (Fig. 1).

Among patients undergoing right colectomy, baseline characteristics were similar between MOABP and NBP groups except that metastatic malignancy was more frequent in the NBP group (Table 1). Among patients undergoing left colectomy, patients in the MOABP group were slightly older and had more coronary and peripheral vascular disease, but baseline characteristics were otherwise similar in the two groups. The duration of operation, timing of preoperative intravenous antibiotics, and blood loss were similar in both groups among patients undergoing right or left colectomies (Table 2).

Right colectomy

Among patients undergoing right colectomy, the rate of SSI was similar in the MOABP and NBP groups: seven (7 per cent) and 10 (9 per cent) patients respectively (OR 0.71, 95 per cent c.i. 0.26 to 1.95; \( P = 0.510 \)) (Table 3). All secondary outcomes were similar between MOABP and NBP groups. There were nine readmissions (8 per cent) in the MOABP group and six (5 per cent) in the NBP group. The reoperations were for anastomotic dehiscence in two patients, suspected anastomotic dehiscence in one, fascial dehiscence in three, intestinal ischaemia in one, ileus in one, and haemorrhage in one patient in the MOABP group, and for postoperative haemorrhage in one, fascial rupture in one, anastomotic dehiscence in two, ileus in one, and intestinal ischaemia in one patient in the NBP group. There were three readmissions (3 per cent) in MOABP group and nine (8 per cent) in the NBP group. The reasons for readmission were fever in one patient, intraluminal haemorrhage in one, and ileus in one patient in the MOABP group, and for postoperative haemorrhage in one, fascial rupture in one, anastomotic dehiscence in two, ileus in one, and intestinal ischaemia in one patient in the NBP group. Two patients died in the NBP group, one (ASA grade IV, Charlson Co-morbidity Index score 6) because of vomiting and pneumonia, and another
Among patients undergoing left colectomy, SSI was detected in five patients (6 per cent) in the MOABP group and eight (10 per cent) in the NBP group (OR 0.57, 95 per cent c.i. 0.18 to 1.82; P = 0.338) (Table 4). All secondary outcomes were similar between MOABP and NBP groups. Reoperation was required in six patients (7 per cent) in MOABP group and six (8 per cent) in the NBP group. The reoperations were for anastomotic dehiscence in four patients, a ureter lesion in one, and intra-abdominal bleeding in one patient in the MOABP group, and for anastomotic dehiscence in four and fascial dehiscence in two patients in the NBP group. There were nine readmissions (11 per cent) in the MOABP group and six (8 per cent) in the NBP group. The readmissions were for anastomotic dehiscence in one patient, fever in one, abdominal pain in one, ileus in two, pyelonephritis in two, urinary retention in one, and diarrhoea in one patient in the MOABP group, and for abdominal pain in one patient, anastomotic dehiscence in one, and ileus in one patient in the NBP group.

**Discussion**

This was a subgroup analysis of the MOBILE trial that compared MOABP with NBP in patients undergoing colonic surgery. The original trial did not find any difference in outcomes between the MOABP and NBP groups in the whole cohort of patients undergoing either right or left colectomy. In this subgroup study, no difference was documented between MOABP and NBP in the rate of SSI or overall postoperative morbidity in patient subgroups undergoing either right or left colectomy. Although the overall postoperative morbidity rate was very similar in MOABP and NBP groups among patients undergoing right colectomy, more postoperative complications were observed in the MOABP group among patients undergoing left colectomy, but this difference did not reach statistical significance.

The effect of MOABP versus NBP was studied in previous retrospective series in both subcohorts of patients undergoing right or left colectomy. An ACS-NSQIP database study suggested an association with MOABP and decreased rate of SSI in patients undergoing either right or left colectomy, but this study had serious selection bias as patients in the MOABP group were younger, more often underwent minimally invasive surgery, and were less often taking preoperative steroids, malnourished or suffering from inflammatory bowel disease. Another retrospective series from the same database reported outcomes of patients undergoing left colectomy only, and also reported an association between MOABP and reduction in SSI. Furthermore, a meta-analysis indirectly estimated that MOABP diminishes SSI compared with NBP (OR 0.6, 95 per cent c.i. 0.45 to 0.79).

The ESCP collaborating group’s multicentre prospective audit of left colectomies reported anastomotic leak rates of 6.1 per cent for MOABP and 8.7 per cent for NBP, which are comparable to those in the present study (MOABP 5 per cent, NBP 6 per cent). The difference in the ESCP study was statistically significant only because of extensive postoperative intra-abdominal bleeding, two relaparotomies, myocardial infarction, and stroke.

**Left colectomy**

Among patients undergoing left colectomy, SSI was detected in five patients (6 per cent) in the MOABP group and eight (10 per cent) in the NBP group (OR 0.57, 95 per cent c.i. 0.18 to 1.82; P = 0.338) (Table 4). All secondary outcomes were similar between MOABP and NBP groups. Reoperation was required in six patients (7 per cent) in MOABP group and six (8 per cent) in the NBP group. The reoperations were for anastomotic dehiscence in four patients, a ureter lesion in one, and intra-abdominal bleeding in one patient in the MOABP group, and for anastomotic dehiscence in four and fascial dehiscence in two patients in the NBP group. There were nine readmissions (11 per cent) in the MOABP group and six (8 per cent) in the NBP group. The readmissions were for anastomotic dehiscence in one patient, fever in one, abdominal pain in one, ileus in two, pyelonephritis in two, urinary retention in one, and diarrhoea in one patient in the MOABP group, and for abdominal pain in one patient, anastomotic dehiscence in one, and ileus in one patient in the NBP group.
after adjustment in a multivariable model (OR 0.52, 0.30 to 0.92; 
\( P = 0.02 \)). Although it was a prospective cohort study, it was not a  
randomized trial, and the estimates suffered similarly from selec-
tion bias as in previous retrospective series.  

A recent randomized trial (SELECT)\(^{26}\) compared selective peri-
operative decontamination of the digestive tract using oral colis-
tin, tobramycin, and amphotericin B versus no oral antibiotics in  
patients undergoing colorectal cancer surgery. All patients un-
dergoing left colectomy, sigmoid or anterior resection underwent  
mechanical bowel preparation. The SELECT trial reported that  
oral antibiotics reduced infectious complications (especially SSI),  
but not anastomotic leakage. Because mechanical bowel prepara-
tion was done before all left-sided colectomies (and before none  
of the procedures on the right side), the results are not compara-
tible to those of the MOBILE trial, which compared MOABP with  
NBP. Furthermore, the SELECT trial did not report patients under-
going right and left colectomy separately, and it is unclear  
whether the reduction in SSI rates applied to both right and left  
colectomies.
The original MOBILE trial was criticized for including low-risk right-sided anastomoses, and this was one of the reasons for the present subgroup analysis. In contrast to the study hypothesis, MOABP was not more effective in preventing SSI or complications in patients undergoing left colectomy, but seemed to increase complications in left colectomy as the cumulative burden of postoperative complications was higher in MOABP group; however, this finding was not statistically significant.

This study has several limitations, including those of the original trial. The original study was powered to detect an 8 per cent absolute difference in SSIs, and the post hoc subgroup analyses of patients undergoing right or left colectomy have even less statistical power. Absolute differences of 2 per cent in SSI rate in patients undergoing right colectomy, and 4 per cent among those undergoing left colectomy were documented. These differences were not significant, but the analysis may suffer from type II error. However, as in the original trial, the overall cumulative postoperative complications are more important for the patient. The differences in these (–1.1 CCI points for right colectomy and 3.7 CCI points for left colectomy) and their 95 per cent confidence intervals do not suggest any benefit of MOABP over NBP in either right or left-sided resections, even if studied in larger cohorts of patients. A total of 10 CCI points is
considered to be clinically significant as it reflects one Clavien–Dindo grade difference in complication burden.

The study also has several strengths. It was a multicentre trial carried out in both university and non-university hospitals, increasing the external validity of the results. The patients were on average 70 years old and nearly half had an ASA physical status grade of III–IV, indicating that a real-life mix of patients was recruited into the trial. Postoperative morbidity was collected using the most sensitive method available, the CCI.

The main finding was that MOABP did not decrease the rate of SSI or overall postoperative morbidity in patients undergoing either right or left colectomy compared with NBP. Further larger RCTs are needed in these subgroups to confirm the results.

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**Conflict of interests**

The authors declare no conflict of interest.

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**Table 4 Outcomes after left colectomies**

| Outcome                                      | Mechanical and oral antibiotic bowel preparation (n = 84) | No bowel preparation (n = 80) | P† | Effect size‡ |
|----------------------------------------------|----------------------------------------------------------|------------------------------|----|--------------|
| Surgical-site infection                      | 5 (6)                                                    | 8 (10)                       | 0.338 | 0.57 (0.18, 1.82) |
| Superficial§                                | 1 (1)                                                    | 1 (1)                        |    |              |
| Deep§                                       | 0                                                        | 1 (1)                        |    |              |
| Organ /space infection§                     | 4 (5)                                                    | 6 (8)                        | 0.053 | 3.68 (–0.06, 7.42) |
| **Comprehensive Complication Index score**   | 10.2 (13.1)                                              | 6.5 (11.0)                   |    |              |
| Anastomotic dehiscence                       | 4 (5)                                                    | 5 (6)                        | 0.742 | 0.75 (0.19, 2.90) |
| Reoperations                                 | 6 (7)                                                    | 6 (8)                        | 0.930 | 0.95 (0.29, 3.07) |
| Readmissions                                 | 9 (11)                                                   | 3 (4)                        | 0.087 | 3.08 (0.80, 11.82) |
| **Duration of hospital stay (days)**‡        | 4.8 (2.6)                                                | 4.8 (3.7)                    | 0.859 | –0.09 (–1.06, 0.89) |
| **30-day mortality**                         | 0 (0)                                                    | 0 (0)                        |    |              |
| **90-day mortality**                         | 0 (0)                                                    | 0 (0)                        |    |              |
| Any adverse effect of antibiotics            | 8 (10)                                                   | 5 (6)                        | 0.438 | 1.58 (0.49, 5.05) |
| Diarrhoea                                    | 7 (8)                                                    | 3 (4)                        |    |              |
| Clostridium spp. infection                   | 0 (0)                                                    | 1 (1)                        |    |              |
| Allergic reaction                            | 0 (0)                                                    | 1 (1)                        |    |              |
| *Candida* spp. infection                     | 1 (1)                                                    | 0 (0)                        |    |              |
| **Readmissions**                             | 23 of 28 (82)                                            | 24 of 26 (92)                | 0.423 | 0.38 (0.07, 2.18) |

Values in parentheses are percentages unless indicated otherwise; values are * mean(s.d.) and † values in parentheses are 95 per cent confidence intervals. Effect sizes are shown as odds ratios, except ‡ mean difference. § Only the most severe type of surgical-site infection reported here. ¶ Student’s t test.

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**Conflict of interest**

The authors declare no conflict of interest.
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