Bowel preparation: No good?

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SUMMARY

In a well-conducted, multicentric, blinded, randomized clinical trial from Finland, Koskenuovo *et al*. have shown that mechanical and oral antibiotic bowel preparation (MOABP) does not reduce surgical-site infections (SSIs) or overall morbidity in colonic resections. In spite of all the evidence in favour of MOABP, no randomized controlled trial (RCT) had ever been conducted to compare these interventions head to head.

They randomized 417 patients and did a modified intention-to-treat analysis on 396 patients (those randomized to, and who underwent colonic resection with anastomosis, excluding those randomized but did not undergo resection or an anastomosis), comparing MOABP and no bowel prep (NBP). The sample size was calculated assuming an absolute difference of 8% in SSIs, 5% in MOABP and 13% in NBP. These calculations were based on evidence from retrospective studies showing SSIs in 3.2%–8.6% of patients prepared with MOABP and 9%–16.8% of patients who did not undergo any bowel preparation. With power of 80% and significance at 5%, they calculated that 396 patients would be needed.

In retrospect, this difference of 8% was perhaps optimistic and resulted in a relatively small sample size. The actual difference was 4%. One criticism of the study is that the sample size was not large enough to pick up small differences in outcome.

The participants were patients in four Finnish government hospitals who were scheduled for elective colonic resections for a variety of indications. Exclusion criteria included emergency surgery, bowel obstruction, planned colonoscopy, allergy to drugs used in the trial and age <18 or >95 years.

Randomization was 1:1, in varying block sizes, and stratified according to centre, administered by a web-based service. The sequence was concealed in serially numbered opaque envelopes, opened in numerical order.

Masking was a complicated process, with recruiters, treating physicians, operating surgeons, data collectors and analysts blinded to the allocation. Patients obviously could not be blinded.

Once consent was obtained from eligible patients, they were enrolled into the trial. The study nurse then opened the envelope with the patient in a closed room and instructed the patient to follow the allocation, to prepare or not to prepare the bowel. For those who required MOABP, the required medication and instructions were given to the patient. The nurse then had no further role in the trial.

The two groups were named A and B after all data were collected. Outcomes were analysed without the group names being known. Blinding was removed after analysis. Ineffective blinding was recorded.

Mechanical bowel preparation (MBP) consisted of 2 L of polyethylene glycol and 1 L of clear fluid before 6 p.m. on the evening before surgery. Oral antibiotic (OAB) consisted of 2 g of neomycin at 7 p.m. and 2 g of metronidazole at 11 p.m. on the evening before surgery. Prophylactic antibiotics consisted of cefuroxime 1.5 g and metronidazole 500 mg before incision and repeated if operating time exceeded 3 hours or blood loss was >1.5 L. A nurse checked if the allocated intervention had been taken by the patient and any deviation was reported only after analysis.

An enhanced recovery after surgery (ERAS) protocol was followed. Follow-up was at 30 days and 6 months.

The primary outcome was SSI within a month of operation. SSIs were divided into superficial incisional, deep incisional or organ space, according to the Centers for Disease Control and Prevention criteria.

Secondary outcome measures were Comprehensive Complication Index score within 30 days. Charlson Comorbidity Index (CCI) score was calculated by weighting Clavien–Dindo scores and adding them. Death was CCI 100.

Anastomotic dehiscence, readmission within 30 days, length of hospital stay, mortality at 30 and 90 days, adverse events of antibiotics within 30 days and prevalence of adjuvant therapy were also assessed.

The study was conducted between March 2016 and August 2018. A total of 196 patients were randomized to MOABP and 200 to NBP. Baseline characteristics and preoperative details were similar in both groups.

SSI was detected in 7% in the MOABP group and 11% in the NBP group (odds ratio 1.65, CI 0.80–3.4, p=0.17).

The types of SSI and CCI were similar between the two groups.

Anastomotic dehiscence was found in 4% of patients in the MOABP group and 4% in the NBP group. All leaks in the MOABP group were dehiscence requiring re-laparotomy. Seven of the eight leaks in the NBP group required exploration. Other reasons for exploration were bowel obstruction, wound dehiscence, bleeding, bowel ischaemia and ureteric injury.

There were re-admissions in both groups: 6% in the MOABP group and 7% in the NBP group. Reasons for re-admission were abdominal pain, SSI, ileus, intra-abdominal bleeding and diarrhoea.

There were no deaths within 90 days in the MOABP group. Two patients died in the NBP group.

Importantly, there were no patients in the MOABP group who developed *Clostridium difficile*-associated diarrhoea. One patient in the NBP group did; this was not significant.

Adjuvant therapy was given in 83% and 85% in the MOABP and NBP groups, respectively. The types of resection were evenly distributed between the two groups.

Over 50% of cases were right-sided resections, where the role of bowel preparation is questioned anyway, and bowel preparation is rarely used by most surgeons around the world. Only 2% of cases were anterior resections in the MOABP group and 3% in the NBP group.

Seventy-seven per cent of resections were carried out laparoscopically in the MOABP group and 80% in the NBP group. The conversion rate was similar (10% *v*. 9%).

COMMENT

Perhaps no subject has raised as much interest in colorectal surgery as the controversies surrounding the use of bowel preparation.

With the advent of microbiological techniques to grow and quantify bacteria in the early 1900s, it was recognized that the colon has a heavy bacterial load. As surgery became safer and more bowel resections were undertaken, it became evident that the high rate of infective complications in colonic resections was related to contamination by these bacteria at the time of operation.

In the late 1930s and early 1940s, Poth *et al*.[1] showed a reduction in bacterial load with MBP and also that MBP was necessary to allow antimicrobials to act effectively.

Nichols *et al*.[2] then showed that by using MOABP the rate of SSIs and anastomotic leaks could be reduced from 39% to 9% and 10% to 0%, respectively.

MOABP became the accepted modality of preoperative bowel preparation for decades. Antibiotic prophylaxis was introduced later and was universally adopted. Numerous studies showed that MBP alone did not reduce the rate of infective complications.[3,4]

MOABP required patients to be admitted a few days preoperatively. With a worldwide move to reduce hospital stay, and the introduction of ERAS programmes, MBP was increasingly self-administered at home. More studies showed that MBP was not necessary or even harmful before colorectal surgery, and MBP gradually fell out of favour, particularly in Europe and with it, the use of OABs.

Practice varied widely in the 2000s, with evidence for and against bowel preparation.

In 2011, a Cochrane systematic review[5] seemed to lay the issue to rest, by categorically stating that MBP was unnecessary. Opinion seemed to be divided between evidence from large (American) cohort studies[6,7] and meta-analyses in favour of MOABP and studies opposing MBP.[3,4]

After 2010, OABs began to make a comeback and American guidelines recommended MOABP. MOABP began to be reintroduced gradually around the world. The controversy seemed to be settling down.

The applecart was upset yet again with this study from Finland.

This distribution of laparoscopic surgery and right-sided resections could perhaps explain the low SSI and infective complication rate and is one of the criticisms of this study.[8]

Strengths of the trial are that it is multicentric, with a pragmatic case mix of patients usually seen in clinical practice in developed nations (age >70 years, American Society of Anesthesiologists 3–4), distributed between university and non-university hospitals. Meticulous data collection and recording of all complications with weighting are other strengths.

One major limitation of the study is that it is underpowered to detect a small difference, as alluded to before. Blinding of patients would have been ideal but is impractical. No planned subgroup analysis was carried out between right- and left-sided resections. The paucity of left-sided and low left-sided anastomoses would probably not have produced meaningful results. Rectal resections have not been included. Lastly, the OAB regimen (single-dose neomycin and metronidazole) used is not one that is universally practised.

In spite of these limitations, this is the first trial to compare MOABP and NBP. Previous randomized trials have compared MOABP to MBP, with results in favour of MOABP.

This study has failed to show a significant difference in infective complications with the use of MOABP when compared to NBP. The authors conclude that colonic resections can safely be carried out without MOABP and that the low risk of infective complications is worth taking if patients can be spared the discomfort of MBP and OABs.

We await the results of a French double-blind RCT looking at SSI with MOABP, OAB, MBP and NBP in colon surgery.

Conflicts of interest. Nil

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