



# Oral antibiotic preparation in colorectal surgery: is there more to debate?

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The use of non-absorbable oral antibiotic preparation (OAB) in colorectal surgery was first proposed by Rosenberg and colleagues in 1971 (1), who in their randomised controlled trial (RCT) of combined mechanical bowel preparation (MBP) and one (phthalylsulphathiazole) or two oral antibiotics (phthalylsulphathiazole and neomycin) found a significant reduction in surgical site infection (SSI) and anastomotic leak rates in a population of patients undergoing large bowel surgery after combined OAB and MBP when compared with those who received MBP alone. This was followed by studies (2,3) which demonstrated similar reductions in the incidence of postoperative infection. However, the preparation protocols typically required large volumes, prolonged preoperative hospital stays and carried a significant risk of electrolyte disturbance and dehydration. These issues resulted in combined preparation falling from favour, with MBP alone becoming an increasingly popular strategy. Relatively recent evidence from RCTs and meta-analyses (4,5) has suggested that MBP alone does not convey any benefit in patients undergoing colorectal surgery and, hence, it is no longer recommended as part of perioperative care protocols.

In recent years, there has been a significant revival of interest in OAB (6) as it has been shown to reduce complications after colorectal surgery, with a decrease in SSI being the most common benefit (7). Much of the recent literature has been driven by large cohort studies (8-11),

many of which have originated from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database. Meta-analyses (12,13) have been published recently with the aim of analysing the potential benefits of OAB more systematically, either with or without MBP, and have demonstrated significant reductions in the incidence of SSI and anastomotic leaks with a combination of OAB and MBP, when both RCTs and cohort studies were considered. The use of OAB prior to elective colorectal surgery is currently very much a topic in evolution, with significant debate in the literature whether the combination of MBP and OAB is superior to OAB alone (14,15).

The most recent publication to arise from the ACS NSQIP database (16) focuses on a cohort of 5,729 patients undergoing elective left-sided laparoscopic and open restorative colorectal surgery with or without faecal diversion and uses primary outcome measures of overall, superficial, deep and organ/space SSI. The authors found that combined MBP and OAB was associated with a significant reduction in the incidence of overall SSI when compared with no preparation (OR 0.46, 95% CI: 0.36 to 0.59,  $P < 0.0001$ ), with this combination remaining a predictor of lower incidence of SSI on multivariate modelling. The OAB alone group had a trend towards a reduction in SSI, but this was not statistically significant (univariate OR 0.84, 95% CI: 0.51 to 1.38,  $P = 0.49$ ). The

combination of MBP and OAB was associated with a reduction in SSI in patients undergoing both laparoscopic and open surgery. However, on multivariate analysis, this significance was lost for patients undergoing laparoscopic resection (adjusted OR 0.44, 95% CI: 0.19 to 1.04,  $P=0.062$ ). Combined MBP and OAB also had a negative association with anastomotic leak rates, but there was no association between OAB alone and leak rates. Finally, the administration of MBP and OAB or OAB alone was not associated with any significant difference in *Clostridium difficile* infection rates when compared with no preparation (1.2% vs. 1.0% vs. 1.3%). This is in concordance with previous publications which have not reported an increased risk of *C. difficile* infection rates (12,17).

This study (16) provides additional information surrounding the beneficial effects of combined MBP and OAB in left-sided restorative colectomy with pelvic anastomosis with or without faecal diversion and was able, through careful uni- and multi-variate analysis, analyze the factors associated with SSI and anastomotic leak rates. It also provides more detailed information than many previous studies regarding the impact of these bowel preparation regimens in open compared with laparoscopic surgery. It represents another of a multitude of studies originating from the ACS NSQIP database, many of which have been likely to have presented data and conclusions based upon overlapping patient populations. However, whereas many of the previous publications have focused upon patients operated on between 2012 and 2014 (12), this study is based on data from 2015 and is, therefore, less likely to be subject to duplication of participants than previous studies originating from the same database.

As with other retrospective database studies on the subject, the proportion of patients receiving OAB alone was low, representing just 3.5% of the overall cohort (16). This makes interpretation of any conclusions based on OAB alone difficult. There were also several potentially significant sources of bias in the baseline patient populations, including an increased prevalence of medical comorbidities in those participants in the no preparation and MBP alone groups, as measured by the American Society of Anesthesiology class, and this may have impacted upon the incidence of postoperative complications. In addition, there was a greater proportion of patients with diabetes in the no preparation group compared with other groups, which again is likely to have exerted a significant selection bias and resulted in an increased incidence of surgical infection in this group, which may not be wholly

explained by the lack of preparation. Moreover, the benefit of OAB with or without MBP in patients undergoing laparoscopic surgery is not proven when compared with those undergoing open surgery both in the cohort study being discussed (16) and a recent meta-analysis (12).

As has been identified by the authors (16), a definitive large four-arm RCT seems necessary to more definitively answer the question regarding the best method for preparation of the colon prior to elective colorectal surgery. Participants should be stratified according to whether they have open or laparoscopic surgery and then randomised to (I) no bowel preparation, (II) MBP, (III) OAB and (IV) OAB + MBP.

Several recent survey-based studies have documented low rates of routine prescription of OAB, either alone or when combined with MBP, particularly in the UK and Europe (18,19), suggesting that despite the ongoing publication of studies supporting the role of MBP and OAB prior to elective colorectal surgery, this is yet to have an impact upon clinical practice. Definitive evidence from a large scale, well designed and conducted RCT may be necessary before this becomes routine clinical practice.

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