



Bowel preparation in colorectal surgery: back to the future?

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Mechanical bowel preparation (MBP) for colorectal surgery aims to reduce fecal mass and bacterial count with the objective to decrease surgical site infections (SSI) rate, including anastomotic leakage [1].

Many randomized studies (RCT) and meta-analysis [2, 3] comparing MBP versus no MBP have been published to date in colorectal surgery. No benefit of MBP in terms of SSI rate or anastomotic leakage has been suggested in all of these studies which mainly included patients operated for colonic surgery. We performed the only randomized study dedicated to rectal cancer surgery, the Greccar III [4] trial, which on the opposite demonstrated that after sphincter-saving rectal resection, 30-day overall (27% with MBP vs 44% without; $p=0.018$) and infectious (16% vs 34%; $p=0.005$) morbidity rates were significantly lower in MBP versus no MBP group.

Thus, to date, MBP is recommended only for rectal cancer surgery and not for patients undergoing colonic surgery.

In the 1970s, some studies [5, 6] on the association of MBP and oral antibiotic (OA) have been appearing in literature and already at that time, it had been demonstrated that MBP + OA was associated with reduced rates of SSI compared with MBP alone. Already in 1973, Nichols et al. [5] wrote that “elective colon resection should be approached with adequate preoperative mechanical and oral antibiotic preparation”. However, these old studies have not convinced colorectal surgeons. And after these old papers, all the RCT have evaluated only MBP alone versus no MBP in colorectal surgery.

However, since these RCT and meta-analysis compare only MBP vs no MBP, recent large national surveys, including a huge number of patients from large databases, coming especially for US have suggested the possible benefits of oral

antibiotics (OA) before colorectal surgery with a significant impact on SSI rate after colorectal surgery.

For this reason, in the last American 2019 clinical practice guidelines [7] concerning MBP for elective colorectal surgery, it is proposed that MBP combined with preoperative OA is typically recommended for elective colorectal resections with a strong grade of recommendation, based on moderate-quality evidence (grade 1B). Although this statement is mainly based on retrospective studies, the impact of OA seems very important in terms of reduction of SSI.

Ohman et al. [8] analyzed patients from the American College of Surgeons NSQIP and observed among their patients that those who received a full bowel preparation with both OA and MBP, a SSI rate of 2.7% was observed versus 15.8% without ($p < 0.001$). On multivariate analysis, full bowel preparation was independently associated with significantly fewer SSI (adjusted odds ratio 0.2; 95% CI 0.1–0.9; $p=0.006$). They concluded that the combination of oral antibiotics with a mechanical bowel preparation was the strongest predictor of decreased SSI.

A recent retrospective study, from Koeller et al. [9], involving 32,359 patients, from the American College of Surgeons National Survey Quality Improvement Program database, who underwent elective colorectal resections from 2012 to 2014 and divided into four groups (no MBP, MBP only, OA only and MBP + OA) have demonstrated (a) first, that the use of MBP alone before elective colorectal resection is ineffective to prevent SSI and should be abandoned; (b) second, in contrast, OA only and MBP + OA are associated with significantly decreased risks of SSI and are not associated with increased risks of other adverse outcomes compared with MBP or with no preparation. In multivariate analysis, odd ratios for MBP + OA ranged from 0.43 to 0.57 for SSI, leakage rate and death, suggesting a very important effect of the use of MBP plus OA. Which is also to be noted is that OA only also did better than MBP alone or no MBP with odd ratios ranging from 0.37 to 0.63 for the same criteria. This result suggested that maybe OA only is enough before colorectal surgery. Authors concluded that prospective studies to determine the efficacy of OA are required

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but that in the interim, MBP + OA should be used routinely before elective colorectal resection.

Although many randomized studies and meta-analyses have already suggested that the adjunction of OA to systemic antibiotics reduced the risk of SSI before colorectal surgery [10], to our knowledge, there is no RCT evaluating the respective benefit of OA and MBP before colonic and rectal surgery. For example, Hata et al. [11] published in 2016 a RCT comparing OA versus OA plus systemic antibiotics (SA) before colorectal surgery. They demonstrated that SSI was reduced in patients receiving OA + SA versus SA only (7.3% vs 12.8%; $p=0.028$), but in this study, patients included presented either colonic or rectal cancer, which is confusing for the interpretation of the results. Furthermore, MBP was given in some patients but was not assessed in this study. Similarly, Ikeda et al. [12] published a RCT including also colonic and rectal surgery, with approximately 85% of patients undergoing MBP in both groups making interpretation of the possible benefit of both OA + MBP impossible.

Very recently, a RCT that focused only on patients with Crohn's disease [13] was also published: 335 patients scheduled to undergo intestinal resection with an open approach were randomly assigned to receive both preoperative OA and SA prophylaxis versus SA alone. The incidence of incisional SSI was significantly lower after OA + SA than after SA only: 7.4% vs 16.7% ($p=0.01$). However, all the patients received MBP and both small bowel and colorectal surgery were included in the same study.

One of the concerns using possibly OA in all the patients undergoing colorectal surgery is the potential risk of *Clostridium difficile* (CD) infection. Al-Mazrou et al. [14], evaluated the impact of OA on the development of CD infection in patients undergoing colectomy: CD occurs in ≈ 1 to 7% of patients after colorectal surgery [15]. Comparing patients with OA and MBP to those who did not, Al-Mazrou et al. [14] showed that OA was associated with significantly lower postoperative CD infection and infectious complications, unplanned reoperations, mortality, length of stay and unplanned readmission. Also on multivariate analysis, OA reduced the odds for CD infection after colectomy. Additionally, in subgroup analysis of patients who did not develop any postoperative infectious complication, OA was associated with lower risk of CD infection.

These results confirm what has already been shown by Kim et al. [16] using a large observational cohort study data from the Michigan Surgical Quality Collaborative-Colectomy Best Practices Project: they provided insight into the effect of bowel preparation on rates of CD infections in a study population of 2475 patients creating 957 paired cases ($n=1914$) and comparing patients receiving MBP with OA with patients with no MBP; patients with MBP + OA were actually less likely to develop postoperative CD infections than those who received no bowel preparation.

In conclusion, this risk of CD infection seems not to a real problem in receiving OA before colorectal surgery.

In conclusion, in 2019, there is a lot of evidence suggesting that MBP + OA should be the new gold standard for colorectal surgery. But because randomized studies are still lacking, we do not know exactly if it is true for both colonic and rectal surgery. Furthermore, we still need to assess if only OA is enough or if both MBP and OA must be given to all the patients undergoing colorectal surgery. Nowadays, no randomized studies with homogeneous groups of patients are available in the literature; patients undergoing rectal cancer surgery must be separate from those undergoing colonic cancer surgery. That is why randomized trials with specific arms are needed [17].

In France, we have organized two randomized studies that started last year: one concerning patients undergoing surgery for colonic cancer (COLONPREP) and comparing four groups (none versus MBP versus OA alone versus both), and the another concerning rectal cancer patients (PREPACOL2) comparing two groups (MBP alone versus both MBP + OA). Before the results of these two studies, and the results of similar studies in progress worldwide, at least in France, we still continue to propose MBP for rectal cancer surgery but not for colonic cancer surgery.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants and/or animals This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study, formal consent is not required.

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