Review Article

Bowel preparation with oral antibiotics for elective colorectal surgery: back to the future?

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Abstract: There is controversy regarding the use of preoperative mechanical bowel preparation (MBP) before elective colorectal surgery. Factual data have led many European learned societies not to recommend MBP whereas its use remains widespread among US surgeons. This review was assessed to clarify the role of preoperative MBP and oral antibiotics. We searched PubMed, Embase, and the Cochrane Library for relevant literature. Search terms included preoperative bowel preparation, oral antibiotics, colorectal surgery and postoperative morbidity. MBP combined with oral antibiotics before elective colorectal surgery remains a present subject of debate within the surgical community. Over a century ago, MBP was considered, dogmatically, as a standard surgical practice. But, the gradual spread of minimally invasive surgery as laparoscopy in colorectal procedures added to enhanced recovery after surgery (ERAS) program promoted its abandonment. Therefore, several large retrospective studies recently questioned the abandonment of MBP suggesting that its omission was deleterious in terms of surgical sites infection (SSI) and anastomotic leakage, especially when MBP was combined with oral antibiotics.

Keywords: Mechanical bowel preparation (MBP); colorectal surgery; postoperative morbidity; anastomotic leakage; septic complications

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Introduction

Over a century ago, preoperative mechanical bowel preparation (MBP) before elective colorectal surgical resection was considered, dogmatically, as a standard surgical practice to reduce the total fecal load leading to decrease the pressure on the anastomosis and to minimize the risk of postoperative anastomotic leakage (1).

Over the past decade, perioperative management in colorectal cancer has dramatically changed. Indeed, minimally invasive surgery as laparoscopy is now widely used leading to well-known benefits with similar oncologic results (2,3). It should be noted that many studies evaluated the use of MBP for open colorectal surgery. It is unclear if results can be extrapolated to laparoscopic colorectal surgery.

Moreover, concomitant with these technical progresses, the enhanced recovery after surgery (ERAS) pathway was developed to accelerate patient recovery (4).

In the same way, recent literature questioned this dogma and provided strong evidence in showing no benefit to MBP before elective colorectal surgery. Thus, many recent randomized studies and meta-analysis (5-9) clearly called into question the interest of MBP underlining its detrimental effect by increasing the risk of postoperative infectious complications and/or anastomotic leakage. These

factual data have led many European learned societies not to recommend MBP for elective colorectal surgery (10,11).

Therefore, very recently, large retrospective studies (12-16) questioned the abandonment of MBP, suggesting that its omission was deleterious in terms of surgical sites infection (SSI) and anastomotic leakage, especially when MBP was combined with oral antibiotic administration.

Finally, MBP before elective colorectal surgery remains a present subject of debate within the surgical community.

Searching Medline and the Cochrane Central Register, selecting especially meta-analysis and randomized studies, this narrative review was assessed to clarify the role of MBP in elective colorectal surgery in the light of recent literature data, questioning the real benefits of the combination of oral antibiotic and bowel preparation.

Rationale for MBP

Infectious complications and especially symptomatic anastomotic leakage are the most important surgical complications after colorectal surgery and can cause both postoperative morbidity and mortality leading to bad oncological outcomes and digestive sequelae as risk of definitive stoma (17).

Historically, over a century ago, MBP alone was given before elective colorectal surgery, as an intuitive measure, to reduce both total fecal load and pressure on the anastomosis leading to decrease the potential risk of anastomotic leak and postoperative pelvic sepsis (18). Many authors argued that reducing total fecal load led to decrease the intraluminal pressure of hard, impacted stool and reduce ischemia at the anastomosis (18). Then, MBP has been regarded as an efficient strategy to prevent anastomotic leakage and surgical site infections (SSI).

MBP combined with oral antibiotics (*Table 1*)

Since many years, it seemed logical to add antibiotics to have maximal effect on colonic bacterial concentration and then, antibiotics were subsequently used to further eliminate bacteria. The idea was that, by first emptying the colon, an antibacterial could be delivered along the length of the bowel and reduced microbial concentration at the mucosal surface. Thus, in the 1940s, as a pioneer in the use of oral antibiotics for colonic surgery, Poth *et al.* noted that MBP alone was inadequate to drive down bacterial counts (19). Then, in the 1970s, a combined oral antibiotic and MBP regimen as proposed by Nichols *et al.* (20) was widely practiced. Then, many randomized studies confirmed the efficacy of such combination as oral antibiotics with MBP, inducing a significant decrease of postoperative septic complications (21-23). Washington *et al.* published a large randomized placebo-controlled double-blind study of 116 subjects, who received either oral antibiotics or placebo, and both groups were given preoperative MBP (23). The authors demonstrated that, comparing both placebo *vs.* antibiotics groups, the overall rate of postoperative septic complications was 43% *vs.* 9% (P<0.001), wound complications were 35% *vs.* 9% (P<0.0001) and anastomotic leak was 17% *vs.* 4% (P<0.001), respectively. Historical evidence supported the use of oral antibiotics in combination with MBP for the reduction of postoperative SSI.

Therefore, despite strong evidence for its benefit, this combination was no longer standard.

No benefit for MBP (*Table 2*)

In 1972, a randomized clinical trial published by Hughes *et al.*, already questioned this combination suggesting that "vigorous mechanical bowel preparation combined with oral antibiotics" was not necessary and that such omission would be welcome by both patient and nursing staff (24).

Since, over the past decade, several randomized studies and meta-analyses published from 2008 to 2009 (9,25,26), have been concordant in showing no benefit to oral MBP before colorectal surgery, whether the agent used was polyethylene glycol or phosphosoda. An updated Cochrane meta-analysis comparing MBP with no preparation (26) before elective colorectal surgery suggested that MBP had not be proven to be valuable for patients and that it should be abandoned. Many authors called into question the dogma of preoperative MBP underlining its detrimental effect by increasing the risk of postoperative infectious complications and/or anastomotic leakage rate. A meta-analysis (9), including 14 randomized trials with more than 4,800 patients, confirmed the safety of elective colonic surgery without MBP and oral antibiotics but, in contrast with all previous published data, failed to demonstrate the negative effect of MBP in terms of anastomotic leakage, showing no statistical difference between the 2 groups, 3.4% after no-MBP *vs.* 4% in MBP patients (P=0.46). In this latter meta-analysis, only the rate of SSI was significantly lower in no-MBP versus MBP patients, 14.5% *vs.* 15.7% (P=0.02).

At the same time, the gradual spread of minimally invasive surgery as laparoscopy in colorectal procedures in addition with the concept of ERAS promoted the

Table 1 Historical studies comparing the postoperative surgical site infection rate (SSI) of mechanical bowel preparation (MBP) combined with oral antibiotics (OA) *vs.* no MBP and no OA before elective colorectal surgery

Authors	Patients (n)	Surgical site infection rate (%)		P
		MBP + OA	No MBP + No OA	
Washington, 1974	200	43	5	S
Clarke, 1977	116	43	35	S
Matheson, 1978	120	40	25	S

MBP, mechanical bowel preparation; OA, oral antibiotics; S, significant comparison.

Table 2 Recent meta-analyses comparing the postoperative surgical site infection rate (SSI) of mechanical bowel preparation (MBP) *vs.* no MBP before elective colorectal surgery

Authors	Randomized studies (n)	Patients (n)	SSI (%)	AL (%)
Slim, 2009	14	4,800	15.7 *vs.* 14.5 (NS)	4 *vs.* 3.4 (NS)
Guenaga, 2011	18	5,805	9.8 *vs.* 8.3 (NS)	4.4 *vs.* 4.5 (NS)

SSI, surgical site infection; AL, anastomotic leakage; NS, no significant.

abandonment of MBP and therefore jointly of oral antibiotics (2-4). Thus, colorectal surgery without preoperative MBP has been proposed (and in laparoscopy, minimal abdominal drainage, early diet and ambulation) as a "more friendly approach" for the patient and especially, to accelerate patient recovery. This strategy was welcomed by both patients and nursing staff. Indeed, the preparation procedure was time-consuming and expensive, unpleasant to the patients, and sometimes dangerous, exposing the elderly population to the particular risk of fluid and electrolyte imbalance. During this period, MBP fell out of favor and intravenous antibiotics administration at induction in clean contaminated surgery became increasingly both routine and mandatory.

These factual data have led many European learned Societies not to recommend MBP for elective colon surgery (10,11). By contrast, SAGES guidelines (27) suggested that MBP was recommended to facilitate manipulation of the bowel especially during the laparoscopic approach and to facilitate intraoperative colonoscopy when needed. Thus, a US 2003 survey showed that more than 99% of colorectal surgeons routinely used MBP (6) and a recent [2007–2009] study of 24 Michigan hospitals reported the use of MBP in 86% of all colorectal surgeries (28).

But, as highlighted by Dellinger *et al.* in its editorial (29), a careful reading of the most recent meta-analysis published by Guenaga revealed that although the most of the trials included omitted oral antibiotics in both MBP and not groups, three studies did administer oral antibiotics to both arms (26). Thus, separating trials with and without oral antibiotics, the results contained the hint that oral antibiotics alone, even without MBP, might reduce the SSI rate (29). The authors clearly showed that the most favorable option for reducing postoperative SSI was oral antibiotics with no MBP, i.e., 6% for antibiotics alone *vs.* 8% for MBP and antibiotics *vs.* 10.6% for MBP with no antibiotic *vs.* 10.3% for patients having no MBP and antibiotic.

Recent data (*Table 3*)

Recent literature has brought new reliable data on this question. Indeed, several large retrospective US studies have been recently published and called into question the dogma of MBP (12-16). Indeed, the unified message was that MBP alongside oral and IV antibiotics provided optimal outcomes following colorectal surgery.

Kim *et al.* analyzing 2,475 patients undergoing colectomy from the Michigan Surgical Quality Collaborative (MSQC) database, showed that patients receiving combined MBP with oral antibiotics were less likely to have postoperative SSI (5% *vs.* 9%, P=0.0001) and *C difficile* Colitis (0.5% *vs.* 1.8%, P=0.01) (12).

These data were consistent with the results of four other retrospective studies analyzing the same administrative database, i.e., the American College National Surgical

Table 3 Recent large retrospective studies comparing the postoperative surgical site infection rate (SSI) of mechanical bowel preparation (MBP) combined with oral antibiotics (OA) *vs.* MBP alone *vs.* OA alone *vs.* no MBP and no OA

Authors	Patients (n)	Surgical site infection rate (SSI) (%)				
		MBP + OA	MBP alone	OA alone	No MBP, no OA	P
Kim	2,475	5	–	–	9	S
Morris	8,415	6.5	12.5	–	–	S
Moghadamyeghaneh	5,021	6.2	12.1	19.8	14.7	S
Kiran	8,842	19.8	26.3	–	29	S
Scarborough	4,999	2.8*	–	–	5.7 *	S

MBP, mechanical bowel preparation; OA, oral antibiotics; S, significant comparison; *, postoperative symptomatic anastomotic leakage.

Quality Improvement Program (AS NSQIP).

Thus, Morris *et al.* provide data on 8,415 colorectal procedures including laparoscopy in 63% of cases, from 121 hospitals in the years 2011 and 2012. The authors demonstrated a clinically and statistically significant 50% reduction in SSI with the use of OABP (6.5%) compared with MBP alone (12%) (P<0.001) (15). A multivariate analysis showed OABP as significant independent criteria associated with lower SSI (OR=0.46, 95% CI: 0.36–0.59). They concluded that OABP was associated with significant reduced SSI rates and fewer readmissions.

Another study, assessing data from the years 2012 and 2013, reported 5,021 patients with colectomy (16). The authors confirmed, with the combination of mechanical and oral antibiotic preparations for left side colon resections, the significant decrease of overall morbidity (OR=0.63, P<0.01), SSI (OR=0.31, P<0.01) and anastomotic leak rates (OR=0.44, P<0.01).

Moreover, another retrospective study from the same NSQIP database (14), showed that, among 8 842 patients undergoing colectomy in 2012, OABP was associated with lower anastomotic leak rate than no preparation (OR=0.45, 95% CI: 0.35–0.94). On multivariate analysis, OABP was independently associated with reduced anastomotic leak (OR=0.57) and SSI (OR=0.40). The authors concluded that OABP reduced by nearly half SSI and anastomotic leak, the most common complications following colorectal surgery.

Finally, Scarborough *et al.* reported from the 2012 AC NSQIP database with 4,999 patients, similar results; assessing the significant improved postoperative results in the OABP group compared to no preparation, i.e., anastomotic leakage (2.8% *vs.* 5.7%, P=0.001), readmission (5.5% *vs.* 8%, P<0.03) (14). Moreover, the outcomes of patients who received either MBP or oral antibiotics did not differ significantly from those with no preparation.

So, all these latter studies should mean that we were wrong about MBP and that we have to revisit the guidelines against bowel preparation before colorectal surgery. Such latter data deserve critical comments. The number of patients is very large but these studies are challenged by multiple biases. Retrospective studies explain that all groups are not similar especially according to comorbidities for patients with no MBP undergoing more significantly advances stage colorectal cancer, corticosteroid use...) and we know the strong correlation between these latter criteria and the risk of postoperative sepsis (14). Finally, a very recent meta-analysis confirmed the superiority of a regime including MBP with oral antibiotics over MBP with intravenous antibiotics in terms of SSI after elective colorectal surgery (30). Another bombshell against MBP was showed by a Swedish trial published in 2014 (31). The authors showed, surprisingly, that no MBP was associated with an increase of the local recurrence rate and a worst disease-free survival. The hypothesis was mechanical with a forceful preparation cleaning leading to a cleaning of potential circulating cancer cells from the tumor and a decrease of the risk of spread. Another reason could be that an empty colon is easier to handle during surgery facilitating the operation leading to a higher quality of surgical resection in terms of margins and mesocolon resection. But, this study included, also, several bias as a higher rate of grade 3 tumors in the no MBP group, a lack of analysis based on adjuvant therapy and follow-up monitoring. Thus, this study was very methodologically questionable because it was a posthoc analysis of a previous multicenter randomized study which answered to a question which was not raised by the protocol design. Moreover, these data were not confirmed by Van't Sant *et al.* who demonstrated that MBP

did not seem to influence long-term survival in patients surgically treated for colorectal cancer (32).

So, because of many biases, we think that neither the US retrospective studies nor the Swedish trial permit the conclusion that the absence of MBP is deleterious in terms of morbidity or survival after colorectal surgery. They do not negate the recommendations of the European learned Societies.

Moreover, a few recent data have been published about the role of probiotics as a pre-surgical nutritional supplement to improve bowel recovery and promote the return of normal gut function (33,34). Tan *et al.* published a randomized study about presurgical administration of microbial cell preparation in colorectal cancer patients (33). Patients (n=40) were randomized to receive either probiotics or placebo for 7 days prior to elective surgery. The authors showed a significantly faster return of normal gut function with a median of 180.5 h which was 18 h earlier than the placebo group. They concluded to the benefit of probiotics in terms of faster recovery and shorter duration of hospital stay. A review (34) confirmed these encouraging results but highlighting the lack of factual evidence in literature. Indeed, despite the positive results, various combinations and concentration, the inconsistency in administration, the inhomogeneity of comparison groups and lack of similar clinical endpoints remain to date many limits to concluded to a definitive clinical strategy. Further work is warranted to have better understanding of probiotics' clinical value.

Outstanding issues in 2017

It means that we should revisit the guidelines against MBP before elective colorectal surgery and come back to the "old practices"? Indeed, several very recent retrospective studies based on good quality and large multi institutional clinical database suggested the unified conclusion that preoperative MBP alongside oral antibiotics provides optimal outcomes following elective colorectal surgery. In fact, rather than questioning the role of MBP, these very recent data highlighted the strong benefit of preoperative intestinal bacterial decontamination with oral antibiotics. Therefore, focusing only on MBP, some authors argue that, because of many methodological bias, such latter trials cannot permit the conclusion that no MBP is deleterious in terms of morbidity and mortality after colorectal surgery.

Moreover, two other points must be questioned. It should be noted that most of the studies evaluated the use of MBP for open colorectal surgery. Regarding literature, only two studies focused on totally laparoscopic colorectal surgery and MBP (35,36). To date, it remains unclear if results can be extrapolated to laparoscopic colorectal surgery. It seems logical that MBP facilitates manipulation of the bowel during laparoscopic resection and readies the colon for intraoperative colonoscopy when it is required for lesion localization or to assess anastomoses. Secondly, these findings cannot be applied to specific rectal surgery because of insufficient published data. Indeed, rectal cancer location was considered as a non-inclusion criterion in most of previous published trials. It is currently admitted that the risk of septic complications after rectal resection, as a result of the well-known risk factors, is higher than after colonic resection. Thus, most of colorectal surgeons consider that no preparation regimen in rectal cancer surgery could represent an additive risk factor for postoperative morbidity.

Regarding rectal surgery without preoperative MBP, only 2 studies for open surgery (26,37) and 1 for laparoscopy (36) are available in the literature to date. The Cochrane Group (26) among 4,700 patients included in all the 14 randomized studies on MBP and colorectal surgery, performed a subgroup analysis of patients with intraperitoneal colorectal anastomosis and it failed to show any benefit of MBP. This subgroup analysis reported an anastomotic leakage rate of 6.6% in no-MBP patients versus 10% after MBP (NS). A second subgroup analysis (37) performed among 449 patients undergoing low pelvic anastomosis, extracted from a randomized study including 1,700 patients, was performed. In this subgroup analysis, in fact, only 48 patients presented a very low anastomosis with a temporary stoma, as it is the rule in rectal cancer surgery. In this analysis, the anastomotic leakage rate was similar between both no-MBP and MBP groups (6.6% *vs.* 7.6%, NS).

We have conducted the first randomized trial focusing on MBP in patients undergoing rectal cancer surgery (37). We demonstrated that rectal resection without MBP was significantly associated with an increase of both the 30-day overall morbidity rate (44% *vs.* 27%, P=0.01) and the infectious complications rate (34% *vs.* 16%, P=0.005). Moreover, although not significant, there was, in no-MBP patients, a trend toward a 2-fold risk of anastomotic leakage (19% *vs.* 10%) and peritonitis (7% *vs.* 2%). This study suggested to continue to perform preoperative MBP before elective rectal resection for cancer. But, we can, therefore, consider that we need more data about MBP before specific laparoscopic colorectal surgery. Moreover, the question about antibiotic use has not been addressed.

Conclusions

Regarding the role of MBP, it is time to rethink the rules... or think about the past. Indeed, historical evidence supports the use of oral antibiotics for the reduction of postoperative infectious complications following colorectal surgery. In 2017, it is clear that the best postoperative surgical outcomes can be achieved when MBP and oral antibiotics are given in combination leading to a significant decrease of colorectal resection-specific outcomes.

A multicenter randomized study on this topic would be very timely, providing the level of evidence required to give surgical guidelines into line with current best evidence.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ales.2019.11.04). The authors have no conflicts of interest to declare.

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