

Does mechanical bowel preparation have a role in preventing postoperative complications in elective colorectal surgery?

A meta-analysis

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Summary

Background: mechanical bowel preparation (MBP) consists of orthograde fluid preparation to clean the bowel. MBP is considered to prevent postoperative complications.

Methods: meta-analysis of prospective randomised clinical trials (RCT) evaluating MBP versus no MBP.

Results: following a medline search we retrieved 15 prospective trials of which only 5 were RCT comparing MBP versus no MBP in elective colorectal surgery. For the randomised studies, there were respectively 186, 179, 149, 267 and 380 patients, including all type of resections. The total number of patients in these 5 studies was 1144 (565 with MBP and 579 with no preparation). All patients received perioperative antibiotic prophylaxis. Only one of these RCT show a significant decrease in anastomotic leak (AL), but among all the patients enrolled, AL is significantly more fre-

quent in the group with MBP (Odds Ratio 1.8). Wound infection, re-operation and intra-abdominal abscess rates were more frequent in the MBP group but the difference did not reach statistical significance and the odds ratios for a 95% confidence interval were extremely large.

Conclusion: there is limited evidence in the literature to support the use of MBP in patient undergoing elective colorectal surgery. Available data tend to suggest that MBP could be harmful with respect to the incidence of anastomotic leak. Moreover, MBP does not reduce the incidence of other infectious complications. Further RCTs are needed to establish an evidence-based rationale for the use of MBP in elective colorectal surgery.

Key words: colon surgery; meta-analysis; human; preoperative care; cathartics; postoperative complication; surgical anastomosis

Introduction

Mechanical bowel preparation, either by orthograde fluid ingestion or enema, is commonly used to prepare patients before colorectal surgery [1-3]. In a survey among colorectal surgeons, in 1997, Nichols [4] showed that 100% of responders used MBP in their patients and 87% used antibiotic prophylaxis. MBP is used because it is considered to decrease the rate of postoperative infectious complications and enable the surgeon to work with a clean bowel. In 1966, Plumley [5] developed a new regimen for bowel preparation and claimed that MBP should be performed in patients undergoing colorectal surgery arguing that the "usefulness of bowel cleaning has been recognised by world war surgeons". In 1971, Goligher [6], in accordance with Everett [7], claimed that MBP should be performed in patients with inflamma-

tory bowel disease before surgery, because gross faecal loading of the bowel was associated with an increase in wound infection incidence, but no increase in anastomotic leak rate. Similarly, Dunphy [8] advocated that MBP should be done for patients before colorectal surgery on the basis of the results published by Stearns et al in 1971 [9]. MBP was then nearly uniformly accepted as a "dogma" in the seventies [10].

MBP in patients undergoing colorectal surgery has many potential attractions. It may decrease the intraluminal content of bacteria thus decreasing intraoperative bacterial contamination load of the peritoneal cavity. MBP does not enhance bacterial translocation through bowel wall, provided the mucosal barrier is not disrupted [11]. But if MBP decreases the amount of solid faeces,

it does not alter the concentration and only slightly alters the relative composition of the intraluminal faecal flora [12–15]. In patients undergoing colorectal surgery the number of isolates per patient is not influenced by MBP [16]. MBP may prevent anastomosis disruption by the passage of hard faeces. It may also decrease the operative time by improving bowel handling during anastomosis construction by avoiding having to clear gross faeces at every turn. In addition, MBP is generally well tolerated by the patient [3, 17].

Antibiotic prophylaxis is effective in decreasing postoperative infection rates [18]. Retrospective studies have been published analysing the outcome of emergency colon surgery in patient without MBP showing low postoperative infectious complication rates and an experimental study was unable to show an advantage of MBP in terms of anastomotic leak incidence [19, 20]. The aim of this meta-analysis was to evaluate the role of MBP in patients undergoing colorectal surgery with antibiotic prophylaxis in terms of postoperative complication rates.

Methods

Criteria for inclusion in this meta-analysis were published prospective clinical trials in which there was random allocation of patients to mechanical preparation or no mechanical preparation of the bowel before elective colon surgery. A computerised search (medline and oldmedline) from 1958 to 2003 was done using the terms: “bowel cleaning”, “bowel preparation” and “cathartics”. The set was limited to human subjects. In addition to the computerised search, a manual search was done on the reference list cited in selected trials and in review articles on mechanical bowel preparation. Randomised studies on mechanical bowel preparation were reviewed and appraised using the method described by Hall JC et al. [21]. Information was extracted from each trial, including aspects of the methodology, number of patients included and randomisation to each group, number of patients excluded, mean age of included patients, type of mechanical preparation for the prepared group, type of antibiotic pro-

phylaxis, indication for surgery and type of colon resection. Outcomes measure analysed were wound infections rates, anastomotic leak rates, intra-abdominal infection rates, re-operation for abdominal complication (ie, anastomotic leak, haemorrhage or intra-abdominal abscess) rates and mortality. Statistical analysis was done according to the Fleiss JL approach [22] using the S-Plus software (Version 3 from “StatSci division of MathSoft”). Odds ratios with a 95% confidence interval (according to random effects estimates), as well as P values, were calculated for each outcome measure. Odds ratios of more than 1 are in favour of mechanical bowel preparation avoidance. The number needed to treat (NNT), which represent the inverse of the risk difference, was derived to aid in clinical interpretation of the results. A positive NNT number favours no MBP. A P value of less than 0.05 was considered statistically significant.

Results

Among 15 prospective trials published in the world literature, only 5 were randomised trials evaluating MBP versus no MBP in patients undergoing elective colorectal surgery with only these being eligible for this meta-analysis [16, 23–26] (table 1). Others trials evaluated different mechanical bowel preparation methods either be-

fore colonoscopy or surgery, but none of them compared them to avoidance of bowel preparation. None of these five trials favour the use of MBP for elective colorectal surgery in patient receiving an antibiotic prophylaxis, and some suggest that MBP could be deleterious in terms of postoperative complication rates. If these studies were all ran-

Table 1
Randomised prospective trials evaluating mechanical bowel preparation in elective colorectal surgery.

RCT	Brownson et al. 1992 [21]	Burke et al. 1994 [22]	Santos et al. 1994 [16]	Miettinen et al. 2000 [23]	Zmora et al. 2003
Number of patients included	179	186	149	267	415
Number of patients excluded	Not given	17	8	12	35
Number of patients (MBP & no MBP group)	86 & 93	82 & 87	72 & 77	138 & 129	187 & 193
Mean age of patients (MBP & no MBP)	Not given	65 and 64	52 and 50	61 and 64	68 and 68
Patients with colon cancer (MBP & no MBP)	Not given	85% and 72%	49% and 43%	46% and 55%	78% and 78%
Type of bowel preparation	Polyethylene glycol	Sodium picosulfate	Laxative, enema and Mannitol	Polyethylene glycol	Polyethylene glycol (with enema for rectal surgery)
Antibiotic prophylaxis	Yes	Yes	Yes	Yes	Yes

Results for those patients receiving mechanical bowel preparation are given in boldface print; MBP = mechanical bowel preparation

Table 2
Assessment of the
randomised trials.

Study	Brownson et al. [21]	Burke et al. [22]	Santos et al. [16]	Miettinen et al. [23]	Zmora et al.
Randomisation	yes	yes	yes	yes	yes
Clearly stated aim	no	yes	no	yes	yes
Adequate control group	yes	yes	yes	yes	yes
Account of the selection process	no	yes	no	yes	no
Prospective definition of the sample size	no	no	no	no	no
Description of the randomisation technique	no	no	yes	no	yes
Demonstration of baseline equivalence between the study groups	no	yes	yes	yes	yes
Definition of the study end points	no	no	yes	no	yes
Unbiased assessment of study end points	no	no	no	no	no
Description of the intervention studied	yes	yes	yes	yes	yes
Clear documentation of adverse events	yes	yes	yes	yes	yes

domised with an adequate control group (no MBP), all of them failed to complete all the items described by Hall JC [21, 27] (table 2). Of importance, none of these trials prospectively defined the sample size, which is critical in determining the power of the trial. In addition, none of these studies described the reasons for stopping the trial. These five studies have a low power and are perhaps therefore unable to bring to the fore a low magnitude difference of clinical importance. However, these trials can rule out an effect of large magnitude which could be of utmost clinical importance. The main objective of this meta-analysis is then to combine these small sample studies to determine the potential differences in outcome.

In 1992, Brownson P et al. [25] compared orthograde MBP, with polyethylene glycol solution, versus no MBP in patients undergoing elective colorectal surgery (table 1). All patients received intravenous antibiotic prophylaxis. This study was published only as an abstract and no precise data are given on to the type of colorectal surgery performed or on anastomosis technique. Furthermore no description of the patient selection criteria is given and the basal equivalence between the study group is not demonstrated. In the publish abstract, absence or presence of patient exclusion is not mentioned. This study enrolled a total of 179 patients, and according to their analysis there was a significant increase in the rate of intra-abdominal infection and anastomotic leak in patient receiving MBP compared to the patients of the control group. There was a slight decrease, not statistically significant, in the rate of wound infection in the MBP group.

In 1994, Burke P et al. [23] compared orthograde MBP, with sodium picosulfate solution, versus no MBP in patients undergoing elective colorectal surgery (table 1). All patients had a complete liquid diet for the last 24 hours before surgery. All patients received intravenous antibiotic prophylaxis (ceftriaxone and metronidazole) during and after surgery for 24 hours. Patients who could not tolerate MBP were not eligible for the

study, but the criteria for this selection are not detailed. All patients enrolled had a left-sided colon resection. The anastomosis technique was either manual or mechanical. 17 patients were excluded because bowel continuity was not restored after surgery or a colostomy was performed. This study enrolled a total of 186 patients with 79% (133 patients) suffering a neoplastic condition. No statistical difference in wound infection and anastomotic leak rates were seen between the two groups. There was a slight decrease of the re-operation rate and of the postoperative mortality rate in the group without MBP.

In 1994, Santos JC et al. [16] compared a combination of orthograde and retrograde MBP, with laxative, mannitol and enema, versus no MBP (table 1). All patients had a low residue diet and a liquid diet 24 hours before surgery. All patients received an antibiotic prophylaxis (cephalothin and metronidazole) during and after surgery for 24 hours. Right-sided colon resections were performed in 8% and 10% of the MBP and no MBP group respectively and 6% and 12% of patients in the MBP and no MBP group had an ileorectal or ileoanal anastomosis. Anastomoses were performed manually. This study enrolled a total of 149 patients with 46% (68 patients) suffering a neoplastic condition. According to their analysis there was a statistically significant decrease in the rate of local complications (anastomotic leak and/or wound infection) in the no MBP group. Anastomotic leak, wound infection and re-operation rates were slightly decreased in the no MBP group.

In 2000, Miettinen RP et al. [24] compared orthograde MBP, with polyethylene glycol solution, versus no MBP (table 1). All patients received intravenous antibiotic prophylaxis (ceftriaxone and metronidazole) during surgery. Right-sided colon resections were performed in 20% and 26% of the MBP and no MBP group respectively. The anastomosis technique was either manual or mechanical. This study enrolled a total of 267 patients with 50% (134 patients) suffering a neoplastic condition. There was a non statistically significant de-

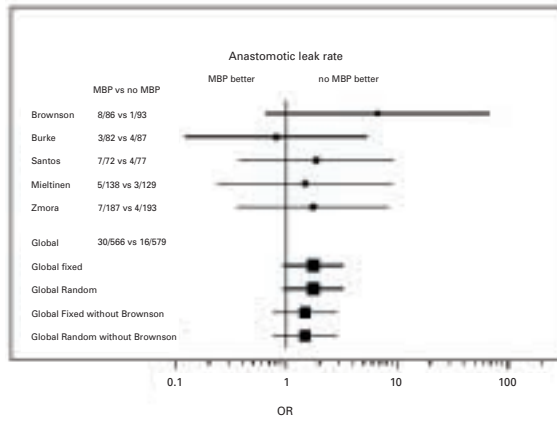


Figure 1
Anastomotic leak rate (odds ratio >1 favours No MBP).

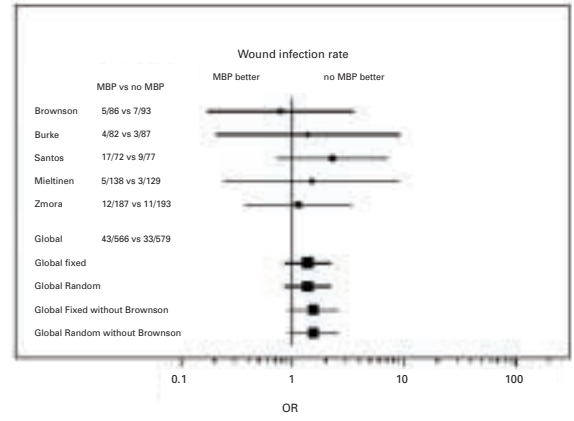


Figure 2
Wound infection rate (odds ratio >1 favours No MBP).

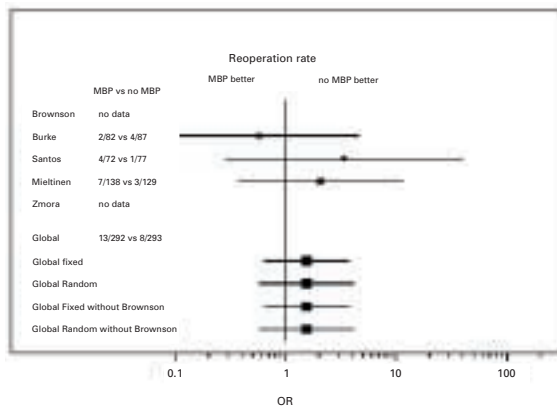


Figure 3
Re-operation rate (odds ratio >1 favours No MBP).

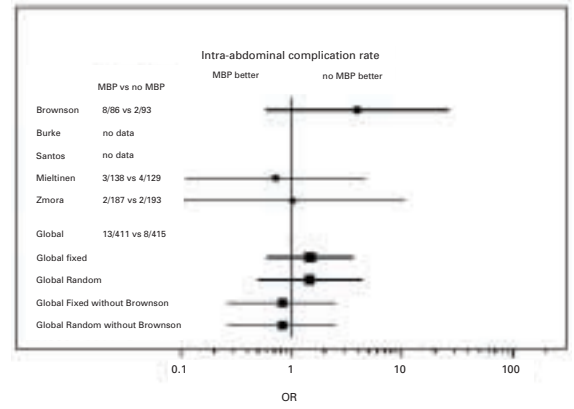


Figure 4
Intra-abdominal complication rate (odds ratio >1 favours No MBP)

crease in anastomotic leak, wound infection and re-operation rates in the no MBP group ($p > 0.05$). The intra-abdominal infection rate was similar in the two groups.

In 2003, Zmora O et al. [26] compared orthograde MBP, with polyethylene glycol solution, versus no MBP (table 1). All patients received intravenous antibiotic prophylaxis before and during surgery (neomycin and erythromycin). Right-sided colon resections were performed in 31.6% and 28% of the MBP and no MBP group respectively. No information on anastomosis technique is given. This study enrolled a total of 380 patients with 78% (296 patients) suffering a neoplastic condition. There was a non statistically significant decrease in anastomotic leak, wound infection and abdominal abscess rates in the no MBP group ($p > 0.05$). Six deaths were recorded in this study (3 in each group). Two of the three patient deaths in the MBP group were associated with the presence of either wound infection or anastomotic leak. Non-surgical complications rates were similar in the two groups, however diarrhoea were statistically significantly more frequent in the MBP group which could be related to the mechanical bowel preparation.

A meta-analysis was then performed on these five randomised clinical trials. The total number

of patients included in these 5 studies [16, 23–26] was 1144 (565 with MBP and 579 with no MBP). Among these five studies one was only published as an abstract [25]. As it could add bias in the meta-analysis we have performed analysis either with or without including the Browson et al study. When excluding the Browson et al study the total number of patients remaining among the four trials [16, 23, 24, 26] was 965 (479 with MBP and 486 with no MBP). This meta-analysis was performed for four end points: wound infection, anastomotic leak, intra-abdominal infection and re-operation rates, with the results available for each point among these five trials (figures 1 to 4). For all end points, exclusion of the Browson study did not influence the results significantly. It revealed a statistically significant higher incidence of anastomotic leak in patients receiving MBP versus no MBP (odds ratio 1.76; CI 95% 0.96–3.22) (fig. 1). However, odds ratio or relative risk can be difficult to interpret. Therefore, a number needed to treat was calculated to provide an absolute measure of risk. With an incidence of 5% of anastomotic leak, 39 (CI 95%: 25–1106) patients would have to be operated without MBP to prevent one leak from a patient receiving MBP before surgery. The rate of wound infection was also slightly higher in patients receiving MBP versus no MBP

(odds ratio 1.37, CI 95% 0.86–2.19) (figure 2). In accordance with the higher rate of anastomotic leak in patients receiving MBP, the rate of re-operation was slightly higher in the MBP group in comparison to the control group (no MBP) (odds ratio 1.54, CI 95% 0.64–3.72) (figure 3). Re-operation (n = 21) was mainly for anastomotic leak (17 cases; 10 in the MBP group and 7 in the control group). 2 patients were re-operated for wound dehiscence and 2 for miscellaneous conditions. No statistical difference was detected for intra-

abdominal infection (odds ratio 1.48, CI 95% 0.62–3.56) (figure 4). Deaths were only reported in two studies [23, 26] (odds ratio 1.42, CI 95% 0.37–5.45). Only 2 deaths were reported in the MBP group in the first study [23], while 6 deaths (3 in each group) were reported in the second [26]. General complication rates are only reported by Miettinen et al. [24] and Zmora et al. [26]. In these studies the complication rates were similar between the two groups (MBP vs no MBP).

Discussion

It is difficult to have faith in conclusions that are drawn from clinical trials that contain flawed methodology. As mentioned, none of these RCTs prospectively defined the sample size or had an unbiased assessment of end points. Most of them failed to clearly state the aim of the study and the reason to stop it. Between 5 and 10% of the selected patients were excluded in the different studies, while reasons for exclusion are not clearly stated. Such deficiencies weaken the conclusions made in these 5 RCTs. Moreover, as in all meta-analysis there is a risk of publication bias. One of these 5 RCTs has been published only as an abstract and it is the only one with statistically significant results concerning anastomotic leak. Not all end-points were published in all studies allowing another bias of publication. A minimal sample size for a RCT on MBP with a power of 80% ($\alpha = 5\%$) would be 950 patients (assuming a variation in end point incidence from 10% to 5%). It is difficult for one institution to accrue such a large number of patients in a short period. Multicentre studies expedite patient accrual, however, this may compromise the homogeneity of the treatment, however this may also increase the reproducibility of the results. According to the results of the present meta-analysis, we have started a randomised multicentre trial evaluating MBP for elective colorectal surgery. The preliminary results have been recently presented and favour the avoidance of MBP before elective left-sided colorectal surgery [28]. Because of this the current common practice of MBP is based mainly on historical non-controlled, small sample studies published before the routine introduction of antibiotic prophylaxis and on a small number of animal studies as well as surgical tradition [29].

Conclusion

Bowel cleaning by the means of mechanical bowel preparation has not been demonstrated to reduce post-operative complication rates in randomised clinical trials. Furthermore, RCTs evaluating mechanical bowel preparation in elective colorectal surgery either show no benefit or a deleterious effect of mechanical bowel cleaning. Yet, none of these trials are sufficiently reliable to detect advantages or disadvantages of mechanical bowel cleaning. This meta-analysis suggests that mechanical bowel preparation may be deleterious in terms of post-operative complications incidence. This raises the need for randomised clinical trials, with adequate sample size, evaluating the role of mechanical bowel preparation in post-operative complication incidence. To date, the current use of mechanical bowel preparation before elective colorectal surgery still remains routine, however avoidance of mechanical bowel preparation for elective colon and rectal surgery might be considered.

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