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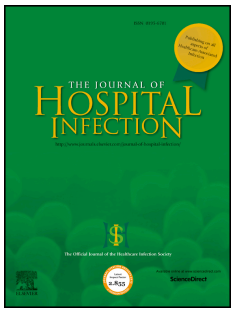

Preoperative Mechanical and Oral Antibiotic Bowel Preparation to Reduce Infectious Complications of Colorectal Surgery – The Need for Updated Guidelines

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Title Page

Preoperative Mechanical and Oral Antibiotic Bowel Preparation to Reduce Infectious Complications of Colorectal Surgery – The Need for Updated Guidelines.

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Running title: Bowel Preparation for Colorectal Surgery

Summary

Background
Increasing evidence indicates that combined mechanical and oral antibiotic bowel preparation reduces the infectious complications of colorectal surgery. Anecdotal evidence suggests the combination is rarely used in the UK & Europe.

Aim
To establish colorectal surgeons' current use, and awareness of the benefits of such bowel preparation amongst, and to identify decision-making influences surrounding preoperative bowel preparation.

Method
An electronic survey was emailed to all members of the Association of Coloproctology of Great Britain and Ireland, and promoted via Twitter.

Findings
495 respondents completed the survey: 413 (83.2%) UK, 39 (7.9%) other European, 43 (8.7%) non-European. Respondents used oral antibiotics for 12%-20% of cases. Mechanical bowel preparation (MBP), phosphate enema, and no preparation respectively ranged between 9%-80%. Combined MBP and oral antibiotic bowel preparation ranged between 5.5%-18.6%.

53% (260/495) agreed that combined mechanical and oral antibiotic bowel preparation reduces surgical site infection. 32% (157/495) agreed that the combination reduces risk of anastomotic leak.

Kappa statistics between 0.06-0.27 indicate considerable incongruity between surgeons' awareness of the literature, and day-to-day practice.

24% (96/495) believed MBP to be incompatible with ERAS. 41% (204/495) believe that MBP delays return to normal intestinal function.

Conclusions
Few UK and European colorectal surgeons use mechanical and oral antibiotic bowel preparation, despite evidence of its efficacy in reducing infectious complications. The influence of ERAS pathways and UK and European guidelines may explain this. In contradiction to the UK and Europe, North American guidelines recommend incorporating MBP/OAB, into ERAS programmes. We suggest future UK and European guidelines incorporate MBP/OABP into the ERAS pathway.

Keywords: Bowel preparation, complications, surgical site infection

Introduction

Infectious complications of colorectal surgery continue to present a significant burden to both patients and healthcare providers. Complications such as surgical site infection (SSI) and anastomotic leak (AL) cause considerable morbidity and mortality, cost, prolonged length of stay (LOS) and impaired quality of life (QOL)(1, 2). Colorectal surgery accounts for the greatest number, and most costly SSIs within NHS hospitals in England (3). Despite the scale of the problem, recording and reporting of SSIs is currently very poor; to reduce the incidence of this problem requires recognition of the nature of the problem, and clinical leadership to drive change (3, 4). It is well recognised that rates of SSI can be significantly reduced by using infection control bundles. Combined mechanical bowel preparation and preoperative oral antibiotic preparation (MBP/OABP) are common in such bundles (5-7).

Establishing an optimal bowel preparation regime to reduce the incidence and burden of infectious complications in colorectal surgery has been the subject of debate for over a century (8). The use of mechanical bowel preparation (MBP), oral antibiotic bowel preparation (OABP), or the combination of both, has fallen in and out of favour over the decades(8).

The use of MBP and OABP in elective colorectal surgery remains the subject of considerable debate, reflected in the discrepancy observed between guidelines issued by various authorities around the world. NICE Guidelines (Clinical Guideline 74) recommend against the routine use of MBP, citing the 2011 Cochrane review; these are currently the only published guidelines pertinent to UK practice(9). European Society for Coloproctology (ESCP) guidelines also advise against the use of MBP(10).

There has been an increasing volume of recent evidence to suggest that the preoperative use of combined mechanical bowel preparation and oral antibiotics is associated with significant reduction in the incidence of infectious complications of elective colorectal surgery (8, 11-16). The use of combined MBP and OABP is supported by randomised controlled trial data, especially for

reducing SSI, however, much of the support for the use of combined MBP/OABP is from large North American cohort studies, including American College of Surgery National Surgical Quality Improvement Program (ACS NSQIP) data. (13)

In contrast to UK and European guidelines, North American guidelines recommend routine use of combined MBP/OAB for elective colorectal surgery(17). One reason for this discrepancy is that some European authors are critical of the use of NSQIP data as studies are based on retrospective analysis of prospectively collected data, rather than data collected within a randomised trial setting and all of the studies are based on the same database. Due to the nature of the data collection, it is not always possible to establish the MBP/OAB regime employed. It is also the case that there is insufficient data comparing oral antibiotic preparation alone, with combined MBP and OAB.(10)

The benefits of combined MBP/OAB is further supported by the recent ESCP Left Sided Colorectal Resection audit (18). This was a prospectively designed study, with AL as a primary endpoint, and detailed data regarding nature of preparation, and other risk factors for AL was collected. Of 3676 patients from 52 countries, 618 (16.8%) received MBP & OABP, 1945 MBP (52.9%) and 1099 patients were in the NBP group (received no MBP and no OABP) (29.9%). Patients undergoing MBP & OABP had the lowest overall rate of anastomotic leak (6.1%, 9.2%, 8.7% respectively) and by mixed-effects multivariable regression MBP & OABP was associated with a two-fold reduction in the anastomotic leak (OR 0.52, 0.30-0.92, p=0.02) but MBP alone did not reduce anastomotic leak risk (OR 0.92, 0.63-1.36, p=0.69) compared to NBP (18). A randomised controlled trials, COLONPREP, designed to compare MBP/OABP with OABP alone is due to commence recruitment in the near future. The trial has SSI as a primary endpoint, with AL as a secondary endpoint. The outcomes may be informative with regard to preventing SSI, but it is unlikely that the trial will be adequately powered to evaluate the effect of preparation regime in reducing risk of AL.

Prior to the introduction of enhanced recovery after surgery (ERAS) pathways, MBP was regarded as standard practice. As ERAS has become increasingly popular, use of MBP has reduced, on the basis that the physiological response to the depletion of fluids and electrolytes prolongs postoperative recovery, MBP is unpleasant for the patients, and the lack of data to demonstrate benefits from its use(9, 14). The evidence, however, suggests that combined MBP and OABP does not delay time to discharge, and may even reduce length of stay(13). Oral antibiotic use alone has been investigated as an alternative to MBP, with some data to show reduced SSI and AL rates (11, 19).

Despite the evidence to support use of MBP/OABP in reducing infectious complications of elective colorectal surgery, anecdotal evidence suggests that the use of MBP and OABP regimes amongst colorectal surgeons is variable. This study aimed to survey current practice within the UK, and to extend the reach of the survey to the wider colorectal surgical community using social media. In addition to describing current practice, we also sought to investigate factors that influence decision-making regarding use of MBP and OABP, especially within the setting of ERAS, which has been widely adopted by colorectal surgeons throughout the world.

Methods

An electronic survey was emailed to all members of the Association of Coloproctology of Great Britain and Ireland (ACPGBI). The survey was in English and the data collection period lasted for one month (19/3/18-18/4/18).

Promotional links were sent via Twitter in the week prior to launching the survey, on the day of the launch and regularly during the survey, with the #colorectalsurgery link, to disseminate the survey to a wider audience. Regular reminders were also sent via email, the ACPGBI newsletter and Twitter. Questions assessed use of MBP and OAB for various colorectal procedures, nature of respondent's practice (consultant or trainee), use of ERAS pathways, and opinions on the influence of MBP and OAB on the incidence of SSI and AL.

The strength of agreement between reported current practice and opinions regarding SSI and AL in relation to the use of MBP and OABP was tested using Kappa statistic. A Kappa value of ≤0.20 was interpreted as 'Poor', 0.21-0.40 as 'Fair', 0.41-0.60 as 'Moderate', 0.61-0.80 as 'Good', and 0.81-1.00 as 'Very good' (20). Data analysis was with carried out with SPSS (v21.0; IBM Corp, Armonk, NY).

Results

495 respondents completed the survey, with 33 countries represented. 413 (83.2%) were from the UK, 39 (7.9%) from other European countries and 43 (8.7%) from non-European countries. 443 (89%) of respondents were consultant colorectal surgeons; 52 (11%) were trainees with an interest in colorectal surgery. 126 (26%) have been practising ERAS for less than 5 years, 247 (50%) for 5-10 years, and 122 (24%) for over 10 years.

Oral Antibiotics and Mechanical Bowel Preparation

Use of mechanical bowel preparation, phosphate enemas and oral antibiotics for various colorectal procedures is detailed in Table I. Use of MBP was predominantly seen in left sided resections, especially those with a planned defunctioning stoma, but remains low for other procedures. Between 30% and 47% of respondents used phosphate enemas as a substitute for MBP in left sided procedures. The use of oral antibiotics alone was generally low for all procedures; consequently the use of combined MBP and OABP was also low for all procedures.

53% (260/495) agreeded that combined MBP and OAB reduces surgical site infection. 32% (157/495) agreed that MBP and OAB reduces risk of AL.

Opinion regarding effect of MBP and OAB on SSI and AL

Kappa statistics are given for respondents' agreements with the statements regarding effect of OABP (Table II) and MBP (Table III) on the reduction of SSI and AL, and what those respondents did in their own practice. The Kappa values are below 0.21 for OABP and MBP practice for all procedures except left sided resection without a stoma. For left sided procedures without a stoma the Kappa values between 0.23 and 0.27 indicate a fair agreement between the surgeon's opinion and practice.

MBP and ERAS

24% (96/495) believed MBP to be incompatible with ERAS. 41% of respondents (204/495) believed that MBP delays return to normal intestinal function.

Discussion and Conclusions

We have demonstrated a considerable variation in the use of mechanical bowel preparation and oral antibiotic preparation, both individually and in combination, amongst practising colorectal surgeons. Despite European and UK guidelines advising against routine use of MBP, surgeons continue to use MBP, especially for left sided resections with a planned stoma. Oral antibiotic preparation was used between 12% and 20%, with very few surgeons using the combination of MBP/OABP, suggesting that some surgeons use oral antibiotics as an alternative to MBP to reduce infectious complications of colorectal surgery. We also demonstrated a wide variation in practice depending upon the operation being carried out. It is particularly interesting to note the data from this study showing the low rate of both MBP and OABP for patients undergoing panproctocolectomy and APER; deep organ space infection, and perineal wound infections carry a major burden for this population(21). The findings suggest that decision-making with regard to bowel preparation is driven by reducing the risk of AL from low anterior resection, rather than preventing SSIs, or AL from other resections. Recent American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) data supports the use of combined MBP/OAB for all colectomies(14).

Although few surgeons prescribe MBP/OAB, 53% of respondents believe that combined MBP/OABP reduces SSI; 32% believe that the combination reduces anastomotic leak, indicating a discrepancy between awareness of the benefit of MBP/OABP and day-to-day practice. Based on data from previous surveys, it was anticipated that surgeons prescribing combined MBP/OABP would be in the minority (22), we therefore sought to investigate whether ERAS protocols might influence decision-making. We postulated that surgeons who omit MBP do so on the basis that it is not compatible with ERAS. 41% of respondents believe that MBP delays return to normal intestinal function, however only 24% of respondents believe that MBP is incompatible with ERAS. It is possible that despite awareness of the benefit of MBP/OAB, most surgeons have not yet modified their ERAS pathways. Whilst most ERAS pathways do not include MBP, avoidance of MBP was not one of the central tenets described by Kelhlet (23), and it has been shown that MPB/OABP can be incorporated into ERAS pathways(2, 17). A further barrier to change in practice may be the lack of clarity regarding the precise MBP/OABP preparation. Various combinations of kanamycin, metronidazole, neomycin and erythromycin have been used with variable dosing (13), however detailed advice to support decision making remains scarce.

We have also explored the relationship between surgeon's views on the effects of MBP and OABP on SSI and anastomotic leak, and their own practice. (Tables II and III). As there were two options for each criteria (agree/disagree; prescribe/don't prescribe), responses fell into one of 4 groups (e.g. agree/prescribe; agree/don't prescribe). Scrutiny of the outcomes indicated considerable incongruity between individual surgeon's agreement with the statements, and their actual practice. The relationships were quantified with kappa agreements, which showed either a poor or fair agreement for all outcomes. These weak agreements indicate that a large proportion of surgeons agreed with the questions, and believe that combined MBP/OABP reduces SSI and anastomotic leak, but do not currently prescribe such a regime. Data from this study also indicates that a considerable number of respondents were either

unaware of current literature or did not agree with it, e.g., respondents who did not believe that MBP/OABP reduces SSI and AL.

Conclusions

Although many surgeons recognise the benefit of MBP/OAB, very few UK surgeons currently employ the regime as a routine element of pre-operative management. The recent influence of ERAS pathways may have contributed to the omission of MBP/OAB, especially as UK and European ERAS guidelines do not endorse routine use of MBP/OAB. In contradiction to the UK and Europe, North American guidelines do recommend the routine use of MBP/OAB, within the context of an ERAS pathway. Infectious complications of colorectal surgery are likely to counteract many of the advantages gained from ERAS. It is therefore reasonable to suggest that future iterations of UK and European guidelines for elective colorectal surgery should recognise the data that supports the use of MBP/OABP, and empower colorectal surgeons to incorporate combined MBP/OABP into ERAS pathways.

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Table 1: Summary of reported bowel preparation practice for elective colorectal resections according the survey responses

Operation Type % [n/495]	Mechanical Bowel Prep		Phosphate Enema		No Prep		Oral Antibiotics		OAB and MBP	
Right hemicolectomy	10%	[48/495]	9%	[47/495]	81%	[400/495]	12%	[60/495]	5.4%	[27/495]
Left sided resection* without a planned defunctioning stoma	43%	[211/495]	47%	[235/495]	10%	[49/495]	18%	[88/495]	13.3%	[66/495]
Left sided resection* with a planned defunctioning stoma	80%	[395/495]	16%	[81/495]	4%	[19/495]	20%	[101/495]	18.6%	[92/495]
Panproctocolectomy	18%	[90/495]	30%	[149/495]	52%	[256/495]	14%	[71/495]	7.1%	[35/495]
Abdominoperineal excision resection	18%	[90/495]	43%	[211/495]	39%	[194/495]	15%	[73/495]	7.9%	[39/495]

***Includes (low) anterior resections. OAB, oral antibiotics. MBP, mechanical bowel prep.**

Table 2: Comparison between the strength of agreement of surgeon's reported current OABP practice and their view on the role of combined mechanical and oral antibiotic bowel preparation for preventing SSI and anastomotic leak.

MBP with oral antibiotics reduces risk of **surgical site infection?**				
	Current Practice	Agrees with Question	Disagrees with Question	Kappa Agreement
Right Hemicolectomy	Use OABP	10.7%	1.4%	0.17
	Do not use OABP	41.8%	46.1%	
Left sided resection **without** stoma	Use OABP	15.2%	2.6%	0.23
	Do not use OABP	37.4%	44.8%	
Left sided resection **with** stoma	Use OABP	16.0%	4.4%	0.20
	Do not use OABP	36.6%	43.0%	
Panproctocolectomy	Use OABP	11.9%	2.4%	0.17
	Do not use OABP	40.6%	45.1%	
Abdominoperineal excision	Use OABP	12.3%	2.4%	0.18
	Do not use OABP	40.2%	45.1%	
MBP with oral antibiotics reduces risk of **anastomotic leak?**				
		Agrees with Question	Disagrees with Question	Kappa Agreement
Right Hemicolectomy	Use OABP	7.1%	5.1%	
	Do not use OABP	24.6%	63.2%	0.18
Left sided resection **without** stoma	Use OABP	9.3%	8.5%	
	Do not use OABP	22.4%	59.8%	0.19
Left sided resection **with** stoma	Use OABP	9.7%	10.7%	
	Do not use OABP	22.0%	57.6%	0.16
Panproctocolectomy	Use OABP	7.5%	6.9%	
	Do not use OABP	24.2%	61.4%	0.16
Abdominoperineal excision	Use OABP	7.7%	7.1%	
	Do not use OABP	24.0%	61.2%	0.16

These are listed according to operation type. Green box, current practice is consistent with the response to the question; blue box, agree with question but not in practice; red, surgeon uses OABP but not for this reason. OABP, oral antibiotic bowel preparation.

Table 3: Comparison between the strength of agreement of surgeon's reported current MBP practice and their view on the role of combined mechanical and oral antibiotic bowel preparation for preventing SSI and anastomotic leak.

MBP with oral antibiotics reduces risk of **SSI?**				
	Current Practice	Agrees with Question	Disagrees with Question	Kappa Agreement
Right Hemicolectomy	Use MBP	7.5%	2.2%	
	Do not use MBP	45.1%	45.3%	0.09
Left sided resection **without** stoma	Use MBP	29.3%	13.3%	
	Do not use MBP	23.2%	34.1%	0.27
Left sided resection **with** stoma	Use MBP	44.2%	35.6%	
	Do not use MBP	8.3%	11.9%	0.10
Panproctocolectomy	Use MBP	13.1%	5.1%	
	Do not use MBP	39.4%	42.4%	0.14
Abdominoperineal excision	Use MBP	12.5%	5.7%	
	Do not use MBP	40.0%	41.8%	0.12
MBP with oral antibiotics reduces risk of **anastomotic leak?**				
		Agrees with Question	Disagrees with Question	Kappa Agreement
Right Hemicolectomy	Use MBP	5.7%	4.0%	
	Do not use MBP	26.1%	64.2%	0.15
Left sided resection **without** stoma	Use MBP	19.0%	23.6%	
	Do not use MBP	12.7%	44.6%	0.23
Left sided resection **with** stoma	Use MBP	27.5%	52.3%	
	Do not use MBP	4.2%	16.0%	0.07
Panproctocolectomy	Use MBP	7.7%	10.5%	
	Do not use MBP	24.0%	57.8%	0.10
Abdominoperineal excision	Use MBP	6.9%	11.3%	
	Do not use MBP	24.8%	57.0%	0.06

These are listed according to operation type. Green box, current practice is consistent with the response to the question; blue box, agree with question but not in practice; red, surgeon uses MBP but not for this reason. MBP, mechanical bowel preparation.