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Oral antibiotics before colorectal surgery?

Adding an oral agent may reduce surgical site infections says new trial

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Most patients undergoing elective colorectal surgery will have an uncomplicated postoperative course. For some, however, their lives will be affected by potentially life threatening surgical site infection requiring readmission to hospital, and the decreased quality of life associated with, for example, a stoma.¹ For this reason extensive research has been performed on ways to decrease the risk of surgical site infection after colorectal surgery.²

The perioperative use of prophylactic oral antibiotics has been studied for over 60 years,^{3,4} following the dogma of maximising the reduction of bacterial bioburden in the gut lumen.⁵ The same principle guides mechanical bowel preparation and enemas. Despite this dogma, the effects of either intervention on the gut microbiome and the effects of the gut microbiome on risk of surgical site infection are only recently being investigated.^{5,6}

In a linked paper, Futier and colleagues (doi:10.1136/bmj-2022-071476) report a multicentre placebo controlled trial in 11 French hospitals on the efficacy of adding a preoperative oral antibiotic, ornidazole, to the usual perioperative intravenous antibiotic for preventing surgical site infection after colorectal surgery.⁷ This pragmatic clinical trial reports impressive reductions in risk of surgical site infection with a single antibiotic dose administered 12 hours before surgery, including a number needed to treat of 12 (for organ space surgical site infection this number rises to 29). This well conducted trial adds to a growing body of evidence suggesting that preoperative oral antibiotics in addition to standard perioperative intravenous antibiotic prophylaxis may be a beneficial strategy for reducing risk of surgical site infection and anastomotic leakage. The authors report statistically and clinically significant reductions in the risk of anastomotic leak (a secondary outcome of the study) associated with receipt of ornidazole.

Implementing Futier and colleagues' findings in real life will be challenging, however, for several reasons. Firstly, microbiologists and infectious disease doctors may argue that the effect of the intervention was mediated mainly by ornidazole's improved antimicrobial activity against anaerobic bacteria, and not the effect of an additional oral antibiotic in itself. The intravenous antibiotic used, cefoxitin, has suboptimal coverage of anaerobes, as evidenced by an update of French national guidelines that occurred during the trial.⁸ This calls into question the relevance of the findings where complete intraoperative anaerobic coverage by metronidazole is the rule.

Secondly, the authors' choice of the study drug, ornidazole, is also arguable. Previous clinical trials

used non-absorbable antibiotics such as neomycin, whereas others used antibiotics with systemic absorption and activity against aerobic bacteria, such as ciprofloxacin.⁹ The heterogeneity of antibiotic regimens evaluated in the existing literature could hamper widespread adoption.

Thirdly, patients with a body mass index of more than 35 were excluded from the trial, which is regrettable because obesity is an increasingly prevalent risk factor for surgical site infection after colorectal surgery,¹⁰ and these patients are likely to benefit the most from additional preventive measures.

Finally, the overall risk of surgical site infection in the placebo group (22%) was unexpectedly high for elective colorectal surgery.¹¹ Experienced surgeons could argue that this high rate is unlikely to reflect usual practice and that other preventive measures should be optimised before introducing an additional prophylactic antibiotic regimen with potential adverse effects.

Unfortunately, Futier and colleagues' trial does not provide a definitive answer to the most pressing question of whether mechanical bowel preparation is a useful adjunct to oral antibiotics.¹² As the trial was a pragmatic study, use of mechanical bowel preparation was left to the surgeons' discretion, and it was given to a third of all participants. A prespecified subgroup analysis suggested that the reduction in risk of surgical site infection associated with ornidazole was greater for patients treated with mechanical bowel preparation (compared with those treated without). Bowel preparation without oral antibiotics is, however, associated with higher risk of surgical site infection, which is why the World Health Organization recommends strongly against this practice.¹³ This was confirmed in the current trial: among participants given a placebo, the authors found a significantly increased risk of surgical site infection associated with mechanical bowel preparation compared with no mechanical bowel preparation.

Use of bowel preparation (and oral antibiotics) before colon surgery still varies widely—from 30% in Europe (mostly without oral antibiotics)¹⁴ to 55% in Australia (mostly with oral antibiotics)¹⁵ to around 80-95% in the United States (mostly with oral antibiotics).¹⁶ Although a recent network meta-analysis¹⁷ suggests that oral antibiotics alone are superior to oral antibiotics plus mechanical bowel preparation for reducing surgical site infections, additional evidence is still required to convince clinicians to change practice.

For this reason, the results of the ORALEV2 study¹⁸ comparing oral antibiotics with placebo in patients

not receiving bowel preparation is eagerly awaited. Until then, researchers designing further studies should compare different oral antibiotic agents head to head, avoid trial arms where mechanical bowel preparation is administered without oral antibiotics, and plan studies of the gut microbiome in patients having colorectal surgery (with an additional focus on development of antibiotic resistance).²⁰

Adding a preoperative oral antibiotic is one of several interventions, across different indications, which opposes conventional wisdom to limit antibiotic use to reduce antimicrobial resistance. The findings of this study and others suggest that there may be occasions when using more antibiotics provides additional benefits that outweigh the risks.²¹

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