



Role of oral and intravenous pre-operative antibiotics in elective colon surgery

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Pre-operative antibiotic administration remains a controversial issue in colorectal surgery. The high bacterial burden of the colon predisposes patients undergoing colorectal surgery to develop surgical site infections (SSI). The increased morbidity and healthcare costs associated with these SSI has further heightened the need for high quality studies to determine the most efficacious practices. Currently, the majority of healthcare practitioners employ a combination of oral antimicrobials and mechanical bowel prep to decrease the bacterial burden within the colon. However, the use of oral antibiotics are controversial and there consequently is not one accepted standardized routine in current clinical practice. In the May 2016 issue of *British Journal of Surgery* (epub ahead of print), Ikeda and colleagues proposed an intriguing article: “Randomized clinical trial of oral and intravenous *versus* intravenous antibiotic prophylaxis for laparoscopic colorectal resection” to compare the use of oral and IV antibiotics versus IV antibiotics alone (1).

In order to investigate the use of pre-operative antibiotics in laparoscopic colon cancer patients, the authors conducted a single center study in Japan of 515 cancer patients randomly assigned to two different treatment groups: group 1 combined oral antibiotics (metronidazole and kanamycin) and perioperative intravenous antibiotics (cefmetazole) (oral/IV group, n=255) or group 2 perioperative intravenous antibiotics (cefmetazole) alone (IV-only group, n=256). Patients were well-matched in terms of pre-operative characteristics, including type of operation (colonic surgery, anterior resection, or abdominoperineal resection),

preoperative use of mechanical bowel preparation, preoperative chemoradiotherapy, and pre-existing diabetes mellitus.

The primary endpoint was the overall rate of SSI at 30 days after surgery with secondary endpoints of incisional site infection rate, organ/space infection, anastomotic leakage, intra-abdominal abscess, adverse events, and postoperative complications. The authors found no difference in the incidence of SSI between the two groups. In addition, there was no statistical difference in secondary outcomes ($P>0.05$). Thus, the authors concluded that IV antibiotics alone before laparoscopic colon surgery is an acceptable practice.

This study is unique in that the investigators specifically looked at laparoscopic colon surgery, which already has an established lower rate of SSIs compared to open colon surgery (2). The authors hypothesized that the use of pre-operative antibiotics is unnecessary for laparoscopic procedures in patients undergoing colon resection for cancer. This could help to decrease associated healthcare costs and also avoid complications associated with antibiotic use, including *Clostridium difficile* colitis and disruption of the normal bacterial flora of the colon. Thus, the reduced use of pre-operative antibiotics in the study population could have significant effects on healthcare costs.

There are several limitations of the study by Ikeda and colleagues. First, the authors used an absorbable antibiotic (metronidazole) combined with a non-absorbable antibiotic (kanamycin). This combination differs from the original oral bowel prep proposed by Nichols and Condon (3). Oral

metronidazole is problematic as metronidazole is absorbed by the gastrointestinal tract and has both an intraluminal and systemic effect (4). Another issue was the inconsistent use of mechanical bowel prep by patients enrolled in the study prior to surgery. The use of mechanical bowel prep remains controversial. Several recent studies have demonstrated improved outcomes when employing pre-operative antibiotics when combined with mechanical bowel prep or antibiotics alone (5-7) while other studies have failed to demonstrate an effect (8). Thus, this confounding factor could have affected the validity of the results of the study. Finally, the authors report the overall SSI rate of their study is significantly lower compared to other studies, which may make these results less generalizable to other patient populations.

Several previous randomized controlled clinical trials have been conducted on this topic previously (9,10). Bellows and colleagues conducted a large meta-analysis of RCTs to compare the effectiveness of combined oral non-absorbable and intravenous antibiotics to reduce SSIs (9). The results of this study found that patients receiving a combination of oral and IV antibiotics had decreased SSIs compared to patients receiving only IV antibiotics. Thus, the authors concluded that both oral non-absorbable and IV antibiotics are necessary. However, this analysis included studies that combined laparoscopic and open surgical procedures. Also, the protocol of antibiotic regimens was not standardized. Thus, the need for a prospective randomized clinical trial investigating a standard pre-op antibiotic regimen in patients undergoing elective laparoscopic colon surgery remains necessary. Furthermore, a recent meta-analysis by Nelson and colleagues confirmed the results of Bellows *et al.*, but did not give specific recommendations on pre-operative antibiotic regimens.

In conclusion, the data supporting the use of a universal pre-operative oral antibiotic regimen and route of administration for colorectal surgery remains unclear. Ikeda and colleagues present a well-designed study that further investigates this topic, specifically in laparoscopic surgery, which always has a lower rate of SSI that contributes to the existing body of literature. However, additional prospective randomized studies are needed to further elucidate the most efficacious strategy to improve post-operative outcomes in colorectal surgery.

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