Should Carbapenem be Used for Elective Colorectal Surgery in Developing Countries?

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To Editor,

In a recent industry-sponsored study, Itani and colleagues reported the superiority of ertapenem over cefotetan for adverse events after elective colorectal surgery.1 Of the 1,002 patients randomly assigned to study groups, 901 (451 in the ertapenem group and 450 in the cefotetan group) qualified for the modified intention-to-treat analysis, and 672 (338 in the ertapenem group and 334 in the cefotetan group) were included in the per-protocol analysis. After adjustment for strata, in the modified intention-to-treat analysis, the rate of overall prophylactic failure was 40.2 percent in the ertapenem group and 50.9 percent in the cefotetan group (absolute difference, -10.7%; 95% confidence interval [CI], -17.1 to -4.2); in the per-protocol analysis, the failure rate was 28.0 percent in the ertapenem group and 42.8 percent in the cefotetan group (absolute difference, -14.8%; 95% CI, -21.9 to -7.5). Both analyses fulfilled statistical criteria for the superiority of ertapenem. In the modified intention-to-treat analysis, the most common reason for failure of prophylaxis in both groups was surgical-site infection: 17.1 percent in the ertapenem group and 26.2 percent in the cefotetan group (absolute difference, -9.1; 95% CI, -14.4 to -3.7).

While I congratulate the investigators on the completion of such an extensive study, important considerations should be made prior to the translation of this study finding into practice, especially in developing countries. First, the adverse event rates of 40 percent for ertapenem and 51 percent for cefotetan, while similar to historical controls, suggest that measures beyond antimicrobial prophylaxis need to be prioritized for these elective colorectal surgical cases. Several of the independent risks in the final model suggest potentially modifiable risks such as pre-operative weight reduction, appropriate hair removal, tobacco cessation, and improved surgical techniques to reduce inadvertent perforation and fecal spillage. Second, it is probably true that a single dose of antimicrobial prophylaxis is less likely to produce the emergence of drug-resistant microorganisms than is repeated administration. However, only 67 percent of surgeons discontinued antibiotic prophylaxis within 24 hours of surgery, and thus carbapenem resistance associated with widespread use of ertapenem prophylaxis is of concern.2-4 Third, excess costs of a new drug need to be considered in practice-change scenarios, especially in developing countries. Furthermore, in developing countries a few, if any, antibiotic control programs exist, multidrug-resistant Gram-negative bacilli are prevalent and the duration of post-operative antibiotic use often goes unchecked.5-6 I, therefore, emphasize the need of caution as the

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findings in this study are balanced with anticipated ongoing drug supplies and future antibiotic prophylaxis guidelines.

References