Intra-abdominal Infections: Do we Need to Change Our Antibiotic Coverage in this Era of Gram Negative Resistance?

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Antimicrobial resistance in Gram negative bacteria has been on the rise in India, and the year 2010 has witnessed the emergence of a novel carbapenemase as a mechanism of resistance in Enterobacteriaceae. However, well before carbapenemase production emerged in E.coli and Klebsiella, these organisms were producing extended spectrum beta-lactamases (ESBLs), which rendered them non-susceptible to most antibiotic classes. Clinicians in Indian hospitals have therefore come to rely on beta-lactam/beta-lactamase combinations and, for serious infection, carbapenems for the empirical therapy of infectious disease syndromes where ESBL producers may be present.

Intra-abdominal infections are common diagnoses in hospitalized patients and require optimal surgical management, in addition to appropriate antibiotics, for an optimal outcome. Surgical source control is central to the management and sometimes, as in acute appendicitis, the only intervention needed. Depending on the site of the infection, bowel anaerobes and Enterobacteriaceae are the target pathogens against which adjunctive empirical antimicrobial therapy is directed. Recent international guidelines emphasize these principles, including the need to factor in local antimicrobial susceptibility patterns when selecting an appropriate empiric regimen.

This issue of JAPI carries two valuable but seemingly contradictory articles on the microbiology of, and antibiotic treatment options for, intra-abdominal infections. Chaudhuri and co-authors have studied a large compilation of isolates from patients admitted with intra-abdominal infections in 9 tertiary care hospitals spread all over India. They took care to include only samples obtained by aseptic aspiration or at surgery and specifically excluded cultures from drains or stools, which would probably reflect colonization. The majority of the isolates (82%) were either E.coli or Klebsiella, and as expected, 79% and 70% of these respectively were ESBL producers. While carbapenems generally remained effective against the majority of isolates, amikacin and piperacillin-tazobactam showed significantly less activity against ESBL producers, this drop-off being more pronounced for Klebsiella. A drawback of this otherwise well done microbiological study includes the lack of testing for susceptibility versus cefoperazone-sulbactam and tigecycline, which are both valuable drugs in intra-abdominal infections. The absence of clinical data, antibiotic exposure and data on outcome also limit our ability to draw clinical conclusions. However this large study reinforces the need to consider empiric coverage for ESBL producers in patients with severe intra-abdominal infections.

A second smaller study by Gupta and co-authors attempts to clinically correlate clinical outcomes with antibiotic selection in intra-abdominal infections. About one half of the 221 patients they studied did well with surgery alone. Even among the patients with complicated infections who got initially inappropriate antibiotics, only one needed to switch to a carbapenem. The authors conclude that routine use of carbapenems or beta-lactam/beta-lactamase inhibitors for ESBL coverage in intra-abdominal infections is unnecessary and pathogen directed therapy with older antibiotics suffices in most cases. A small sample size and the non-randomized retrospective nature of this study are obvious limitations.

Are these results contradictory? Not really. As any surgeon will tell you, the key intervention in any intra-abdominal infection is timely and adequate surgical intervention. The patient with acute appendicitis who goes to the operating theater early will do well even without antibiotics. Even when there is a severe infection such as an abscess or a perforation, thorough source control and reasonably narrow spectrum antibiotics will suffice. However if the same patient presents a few days later or is not operated on early and adequately, broad spectrum antibiotics active against ESBL producers may be needed as a life saving measure. One may even need to cover for carbapenemase producers in severely ill patients who have been exposed to antibiotics earlier.

So what is the take home message in intra-abdominal infections? Call the surgeon quickly; if not, you may well need to broaden your antibiotic spectrum in this era of Gram negative resistance.

References
