Empirical Enterococcal Coverage for Complicated Intra-Abdominal Infection

To the Editor—All new or updated Infection Diseases Society of America (IDSA) guidelines allow us to be in a privileged position to take advantage of an authoritative review of current knowledge and best practices on a given topic. The recent IDSA guidelines on the diagnosis and management of complicated intra-abdominal infection in adults and children [1] are no different, and I commend the authors for the amount of work that was necessary to write the manuscript.

However, on the topic of empirical enterococcal coverage for abdominal infections, there are some inconsistencies that should be addressed to clarify the recommended approach. Whether enterococci are significant pathogens in intra-abdominal infections has been a matter of much debate and research. On one hand, there have been several well-designed trials showing no clinical benefit associated with empirical enterococcal coverage [2, 3]. Conversely, prospective trials have demonstrated increased mortality among patients with documented enterococcal infection, particularly in those patients with health care–associated intra-abdominal infection [4, 5]. On the basis of these data, I agree with the position stated on pages 150 and 151 of the guidelines that it seems reasonable and appropriate to provide empirical enterococcal coverage both for high-risk community-acquired intra-abdominal infections and for all health care–associated intra-abdominal infections.

Recommendations at odds with the above are, however, to be found in Table 2 of the guidelines, in which “Cefepime, ceftazidime, ciprofloxacin, or levofloxacin, each in combination with metronidazole” are suggested as appropriate regimens for high-risk, community-acquired intra-abdominal infections. These regimens provide no—or, in the case of levofloxacin, extremely poor—enterococcal coverage. This is clearly inconsistent with the statement in point 42: “Empirical use of agents against enterococci is recommended” [1, p 136].

Along the same lines, point 34 states that “Empiric coverage of Enterococcus is not necessary with community-acquired intra-abdominal infection” [1, p 136]. This is under the heading of mild-to-moderate infections and is therefore congruent with the rest of the guidelines. Nevertheless, for clarity, this statement should probably be revised to state, “Empiric coverage of Enterococcus is not necessary with mild-to-moderate community-acquired intra-abdominal infection.”

Similar issues can be found in the recommendations for healthcare-associated infections. Table 3 offers “Ceftazidime or ceftazidime, each with metronidazole” for the aforementioned indication in institutions with a low prevalence of multidrug-resistant infections with gram-negative organisms. This is at odds with the statement in point 55: “Empiric anti-enterococcal therapy is recommended for patients with health care–associated intra-abdominal infection, particularly those with post-operative infection, those who have previously received cephalosporins or other antimicrobial agents selecting for Enterococcus species, immunocompromised patients, and those with valvular heart disease or prosthetic intravascular materials” [1, p 137].

These incongruities do not detract from the overall quality of the guidelines. In my opinion, an update to clarify these points would, nonetheless, be welcomed.

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References

For the Editor—In his excellent assessment of the recent literature and guidelines, Tarchini [1] highlights the difficulties in making evidence-based recommendations for the management of enterococci in intra-abdominal infections [2]. The panel discussed at some length the placement of the enterococcal therapy recommendations, particularly those for high severity community-acquired infections. There was not sufficiently broad consensus for any approach to warrant any level of recommendation. It was decided, therefore, to mention this in text without implying that this carried the same level of evidence or comfort as did the other elements in Table 2.

Regarding the addition of anti-enterococcal therapy to empirical therapy for health care–associated infection, my colleagues and I agree with the concern Tar- chini [1] has regarding a close connection between Table 3 and recommendation 55. However, that table, as with all of the tables, was intended as a summary of the more complete material in text. Therefore, how much detail to insert in the tables became an assessment of relative priorities.

Piacenti [3] raises several important points that focus attention on our handling of stewardship concerns. An overarching concern to the panel was for the incorporation of material on how these guidelines would fit into antibiotic stewardship efforts. We chose to handle this by recommending that local hospitals develop a specific pathway for handling appendicitis, a disease that accounts for a predominant share of complicated intra-abdominal infections. This specific disease was chosen simply because these patients are overwhelmingly a unique group and do not have those patient-specific factors that would frequently alter antimicrobial or interventional strategies. Such necessary changes in an individual patient’s treatment was felt to vastly complicate broader pathways to the point of this pathway being useless.

In constructing recommendations for mild-to-moderate severity disease for an evidence-based review, we included erta- penem, moxifloxacin, and tigecycline because there are data from level 1 studies on their use in this setting. These agents have been approved by the US Food and Drug Administration for the treatment of complicated intra-abdominal infections and are used for this indication. Table 2 is not entitled, “recommended Agents,” but rather “Agents and Regimens That May Be Used for the Initial Empiric Treatment of Extra-biliary Complicated Intra-abdominal Infections.”

The evidence summary describes stewardship concerns for empirical therapy directed at extended-spectrum β-lacta- mase–producing organisms when these are locally uncommon and for coverage of methicillin-resistant Staphylococcus au- reus when it is an unlikely pathogen. Recom- mendation 39 is given over to these concerns. In other text, the benefits of generic agents and cephalosporin/metroni- dazole combinations are mentioned.

Recommendation 39 deals with the percentage incidence of resistance that requires a change in empirical regimens for common isolates, including Escherichia coli and Bacteroides fragilis. Quinolon-re- sistant E. coli is commonly an extended- spectrum β-lactamase (ESBL)–producing organism. The recommendation is specific for quinolones, but it was part of a broad recommendation that specifically dealt with ESBLs in Table 8.

Piacenti [3] is also concerned about the use of a 1987 study and describes his concerns regarding the microbiological aspects of that study. We did not include that study as evidence for or against single-agent or combination therapy. That study was included because it provided the strongest data available on the importance of empirical therapy given at the time of operation. This is accepted surgical prac- tice. I doubt any surgeon or institutional review board would allow a controlled trial involving withholding of such therapy.

With regards to the concerns about our recommendation for the use of agents such as piperacillin-tazobactam, cefepime- metronidazole, or carbapenems for high- severity, high-risk infection, our recom- mendation was not made on the basis of clinical trials data showing superior outcome. We clearly stated this in the evidence summary. Conversely, none of the panel members suggested administration of first- or second-generation cephalosporins in these critically ill patients.

Piacenti [3] is further concerned that the definition we provided for high-se- verity, high-risk infection incorporates most infections among admitted pa- tients. The distribution of severity of ill- ness measures (for example, the Acute Physiology and Chronic Health Evaluation [APACHE] II score) is well known for complicated intra-abdominal infections and is heavily weighted to a younger, healthier group with low scores. This is because appendicitis is the most common complicated intra-abdominal infection treated. Similarly, “immuno- compromise,” as defined in this guide- line, is not common.

Experienced microbiologists and infectious disease practitioners on this panel uniformly agreed ampicillin-sulbactam should not be used. I regret the inaccurate citation but believe that problems with this agent are widely and well known. I appreciate Piacenti supplying the correct citations.

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