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Surveillance

Antimicrobial susceptibility of common pathogens isolated from postoperative intra-abdominal infections in Japan

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ABSTRACT

The principle of empirical therapy for patients with intra-abdominal infections (IAI) should include antibiotics with activity against Enterobacteriaceae and *Bacteroides fragilis* group species. Coverage of *Pseudomonas aeruginosa*, *Enterobacter cloacae*, and *Enterococcus faecalis* is also recommended for hospital-associated IAI. A nationwide survey was conducted to investigate the antimicrobial susceptibility of pathogens isolated from postoperative IAI. All 504 isolates were collected at 26 institutions and referred to a central laboratory for susceptibility testing. Lower susceptibility rates to ciprofloxacin and cefepime were demonstrated in *Escherichia coli*. Among *E. coli*, 24.1% of strains produced extended-spectrum β-lactamase (ESBL). Carbapenems, piperacillin/tazobactam, cephamycins/oxacephem, aminoglycosides, and tigecycline had high activity against *E. coli*, including ESBL-producing isolates. Among *E. cloacae*, low susceptibility rates to ceftazidime were demonstrated, whereas cefepime retained its activity. *P. aeruginosa* revealed high susceptibility rates to all antimicrobials tested except for imipenem. Among *B. fragilis* group species, low levels of susceptibility were observed for cefoxitin, moxifloxacin, and clindamycin, and high susceptibility rates were observed for piperacillin/tazobactam, meropenem, and metronidazole. Ampicillin, piperacillin, and glycopeptides had good activity against *E. faecalis*. Imipenem had the highest activity against *E. faecalis* among carbapenems. In conclusion, we suggested the empirical use of antimicrobials with the specific intent of covering the main organisms isolated from postoperative IAI. Piperacillin/tazobactam, meropenem, or doripenem, are appropriate in critically ill patients. Combination therapy of cefepime (aztreonam in patients with β-lactam allergy) plus metronidazole plus glycopeptides, imipenem/cilastatin or cephamycins/oxacephem plus ciprofloxacin plus metronidazole are potential therapeutic options.

1. Introduction

Complicated intra-abdominal infections (IAI) lead to abscess formation or generalized peritonitis, and patients with IAI are at risk of sepsis and mortality. Clinical guidelines [1–4] include recommendations for source control and appropriate selection of antimicrobial agents on the basis of high-quality evidence. A treatment effect of antibiotics would not be expected unless source control was adequately performed [5]. However, late treatment failure occurring after 48 h is likely a failure of antimicrobial therapy caused by resistant organisms [2]. As resistant organisms could cause infection in patients with postoperative IAI, alternative selection of empirical antimicrobial therapy is recommended compared with community-acquired IAI [1,2]. Recent guidelines by the Surgical Infection Society (SIS) [2] recommended carbapenems except for ertapenem, piperacillin/tazobactam (PIPC/TAZ), and combination therapy with cefepime (CFPM) plus metronidazole (MNZ) in patients with healthcare- or hospital-associated IAI.

Because prevalence of resistant organisms has been increasing, it is reasonable that the choice of empirical antimicrobial therapy in patients with postoperative IAI is modified in reference to contemporary antibiotic susceptibility data among common isolates from postoperative IAI. The results of Japanese nationwide surveillance of antimicrobial susceptibility of organisms isolated from surgical site infections (SSI) were published recently [6,7]. To better understand the results, we carried out a post-hoc analysis of the data to explore antimicrobial susceptibility patterns of common organisms isolated from postoperative IAI and suggested appropriate primary and alternative antibiotic therapies for patients with postoperative IAI with the specific intent of covering these common organisms isolated from postoperative IAI.

2. Methods

This study was performed based on the post-hoc analysis of nationwide surveillance data of antimicrobial susceptibility of organisms isolated from SSI conducted by the Japanese Surveillance Committee, which comprised the Japanese Society of Chemotherapy, the Japanese Association for Infectious Diseases, and the Japanese Society for Clinical Microbiology [7]. This study was approved by the research ethics committee of Hyogo College of Medicine (No. 2858).

Postoperative IAI was diagnosed by radiological examination or intraoperative observation within 30 days after an operation. Samples obtained from surgical intervention (laparotomy or percutaneous drainage of an abscess), intra-abdominal drain inserted intraoperatively, or biliary drainage tube were cultured. Seven main organisms isolated from postoperative IAI (*Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Pseudomonas aeruginosa*, *Bacteroides fragilis* group species, *Staphylococcus aureus*, and *Enterococcus faecalis*) were collected at 26 medical centers around Japan between January 2014 and February 2015 and referred to a central laboratory (Research Center for Anti-infective Drugs at Kitasato Institute, Tokyo, Japan) for testing. MALDI Biotyper (Bruker Daltonics K.K., Kanagawa, Japan) was used for the identification of *B. fragilis* group species. All isolates were tested for antimicrobial susceptibility using the broth microdilution method, as described by the Clinical and Laboratory Standards Institute (CLSI) [8], and CLSI breakpoints were adopted. European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints [9] were used when CLSI breakpoints were unavailable. The following formula was used to calculate the geometric mean minimum inhibitory concentration (MIC):

$$\overline{x}_g = \left(\prod_{i=1}^{n} x_i \right)^{\frac{1}{n}}$$

where n is the total number of values and x_i (x_2, x_1, …,x_n) are the individual numbers in the data set.

Tested antibiotics are listed in Table 1. Susceptibility testing was not performed if organisms were considered to have natural resistance. For susceptibility testing of PIPC/TAZ, the concentration of tazobactam was fixed at 4 μg/mL. The Cica-Beta Test (Kanto Chemical, Tokyo, Japan) was used to detect extended-spectrum β-lactamase (ESBL)- and carbapenemase-producing

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