Journal of Infection (2014) 68, 71–76

BIAMM British Infection Association

www.elsevierhealth.com/journals/jinf

Susceptibility of gram-negative aerobic bacilli from intra-abdominal pathogens to antimicrobial agents collected in the United States during 2011

Stephen P. Hawser [a,*], Robert E. Badal [b], Samuel K. Bouchillon [b], Daryl J. Hoban [b], Meredith A. Hackel [b], Douglas J. Biedenbach [b], Debra A. Goff [c]

[a] *IHMA Europe Sàrl, 1066 Epalinges, Switzerland*
[b] *International Health Management Associates, Inc., Schaumburg, IL 60173-3817, USA*
[c] *The Ohio State University Wexner Medical Center, Columbus, OH 43210, USA*

Accepted 1 September 2013
Available online 7 September 2013

KEYWORDS
Ertapenem;
Susceptibility;
Trends;
SMART;
Intra-abdominal;
USA

Summary *Objectives:* During 2011, a total of 1442 gram-negative pathogens from intra-abdominal infections were collected as part of the Study for Monitoring Antimicrobial Resistance Trends (SMART) from 19 hospital sites within the United States. Susceptibility to ertapenem and comparators and molecular analysis of ertapenem resistant isolates was performed.
Methods: Extended-spectrum beta-lactamase ESBL (ESBL) isolates were determined using the Clinical and Laboratory Standards Institute's recommended phenotypic test. Isolates were identified to the species level, and tested for antimicrobial susceptibility using custom MicroScan dehydrated broth microdilution panels ESBLs and carbapenemases were characterized using the Check-Points microarray. Strain typing of *Klebsiella pneumoniae* was performed by rep-PCR on the DiversiLab System.
Results: The majority of isolates were *Escherichia coli* (36%), *K. pneumoniae* (18.6%), *Pseudomonas aeruginosa* (12.1%) and *Enterobacter cloacae* (8.4%). Incidence of ESBL-positive isolates was 12.7%, 9.7%, 3.6% and 3.1% for *K. pneumoniae*, *E. coli*, *Proteus mirabilis* and *Klebsiella oxytoca*, respectively. Against the majority of isolates and species tested, the most active antibiotics were amikacin, ertapenem, and imipenem, with the carbapenems being the most active *in vitro*, including against ESBL-positive isolates of *E. coli*. All other antibiotics exhibited diminished activity. Against *K. pneumoniae*, the carbapenems were notably less active against ESBL-positive isolates though their activity against this sub-population was still the highest of

* Corresponding author. IHMA Europe Sàrl, 9A Route de la Corniche, 1066 Epalinges, Switzerland. Tel.: +41 216519030; fax: +41 216519009.
E-mail address: shawser@ihmainc.com (S.P. Hawser).

http://dx.doi.org/10.1016/j.jinf.2013.09.001

all antibiotics tested; however, 41.1% (14 of 34) of the phenotypically ESBL-positive *K. pneumoniae* co-produced a carbapenemase (KPC2 or KPC3), and >90% of the isolates producing only an ESBL remained susceptible to ertapenem.
Conclusions: Further monitoring of susceptibility of intra-abdominal isolates is warranted due to limited therapeutic options available to physicians.

Introduction

Intra-abdominal infections (IAIs), including those from surgical sites, are frequently encountered in the healthcare setting and the majority of pathogens are Gram-negative bacilli from IAIs. These Gram-negative pathogens contribute to increased mortality, healthcare costs and length of stay.[1,2] The most commonly isolated aerobic gram-negative species in IAIs are *Escherichia coli* and *Klebsiella* spp., including extended-spectrum beta-lactamase (ESBL) producing isolates, *Proteus* spp., *Enterobacter* spp., and *Pseudomonas aeruginosa*.[3] A variety of antimicrobial agents are recommended for the treatment of IAIs but the utility of many of these agents have become restricted over time due to increasing resistance rates. Recommended agents include the carbapenems (ertapenem, imipenem, and meropenem) and piperacillin-tazobactam. Cephalosporins and fluoroquinolones, with the exception of moxifloxacin which can be used as monotherapy, are also recommended though their utility is evident only when used in combination with other drugs.[3]

The SMART program monitors the susceptibility of gram-negative bacilli from IAIs to ertapenem and comparators, and has been ongoing since 2002, with nearly 200 hospitals participating worldwide in 2011. A total of nineteen hospitals were involved in SMART in the United States (US) during 2011. To date, the data from this study have demonstrated generally high worldwide and regional ertapenem susceptibility.[4–8] While ertapenem and carbapenem susceptibilities have remained high it is noteworthy to mention that since the emergence of metallo-beta-lactamases and carbapenemases the effectiveness of carbapenem therapy is speculated to become more limited.[9–12] The current report describes data from SMART 2011 from the United States and highlights susceptibility of the major gram-negative pathogens isolated including ESBL-positive isolates.

Materials and methods

Clinical isolates

A total of 1442 clinical isolates from both community- and hospital-associated IAI, were collected from 19 hospital sites throughout the United States during 2011. Most of the centers, 80%, were from the Eastern United States while 20% were from the Pacific and Mountain regions. The majority of the isolates, 60%, came from nine university/teaching centers and one reference laboratory, while 40% came from nine private/community hospitals. The size of the collection centers ranged from 110 to 2000 beds. All organisms were deemed clinically significant by local participant criteria. Isolate inclusion was independent of antimicrobic use, age, or gender. Only one isolate per species per patient was accepted into the study. Up to 100 consecutive, non-selected gram-negative aerobic and facultative bacilli from each participating hospital were cultured from specimens from intra-abdominal body sites (e.g., appendix, peritoneum, colon, bile, pelvis, and pancreas). The majority of intra-abdominal specimens were obtained during surgery, though some paracentesis specimens were also accepted. Sixteen percent of isolates were obtained from ICUs, 70% were obtained from general medical units, and 14% came from unspecified locations. Isolates from blood, urine, and perirectal abscesses were excluded. No identifiable patient-specific information, including symptoms, diagnosis or accession numbers, was recorded; IRB approval was obtained at the local institutional level as required.

Susceptibility testing

Isolates were identified to the species level, and tested for antimicrobial susceptibility using custom MicroScan dehydrated broth microdilution panels (Siemens Medical Solutions Diagnostics, West Sacramento, CA, USA) at a central laboratory (Laboratories International for Microbiology Studies, a subsidiary of International Health Management Associates, Inc., Schaumburg, Illinois, USA). Development and maintenance of a combined database of study results was managed by the central laboratory.

MicroScan minimum inhibitory concentration (MIC) panels were set up following the manufacturer's and Clinical and Laboratory Standards Institute (CLSI) guidelines.[13] The following antimicrobial agents were included on the panels with their dilution ranges (expressed in mg/L): ertapenem 0.03—4, imipenem 0.06—8, cefepime 0.5—32, ceftazidime 0.5—128, ceftazidime-clavulanic acid 0.12/4—16/4, cefoxitin 2—16, ciprofloxacin 0.25—2, amikacin 4—32, levofloxacin 0.5—4, cefotaxime 0.5—128, cefotaxime-clavulanic acid 0.12/4—16/4, piperacillin-tazobactam 2/4—64/4, ampicillin-sulbactam 2/2—16/2, and ceftriaxone 1—32. MIC interpretive criteria of the CLSI were followed.[14] Using CLSI guidelines, *E. coli* were classified as ESBL producers if there was at least an eight-fold reduction (i.e., three doubling dilutions) of the MIC for ceftazidime or cefotaxime tested in combination with clavulanic acid versus their MICs when tested alone.[14]

Quality control

Quality control testing (QC) was performed each day of testing using the CLSI recommended QC strains: *E. coli*