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Epidemiology and trends in the antibiotic susceptibilities of Gram-negative bacilli isolated from patients with intra-abdominal infections in the Asia-Pacific region, 2010–2013

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ABSTRACT

This study was conducted to investigate the epidemiology and antimicrobial susceptibility patterns of Gram-negative bacilli (GNB) isolated from intra-abdominal infections (IAIs) in the Asia-Pacific region (APR) from 2010–2013. A total of 17 350 isolates were collected from 54 centres in 13 countries in the APR. The three most commonly isolated GNB were *Escherichia coli* (46.1%), *Klebsiella pneumoniae* (19.3%) and *Pseudomonas aeruginosa* (9.8%). Overall, the rates of extended-spectrum β-lactamase (ESBL)-producing *E. coli* and *K. pneumoniae* were 38.2% and 24.3%, respectively, and they were highest in China (66.6% and 38.7%, respectively), Thailand (49.8% and 36.5%, respectively) and Vietnam (47.9% and 30.4%, respectively). During 2010–2013, the rates of ESBL-producing *E. coli* and *K. pneumoniae* isolates causing community-associated (CA) IAIs (collected <48 h after admission) were 26.0% and 13.5%, respectively, and those causing hospital-associated (HA) IAIs were 48.0% and 30.6%, respectively. Amikacin, ertapenem and imipenem were the most effective agents against ESBL-producing isolates. Piperacillin/tazobactam displayed good in vitro activity (91.4%) against CA ESBL-producing *E. coli*. For other commonly isolated Enterobacteriaceae, fluoroquinolones, cefepime and carbapenems exhibited better in vitro activities than third-generation cephalosporins. Amikacin possessed high in vitro activity against all GNB isolates (>80%) causing IAIs, except for *Acinetobacter calcoaceticus–baumannii* (ACB) complex (30.9% for HA-IAI isolates). All of the antimicrobial agents tested exhibited <45% in vitro activity against ACB complex. Antimicrobial resistance is a persistent threat in the APR and continuous monitoring of evolutionary trends in the susceptibility patterns of GNB causing IAIs in this region is mandatory.

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1. Introduction

Intra-abdominal infections (IAIs) are common infectious diseases caused by Gram-negative bacilli (GNB). They result in high mortality and morbidity rates in the intensive care unit clinical setting [1] and 3–30% mortality rates in community-acquired IAIs [2]. The cost of care is closely related to the incidence of inappropriate initial therapy and subsequent clinical failure [2]. Increasing antimicrobial resistance of GNB has been observed globally [3] and is a great medical burden.

The Study for Monitoring Antimicrobial Resistance Trends (SMART) is a global surveillance programme initiated in 2002 to investigate the antimicrobial susceptibility of GNB in IAIs and to serve as a horizontal and longitudinal observation of epidemiological trends. A high level of antimicrobial resistance in the Asia-Pacific region (APR) has been well described by many prior reports from the SMART programme [4,5]. The particularly high prevalence rates of extended-spectrum β-lactamase (ESBL)-producing isolates in the APR are also well known [5–7] and they pose great challenges for physicians making decisions regarding empirical treatment. The present study updates the epidemiology and antimicrobial resistance patterns among common Gram-negative pathogens isolated in IAIs in the APR from 2010–2013. Part of these study data regarding the distribution of ESBLs, AmpC β-lactamases and carbapenemases among Enterobacteriaceae isolates causing intra-abdominal and urinary tract infections have been recently published [8].

2. Patients and methods

2.1. Study centres and isolates

There were 54 centres in 13 countries in the APR included in the SMART programme of IAIs from 2010–2013, namely Australia (5 centres), China (17), Hong Kong (2), Japan (3), Kazakhstan (1), Malaysia (2), New Zealand (4), Singapore (2), South Korea (2), Taiwan (8), Thailand (2), The Philippines (2) and Vietnam (4). A total of 100 consecutive, non-duplicate GNB isolates causing IAIs were prospectively collected from all participant sites each year. All isolates were cultured from specimens obtained from intra-abdominal body sites (appendix, peritoneum, colon, bile or pancreas). Isolates recovered from blood, urine and perirectal abscess sources outside the intra-abdominal body sites were excluded by protocol. Isolates were categorised as community-associated (CA) or hospital-associated (HA) depending on the length of time between collection of clinical specimens for the recovery of isolates and hospitalisation; isolates were classified as CA if they were obtained within 48 h after admission and as HA if they were collected ≥48 h after admission.

2.2. Antimicrobial susceptibility testing

Antimicrobial susceptibility was determined by the agar dilution method and the results were interpreted according to the minimum inhibitory concentration (MIC) interpretive breakpoints recommended by the Clinical and Laboratory Standards Institute (CLSI) in 2013 [9]. The tested antimicrobial agents included amikacin (AMK), ampicillin/sulbactam (SAM) (at a 2:1 ratio), cefoxitin (FOX), ceftazidime (CAZ), ceftriaxone (CRO), cefotaxime (CTX), piperacillin/tazobactam (TZP) (at a fixed tazobactam concentration of 4 mg/L), cefepime (FEP), ertapenem (ETP), imipenem (IPM), ciprofloxacin (CIP) and levofloxacin (LVX). The double-disk synergy test was applied to determine ESBL production among isolates of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Klebsiella oxytoca* as recommended by the CLSI [9]. The reference isolates *E. coli* ATCC 25922, *E. coli* ATCC 35218 and *Pseudomonas aeruginosa* ATCC 27853 were used as positive quality control isolates.

2.3. Statistical analysis

Categorical variables were compared using the χ^2 or Fisher's exact test as appropriate. A *P*-value of <0.05 was considered statistically significant. All statistical analyses were performed using the statistical package PASW Statistics for Windows v.18.0 (SPSS Inc., Chicago, IL).

3. Results

3.1. Aetiology of intra-abdominal infections

During the study period, a total of 17 350 isolates were collected in the APR. *Escherichia coli* was the most frequently isolated pathogen (*n* = 8001; 46.1%), followed by *K. pneumoniae* (*n* = 3355; 19.3%) and *P. aeruginosa* (*n* = 1694; 9.8%). *Escherichia coli* was more commonly encountered in CA-IAIs than in HA-IAIs (51.2% vs. 43.3%). Higher rates of *P. aeruginosa* (10.8% vs. 7.9%) and *Acinetobacter calcoaceticus–baumannii* (ACB) complex (5.1% vs. 2.1%) were found in HA-IAIs than in CA-IAIs.

3.2. Distribution of extended-spectrum β-lactamase-producing isolates by country and by association with community-associated and hospital-associated infections

Fig. 1 depicts the ESBL-positive rates of *E. coli* and *K. pneumoniae* for IAIs in the APR during 2002–2013 stratified by country (Fig. 1A) and by CA- and HA-IAIs (Fig. 1B) using data obtained from previous SMART programme IAI reports [4,10,11] (data from 2009 were not available). Rates of ESBL-producing *E. coli* and *K. pneumoniae* in the APR were 38.2% and 24.3%, respectively, and they were highest in China (66.6% and 38.7%, respectively), Thailand (49.8% and 36.5%, respectively) and Vietnam (47.9% and 30.4%, respectively) in comparison with other countries in the APR. The rates of ESBL-producing *E. coli* and *K. pneumoniae* isolates (2010–2013) causing CA-IAIs were 26.0% and 13.5%, respectively, and those causing HA-IAIs were 48.0% and 30.6%, respectively. There was a trend towards rising ESBL-positive rates for *E. coli* from 2002–2007 irrespective of whether they were isolated from HA-IAIs (24.6% in 2002 and 50.7% in 2007) or CA-IAIs (6.3% in 2002 and 28% in 2007); these rates were stationary from 2007–2013. In contrast, there was no obvious increasing trend of ESBL-producing *K. pneumoniae* causing either CA- or HA-IAIs. China, South Korea, Thailand and Vietnam had high ESBL-positive rates of >20% among CA infections with *E. coli* and *K. pneumoniae* alike. Australia had the lowest ESBL-positive rates of <10% both in CA and HA infections.

3.3. Antimicrobial susceptibilities of the isolates

SAM was the least active agent, displaying ≤50% susceptibility against most of the isolates causing CA- and HA-IAIs, with the exception of the non-ESBL-producing isolates of *K. pneumoniae*, *K. oxytoca* and *P. mirabilis* (63.3–82.8%) (Table 1). CIP and LVX exhibited poor potency among all ESBL-producing isolates, particularly *E. coli*, which had <30% susceptibility to these agents.

Third- and fourth-generation cephalosporins and TZP resulted in >90% susceptibility in non-ESBL-producing isolates of *E. coli*, *K. pneumoniae*, *K. oxytoca* and *P. mirabilis*. However, reduced activities were observed with CRO, CTX and CAZ against other commonly isolated Enterobacteriaceae. ETP and IPM exhibited good activity with >90% susceptibility against most Enterobacteriaceae. It is of note that IPM had reduced potency against *Citrobacter freundii*, *Enterobacter cloacae*, *Enterobacter aerogenes* and *Serratia marcescens* (78.2–93.0%) and very low potency (14.0%–45.5%) against *Morganella morganii* and *P. mirabilis* isolates.