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Review

Antibiotic management of complicated intra-abdominal infections in adults: The Asian perspective

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HIGHLIGHTS

- We propose updated recommendations for antibiotic management of cIAIs in Asia.
- Literature from Asian and international publications are reviewed and compared.
- Antimicrobial resistance in key pathogens causing IAIs in Asia is presented.
- Expert consensus of the Asian Taskforce members is also included.

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ABSTRACT

Regional epidemiological data and resistance profiles are essential for selecting appropriate antibiotic therapy for intra-abdominal infections (IAIs). However, such information may not be readily available in many areas of Asia and current international guidelines on antibiotic therapy for IAIs are for Western countries, with the most recent guidance for the Asian region dating from 2007. Therefore, the Asian Consensus Taskforce on Complicated Intra-Abdominal Infections (ACT-cIAI) was convened to develop updated recommendations for antibiotic management of complicated IAIs (cIAIs) in Asia. This review article is based on a thorough literature review of Asian and international publications related to clinical management, epidemiology, microbiology, and bacterial resistance patterns in cIAIs, combined with the expert consensus of the Taskforce members. The microbiological profiles of IAIs in the Asian region are outlined and compared with Western data, and the latest available data on antimicrobial resistance in key pathogens causing IAIs in Asia is presented. From this information, antimicrobial therapies suitable for treating cIAIs in patients in Asian settings are proposed in the hope that guidance relevant to Asian practices will prove beneficial to local physicians managing IAIs.

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1. Introduction

Management of complicated intra-abdominal infections (cIAIs) in Asia remains challenging, and differs in important aspects from practices in the West. Disease patterns differ, and available resources including operating facilities, ancillary personnel and imaging equipment vary from one region to another. Importantly, microbial resistance and access to specific antimicrobial agents varies from region to region.

Available guidelines on the management of cIAIs are predominantly written for the Western context [1,2], although Asian guidance on antimicrobial therapy for cIAIs has been previously developed [3]. The current document outlines the microbiological profiles of IAIs in the Asian region for comparison with the West, and explores antimicrobial resistance in key pathogens causing IAIs in Asia. We also provide updated guidance on antimicrobial management of cIAIs in the Asian setting.

2. Methods

The Asian Consensus Taskforce on Complicated Intra-Abdominal Infections (ACT-cIAI) met and discussed current clinical approaches to cIAI management in Asia, international guidelines on cIAI management, microbiological trends of cIAI pathogens in Asia, and the existing antibiotic options. A steering committee was formed to explore differences between Asia and the West. Where applicable, existing guidelines were consulted, including the American Infectious Diseases Society of America (IDSA)/Surgical Infection Society (SIS) guidelines, as well as published recommendations from the Asian region. Microbiology data on cIAI pathogens and data on bacterial resistance rates in Asian countries were obtained from published surveillance studies and the Tigecycline Evaluation and Surveillance Trial (TEST) database.

After a second meeting to review and refine the compiled document, the revised document was circulated to the Taskforce for final review and comments. The final document is endorsed by the International Surgical Infections Study (ISIS) Group.

3. Definitions

In accordance with the American IDSA/SIS guidelines, we are defining cIAIs as an infection that "extends beyond the hollow viscus of origin into the peritoneal space and is associated with either abscess formation or peritonitis" [1].

4. Clinical epidemiology of cIAIs in Asia

4.1. Key pathogens causing cIAIs in Asia

Chief amongst factors influencing the success of management of cIAI in Asia is the high prevalence of antimicrobial resistance, especially amongst Enterobacteriaceae. Data from the Study for Monitoring Antimicrobial Resistance Trends (SMART) [4] provide the best available evidence for the current status of cIAI infections in Asia, but limitations include the small number of contributing sites per country and the selection process for test organisms. These sites are usually major teaching or tertiary-care centers, which potentially creates sample bias. Another limitation is that in vitro susceptibility results do not necessarily predict clinical success or failure. Furthermore, although isolates are divided into those obtained from cultures collected <48 h and ≥48 h after hospital admission to differentiate community-acquired from nosocomial infections, the time of collection may not represent the true time of acquisition of infection [5]. Thus, the SMART results may not accurately reflect the patterns of pathogen distribution in community versus healthcare settings. However, the results are useful in comparing gross trends between Asia and other global regions.

Reports from Asia–Pacific countries participating in SMART confirm the polymicrobial basis for cIAI. Enterobacteriaceae were the most frequently isolated microorganisms in patients with cIAIs, comprising 68.3%–89.5% [6–8]. Of these, *Escherichia coli* and *Klebsiella pneumoniae* were the most common, like the West, with *Enterobacter* spp, including *Enterobacter cloacae*, found at lower rates. Whilst *Pseudomonas aeruginosa* featured across the world as a non-Enterobacteriaceae pathogen, *Acinetobacter baumannii* was more prominent in the Asian setting. In some areas, including Asia, *Aeromonas hydrophila* and *Citrobacter freundii* have also been implicated in these polymicrobial infections [9]. However, the pattern of bacterial causes of cIAI infections varies across the Asia–Pacific region. Table 1 shows the most common pathogens causing IAIs in selected Asian countries, alongside data from the USA and Europe [7,9–18].

4.2. Antimicrobial resistance in pathogens causing cIAIs in Asia

Isolates from Asia–Pacific countries showed the highest levels of antimicrobial resistance of the global regions included the SMART study, and a trend of increasing resistance continues year by year [5,10]. Within the region, resistance rates can vary between countries; for example, resistance in Enterobacteriaceae in China and India was higher than in the other countries of this region, especially to ampicillin–sulbactam, fluoroquinolones, and cephalosporins [8]. Updated results from ongoing monitoring continue to confirm high levels of resistance [8,18]. The high resistance rate of Enterobacteriaceae isolates to ampicillin–sulbactam supports the guideline recommendation against using ampicillin–sulbactam for patients with IAIs, especially in severe cases [1,3].

Production of β-lactamases is among the most common and clinically significant of the resistance mechanisms for Gram-negative bacilli [19]. Multiple types of β-lactamases exist (Table 2) [19,20], and bacteria usually carry several simultaneously. Clinically, the extended-spectrum β-lactamases (ESBLs) are a particular concern. [20]

4.3. ESBLs in Asia and ESBL-producing pathogens causing IAIs

ESBLs almost certainly emerged *de novo* in Asia, with early resistance studies detecting elevated levels of ESBL phenotypes, particularly among *Klebsiella* isolates and particularly in China, South Korea, Japan and India [21].

Data from the SMART study for 2005–2010 show that the Asia–Pacific region has consistently had the highest ESBL positivity rates for *E. coli*, *K. pneumoniae* and *Klebsiella oxytoca* isolated from IAIs (Fig. 1) [22]. As of 2012, ESBL production amongst targeted Enterobacteriaceae isolates in the Asia–Pacific region was higher than other geographic areas, at nearly 40% [23]. Amongst isolates from ICU patients in Vietnam and the Philippines, the prevalence of ESBL-producers was as high as 81.0% and 58.8%, respectively [23]. However, this trend is not uniform across Asia. In Taiwan, the rates of ESBL-producing *E. coli* and *K. pneumoniae* were 7.5% and 7.0%, respectively, among 610 Enterobacteriaceae isolates [8]. ESBL positivity rates were lower among isolates recovered from patients with community-acquired IAIs than those with hospital-acquired infections (3.6% vs. 13.9% for *E. coli* and 2.4% vs. 13.3% for *K. pneumoniae* isolates, respectively) [8]. Fig. 2 illustrates the marked variability across the Asia–Pacific region in the prevalence of ESBL-producing *E. coli* and *K. pneumoniae* isolates from IAIs [18].

Although not as prevalent as enterobacteria, multidrug-resistant *A. baumannii* and *P. aeruginosa* are also implicated in