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Antibiotic consumption versus the prevalence of multidrug-resistant *Acinetobacter baumannii* and *Clostridium difficile* infections at an ICU from 2014–2015

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ABSTRACT

Background: Acinetobacter baumannii strains are currently the most commonly isolated non-fermenting rods at Polish intensive care units (ICUs), and they are the dominant aetiological agents of pneumonia. This study aimed to evaluate the prevalence of *A. baumannii* isolated from patients who were hospitalised at Sosnowiec Hospital's ICU. We also investigated the drug sensitivity of *A. baumannii* in relation to antibiotic consumption expressed as the defined daily dose (DDD) and *Clostridium difficile* infection (CDI).
Methods: We performed a retrospective, laboratory-based study, which comprised consecutive, non-repetitive *A. baumannii* isolates from bloodstream infections and patients with pneumonia who were hospitalised from 2014–2015.
Results: In the analysed period, 187 *A. baumannii* strains constituted 13.5% of all pathogens from clinical samples. A total of 76.5% of these strains were extensively drug resistant. Resistance of *A. baumannii* to fluoroquinolones, amikacin, and trimethoprim/sulfamethoxazole exceeded 90%. A total of 95% of strains were resistant to imipenem and meropenem, and 100% were resistant to cephalosporins and tetracyclines. Antibiotic consumption was 191.54 DDD for 100 patient-days, and the highest use of antibiotics involved ampicillin with sulbactam. The cumulative CDI incidence rate was 2.4%.
Conclusions: In our ICU, all of the strains were extensively drug resistant and sensitive to colistin. The significantly high consumption of carbapenems, fluoroquinolones, and aminoglycosides should be reduced because the high CDI incidence is probably related to extensive antibiotic consumption.

Introduction

Among healthcare-associated infections (HAIs) in the intensive care unit (ICU), forms of infections that are dangerous to the life of patients can be distinguished, such as pneumonia, bloodstream infection (BSI), urinary tract infection, and others. The incidence of HAIs may be associated with many risk factors, such as the use of invasive diagnostic and therapeutic procedures, the environment of treatment (including technological advancement), underlying diseases, and comorbidities, which are the reasons for hospital treatment. The differences in the incidence rate suggest differences in the complexity of HAI monitoring and surveillance sensitivity in various countries, and these should be monitored to set the current benchmark for the hospital or unit (e.g., ICU). To introduce an international benchmark on healthcare-acquired infections in the

Abbreviations: ATC, Anatomic-therapeutic-chemical; BAL, Broncho-alveolar lavage; BSI, Bloodstream infections; CDI, *Clostridium difficile* infection; CI, Confidence interval; DDD, Defined daily dose; EARS, Antimicrobial Resistance Surveillance Network; ECDC, European Centre for Disease Prevention and Control; EUCAST, European Committee on Antimicrobial Susceptibility Testing; ICU, Intensive care unit; KPC, *Klebsiella pneumoniae* carbapenemase; MBL, Metallo-β-lactamases; MDR, Multidrug-resistant; OMP, Outer membrane proteins; OR, Odds ratio; PBP, Penicillin binding proteins; VAP, Ventilator-associated pneumonia; XDR, Extensively-drug resistant.

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USA, the results of CDC's National Healthcare Safety Network (CDC NHSN) surveillance should be included [1] and the results of data of low and middle income countries, such as data of The International Nosocomial Infection Control Consortium (INICC), should be commented on. Unfortunately, although device use in INICC ICUs was similar to that reported from CDC-NHSN ICUs, device-associated HAI infection rates were higher in INICC ICUs than those reported by the CDC-NHSN [2]. Data according HAIs incidence from Poland are alarming. Single-centre studies conducted in the ICU in Wrocław [3] showed that the incidence of catheter-associated urinary tract infection was higher than that in the INICC and in the NHSN report [1,21] and additionally the incidence of ventilator-associated pneumonia (VAP) [4] was 10-fold higher than that in the NHSN/CDC report [1].

HAI in ICUs have adverse effects, such as an extra length of stay and mortality. Data in Poland showed that the length of stay of patients without HAIs was 6.9 days, and it was 10.0–15.5 days longer for patients with HAI [5]. HAI-related mortality (directly and indirectly) in Polish ICUs in multicentre study in 2013–14 was 10.8% [6] same as mortality found in the European Centre for Disease Prevention and Control (ECDC) report of 2012, where the mean mortality accounted for 15% [7].

Acinetobacter baumannii strains are some of the most important opportunistic pathogens, and are responsible for most severe infections at ICUs. These strains are characterised by a high level of resistance to commonly used antibiotics and have a high mortality rate [8,9]. *A. baumannii* strains cause infections, such as VAP, surgical site infections, urinary tract infections, bacteraemia/sepsis, meningitis, endocarditis, peritonitis, and conjunctival sac infections [10,11]. Data from Poland showed that *Acinetobacter* spp. are the predominant microorganisms in HAI [5] and present a serious challenge. The risk factors of these BSIs may be in neoplasms, trauma, surgical procedures, and burns. The sources of bacteraemia are most commonly respiratory tract infections. In adults, *Acinetobacter* spp. may cause surgical site infections, leading to generalised infections, such as sepsis [10]. Antibiotic resistance among *A. baumannii* strains is related to beta-lactamase production, penicillin-binding protein alterations, permeability changes related to outer membrane proteins, and to antibiotic efflux. The genes of these enzymes may be located on plasmids (IMP, VIM enzymes) or chromosomes (OXA enzymes) [10,12]. One *Acinetobacter* spp. strain may produce several beta-lactamases with a concurrent reduction or change in outer membrane proteins or penicillin-binding proteins. This results in resistance to many drugs from the particular antibiotic group. An intensive pharmacological treatment of severe infections caused by *A. baumannii* requires long-term use of antibiotics and exposes patients to adverse effects of such therapy, such as an increased risk of *Clostridium difficile* infection (CDI) [13].

This study aimed to evaluate the prevalence of *A. baumannii* isolated from patients who were hospitalised at Sosnowiec Hospital's ICU. We also investigated the patients' drug sensitivity in relation to antibiotic consumption expressed as the defined daily dose (DDD) and CDI.

Materials and methods

For the 2 years of 2014–2015, at the Clinical Department of Anaesthesiology and Intensive Care of Saint Barbara Specialized Regional Hospital no. 5 Trauma Centre in Sosnowiec, 708 patients were hospitalised (9 688 patient-days), with an average of 13 days of hospitalisation (median length of stay: 13; 1 quartile — 13.0; 3 quartiles — 13.5), and bed occupancy of 0.80. The 16-bed department used in this study is a teaching unit where continuous training of students and residents occurs.

Infections were diagnosed and qualified according to the ECDC definitions. BSI and VAP cases were registered (http://ecdc.europa.eu/en/publications/Publications/healthcare-associated-infections-HAI-ICU-protocol.pdf, accessed 23.06.2017). In each case, clinical samples were collected for microbiological studies to identify the aetiological agent of infection. BSI was indicated by a positive blood culture and VAP was identified by bronchoalveolar lavage with 10^4 cfu/ml. The bacterial strains were analysed at the Department of Microbiology of the Laboratory Diagnostic Centre at Saint Barbara Specialized Regional Hospital no. 5 — Trauma Centre in Sosnowiec. Only non-repetitive isolates of *A. baumannii*, excluding strains originating from one patient or from the same infection case, were analysed.

The strains were identified using BD Phoenix NID cards of the automated Phoenix 100 Becton Dickinson Diagnostic System (Beckton Dickinson, Warszawa, Poland) according to the manufacturer's instructions, without molecular techniques.

Overall, 187 strains of *A. baumannii* were isolated, and these comprised 13.54% of the total bacterial isolates from clinical samples among all clinical types of infection in the ICU (Table 1). Additionally, information regarding 17 cases of CDI was confirmed by a *Clostridium difficile* A + B cassette test (Stamar, Dąbrowa-Górnicza, Poland).

Evaluation of drug sensitivity

Sensitivity of *A. baumannii* to antimicrobials was examined by the automated Phoenix 100 system. NMIC/ID-204 combo panels were used to measure drug sensitivity. The sensitivity to colistin was validated with the COLISTIN CO 256 E-test (BioMérieux, Marcy IÉtoile, France), as per the manufacturer's instructions. The results of drug sensitivity examinations were interpreted according to the European Committee on Antimicrobial Susceptibility Testing criteria [14].

Detection of the carbapenemases metallo-β-lactamase and Klebsiella pneumoniae *carbapenemase*

Testing for metallo-β-lactamase (MBL) was performed using a phenotypic screening test with EDTA [15]. For phenotypic MBL analyses, Becton Dickinson discs with imipenem (10 μg) and ceftazidime (30 μg), and the MBL inhibitor EDTA (GRASO, Starogard Gdański, Poland) were used.

For phenotypic screening tests of *Klebsiella pneumoniae* carbapenemase (KPC), chromogenic media for rapid identification of carbapenem-resistant strains was applied: CHROMagar KPC medium (GRASO, Starogard Gdański, Poland) and meropenemem discs (10 μg) (Becton Dickinson, Sparks, MD, USA) plus boronic acid (GRASO, Starogard Gdański, Poland) [16].

Multidrug resistance

The resistant and intermediate strains were grouped together as drug resistant. Multidrug-resistant strains were defined as not susceptible to one antimicrobial in at least three different antimicrobial classes. Extensively drug resistant (XDR) strains were defined as susceptible to no more than two antimicrobial classes [15,18].

Antibiotic consumption

The aggregate sum of the number of the defined daily dose (DDD) according to the ATC/DDD system of the World Health Organization (Anatomical Therapeutic Chemical, group "J01" [17]). Only antibiotics for systemic use were taken into account — no antifungal (J02), antimycobacterial (J04), or antiviral (J05) drugs were included in the analyses. The data referring to used quantities of

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