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ACINETOBACTER BAUMANNII NOSOCOMIAL INFECTIONS

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Nosocomial infections caused by strains Acinetobacter baumannii strands are a growing clinical problem.The occurrence of multidrug-resistant strands is observed and that limits the ways of therapy considerably.

The aim of the study was to determine the rate of infection and susceptibility spectrum of the species Acinetobacter baumannii isolated from patients treated at Maria Skłodowska-Curie Memorial Hospital in Zgierz with particular emphasis on surgical wards.

Materials and methods. The material consisted of Acinetobacter baumannii isolates were obtained from samples of materials from patients treated at Maria Skłodowska-Curie Memorial Hospital in Zgierz from January to December 2011. Isolated bacterial strains were cultured at microbiological substrates. Isolates were identified to species using the VITEK 2 GN card (bioMérieux) and Vitek 2 automated system (bioMérieux). Susceptibility towards antibiotics of particular strains was determined by the means of AST NO 93 card. In the case of resistance towards carbapenem, the MIC was marked by E-test with Mueller Hinton substrate. The occurrence of MBL was verified by the means of disc system with Mueller Hinton substrate.

Results. We have shown that total number of Acinetobacter baumannii infections at hospital was 140 (10,31% of total results of cultures). Percentage of Acinetobacter baumannii infections at wards: Intensive Care Unit 48%, Surgical Departments 20%, Internal Diseases Department 16%, Neurology 13%, other wards – 3%.

The susceptibility percentage of Acinetobacter Baumannii against antibiotics: colistin 90%, imipenem 64%, meropenem 43%, ampicillin-sulbactam 28%, amikacin 27%, gentamicin 24%, cefepime 9%, ceftazidime 7%, ciprofloxacin 7%

Conclusions. Acinetobacter baumannii infections are a significant proportion of nosocomial infections. Most relate to surgical wards and ICUs. Acinetobacter baumannii is resistant against most antibiotics. The highest percentage of sensitivity demonstrated for colistin and carbapenems.

Key words: Acinetobacter baumannii, nosocomial infections, multidrug-resistant

Acinetobacter baumannii (A. baumannii) infections are a growing clinical problem affecting all countries of the world. A. baumannii is one of the most prevalent bacterial species isolated from biological material from hospitalised patients (1).

A. baumannii is a Gram-negative, aerobic, immotile, glucose non-fermentative, oxidase negative, catalase positive bacterium (2). It belongs to the genus Acinetobacter which comprises many species discovered during the last 3 decades, including A. baumannii, A. johnsonii, A. haemolyticus, A. calcoaceticus, A. junii and A. lwoffii. By nature, species belonging to Acinetobacter spp. are less susceptible to antibiotics than other bacteria, especially in comparison with the species of the Enterobacteriaceae family (3). Due to an exceptional ability to adapt to unfavourable hospital conditions and resistance to antibiotics and disinfectant agents, Acinetobacter baumannii poses a significant threat to patients. Low

nutritional requirements and the ability to form biofilms ensure greater resistance to desiccation, allowing the species to survive about 27 days on dry surfaces (4). Moreover, strains isolated from dry environments have higher survivability than those from wet environments (5). The ability to form biofilms may explain the endemic occurrence of outbreaks in particular hospitals (6). The pathogen is often carried by medical personnel, contributing to the spreading of A. baumannii.

A. baumannii causes opportunistic infections, mainly in immunocompromised patients. The risk factors for A. baumannii infection include hospitalisation, poor overall condition, circulatory system insufficiency, respiratory system insufficiency, mechanical ventilation, prior antibiotic therapy and presence of foreign materials (such as venous, arterial and urinary catheters) (7).

A. baumannii colonisation and infections are often downplayed by physicians. However, longer hospitalisation periods and higher mortality rates have been shown in patients with confirmed A. baumannii infections (8, 9).

A. baumannii wound infections, especially with strains resistant to multiple antibiotics, pose a significant problem at surgical wards. A. baumannii strains are defined as multidrug-resistant (MDR) if they are insensitive to antibiotics pertaining to three of five classes of antibiotics (cephalosporines, carbapenems, fluorochinolones, aminoglycosides and ampicilin with sulbactam) (2). Strains are defined as pandrug-resistant (PDR) if they are resistant to all commercially available classes of antibiotics, i.e. penicilins, cephalosporines, carbapenems, monobactams, fluorochinolones, aminoglycosides, polymyxins, tetracyclines (including tigecycline) and sulbactam (10). These aspects combined cause A. baumannii to present a significant threat to hospitalised patients and a significant clinical problem for physicians trying to choose the appropriate therapeutic regimen. Studies show that the mortality rate of hospitalised patients infected with A. baumannii is 8-23%, and 10-43% at intensive care units (ICUs) (8).

The aim of this study was to determine the infection rate and sensitivity spectrum of A. baumannii strains isolated from patients treated at the Maria Sklodowska-Curie Memorial Hospital in Zgierz, with particular emphasis on surgical wards and the intensive care unit.

MATERIAL AND METHODS

The analyses were performed on samples of materials collected from patients treated at the Maria Skłodowska-Curie Memorial Hospital in Zgierz from 1st January to 31st December 2011. The analysed material included wound swabs, blood, bronchial secretions, peritoneal fluid, throat swabs, sputum and urine. A. baumannii isolates were obtained from bacterial cultures on the following microbiological substrates: Columbia agar with 5% sheep blood, Columbia CNA agar with 5% sheep blood, MacConkey agar. Particular strains were isolated and antibiograms were performed. Species were identified using the VITEK 2 GN card (bioMérieux) and the Vitek 2 automated system (bioMérieux), according to the procedure recommended by the producer. The susceptibility of particular strains to antibiotics was determined using the AST NO 93 card. In case of resistance to carbapenem, MIC was determined using the E-test with the Mueller Hinton substrate. The occurrence of MBL was verified by means of the disc system with the Mueller Hinton substrate.

RESULTS

In 2011, 4765 patients were included in microbiological analyses. Infection was confirmed in 1358 cases (28.5%), yielding 1902 bacterial isolates. The total number of Acinetobacter baumannii infections at the hospital was 140 which constitutes 10.31% of all positive culture results and 7.36% of the total number of isolates.

The number and percentage rate of Acinetobacter baumannii infections in 2011 at particular wards, according to prevalence, was as follows: ICU – 67 (48% of all infections), Department of Internal Medicine – 22 (16%), Neurology Department – 18 (13%), surgical wards – 28 (20%), out of which the Department of General and Oncological Surgery – 12 (8%), other wards – 5 (3%).

Figure 1 shows the number of patient-derived materials used for the culture of the analysed Acinetobacter baumannii strains.

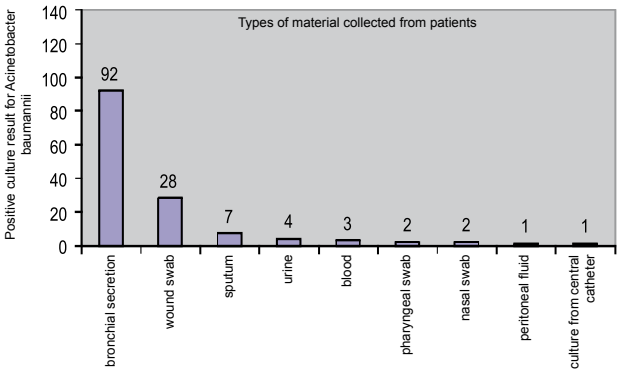

Fig. 1. Number of materials collected in 2011 from patients hospitalised at the Maria Skłodowska-Curie Memorial Hospital in Zgierz from which the analysed Acinetobacter baumannii strains were cultured

Figure 2 shows the sensitivity of A. baumannii strains to antibiotics. The bacteria showed greatest sensitivity to colistin – 90%, followed by carbapenems: 64% for imipenem and 43% for meropenem. A lower sensitivity of approximately 20-30% was found for aminoglycoside antibiotics and the combination of ampicilin with sulbactam. A. baumanii showed sensitivity below 20% for aztreonam, cefepime, ceftazidime, ciprofloxacin, piperacilin with tazobactam, ticarcilin, ticarcilin with clavulanic acid, tobramycin and trimethoprim with sulfamethoxazole.

The susceptibility of Acinetobacter baumannii to antibiotics at particular wards was varied. High sensitivity to colistin, reaching 100%, was observed for isolates from surgical wards and the Department of Internal Medicine. Lower sensitivity was observed at the Department of Neurology and the ICU – 83% and 85%, respectively. The highest sensitivity rate to imipenem (77%) and meropenem (73%) was found at the Department of Internal Medicine, while the lowest to imipenem (44%) was observed at the Neurology Department, and to meropenem (32%) at surgical wards. Sensitivity to ampicilin with sulbactam ranged from 43% to 28%, with the highest rate observed at surgical wards and the lowest at the ICU. Among aminoglycoside antibiotics, gentamicin is worth pointing out. Sensitivity to the antibiotic was 50% at the Department of Internal Medicine and 13% at the ICU.

The susceptibility of Acinetobacter baumannii strains to antibiotics at particular wards is shown in fig. 3, 4, 5 and 6.

DISCUSSION

The results of the study performed in 2011 at the Maria Skłodowska-Curie Memorial Hospital in Zgierz show that the number of Acinetobacter baumannii infections is highest at the ICU and surgical wards, i.e. where severely ill and often immunocompromised patients, vulnerable to nosocomial infections related to invasive medical procedures, are hospitalised. A higher number of infections was also observed at the neurology and internal medicine wards, possibly as a result of long hospitalisation periods and patients' poor overall condition (7).

According to American and British studies concerning infections in soldiers wounded dur-

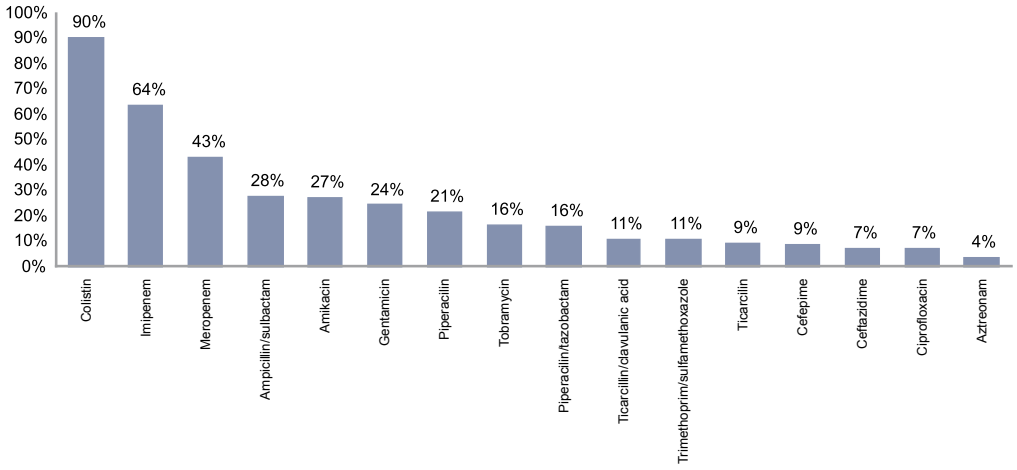

Fig. 2. Resistance rate of Acinetobacter baumannii to antibiotics at the Maria Skłodowska-Curie Memorial Hospital in Zgierz in 2011

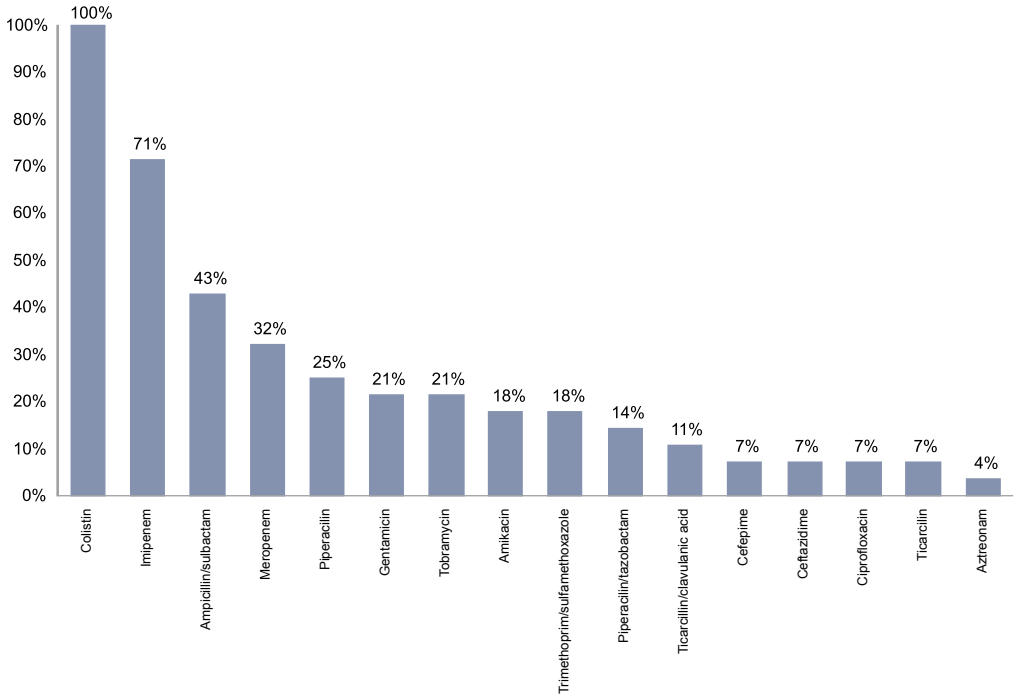

Fig. 3. Resistance rate of Acinetobacter baumannii to antibiotics at surgical departments in 2011

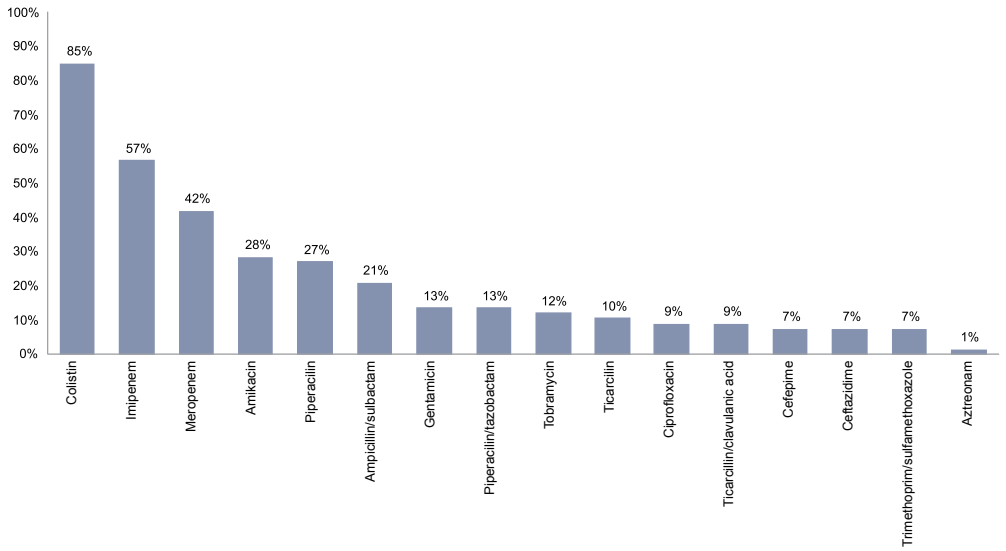

Fig. 4. Resistance rate of Acinetobacter baumannii to antibiotics at the Intensive Care Unit in 2011

ing armed conflict in Iraq and Afghanistan, A. baumannii was one of the most frequently isolated bacterial species. Earlier hypotheses that A. baumannii naturally occurring in the countries of armed conflict could be the source of infections were not confirmed. The isolated microbes were found to be nosocomial strains. The studies also found that the percentage of MDR strains isolated from field hospitals increased over the years (11).

The susceptibility pattern of A. baumannii to the analysed antibiotics supports the notion of the microbe's worldwide tendency of increasing resistance. A. baumannii strains have multiple mechanisms at their disposal which make them potentially resistant to antibiotics of all families. The most important of these mechanisms include: metallo-ß-lactamases (MBLs), oxacillinases, aminoglycoside-modifying enzymes, protective changes in rRNA, modifications of penicillin-binding proteins (PBPs) and other antibiotic binding sites, modifications of porins, modifications of the outer membrane and the lipopolysaccharide layer, and pumps that remove antibiotics (2). What is more, resistance-coding genetic mate-

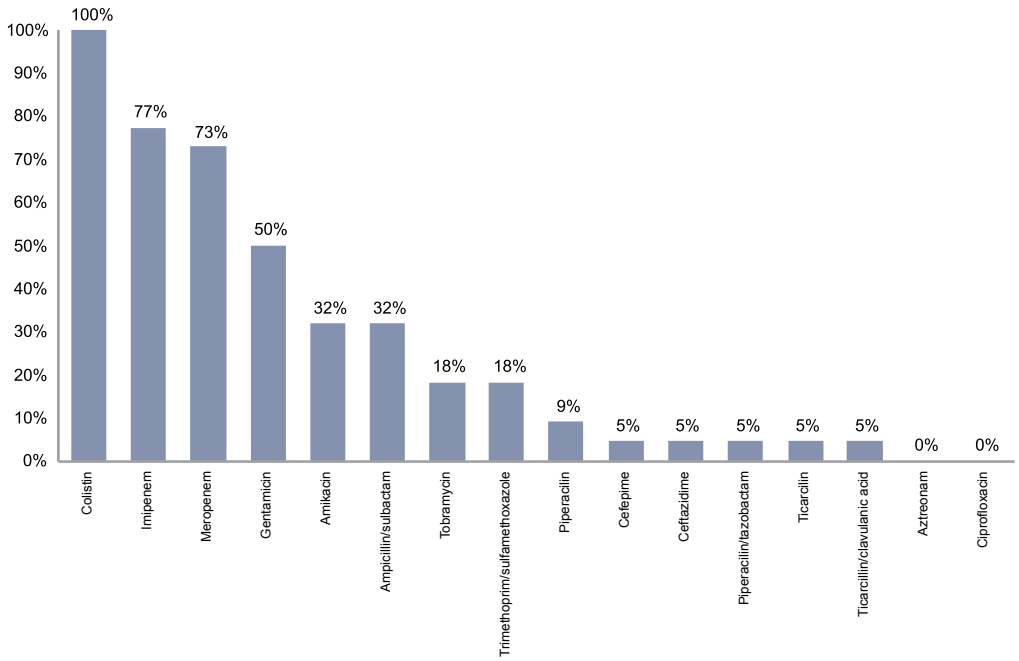

Fig. 5. Resistance rate of Acinetobacter baumannii to antibioticsat the Department of Internal Medicine in 2011

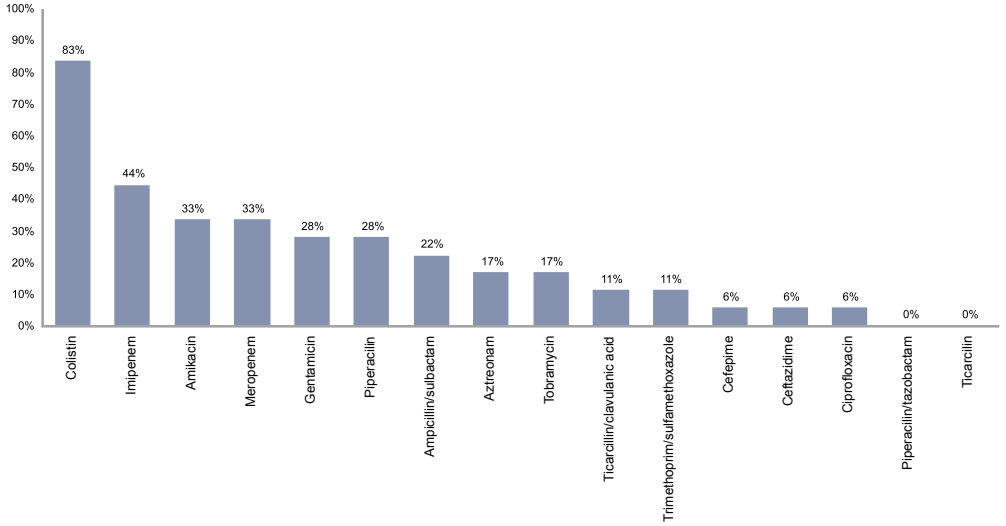

Fig. 6. Resistance rate of Acinetobacter baumannii to antibioticsat the Neurology Department in 2011

rial can quickly be transferred vertically from one bacterium to another with plasmids and/or transpozons (12). Due to the wide range of resistance mechanisms compared with other Gram-negative pathogens, A. baumannii is at the very forefront of multidrug-resistant microbes. Consequently, physicians are forced to introduce significantly toxic drugs in patient therapy. Until the 1970s, Acinetobacter spp. infections were treated with most antibiotics pertaining to the ß-lactam, aminoglycoside and tetracyclin families; the effectiveness of these antibiotics decreased with time (13).

In recent years, A. baumannii infections have been treated primarily with carbapenems. At our hospital, carbapenem sensitivity was 64% and 43% for imipenem and meropenem, respectively. This coincides with data from other centres, suggesting a clear increase in resistance. In the years 1998-2001, the percentage of carbapenem-sensitive isolates in the USA was 90% (1, 14). Studies from recent years concerning A. baumannii infections at hospitals in the USA and South Korea confirm a decline in the susceptibility of A. baumannii strains to 50% (3, 15, 16). The MYSTIC program con-

ducted in European hospitals between 2002 and 2004 showed that the susceptibility of the strains in question decreased to approx. 75% for meropenem and imipenem (14). Improved effectiveness of carbapenem treatment was shown for regimens where maximum doses of meropenem were used and antibiotic infusion time was extended to 3 hours (17, 18).

The increasing resistance to carbapenems drives the search for other, effective therapeutic regimens. Colistin (polymyxin E), to which A. baumannii sensitivity was found to be 90% in our study, is becoming an alternative for ß-lactam antibiotics. This data coincides with the results of the American CAPITAL study of 2010, where sensitivity to colistin was found to be 95% (16).

High sensitivity to colistin stems from the limited use of the drug, due in turn to its alleged strong nephrotoxicity and neurotoxicity. However, colistin toxicity is not as significant as previously believed and is comparable with aminoglycoside toxicity (19).

Additional advantages of polymyxin E include its post-antibiotic effect towards MDR strains of Gram-negative bacteria and synergy with carbapenems and rifampicin (19, 20). The post-antibiotic effect (PAE) of a drug is its ability to suppress bacterial growth for a long period of time after a brief exposure to the antibiotic.

If colistin administration is to be optimized, its pharmacokinetics must be considered. Therefore, studies are underway concerning different routes of administration, including pressurized inhalation or intrathecal/intraventricular injections in infections of the central nervous system (21, 22, 23). Reports of A. baumannii strains resistant to polymyxin E should call for limiting the use of the drug to patients with a very severe course of infection, with consideration for its bioavailability in tissues (3, 24).

Combined ampicilin and sulbactam treatment may be an alternative. Therapeutic regimens with these antibiotics in A. baumannii infections turned out to be comparable with other drug regimens (24). Although A. baumannii susceptibility at the level of 23% of in our study is not high, it could conceivably increase with other administration regimens. Studies confirm that the main effect on A. baumannii is achieved through sulbactam, however not due to ß-lactamase inhibition but the compound's direct bactericidal properties (25).

In an ex vivo study conducted in 2008 in Argentina, the therapeutically effective bactericidal concentration of ampicilin combined with sulbactam was achieved for 0.5g and 1g doses of sulbactam administered every 4 hours. Sulbactam without ampicilin showed bactericidal properties at a dose of 2g administered every 6 hours. The desired therapeutic effect was also achieved when ampicilin plus sulbactam were administered in prolonged intravenous infusions (26). An additional property of sulbactam is its synergy with multiple antibiotic families, including cephalosporines, aminoglycosides, fluorochinolones, colistin and tigecycline (27).

A. baumanii sensitivity to aminoglycosides in our study was 27% for amikacin and 24% for gentamicin. Despite their adverse effects, these well-known antibiotics should be considered when choosing therapeutic regimens due to their synergic action with other antibiotics, e.g. ß-lactams, and low cost of therapy.

It is worth noting the low susceptibility of A. baumannii strains in our study to cephalosporine and fluorochinolone antibiotics. These broad-spectrum antibiotics are often part of empiric therapy in the treatment of infections of different bodily systems. Comparison of the susceptibility rate to ceftazidime (7%), cefepime (9%) and ciprofloxacin (7%) in our study with data collected in the years 1997-2000 by a Warsaw centre – 81%, 75% and 81%, respectively – serves to show the potential of A. baumannii in gaining resistance over the years (28).

The susceptibility profile of A. baumannii included in our study does not comprise tigecycline, despite recommendations to use the antibiotic in patients with complicated infections and in poor overall condition (29). Long-term 100% resistance to tigecycline with the MIC breakpoint used in our laboratory caused this antibiotic to be withdrawn from the sensitivity panel for this pathogen. Following the publication of studies confirming high susceptibility of A. baumannii MDR strains to tigecycline in vitro, the antibiotic was among potentially effective treatment regimens. However, a paper published in 2012 concerning tygecycline use in vivo pointed to the development of resistance during treatment (12).

The increasing prevalence of A. baumannii MDR strains in hospital environments results in the need to modify therapeutic options, tak-

ing into account the susceptibility of strains in particular medical centres.

CONCLUSIONS

1. Acinetobacter baumannii infections constitute a large share of the total number of nosocomial infections
2. Most Acinetobacter baumannii infections were found in patients hospitalised at ICUs and surgical wards, confirming the influence of known risk factors for infection
3. Acinetobacter baumannii shows highest sensitivity to colistin
4. The sensitivity of Acinetobacter baumannii to currently used antibiotics is significantly decreasing

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