Acinetobacter baumannii microbiological and phenotypic characteristics of isolates from Intensive Care Unit of the Department of Internal Medicine at the University Hospital Centre in Zagreb over a four-year period

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ABSTRACT

Acinetobacter baumannii is an opportunistic nosocomial pathogen and one of the six most important multidrug-resistant microorganisms in intensive care units (ICU).

The aim of this study was to determine the prevalence of antimicrobial resistant A. baumannii strains in ICU.

We analysed antibiotic susceptibility of A. baumannii isolates collected in University Hospital Centre Zagreb over a four-year period (2011-2014) based on the hospital computer system data (BIS). The data were interpreted according to Clinical and Laboratory Standards Institute criteria.

All strains from 2014 were found to be resistant to meropenem, which is a significant increase when compared to 1.4% in 2011 and 81.8% in 2012. The resistance rate to imipenem increased to 95.8% in 2014 from 91.4% in 2011 and 81.8% in 2012. Colistin resistance, confirmed by E test, was found only in one strain in 2013. The resistance rates of other antimicrobial agents were as follows: ampicillin/sulbactam 8.6% and 73.9%, netilmicin 70.6% and 83.3%, gentamicin 48.6% and 91.7%, amikacin 82.4% and 80.0% and ciprofloxacin 100% and 100% in 2011 and 2014 respectively.

Our data confirmed a multidrug-resistance phenotype in Acinetobacter baumannii strains isolated in ICU at the Clinical Hospital Centre, with a significant increase in resistance rates between 2011 and 2014 against certain antimicrobial agents including ampicilin/sulbactam and carbapenems.

Key words: Acinetobacter baumannii, multidrug resistance, extensively drug resistance, nosocomial pathogen

INTRODUCTION

Acinetobacter spp. are glucose non-fermenting, non-motile, catalase positive, and oxidase negative aerobic gram-negative cocobacilli. (1) The most important species in human medicine is Acinetobacter baumannii. It is nowadays the leading causative agent of health care associated infections and is often called Gram-negative MRSA. (2) Health care associated infections tend to occur in debilitated patients in intensive care units (both children and adults) and among residents of long-term care facilities (particulary facilities caring for ventilator-dependent patients). Additional risk factors include recent surgery, central vascular catheterization, tracheostomy, mechanical ventilation, enteral feedings, and treatment with third generation cephalosporin, fluoroquinolones, or carbapenem antibiotics. (1,3) It has a great capacity of acquiring resistance traits and spreading within the hospital environment. Many factors contributed to the virulence of Acinetobacter species: survival in dry and iron-deficient conditions for a long period of time, the production of a polysaccharide capsule that works with the cell wall liposaccharide to prevent complement activation. The capsule prevents phagocytosis and enables the survival of bacteria in the blood. Colonisation in the lung is facilitated by the ability of Acinetobacter to adhere to human bronchial epithelial cells using fimbriae. (4) In addition, the colonization of environmental surfaces is promoted by adhesion via pili and the subsequent formation of biofilm. Most A. baumannii isolates are highly resistant to most antibiotics available in clinical practice due to intrinsic and acquired resistance mechanisms. A number of resistance mechanisms to many classes of antibiotics are known to exist in A. baumanni, including β-lactamases production (particularly carbapenemases), upregulated efflux pumps, production of aminoglycoside-modifying enzymes, permeability defects and the alteration of target sites. (1) The spread of multidrug resistance determinants in A. baumannii occurs by conjugation, transposon acquisition or integron mobilization to gain clusters of genes encoding resistance to several antibiotics families.(5)

The aim was to analyze the prevalence and antibiotic sensitivity patterns of Acinetobacter baumannii isolates from patients hospitalized at the Department for Intensive Care Medicine, University Hospital Centre Zagreb. The number and the type of microbiological specimens with A. baumannii were determined as well.

MATERIAL AND METHODS

The data are based on a retrospective study conducted between 1 January 2011 and 31 December 2014. The data were collected from the hospital computer system (BIS). Only one isolate per patient was included in the study. Antibiotic susceptibility was determined according to EUCAST guidelines (European Committee on Antimicrobial Susceptibility Testing). The general parameters of ICU (number of beds, number of patients and the total number of bacteriological results) were used to calculate the resistance rates and the proportion of A. baumannii in the total number of positive bacteriological results.

RESULTS

The Department for Intensive Care Medicine has 12 beds. The total number of patients hospitalized in the department in the study period (2011-2014) was as follows: 589, 590, 590, 562 , while the number of patients with A. baumannii isolates was 50, 20, 47, 37 in 2011, 2012, 2013 and 2014 respectively (table 1.). The largest number of A. baumannii isolates originated from respiratory tract specimens (tracheal aspirate, BAL, minilavate) during the whole four-year study period (figure 1).
Resistance rates for meropenem ranged from 81.8 % (2012) to 100% (2014). Similarly, imipenem showed the resistance rate which increased from 81.8% in 2011 to 95.8% in 2014. The highest increase of the resistance rate was observed for ampicilin/sulbactam from 8.6% in 2012 to 73.9% in 2014 and for gentamicin with the range from 48.6% in 2011 to 91.7%. in 2014. No resistance rate to colistin was observed, except for one single strain (figure 2). The resistance rates to amikacin and ciprofloxacin did not change during the study period.

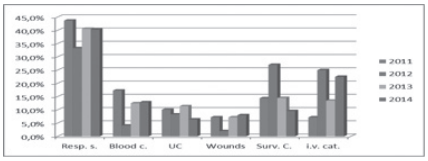

Figure 1. The proportion of A. baumannii isolates from various clinical samples

Blood c.= Blood culture,
i.v. cat.= intravascular catether samples
Resp. s. = respiratory samples,
Surv. c.= surveillancy culture,
UC= urine culture

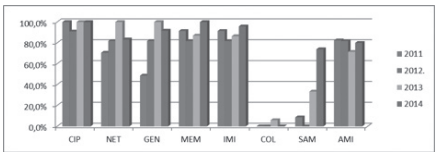

Figure 2. Percentage of A. baumannii strains resistant to various antibiotics over a four year period (2011-2014)

AMI=amikacin
CIP= ciprofloxacin,
COL=colistin,
GEN= gentamicin,
IMI= imipenem,
MEM= meropenem,
NET=netilmicin,
SAM=ampicilin/sulbactam,

DISCUSSION

In our study A. baumannii was isolated in 9-17.2 % of all bacteriological specimens, which is comparable to Prashanth et al. with 10% Acinetobacter isolates (6), Pathwardhan et al. with 13-23% (7) and Purti et al. with 11.96% .(8) The most common site for A. baumannii infection is the respiratory tract and the most common manifestation is VAP (9). This is in concordance with the high number of isolates from the respiratory tract and blood cultures in our study. The ability of Acinetobacter strains to adhere to the surface is an important mechanism in pathogenicity. It frequently causes infections associated with medical devices, e.g. vascular catheters. Biofilm formation is a well-known virulence mechanism in such infections. (10) This explains a high number of strains from vascular catheter swabs and lavates.
Analysis of susceptibility patterns showed that most isolates do not have only the multidrug-resistant phenotype (MDR) but also extensively drug-resistant phenotype (XDR). Proportion of XDR A. baumannii in total number of MDR A. baumannii increased from 24% and 5% in 2011 and 2012 to 40% and 70.2 % in 2013 and 2014. A similar proportion of XDR A. baumannii of 72.4 % was reported in the study byMetan et al. at the bone marrow clinic. (11) The proportion of isolates resistant to carbapenems (imipenem, meropenem) in our ICU reached the peak level in 2014 (100% resistant to meropenem, 95% to imipenem). Guven et al. reported in their study from 2011 the resistance rate to carbapenems of 98.9%, also in ICU. (12) The hospital in general demonstrated in 2014. a smaller resistance rate to carbapenems of 87.8%, compared to ICU. On the national level, there was also an increase from 23% in 2009 to 80% in 2013 in Croatia. (13) Clinical studies showed higher mortality rates of patients infected with carbapenem-resistant strains compared to those infected with carbapenem-susceptible strains. (14, 15) An alarming increase of the resistance rate was reported for ampicilin/sulbactam from 8.6% in 2012 to 73.9% in 2014 in ICU. In the hospital in general the resistance rate for ampicillin/sulbactam was 64%, while in the whole country the rate was 26%. No resistance to colistin was observed except in one single strain. At the University Hospital Centre the resistance rate for colistin was 1.6%, which is slightly higher than at the national level in Croatia (1%). The first study on carbapenem resistance in A. baumannii at the University Hospital Centre Zagreb demonstrated the emergence of OXA-72 betalactamase belonging to OXA-24-like group among isolates from 2008. (16)

CONCLUSION

The total number of A. baumannii in ICU was similar in each year during the study period, but the increase of resistance rates and the increased proportion of XDR A. baumannii compared to the total number of A. baumannii were observed. The increase of resistance rates to carbapenem and ampicillin/sulbactam is worrisome. Early identification, effective strategies to control the use of antibiotics and continuous surveillance and enforcement of specific infection control measures are strongly emphasized.

Table 1. Epidemiological parameters in ICU

Parameter	2011.	2012.	2013.	2014.
The number of patients with A. baumannii isolat	50	20	47	37
Number/1000 bo days (‰)	15,7	6,8	17,2	13,06
Number of microbiological specimens with A.baumannii isolate	69	48	96	62
% of total bacteriological specimens	13,5	9	17,2	11,2

REFERENCES

1. Feng Lin M, Yu Lan C. Antimicrobial resistance in Acinetobacter baumannii: From bench to bedside. World J Clin Cases. 2014; 2(12):787-814.
2. Falagas ME, Bliziotis IA, Siempos II. Attributable mortality of Acinetobacter baumannii infections in critically ill patients: A systematic review of matched cohort and case-control studies. Crit Care. 2006;10: R48.
3. Dijkshoorn L, Nemec A, Seifert H. An increasing threat in hospitals: Multidrug-resistant Acinetobacter baumannii. Nat Rev Microbiol. 2007;5:939-951.
4. Lee JC, Koerten H, van den Broek P, et al. Adherence of Acinetobacter baumannii strains to human bronchial epithelial cells. Res Microbiol. 2006;157:360.
5. Esterly J, Richardson CL, Eltoukhy NS, Qi C, Scheetz MH. Genetic Mechanisms of Antimicrobial Resistance of Acinetobacter baumannii. Ann Pharmacother. 2011.
6. Prashanth K, Badrinath S. Nosocomial infections due to Acinetobacter species: Clinical findings, risk and prognostic factors. Indian J Med Microbiol. 2006;24:39-44.
7. Patwardhan RB, Dhakephalkar PK, Niphadkar KB, Chopade BA. A study on nosocomial pathogens in ICU with special reference to multiresistant Acinetobacter baumannii harbouring multiple plasmids. Indian J Med Res.2008;178-87.
8. Purti CT, Sunita RG, Gopal NA. Clinical and antimicrobial profile of Acinetobacter spp.: An emerging nosocomial superbug. Adv. Biomed. Res. 2014;3:13.
9. Behnia M, LoganSC, Fallen L, Catalano P. Nosocomial and ventilator-associated pneumonia in a community hospital intensive care unit: a retrospective review and analysis. BMC Research Notes. 2014;7:232
10. Gentile V, Frangipani E, Bonchi C, Minandri F, Runci F, Visca P. Iron and Acinetobacter baumannii Biofilm Formation. Pathogens. 2014;3:704-719.
11. Metan G,Pala C, Kaynar L, Cevahir F, Alp E. A nightmare for haematology clinics: extensively drug-resistant (XDR) Acinetobacter baumannii. Infez Med. 2014;1;22(4):277-82.
12. Guven T, Yilmaz G, Guner HR, Kaya Kalem A, Eser F, Tasyaran MA. Increasing resistance of nosocomial Acinetobacter baumannii: are we going to be defeated? Turk J Med Sci. 2014;44(1):73-8.
13. Commitee for antibiotic resistance surveillance in Croatia. Antibiotic resistance in Croatia, 2013. The Croatian Academy of Medical Science. 2014.
14. Sheng WH, Liao CH, Lauderdale TL, Ko WC, Chen YS, Liu JW et al. A multicentar study of risk factors and outcome of hospitalized patients with infections due to carbapenem-resistant Acinetobacter baumannii. Inf J Infect Dis. 2010;14:764-769.
15. Grupper M, Sprecher H, Mashich T, Finkelstein R. Attributable mortality of nosocomial Acinetobacter bacteremia. Infect Control Hosp Epidemiol. 2007;28:293-298.
16. Franolić-Kukina I, Bedenić B, Budimir A, Herljević Z, Vraneš J, Higgins P. Clonal spread of carbapenem-resistant OXA-72 positive Acinetobacter baumannii in a Croatian university hospital. Internation Journal of Infectious Diseases 2011;15:e706- e709).
17. 1Vranić-Ladavac M, Bedenić B, Minandri F, Ištok M, Frančula-Zaninović S, Ladavac R, Visca P. Carbapenem-resistance and acquired class D carbapenemases in Acinetobacter baumannii from Croatia 2009-2010. Eur J Clin Microbiol Infect Dis 2014; 33(3):471-8.