The evolution of carbapenem resistance determinants and major epidemiological lineages among carbapenem-resistant Acinetobacter baumannii isolates in Germany, 2010-2016

Michael Kresken*1,2, Paul Higgins3, Danuta Stefanik3, Julia Wille3, Barbara Körber-Irrgang1, Harald Seifert3,4

1 Antiinfectives Intelligence GmbH, Rheinbach, Germany, 2 Rheinische Fachhochschule Köln gGmbH, Cologne, Germany, 3 Institute for Medical Microbiology, Immunology and Hygiene, University of Cologne, Cologne, Germany, 4 German Center for Infection Research (DZIF), Partner Site Bonn-Cologne, Cologne, Germany

Background: Acinetobacter baumannii is a major pathogen causing healthcare-associated infections, especially in the intensive care unit (ICU). Penicillins and cephalosporins are usually not clinically effective, while carbapenems play an important role in the management of A. baumannii infections. However, A. baumannii possesses intrinsic class D β-lactamase genes (blaOXA-51-like) being able to confer carbapenem resistance. The majority of carbapenem-resistant isolates however possess acquired carbapenemase-encoding genes including blaOXA-23-like, blaOXA-40-like, and blaOXA-58-like. The objectives of the present study were i) to evaluate the occurrence of carbapenem resistance determinants among A. baumannii isolates collected during three multicentre surveillance studies conducted by the Paul-Ehrlich-Society between 2010 and 2016, and ii) to investigate the molecular epidemiology of these isolates.

Materials/methods: Isolates were collected prospectively from hospital in-patients at 18 medical centres in Germany, in each case over a three-month-period in the years 2010, 2013 and 2016. Verification of species identification and susceptibility testing were performed in a reference laboratory. MICs were determined by broth microdilution according to the ISO-standard and interpreted by EUCAST breakpoints (v.8.1). The prevalence of carbapenemase-encoding genes was investigated by oxacillinase (OXA)-multiplex polymerase chain reaction (PCR) and whole-genome sequencing. The molecular epidemiology was examined by repetitive sequence-based PCR (rep-PCR; DiversiLab) and core-genome MLST (cgMLST).

Results: Overall, 236 A. baumannii isolates were collected. There were 61 ICU isolates and 175 non-ICU isolates. Resistance to imipenem and/or meropenem was detected in 49 isolates from 13 centres, of which 41 (83.7%) produced an OXA-23-like carbapenemase. Other carbapenemases detected were OXA-24-like (n=3), OXA-58-like (n=2) and NDM-1 (n=2). The proportion of resistant isolates evolved from 15/74 (20.3%) in 2010 to 21/65 (32.3%) in 2013 and then decreased to 13/97 (13.4%) in 2016 (chi-squared-test for linear trend, p=0.2). One carbapenem-resistant isolate was cross-resistant to colistin. Thirty-seven carbapenem-resistant isolates (75.5%) were associated with the clonal lineage IC 2 (13/15 [86.7%] in 2010, 17/21 [81%] in 2013, 5/13 [38.5%] in 2016) and six with IC 1.

Conclusions: This nationwide study found a pooled rate of non-susceptibility to carbapenems of 20.8% (95%-CI: 15.6-26%) in the period 2010-2016, with a decrease in the rate of IC 2 isolates harbouring the blaOXA-23-like gene.