O9

INSTABILITY OF AMIKACIN RESISTANCE IN A CARBAPENEM-RESISTANT STRAIN OF *ACINETOBACTER BAUMANNII* ISOLATED DURING A HOSPITAL OUTBREAK

A. Nemec[a,b], M. Maixnerová[b], T. J. K. van der Reijden[c], V. Jindrák[d], J. Smíšek[a] and L. Dijkshoorn[c]

[a]3rd Medical School, Charles University, Prague, Czech Republic, [b]National Institute of Public Health, Prague, Czech Republic, [c]Leiden University Medical Center, Leiden, The Netherlands, [d]Hospital Na Homolce, Prague, Czech Republic.

In January 2000, a carbapenem-resistant *Acinetobacter baumannii* strain was isolated in a Prague hospital. A few months later, additional carbapenem-resistant isolates were recovered from multiple patients in the same hospital. These isolates differed in their susceptibility to amikacin even if they were from the same patient. The present study aimed to assess the relatedness of the carbapenem-resistant isolates and to reveal the genetic basis of their variability in susceptibility to amikacin.

In total, 31 clinical isolates of *A. baumannii* from 11 patients hospitalised in the Hospital Na Homolce in Prague were investigated. The index isolate was recovered from a patient admitted from another hospital in January, the other isolates were collected in June 2000. The MICs of all isolates for both imipenem and meropenem were ≥16 mg/L. Genotyping was done by *Apa*I macrorestriction analysis and AFLP fingerprinting. Susceptibility to antibiotics was tested by disk-diffusion and agar dilution, while the genes for the aminoglycoside phosphotransferase APH(3')-VI (*aphA6*) and for OXA-type carbapenemases were detected by PCR.

All isolates yielded indistinguishable macrorestriction profiles and were allocated to the European multidrug resistant clone II by AFLP. They were uniformly resistant or intermediately susceptible to all tested antibiotics, except for tobramycin and ampicillin-sulbactam. The gene encoding carbapenemase OXA-58 was found in all isolates. Twenty-six isolates were resistant to amikacin (MIC >64 mg/L) and carried the *aphA6* gene, whereas this gene was not detected in any of five amikacin-susceptible isolates (MIC 1 mg/L). In laboratory experiments, isolates originally resistant to amikacin showed spontaneous loss of amikacin resistance with a frequency of 5×10^{-3}.

In conclusion, the hospital outbreak was caused by an imported multidrug resistant strain, which harboured the genes for OXA-58 and APH(3')-VI. Susceptibility to amikacin most likely resulted from the loss of *aph6*. Since amikacin-resistant and susceptible variants were present concurrently on the ward, use of amikacin might result in selection of resistant variants and, hence, treatment failure. The study results emphasise the importance of both strain identification and assessment of the genetic basis of resistance in cases of difficult-to-understand treatment failures.

This study was supported by grant IGA MZ ČR 8554-3.