Type: Poster Presentation

Final Abstract Number: 40.037
Session: Antibiotic Resistance
Date: Thursday, April 3, 2014
Time: 12:45-14:15
Room: Ballroom

Impact of carbapenem-resistance on 28-days survival in patients with Gram-negative bacteraemia

N. Kulkova[1], J. Brnova[2], L. Michalikova[2], M. Babalova[3], V. Krcmery[4,*]

[1] *St. Elisabeth University, Bratislava, Slovakia*
[2] *Trnava University, School of Public Health Social Sciences, Trnava, Slovakia*
[3] *Slovak Medical University, Bratislava, Slovakia*
[4] *St. Elizabeth University College of Health and Social Sciences, Bratislava, Slovakia*

Background: Carbapenem-resistant Gram-negative bacteria (CR GNB) are subject of public health concerns and may be associated with worse outcomes. In this study we aimed to assess 28-days survival of patients with bacteraemia due to Gram negative species.

Methods & Materials: Cross-sectional multicentre study was performed in patients with drug-resistant Gram-negative bacteraemia in Slovakia in November 2011- January 2012. Antibiotic susceptibility testing was performed according to the European Committee on Antimicrobial Susceptibility Testing. Kaplan-Meier curves were used to assess 28-days survival and were analysed with Log rank test to compare survival of patients with and without infection caused by CR GNB.

Results: Altogether, 257 cases with drug-resistant GNB bacteraemia were identified (59,4% males; median age 62 years, IQR 50-75), of them 45 (17,5%) were due to CR GNB. Twenty-eight-days mortality, was significantly higher in group of CR GNB cases (42,2% vs. 25,5%, p=0,029), while in overall mortality there was no statistically significant difference (64,4% vs. 49,06%, p=0,086). Median time from positive blood culture to death was 9,5 days in CR GNB group, and 34,5 days in carbapenem-susceptible group (p=0,042). Also, significant difference in 28-days survival was noticed comparing patients with carbapenem susceptible and CR GNB infection (Log rank test p=0,033). Regarding the risk factors, polymicrobial infection (p=0,019), hospitalization in intensive care unit (p<0,001) and hospitalization during the winter and/or spring (p=0,054), were associated with CR infection.

Conclusion: In this study, carbapenem-resistance in GNB species causing bloodstream infection was associated with significantly worse outcome and decreased probability of survival. This is underscoring importance of careful control strategies to avoid spread of CR GNB among patients.

(This study was partially supported with Trnava University Grant, No 7/TU/12).

http://dx.doi.org/10.1016/j.ijid.2014.03.627

Type: Poster Presentation

Final Abstract Number: 40.038
Session: Antibiotic Resistance
Date: Thursday, April 3, 2014
Time: 12:45-14:15
Room: Ballroom

Association between genotypic and phenotypic pyrazinamide resistance in *Mycobacterium tuberculosis*

M.G. Whitfield[1,*], E.M. Streicher[1], T. York[1], I. Mardarowicz[1], L. Scott[2], W. Stevens[2], P.D. van Helden[1], R.M. Warren[1], A. Van Rie[3]

[1] *Stellenbosch University, Tygerberg, South Africa*
[2] *National Health Laboratory Services, Johannesburg, South Africa*
[3] *Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, NC, USA*

Background: Pyrazinamide (PZA) has the unique ability to eradicate semi-dormant bacilli in acidic environments not targeted by other drugs. Addition of pyrazinamide (PZA) has enabled shortening of the duration of tuberculosis (TB) treatment regimens. PZA is likely to continue to play a role in novel TB treatment regimens but little information is available on the prevalence of PZA resistance as PZA drug susceptibility testing (DST) is not performed routinely due to technical difficulties. Studies have suggested an association between mutations in the *pncA* gene and *in vitro* PZA resistance.

Objectives: We aimed to determine the association between mutations in the *pncA* gene and phenotypic resistance to PZA in clinical isolates from patients with rifampicin resistant TB.

Methods & Materials: A total of 233 *Mycobacterium tuberculosis* isolates identified as rifampicin (RIF) resistant by the National Health Laboratory service (routine DST/Xpert MTB/RIF) from three provinces in South Africa were subjected to culture-based PZA drug susceptibility testing using BD BACTEC MGIT 960 PZA Mycobacterial Detection System and targeted DNA sequencing of the *pncA* gene. Isolates were the initial clinical isolates collected prior to initation of tuberculosis treatment.

Results: Based on phenotypic testing, 117 (50%) of the RIF resistant isolates were also resistant to PZA at a concentration of 100 μg/ml. DNA sequencing identified polymorphisms (single nucleotides polymorphisms/insertion/deletion) in 109 (93%) of the phenotypically PZA resistant isolates. All 109 were non-synonymous/insertions/deletions. Eight of the phenotypically PZA susceptible isolates had mutations in the *pncA* gene of which 6 were non-synomymous and 3 were synonymous. A total of 39 different polymorphisms in the *pncA* gene were identified, with the insert at codon 173 (G) being most prevalent. Using phenotypic PZA resistance as the gold standard, sensitivity and specificity of genetic detection of PZA resistance was 93.2% and 95.7%, respectively.

Conclusion: The observed strong association between genotypic and phenotypic PZA resistance in clinical RIF resistant isolates suggests that both methods could be used for detection of PZA resistance. The high (50%) proportion of RIF resistant isolates harbouring PZA resistance highlights the need for routine PZA DST and cautions against the inclusion of PZA in multi-drug resistant TB treatment regimens.

http://dx.doi.org/10.1016/j.ijid.2014.03.628