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Abstract (poster session)

DALI: defining antibiotic levels in intensive care unit patient. Variability of protein binding of teicoplanin and achievement of TDM targets

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Objectives: Teicoplanin is a valuable antibiotic for infections caused by Gram positive bacteria including methicillin resistant Staphylococcus aureus. Teicoplanin has high protein binding which may increase pharmacokinetic variability in critically ill patients, particularly those with hypoalbuminemia given that unbound or free concentrations are responsible for pharmacological activity. The aim of this study was to describe the variability in protein binding of teicoplanin in critically ill patients and the number of patients achieving therapeutic drug monitoring (TDM) target concentrations. Methods: This report is part of the multi-national DALI study which included 68 intensive care units throughout Europe. Patients were recruited and sampled on a single day with blood samples taken at both the mid-point of the dosing interval and the end. Total and unbound teicoplanin was assayed using validated chromatographic methods. Variability in protein binding was interpreted with linear regression. The lower therapeutic range of teicoplanin was defined as total trough concentrations from 10-20 mg/L and the higher range as 10-30 mg/L. Results: Sixteen critically ill patients were included in the analysis. The following are the median (interquartile range (IQR); range) for mid-point total and free concentrations were 13.1 (10.9-16.7; 6.6-27.7) mg/L and 1.1 (0.6-1.8; 0.3-3.1) mg/L respectively. The following are the median (IQR; range) for trough total and free concentrations were 12.4 (10.7-24.9; 4.3-40.5) and 1.8 (0.7-2.4; 0.1-4.5) mg/L respectively. The median (IQR; range) percentage free teicoplanin was 6.1 (4.5-12.3; 2.7-28.7) % for the mid-point samples and 6.5 (5.8-14.5; 3.0-28.6) % for the trough samples. The correlation between total and free antibiotic concentrations for the mid-point concentrations was low, $R2 = 0.23$ and for the trough concentrations was also low $R2 = 0.20$. Only 50% of patients had total trough concentrations between 10-20mg/L with 70% having total trough concentrations between 10-30mg/L. Conclusions: The variability of teicoplanin protein binding is very high in critically ill patients with correlations between free and total concentrations between 20-30% placing significant doubt on the accuracy of total concentrations for TDM. In this point prevalence study, 30-50% of patients did not achieve traditional TDM total concentration targets.