Introduction and Purpose

Daptomycin is a lipopeptide antibiotic commonly used for complicated skin and soft tissue infection caused by resistant gram-positive bacteria, including methicillin resistant *Staphylococcus aureus*. Elevated daptomycin exposures are associated with increased creatine phosphokinase levels\(^1\), while low exposures are associated with poor clinical response. We have provided a UK daptomycin therapeutic drug monitoring (TDM) clinical assay service for 4 years and present a retrospective review of our assay data.

Methods

Daptomycin was assayed using a validated reversed phase HPLC assay\(^2\). For TDM we consider pre dose concentrations greater than 20 mg/L as elevated and those less than 5 mg/L as low.

Results

*Of the pre dose samples (N=335) only 60% were within the recommended range, with 14% being below and 26% above the desirable range; however, concentrations below the recommended range were more frequent in younger patients (Table 1). Mean post dose samples ranged from 45.3 – 56.4 mg/L across the age groups (Table 2),

*Over the study period, there was a slight increase in median pre dose concentration, suggesting an increased dose in many patients (Figure 1).

*Where patients had repeated TDM, concentrations later in the period of monitoring were more likely to be in the recommended range (Figure 2).

Discussion

Not all requests had details on the reasons for TDM referral, but in general these included renal insufficiency, difficult to treat sites of infection and salvage therapy. As such, the data reported here probably represent the more difficult end of the treatment spectrum and it is not surprising that many patients had levels outside of the recommended range. However, for such a patient group it is concerning that so many patients had potentially sub-therapeutic concentrations and that this was particularly an issue in the paediatric population. Post dose concentrations were lower than reported in healthy volunteers but consistent with other patients’ data suggesting volume of distribution changes in sepsis\(^3\).

Conclusion

We conclude that a significant number of patients receiving daptomycin have serum concentrations that are outside of the desirable range, which appears to be a particular issue in paediatric patients. Therapeutic drug monitoring results in an improvement in target therapy attainment in many patients and should be considered as an important adjunct when trying to optimise therapy in the difficult to treat patient.

References