P 1624 Therapeutic drug monitoring of Daptomycin: a 4 year audit of levels from a UK clinical antibiotic service.

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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. Where patients had repeated samples sent, there was evidence that therapy had been adjusted in response to TDM in patients with potentially sub-therapeutic or elevated levels. Post dose concentrations were lower than reported in healthy volunteers but consistent with other patients' data suggesting volume of distribution changes in sepsis[3].

Table 1: Percentage of Daptomycin (DAPT) Pre dose samples within and outside guideline levels of 5-20mg/L by age groups.

Conc. range mg/L	Neo-nates	1m-1y	>1y-<18y	>= 18y	All
	N=5	N=20	N=18	N=292	N=335
<5	40%	30%	28%	12%	14%
>=5-20	20%	70%	44%	61%	60%
>20	40%	0%	28%	27%	26%

Table 2: Daptomycin post dose samples by age groups.

Post dose conc. mg/L	Neonates <=1m	>1m-1y	>1y-<18y	>=18y	All
mean	45.3	44.7	54.1	56.4	55.3
range	25.5 - 69.9	8.3 - 97.7	31.4 - 85.8	1.7 - 154.3	1.7 - 154.3
N	3	17	14	206	240

Figure 1: Daptomycin Pre dose samples assayed between 2007 – 2011 in adult patients.

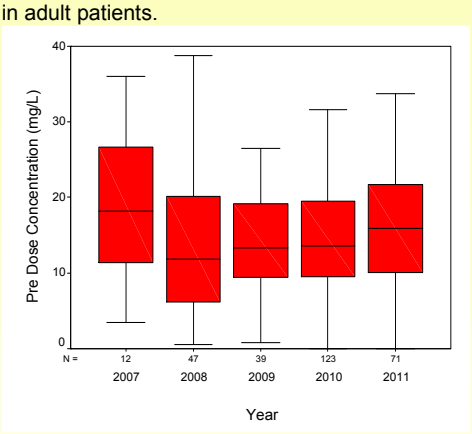
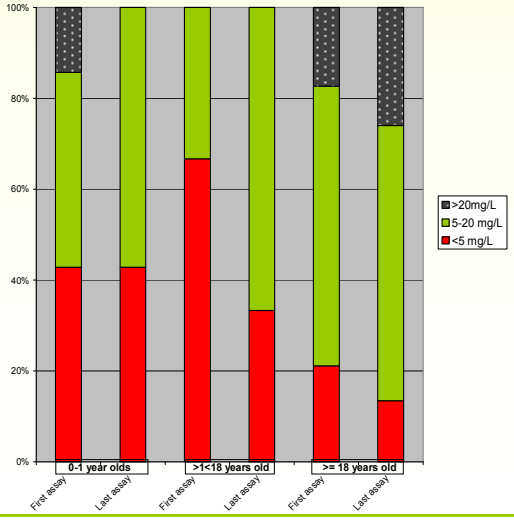


Figure 2: Comparison of patients first and final Daptomycin Pre dose assay concentrations after TDM advice.



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

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