

Daptomycin Trough Serum Levels: Are They Useful in a General Hospital?

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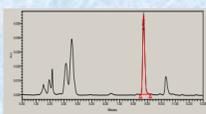
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INTRODUCTION

- ❖ **Therapeutic drug monitoring (TDM)** of daptomycin is not considered routinely necessary, mainly due to the belief that adequate daptomycin serum concentrations are easily reached.
- ❖ However, a wide range of daptomycin doses are used in clinical practice.
- ❖ **Objectives:** to assess interpatient variability in daptomycin blood levels in an inpatient population and to evaluate the potential correlation of dosing, trough levels and clinical outcome.

MATERIAL AND METHODS

- ❖ A **prospective study** performed at a **tertiary care centre** including hospitalized patients who received daptomycin for empirical or targeted treatment and accepted to participate, signing an **informed consent**.
- ❖ **Daptomycin dosage** was at discretion of the attending physicians.
- ❖ Dosage was classified as adequate, low or high according to drug label sheet, indication, weight and renal function. A dosage from **4 to 6 mg/kg** for non-severe skin and soft tissue infections, a dosage from **6 to 10 mg/kg** for other complicated infections and a dosage of **10 mg/kg** for endocarditis were considered adequate.
- ❖ Each patient had one **blood sample drawn** at the end of a dosing interval (within 30 minutes of the next dose), at least **3 days** post-treatment initiation.



- ❖ Serum daptomycin concentrations were determined with **High-Performance Liquid Chromatography**. Trough levels from 6 to 24.3 µg/mL were considered normal.
- ❖ Demographic characteristics, underlying diseases, indication, duration of treatment, microorganisms, laboratory findings and outcome were evaluated.
- ❖ **Clinical outcome** was classified as: a) **poor** –if no clinical response or recurrence or related mortality or if any serious adverse events causing the drug discontinuation (CPK elevations of ≥3 times the upper limit of normal from baseline); b) **favorable** -if clinical improvement or cure occurred and no adverse events were detected.

RESULTS

- ✓ **40 patients** [60% male, median age: 65.6 years (IQR=57.2-75.0)] were included.
- ✓ **Median BMI** was 26.4 m/kg² (IQR=22.5-30.1).
- ✓ Median **Charlson score** was: 4.5 (IQR=3.0-5.7).
- ✓ **Indications** were bacteremia, endocarditis or endovascular infection (n=19), complicated SSTI (12), osteoarticular infection (5) and others (4).
- ✓ **Type of treatment** was Empirical in 13 cases (32.5%) and Targeted in 27 cases (67.5%).
- ✓ **Daptomycin initial dosage** was adequate in 26 cases (65%), lower in 8 (20%) and higher than required in 6 patients (15%).
- ✓ Daptomycin **trough levels** showed large interindividual variability, ranging from 1.9 to 66.0 µg/mL (median:11.1 µg/mL).
- ✓ Out of the 40 patients, 17 (42.5%) were within “normal trough range”, 12 (30%) were below normal trough range (<6 µg/mL) and 11 (27.5%) were above it (>24.3 µg/mL).

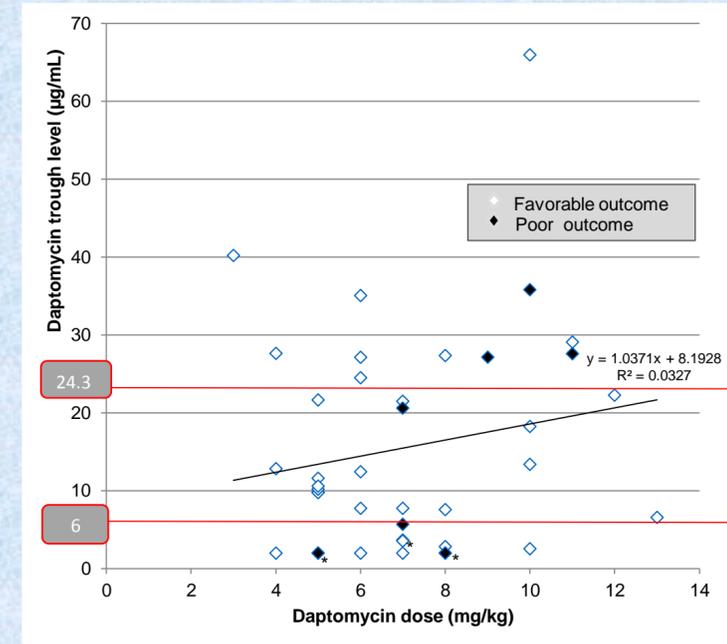


Figure 1. Correlation of dose with trough level and clinical outcome.
* Two patients in the same point.

	Normal range level (N=17)	Out of normal range level (N=23)	P
Non-adequate initial dosage (N=14)	7 (50%)	7 (50%)	0.481
Poor clinical outcome (N=8)	1 (12.5%)	7 (87.5%)	0.107

CONCLUSIONS

- ✓ Treatment with **daptomycin** is associated with a **great interpatient variability** in trough serum levels.
- ✓ There was not a significant relationship between receiving an **inadequate initial dosage** and having an “out of range” trough level.
- ✓ Most of the patients with **poor clinical outcome** had daptomycin trough serum levels out of normal range.
- ✓ Larger clinical trials on daptomycin TDM are needed.