Implementation of a Daptomycin Dosing Nomogram and Assessment of Clinical Outcomes Across a Large Health System

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Background

- Daptomycin is a lipopeptide antibiotic indicated for the treatment of complicated skin and skin structure (cSSSI) and *Staphylococcus aureus* bacteremia, including right-sided endocarditis[1]
- As daptomycin dosing is based on weight and indication, several dosing methods have been studied, which vary from the FDA-approved doses
- Dosing is often complicated when treating off-label infections requiring high-doses and in obese patients[2]
- Optimal dosing weight for daptomycin has remained controversial with limited evidence supporting one optimal weight (e.g., actual body weight, ideal body weight, adjusted body weight)
- A previous study by Schmidt et al. demonstrated benefits with a standardized daptomycin nomogram resulting in reduced medication waste and comparable clinical efficacy as FDA approved dosing strategies[3]
- As more commercially available generic vials are available, including both 350 mg and 500 mg vials, a nomogram could help reduce waste and improve costs[1]

Objective

- In October 2021, AdventHealth (AH) Central Florida (CFDS), a large multi-site health system with over 3,000 inpatient beds, developed and implemented a standardized daptomycin dosing nomogram which included five standardized dosing options:
  - 250 mg, 350 mg, 500 mg, 700 mg, 850 mg 1000 mg
  - Doses were capped at a maximum dose of 1000 mg
  - Nomogram (Figure 1) outlines indications, and dose dispensed based on patient's actual body weight (ABW)
- As the impact of a standardized dosing nomogram at a large health-system is limited, we seek to explore the effects on both clinical and safety outcomes in treating invasive gram-positive infections across AH CFDS

Methods

- This retrospective cohort review compared patients receiving daptomycin across 7 campuses in AH CFDS between September 1, 2020, to December 31, 2020 (pre-implementation) and December 1, 2021, to January 31, 2022 (post-implementation)

Inclusion	Exclusion
Age ≥ 18 and inpatient admission	Ambulatory administration of daptomycin
Invasive Infection (e.g., bone/joint infection, bacteremia, cSSSI, endocarditis)	Uncomplicated skin and skin structure infection (e.g., cellulitis, no surgical intervention required
Duration of daptomycin therapy > 72 hours	One-dose transition to ambulatory therapy of inpatient admission < 72 hours

- Primary outcome was clinical success, defined as:
  - Improvement in signs and symptoms at the end of therapy and/or discharge
  - Absence of repeat positive cultures
- Secondary outcomes included mean length of therapy (LOT), pharmacist adherence to nomogram-guided daptomycin dosing, occurrence of adverse events

Figure 1. Nomogram

Indication	Dose Ordered	Patient ABW	Adult Dose
ABSSSI	4 mg/kg	40-70.9 kg	250 mg
		71-100.9 kg	350 mg
		101-150.9 kg	500 mg
		>151 kg	700 mg
ABSSSI	6 mg/kg	40-49.9 kg	250 mg
		50-69.9 kg	350 mg
		70-94.9 kg	500 mg
		95-124.9 kg	700 mg
		>125 kg	850 mg
MRSA bacteremia and/or endocarditis or osteomyelitis	8 mg/kg	40-55.9 kg	350 mg
		56-75.9 kg	500 mg
		76-90.9 kg	700 mg
		91-115.9 kg	850 mg
		>116 kg	1000 mg
VRE bacteremia	10 mg/kg	40-54.9 kg	500 mg
		55-75.9 kg	700 mg
		76-85.9 kg	850 mg
		>86 kg	1000 mg
VRE bacteremia (enterococcal strains resistant to Penicillin & Aminoglycosides)	12 mg/kg	40-49.9 kg	500 mg
		50-69.9 kg	700 mg
		70-79.9 kg	850 mg
		>80 kg	1000 mg

Figure 2. Demographics

	Pre-Nomogram	Post-Nomogram
Sex	n=100	n=100
Male	53	59
Female	47	41
Age, years (IQR)	56.5 (46-68.2)	59.1 (51-68.5)
Comorbidities		
CKD	8	10
HD	8	8
CRRT	1	0
Statin use	15	15
Statin use + CKD, HD, CRRT	19	18
None	49	49
Average BMI (kg/m^2)	31.4	31.9
Source of Infection		
Bacteremia/Endocarditis	55	55
Bone / Joint Infection	19	27
cSSSI	21	12
Other	5	6

Results

- A total of 200 patients were included, 100 in each group
- For the primary outcome, clinical success was demonstrated in 70% of patients in the pre-implementation group compared to 74% in the post-implementation group (p=0.529)
- In patients with bacteremia and/or endocarditis and repeat cultures, bacterial clearance was demonstrated in 94% of patients in the pre-implementation group and 95% of patients in the post-implementation group (p=0.847)
- Average length of daptomycin therapy was similar between both groups (10.9 days vs. 9.15 days, p=0.191)
- Pharmacist adherence to the dosing nomogram was high in the post-implementation group at 91% compliance
- Rates of adverse events were similar between the two groups with CPK elevations > 200 units/L with elevations occurring in 12% of patients in the pre-implementation group compared to 14% of patients in the post-implementation group (p=0.674)
  - Of the 26 total patients experiencing CPK elevations, 73% of patients were either receiving statin therapy or had existing kidney disease
- *Staphylococcus aureus* was the most frequently isolated pathogen in both cohorts (31% vs. 27%)
- Average BMI was similar between both groups, indicating majority of patients were classified as obese (p=0.727)

Conclusion

- This study demonstrates a safe and effective process for treating invasive gram-positive infections utilizing a standardized daptomycin nomogram
- Given the availability of newer generic formulations, this nomogram could easily be implemented in hospitals seeking alternative dosing strategies

References

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Disclosure

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