Published in final edited form as:
J Perinatol. 2008 March ; 28(3): 233–234. doi:10.1038/sj.jp.7211898.

Daptomycin Use in Infants: Report of Two Cases with Peak and Trough Drug Concentrations

Michael Cohen-Wolkowiez, MD[1], **P Brian Smith, MD MS**[1,2], **Vance G Fowler Jr., MD MHS**[3], **Daniel K Benjamin Jr., MD MPH PhD**[1,2], and **Kelly C Wade, MD PhD**[4]

[1]Department of Pediatrics, Duke University, Durham, North Carolina

[2]Duke Clinical Research Institute, Durham, North Carolina

[3]Department of Medicine, Duke University, Durham, North Carolina

[4]Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

Abstract

We report two infants treated with daptomycin for methicillin-resistant *Staphylococcus aureus* infection and describe peak and trough blood concentrations measured during therapy. The peak concentrations were 41.7 mcg/ml and 36.7 mcg/ml, and the 12-hour trough concentrations were 12.7 mcg/ml and 16.3 mcg/ml, respectively. Even though the infants received higher doses than adults, their drug concentrations were comparable to those observed in adults treated with regular dosing of daptomycin.

Keywords

Staphylococcus aureus; neonates; daptomycin; premature; drug concentration

Introduction

Daptomycin is FDA approved for the treatment of complicated skin and skin structure infections, *Staphylococcus aureus* endocarditis, and bacteremia in adult patients.[2] The drug is not FDA approved for use in neonates and there are no reports of its use in this population. The purpose of our study was to describe peak and trough blood concentrations of daptomycin measured in two infants with methicillin-resistant *Staphylococcus aureus (MRSA) infection*.

Methods

We reviewed the medical records of one neonate and one infant treated with daptomycin for MRSA infection in whom drug concentrations were obtained. Daptomycin blood monitoring is not widely available in clinical practice; the drug concentrations we report were performed by Cubist pharmaceuticals.

Name and address for correspondence: Daniel K Benjamin, Jr. PO Box 17969 Duke Clinical Research Institute Durham NC, 27705 Ph: 919-668-8009 Fax: 919-668-7058 danny.benjamin@duke.edu. Address for reprints if different from that of corresponding author: Same as above..

Results

The first patient was an infant born by spontaneous vaginal delivery at 23 weeks gestational age with a birth weight of 630 grams. At age 2 months, the infant developed MRSA bacteremia. The organism was also resistant to clindamycin, erythromycin, and trimethoprim/sulfamethoxazole, and it was susceptible to rifampin. Susceptibility to gentamicin was unknown. She had persistently positive blood cultures on day 1, 2, and 6 (on day 4 the blood culture was sterile) despite treatment with vancomycin (trough concentrations of 3.3 mcg/ml, 5.8 mcg/ml, 7.9 mcg/ml, 13 mcg/ml, and 19.3 mcg/ml on therapy days 2, 4, 6, 7, and 7, respectively) and central line removal on day three of bacteremia. A transthoracic echocardiogram on day 4 of bacteremia revealed a patent foramen ovale with left-to-right shunt and no vegetations. Because of persistent bacteremia, on day 10 she was started on daptomycin 6mg/kg IV every 12h. Blood cultures drawn 48 hours after and immediately before starting daptomycin were sterile. She received a total of 14 days of daptomycin after negative cultures and 7 days of gentamicin as adjunct therapy. Cerebrospinal fluid was not obtained for evaluation of meningitis and chest radiographs obtained throughout the course of therapy did not reveal evidence of pneumonia. Daptomycin peak and trough plasma samples were collected around dose 22. The peak concentration at the end of the 1-hour infusion was 41.7 mcg/ml and the 12-hour trough concentration was 12.7 mcg/ml. At the time of sample collection the infant had normal creatinine and blood urea nitrogen values (0.5 mg/dl and 3 mg/dl, respectively).

The second patient was a large for gestational age neonate with 11q terminal deletion syndrome born by spontaneous vaginal delivery at 32 weeks with a birth weight of 2670 grams. At 3 weeks of age, she developed signs and symptoms consistent with sepsis, however blood culture was sterile. She was given empirical therapy with vancomycin and gentamicin. After 48 hours of vancomycin therapy, she developed a cervical abscess located in the right anterior submandibular space and piperacillin/tazobactam was started. The abscess was excised on day 4 of vancomycin therapy, and MRSA was isolated. The organism was resistant to clindamycin and erythromycin, but was susceptible to trimethoprim/sulfamethoxazole. This neonate was not evaluated for meningitis and did not have evidence of pneumonia on chest radiograph. She was treated with daptomycin 6 mg/kg IV every 12h for 10 days with resolution of the abscess. After the third dose of daptomycin, the end of the 1-hour infusion peak was 36.7 mcg/ml and 12-hour trough was 16.3 mcg/ml. At the time of sample collection the infant had normal creatinine and blood urea nitrogen values (0.5 mg/dl and 15 mg/dl, respectively). Creatine phosphokinase (CK) measurements were not obtained for these infants.

Discussion

The peak and trough daptomycin blood concentrations obtained in these infants treated with 6mg/kg every 12 hours were consistent with concentrations observed in adults treated with 4 mg/kg/dose every 24 hr (peak 58 mcg/ml, trough 7 mcg/ml).[1] Daptomycin 6 mg/kg every day is approved for treatment of MRSA bacteremia.[2] Preliminary data on the pharmacokinetic properties of daptomycin in children older than 2 years of age indicates that an inverse linear correlation exists between clearance and age when young children are compared with adolescents.[3] This observation suggests that infants may require a higher dose of daptomycin when compared to adults. Pharmacokinetic studies of daptomycin in the neonatal population are needed to better establish these differences. Elevated CK were observed in adults treated with daptomycin[2], but the effect of this drug in infant skeletal muscle is unknown. These two cases suggest that substantial investigation regarding the PK and safety of daptomycin should be obtained prior to its routine use in the nursery; in the interim, physicians treating infants with daptomycin should consider drug and CK concentration monitoring.

Acknowledgments

Statistical support: None.

Sources of support: This work was supported by the Pediatric Pharmacology Research Unit Network. Dr. Cohen-Wolkowiez received support from the Lenox Baker fellowship and is the Lenox Baker Fellow. Dr. Smith received support from T32 (HD-043728-01A2). Dr. Benjamin received support from K23 (HD-044799-01) and 5U10 HD045962-03. Dr. Wade received support from the Pediatric Pharmacology Research Unit (U01 HD037255-06). The assay of daptomycin concentrations was performed by Cubist Pharmaceuticals. We would like to thank Dr. Gordon Worley and the board of directors at the Lenox Baker Children's Hospital for their support during this project.

References

1. Dvorchik BH, Brazier D, DeBruin MF, Arbeit RD. Daptomycin pharmacokinetics and safety following administration of escalating doses once daily to healthy subjects. Antimicrob Agents Chemother Apr; 2003 47(4):1318–23. [PubMed: 12654665]
2. Maryland: Food and Drug Administration. 2003. Fda.gov [homepage on the Internet]Available from: http://www.fda.gov/
3. Kearns, GL., JR; Jafri, HS.; Hong, EF.; Benziger, DP. Pharmacokinetics of Daptomycin in Pediatric Patients. PAS 2007: Pediatric Academic Societies' Annual Meeting, Toronto; Toronto, Canada. 2007 May 5-8; 2007.