JPPT

Editorial

Vancomycin Dosage Regimens for Pediatric Patients

Milap C. Nahata, MS, PharmD

Colleges of Pharmacy and Medicine, The Ohio State University, Columbus, Ohio

KEYWORDS children, dosage regimens, infants, serum concentration, vancomycin

J Pediatr Pharmacol Ther 2009;14:64–65

Intravenous vancomycin is often used to treat serious infections caused by Gram-positive bacteria including those resistant to beta-lactams.

see related article page 86

In the presence of normal renal function, the manufacturer recommends an initial intravenous dose of 15 mg/kg, followed by 10 mg/kg every 12 hours in neonates younger than one week of age and 10 mg/kg every 8 hours for infants one week to one month of age. For older children with normal renal function, the recommended dosage regimen is 10 mg/kg every 6 hours.[1]

The manufacturer recommended vancomycin dosage of 40 mg/kg/day in divided doses for children has not changed for decades despite increasing bacterial resistance over the past decade.[2-4] Thus, the article by Benner et al. correlating vancomycin dosing to serum concentrations in pediatric patients is timely.[5] These authors concluded that vancomycin dosage regimens of 15 mg/kg every 6 to 8 hours produced peak and trough serum concentrations within their target range more frequently than 10 mg/kg every 6 to 8 hours.

Benner et al. have contributed to our knowledge about the relationship between dosage regimens and serum concentrations of vancomycin in pediatric patients.[5] Three hundred seven patients received one of eight dosage regimens with the dose ranging from 30 mg/kg/day to 80 mg/kg/day. Patients ranged from 1 month to 18 years in age and could have had any type of illness. The target ranges for peak and trough serum concentrations were 25-40 mg/L and 5-15 mg/L, respectively. The data were collected retrospectively from January to July 2004. The limitations of this study include retrospective design, heterogenous patient demographics, relatively small number of patients in some groups, and lack of documented clinical outcomes in terms of efficacy or toxicity.

Some authors have suggested that the target trough concentration in adults should be in the range of 10-20 mg/L.[2, 6-9] Although Benner et al.[5] used a target trough concentration of 5-15 mg/L, a specific target range based on clinical evidence in pediatric patients is unknown. This emphasizes the need to conduct prospective efficacy and safety studies in pediatric patients (premature infants to adolescents) for the treatment of various infections.

Benner et al.[5] have raised concerns about the nephrotoxicity and ototoxicity associated with increasing doses of vancomycin in pediatric patients. Previous studies, however, have not established a direct link between recommended doses of vancomycin and toxicity.[10-12] The observed peak and trough serum concentrations of vancomycin ranged from 10-55 mg/L and 2-18 mg/L in one study,[10] and the target ranges for peak and trough serum concentrations were 20-40 mg/L and 5-15 mg/L in another.[11] Nephrotoxicity was not observed in any patient,[10,11] even with concurrent gentamicin therapy with its serum concentration within the therapeutic range.[10] Infants with peak and trough serum concentrations as high as 49.7 and 39.4 mg/L, respectively, also did not develop nephrotoxicity.[12] Thus, the

Address correspondence to: Milap C. Nahata, PharmD, College of Pharmacy, Ohio State University, 500 West 12th Avenue, Columbus, Ohio 43210, email: nahata.1@osu.edu

risk of toxicity associated with vancomycin has not clearly been established in the pediatric age groups with normal renal function.

In summary, intravenous vancomycin continues to be an essential antibiotic for the treatment of serious infections caused by Gram-positive bacteria. At higher doses needed to overcome increasing resistance, we have limited clinical data correlating vancomycin serum concentrations to its efficacy and safety in pediatric patients. Thus, it seems reasonable to selectively monitor its serum concentrations in this population. Implementing explicit criteria can decrease unnecessary vancomycin serum concentration monitoring and costs without adversely affecting health outcomes.[11]

REFERENCES

1. Vancomycin hydrochloride. McEvoy GK, ed. In: AHFS Drug Information. ASHP, Bethesda, MD 2009;478-486.
2. Hidayat LK, Hsu DI, Quist R, et al. High-dose vancomycin therapy for methicillin-resistant *Staphylococcus aureus* infections. Arch Intern Med 2006;166:2138-2144.
3. Soriano A, Marco F, Martinez JA, et al. Influence of vancomycin minimum inhibitory concentration on the treatment of methicillin-resistant *Staphylococcus aureus* bacteremia. Clin Infect Dis 2008;46:193-200.
4. Sakoulas G, Moise-Broder PA, et al. Relationship of MIC and bactericidal activity to efficacy of vancomycin for treatment of methicillin-resistant *Staphylococcus aureus* bacteremia. J Clin Microbiol 2004;42:2398-2402.
5. Benner KW, Worthington MA, Kimberlin DW, Hill K, Buckley K, Tofil NM. Correlation of vancomycin dosing to serum concentrations in pediatric patients: a retrospective database review. J Pediatric Pharmacol Ther 2009;14:86-93.
6. American Thoracic Society. Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171:388-416.
7. Iwamoto T, Kagawa Y, Kojima M. Clinical efficacy of therapeutic drug monitoring in patients receiving vancomycin. Biol Pharm Bull 2003;26:876-879.
8. Wootton M, Walsh TR, MacGowan AP. Evidence for reduction in breakpoints used to determine vancomycin susceptibility in *Staphylococcus aureus*. Antimicrob Agents Chemother 2005;49:3982-3983.
9. Hermsen ED, Toss GH, Rotschafter JC. Glycopeptide pharmacodynamics. In: Nightingale CH, Ambrose PG, Drusano GL, Murakawa T, eds. Antimicrobial pharmacodynamics in theory and clinical practice. 2nd ed. New York, NY: Informa Healthcare USA, Inc.; 2007:189-215.
10. Nahata MC. Lack of nephrotoxicity in pediatric patients receiving concurrent vancomycin and aminoglycoside therapy. Chemotherapy 1987;33:302-304.
11. Lee KR, Phelps SJ. Implementation of vancomycin monitoring criteria in a pediatric hospital. J Pediatr Pharmacol Ther 2004;9:179-186.
12. Bhatt-Mehta V, Schumacher RE, Fair RG, Et al. Lack of vancomycin-associated nephrotoxicity in newborn infants: a case-control study. Pediatrics 1999;103:e48.