

## TEICOPLANIN (Commentary)

## Optimising treatment

There have several small, but relatively good, studies showing how to optimise neonatal treatment, but relatively few published studies looking at treatment in later infancy. Since teicoplanin is almost all excreted unchanged in the urine, and since renal function changes relatively fast in the first few months of life, the dosage regime used to treat a baby 1–2 weeks old cannot be relied upon to produce a sustained therapeutic blood level later in the first year of life. Studies in older patients have shown that treatment with teicoplanin can be very successful as long as the trough level is kept above 10 mg/l (Harding *et al.* 2000) or, for bacterial endocarditis, 20 mg/l (Wilson *et al.*, 1994; Cepeda *et al.*, 2004). Darley and MacGowan also argued in 2004 that trough levels should be monitored more often than they are at present to ensure optimal treatment.

The treatment strategy recommended in most texts (and quoted by the current edition of *BNF for children*) is to give three 10 mg/kg loading doses IV twelve hours apart and then give a maintenance dose of 6 mg/kg IV (or IM) once a day (with a caveat that a 10 mg/kg rather than a 6 mg/kg dose may be more appropriate if there is severe infection). However a study published by Dufort *et al.* in 1996 showed that the trough blood level quite often fell below 10 mg/l when children over a year old were given even a 10 mg/kg daily maintenance dose, and Lukas reported similar findings in 2004. Reed *et al.* came to a similar conclusion in 1997. All concluded that a 15 mg/kg daily maintenance dose might be the best way to *reliably* maintain a trough level of more than 10 mg/l in 1–6 year old children. Clearance is quite variable, but certainly more rapid in children this age than in adult life. While there is only limited evidence that efficacy really *is* compromised if teicoplanin is the only antibiotic being given and the trough level is allowed to fall below 10 mg/l (Sánchez *et al.*, 1999), few clinicians would wish to risk relying on levels this low in a sick baby with a deep-seated staphylococcal infection when there is remarkably little evidence that high levels are toxic.

Because there is still very little published information on how teicoplanin is handled by babies more than a month old, but less than a year old, it seems particularly wise to monitor the trough level in these babies in those centres where this is possible – especially if the baby is overtly unwell. Indeed, a recent UK working party concluded that there were, at the moment, quite strong grounds for using vancomycin rather than teicoplanin when treating methicillin-resistant *Staphylococcus aureus* bacteraemia “unless teicoplanin levels are measured or high dosages are used empirically” (Gemmell, *et al.*, 2006). There is also a very real concern that sub-optimal treatment could speed the emergence of strains of *Staphylococcus aureus* that are resistant to teicoplanin (Cepeda, *et al.*, 2003). There is, on the other hand, good evidence that brief prophylactic use during any high-risk surgical procedure can be both safe and effective (Shime *et al.*, 2007).

**Meningitis** Although teicoplanin, like vancomycin (q.v.), only penetrates the CSF poorly there is one report of intrathecal treatment being used to treat nosocomial Staphylococcal meningitis successfully. One month-old term baby was given 5 mg every 2 days into the ventricles for 4 weeks for *S epidermidis* meningitis; the other was given 10 mg every 3 days for 17 days for *S aureus* meningitis (Kralinsky *et al.*, 1999).

## References

- Terragna A, Ferrea G, Loy A, *et al.* Pharmacokinetics of teicoplanin in pediatric patients. *Antimicrob Agents Chemother* 1988;**32**:1223–6.
- Davey PG, Williams AH. Teicoplanin monotherapy of serious infections caused by Gram-positive bacteria: a re-evaluation of patients with endocarditis or *Staphylococcus aureus* bacteremia from a European open trial. *J Antimicrob Chemother* 1991; **27** Suppl B:51–60.
- Kacet N, Dubos J-P, Roussel-Delvallee M, *et al.* Teicoplanin and amikacin in neonates with staphylococcal infection. *Pediatr Infect Dis J* 1993;**12**:s10–13.
- Kacet N, Dubos JP, Roussel-Delvallee M, *et al.* Teicoplanin and amikacin in neonates with staphylococcal infection. *Pediatr Infect Dis J* 1993;**12**:S10–3.
- Wilson AP, Grüneberg RN, Neu H. A critical review of the dosage of teicoplanin in Europe and the USA. *Int J Antimicrob Agents* 1994;**4**(Suppl 1):1–30.
- Neumeister B, Kastner S, Conrad S, *et al.* Characterisation of coagulase-negative staphylococci causing nosocomial infections in preterm infants. *Eur J Clin Microb Infect Dis* 1995;**14**:856–63.
- Möller JC, Nelskamp I, Jensen R, *et al.* Teicoplanin pharmacology in prophylaxis for coagulase-negative staphylococcal sepsis in very low birthweight infants. *Acta Paediatr* 1996;**85**:638–40.
- Dufort K, Ventura C, Olivé T, *et al.* Teicoplanin pharmacokinetics in pediatric patients. *Pediatr Infect Dis J* 1996;**15**:494–8.
- Reed MD, Yamashita TS, Myers CM, *et al.* The pharmacokinetics of teicoplanin in infants and children. *J Antimicrob Chemother* 1997;**39**:789–96.
- Fanos V, Kacet N, Mosconi G. A review of teicoplanin in the treatment of serious neonatal infections. *Eur J Pediatr* 1997;**156**:423–7.
- Degraeuwe PL, Beuman GH, van Tiel FH, *et al.* Use of teicoplanin in preterm neonates with staphylococcal late-onset neonatal sepsis. *Biol Neonate* 1998;**73**:287–94.
- Kralinsky, Lako J, Dluholucky S, *et al.* Nosocomial staphylococcal meningitis in neonates successfully treated with intraventricular teicoplanin. *Chemotherapy* 1999;**45**:313–4.
- Sánchez A, López-Hercw J, Cueto E, *et al.* Teicoplanin pharmacokinetics in critically ill pediatric patients. *J Antimicrob Chemother* 1999;**44**:407–9.
- Wilson APR. Clinical pharmacokinetics of teicoplanin. *Clin Pharmacokinet* 2000;**39**:167–83.
- Harding I, MacGowan AP, While LO, *et al.* Teicoplanin therapy for *Staphylococcus aureus* septicaemia: relationship between pre-dose serum concentrations and outcome. *J Antimicrob Chemother* 2000;**45**:635–41.

- Sunakawa K, Nonoyama M, Fujii R, *et al.* Pharmacokinetic and clinical studies on teicoplanin for sepsis by methicillin-cephem resistant *Staphylococcus aureus* in the pediatric and neonate field. *Jpn J Antibiot* 2002;**55**:656–77.
- Cepeda J, Hayman S, Whitehouse T, *et al.* Teicoplanin resistance in methicillin-resistant *Staphylococcus aureus* in an intensive care unit. *J Antimicrob Chemother* 2003;**52**:533–4.
- Cepeda JA, Whitehouse Y, Cooper B, *et al.* Linezolid versus teicoplanin in the treatment of Gram-positive infections in the critically ill: a randomized double-blind multicentre study. *J Antimicrob Chemother* 2004;**53**:345–55. [RCT]
- Lukas JC, Karikas G, Gazouli M, *et al.* Pharmacokinetics of teicoplanin in an ICU population of children and infants. *Pharm Res* 2004;**21**:2064–71.
- Darley ESR, MacGowan AP. The use and therapeutic drug monitoring of teicoplanin in the UK. *Clin Microbiol Infect* 2004;**10**:62–9.
- Yalaz M, Cetin H, Akiso M, *et al.* Experience with teicoplanin in the treatment of neonatal staphylococcal sepsis. *J Int Med Res* 2004;**32**:540–8.
- Gemmell CG, Edwards DI, Fraise AP, *et al.* Guidelines for the prophylaxis and treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in the UK. *J Antimicrob Chemother* 2006;**57**:589–608. [SR]
- Shime N, Kato Y, Kosaka T, *et al.* Glycopeptide pharmacokinetics in current paediatric cardiac surgery practice. *Eur J Cardio-Thoracic Surg* 2007;**32**:577–81.
- Kobayashi M, Arima M, Kimura T, *et al.* Population pharmacokinetics of teicoplanin in infants and children. *Jpn J Chemother* 2007;**55**:17–22.

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