

**GENTAMICIN** (Comment)**How accurate does neonatal dosing need to be?**

The childrens' version of the *British National Formulary (BNFc)* is now well established in the UK, and its recommendations are increasingly treated as authoritative. Its general advice on aminoglycoside usage covers most of the key issues well. However, its advice on how to give gentamicin to babies less than one month old using the "extended interval dose regimen" by slow intravenous injection or intravenous infusion over 30 minutes, is:

**Neonate less than 32 weeks postmenstrual age**

4–5 mg/kg every 36 hours

**Neonate 32 weeks and over postmenstrual age**

4–5 mg/kg every 24 hours

**Child 1 month –18 years old: Once daily dose by infusion**

7 mg/kg, then adjusted according to serum gentamicin concentration

**Pharmacokinetics**

Once daily dose regimen: pre-dose ("trough") concentration should be less than 1 mg/litre (2 mg/litre in the first 4 weeks of life).

While these guidelines are very similar to those now being recommended in many other reference texts, they fail to reflect the fact that the half life of gentamicin is controlled almost exclusively by glomerular filtration, and because this almost halves within 1–2 weeks of birth (unless there is renal failure), dosing has to be influenced much more by *postnatal* age than by *postmenstrual* age (as the web commentary for this drug has long stressed). There are also many drawbacks to only giving treatment once every 36 hours. It can be very difficult to remember to give treatment at 36 hour intervals but, more importantly, it can not be assumed that treatment given this infrequently is therapeutic if inhibitory levels are only achieved at such infrequent intervals and for such a relatively short time. While many texts now recommend that the trough blood level in adults should not exceed 1 mg/l rather than 2 mg/l with "once a day" treatment, there is little evidence that such caution is necessary even in adults, and much to suggest that this could easily lead to serious under-treatment (as the differentiated guidance offered by the *BNFc* seems to acknowledge).

In truth most of the current neurosis about gentamicin toxicity is misplaced, because it is extremely uncommon in the neonate unless high blood levels persist for more than a week and/or the child is also being given furosemide at the same time. Although renal tubular function can be mildly affected, this always recovers once treatment is stopped (Giapros *et al.*, 1995; Tugay *et al.*, 2006). Permanent ear damage seems very rare. When it does occur in older patients, it usually affects vestibular function (causing vertigo) much more than cochlear function (causing deafness). The current obsession with not doing harm may well be leaving many children with a genuine infection sub-optimally treated – a concern only partially obscured by the fact that most babies given gentamicin are also being given a second antibiotic at the same time.

Those who express concern that the current recommendation in *BNFc* is wrong (Serane *et al.*, 2009) need to recognise that quite a wide range of treatment options are almost certainly equally safe and equally effective (although this is not quite as true as it is for most other antibiotics). So too do those who express concern that any departure from this is a dosing 'error' (Wong *et al.*, 2008). That such texts continue to list treatment with a dose as low as 2.5 mg/kg once every 18–24 hours as an acceptable option in babies of less than 36 weeks gestation in the first month of life, without giving a first initial loading dose (Gal, *et al.*, 1990), is, however, a recipe for serious under-treatment, because several doses have to be given before a therapeutic peak blood level is achieved with this treatment strategy. The other thing most guidelines continue to ignore is the speed with which clearance increases within 1–2 weeks of birth.

The *BNFc* also, somewhat illogically, advises that although once-a-day treatment can be given as a "slow IV injection" to babies less than a month old, it currently implies that it has to be given as an "IV infusion" over 30 minutes in children older than this. In fact slow administration is really no more necessary in a 2 month old baby than it is in a 2 week old baby, and there is good published evidence that bolus administration over 2–3 minutes is perfectly safe in children of any age (Robinson & Nahata, 2001).

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