

CIPROFLOXACIN (Commentary)

Dosage

The first published study of the way young children handle this drug suggested that the steady-state half life in infancy and childhood was shorter than in adult life (Peltola, *et al.*, 1992). However this finding was not confirmed when the same group later came to study pharmacokinetics using a liquid preparation instead of powdered tablets (Peltola, *et al.*, 1998). There is very little pharmacokinetic data available as yet on children who are less than three months old.

The dose regimen suggested in this *Formulary* is significantly higher than that quoted in most UK publications (including Martindale, the Guy's Paediatric Formulary, and BNF for children), but it is in keeping with the dose used in most of the published reports of the drug's use in young children. While a lower dose *might* be just as effective, there is substantial evidence that the higher dose is safe. The dose recommended here (30 mg/kg a day) is in line with the available pharmacokinetic data (Peltola, *et al.*, 1998). It is also in line with the advice given for children more than a month old in the "Red Book" published by the American Academy of Pediatrics (the Report of the Committee on Infectious Diseases), and in most other North American texts. Similarly, the fact that the average half life is only 4–5 hours, points to the wisdom of recommending 8-hourly rather than 12-hourly treatment in the very ill child. While oral treatment is seldom appropriate in this situation there is a growing consensus that a higher dose is almost certainly appropriate when the drug *is* given by mouth.

The manufacturers have issued little specific advice about use in children because the drug, though increasingly prescribed, has not yet been formally endorsed for use in the US in children less than 18 years old. Similarly it is only formally approved for use in the UK, as yet, in children with cystic fibrosis who are at least five years old. It has been in common use in children in Europe (and particularly in France) for many more years than it has in the UK or North America. Half a million prescriptions for systemic fluoroquinolone treatment were, however, written for children under 18 in the United States in 2002, and the American Academy of Pediatrics came out with a position statement on such use in late 2006. The fact that several other fluoroquinolones had to be withdrawn from the market when toxicity was revealed, quite unexpectedly, during early clinical trials, fueled much of the initial caution. With the publication of several large reviews of efficacy and safety in the last seven years, ciprofloxacin is becoming much more widely used in the management of children with cystic fibrosis. The attitude to use in other conditions is also now changing, especially as the drug can be given by mouth.

However, the drug's use in children less than three months old still remains problematic because, although there are several reports of its use in this age group, there have not yet been any formal pharmacokinetic studies. The dose suggested here is in line with that used in most of the published case reports (and there have been an increasing number of these in the last six years). These reports suggest that the incidence of arthralgia is actually no higher in young children than it is in adult life, and that when it does occur it is almost always transient. 'Benign' intracranial hypertension, though rare, may actually be a potentially more worrying complication.

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Lactation

Mothers taking this drug while breast feeding need to know that the manufacturers are not yet prepared to recommend use in young children. However, they can also be told that their baby is very unlikely to ingest more than 5% of the maternal dose when this is calculated on a weight for weight basis. Indeed in the only study where this was specifically assessed no ciprofloxacin could be detected in the baby's blood (Gardner *et al.*, 1992). Against this, it has to be stressed that there is one anecdotal report of a breast fed baby who inexplicably developed severe pseudomembranous colitis after the mother self-medicated with ciprofoxacin for 6 days (Harmon, *et al.*, 1992). Most reviews suggesting that it is inadvisable for a mother to breast feed while taking this drug (Stoukides, 1991; Fulton and Moore, 1993) date back to a time when there was still much sustained concern that this drug could damage the cartilage of weight bearing joints in children in the same way as it does in some animal species. Given the rarity of skeletal toxicity in man, and the small amount ingested in breast milk, these fears seem greatly exaggerated.

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