

CHLORAMPHENICOL (Commentary)**Side effects of treatment**

Haemolytic anaemia may occur in patients with the Mediterranean variant of G6PD deficiency. There is also a risk of bone marrow suppression at any age if high doses are prescribed for more than 1-2 weeks, but the resultant neutropenia and thrombocytopenia and reduced reticulocyte count are reversible once treatment is withdrawn. Irreversible aplastic anaemia, on the other hand, is not dose-related and typically occurs after therapy is over. There is some suggestion that susceptibility may be genetically determined. Luckily, it only occurs about once every sixty thousand times the drug is prescribed. Both these problems are more commonly seen in children than in neonates. The main toxic symptom of high-dose medication in infancy is the 'grey baby' syndrome with abdominal distension and vasomotor collapse after 2-3 days. Acute toxicity can effectively poison all drug oxidation by the liver for up to three days, and there is no treatment of proven value. Even charcoal haemoperfusion is largely ineffective.

Blood levels

It is probably only worth measuring the peak level (if this can be done) when the drug is used in children less than 4 weeks old. Some texts recommend that trough and peak levels should both be monitored, and there are theoretical reasons for this, because trough levels in excess of 5mg/l can cause damage to cell mitochondria. It is, however, often unrealistic to insist on such a low trough level in the neonate, because biological activation of the administered 'prodrug' proceeds too slowly for the drug to have a definable half life. This is particularly true following oral administration.

Management of neonatal meningitis

A study by Holt (2001) shows that group B streptococci are still the commonest cause of neonatal meningitis. Coliform infection is also common. Cefotaxime (q.v.) is now the drug most frequently used to treat an as yet undiagnosed organism (together with ampicillin or amoxicillin because infection with *Listeria* or enterococci is a real possibility), and mortality has declined since this became the usual approach to treatment. Some 15% of babies still die however, and most survivors suffer some disability. Treatment with vancomycin (q.v.) only seems appropriate once staphylococcal infection has been identified (which is uncommon except as a complication of shunt treatment). Chloramphenicol remains a valid option where drug cost is a major consideration. An uncertain fraction of all neonatal meningitis is viral in origin.

Meningitis in later infancy

Vaccines have now greatly reduced the incidence of meningitis later in infancy in most developed countries, but antibiotic treatment remains the main line of defence in developing countries. Here as many as 170,000 children currently die every year of meningitis, and between a quarter and a half of all the survivors suffer some permanent neurological disability. Unfortunately *H influenzae* is rapidly becoming resistant to chloramphenicol in many of these countries (resistance is said to have increased from 8% to 80% between 1994 and 2000 in Kenya). Treatment with amoxicillin and an aminoglycoside has long been the stand-by strategy in this situation, but ceftriaxone has recently become both an affordable as well as a simpler alternative now that its patent has expired and its cost has fallen. However death still remains common in those who are already drowsy or semi-conscious by the time treatment is started. The scourge of childhood meningitis in the third world will only be defeated when the resources are found to adopt the strategy that has been adopted in the developed world – vaccination.

Further references

- Nahata MC, Powell DA. Bioavailability and clearance of chloramphenicol after intravenous chloramphenicol succinate. *Clin Pharmacol Ther* 1981;**30**:268–72.
- Mulhall A, de Louvois J, Hurley R. The pharmacokinetics of chloramphenicol in the neonate and young infant. *J Antimicrob Chemother* 1983;**12**:629–39.
- De Louvois J, Blackburn J, Hurley R, *et al.* Infantile meningitis in England and Wales: a two year study. *Arch Dis Child* 1991;**66**:603–7.
- Ismail R, The LK, Choo EK. Chloramphenicol in children: dose, plasma levels and clinical effects. *Ann Trop Paediatr* 1998;**18**:123–8.
- Holt DE, Halket S, de Louvois J, *et al.* Neonatal meningitis in England and Wales: 10 years on. *Arch Dis Child* 2001;**84**:F85–9.
- Duke T, Poka H, Dale F, *et al.* Chloramphenicol versus benzylpenicillin and gentamicin for the treatment of severe pneumonia in children in Papua New Guinea: a randomised trial. *Lancet* 2002;**359**:474–80. [RCT]
- Mwangi I, Berkley J, Lowe B, *et al.* Acute bacterial meningitis in children admitted to a rural Kenyan hospital: increasing antibiotic resistance and outcome. *Pediatr Infect Dis J* 2002;**21**:1042–8.
- Duke T, Michael A, Mokela D, *et al.* Chloramphenicol or ceftriaxone, or both, as treatment for meningitis in developing countries. *Arch Dis Child* 2003;**88**:536–9.
- Bryce J, Boschi-Pinto C, Shibuya K, *et al.* WHO estimates of the causes of death in children. *Lancet* 2005;**365**:1147–52.
- Berkley JA, Maitland K, Mwangi I, *et al.* Use of clinical syndromes to target antibiotic prescribing in seriously ill children in malaria endemic area: observational study. *BMJ* 2005;**330**:995–9.
- Nathan N, Borel T, Djibo A, *et al.* Ceftriaxone as effective as long-acting chloramphenicol in short-course treatment of meningococcal meningitis during epidemics: a randomized non-inferiority study. *Lancet* 2005;**366**:308–13. [RCT]

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