

## CEFTRIAZONE

### Use

Ceftriaxone is a versatile and useful cephalosporin antibiotic that only needs to be given once a day. It should only be given with great caution to any child with a high unconjugated bilirubin level.

### Pharmacology

Ceftriaxone is a  $\beta$ -lactamase-resistant 'third generation' cephalosporin first patented in 1979 that is active, like cefotaxime and ceftazidime (q.v.), against some important Gram-positive and most Gram-negative bacteria. Because of good CSF penetration, even when the meninges are not inflamed, it is now often used as a simpler alternative to cefotaxime in the treatment of early meningitis due to organisms other than *Listeria monocytogenes* and faecal streptococci (enterococci). It is also used to treat *Salmonella typhi* infection in countries where this organism is becoming resistant to chloramphenicol (q.v.), and to treat gonorrhoea (*Neisseria gonorrhoea* infection). The drug is excreted unaltered almost equally in bile and urine, so treatment does not normally require adjustment unless there is both renal and hepatic failure. It has a longer half life than other cephalosporins, the plasma half life falling from 15 hours at birth to a value only a little in excess of that found in adults (7 hours) over some 2–4 weeks. It crosses the placenta and also appears in amniotic fluid. There is no evidence of teratogenicity in animals, but only limited information regarding its safety during human pregnancy. Very little appears in breast milk: the baby of any mother treated during lactation would be exposed to less than 1% of the maternal dose on a weight adjusted basis, and little of this would be absorbed.

Ceftriaxone displaces bilirubin from its plasma albumin binding sites, thereby increasing the amount of free, unconjugated bilirubin. This initially made many clinicians reluctant to recommend its use in babies less than six weeks old, and the drug should only be used in babies at risk of developing unconjugated hyperbilirubinaemia if a lower than usual threshold is adopted for starting phototherapy (q.v.). High doses often cause a transient precipitate to form in the biliary tract, and small asymptomatic renal stones occasionally form with sustained use. Ceftriaxone has very occasionally caused severe neonatal erythroderma ('red baby' syndrome). Severe, potentially lethal, haemolysis is another very rare complication. Other problems are very uncommon but the same as for all cephalosporins, as discussed in the monograph on ceftazidime.

### Gonorrhoea

The incidence of this sexually transmitted disease, which can cause vaginal discharge, dysuria and heavy or intermenstrual bleeding, varies greatly in different parts of the world, and a single 250 mg IM dose of ceftriaxone is now widely used to treat maternal infection. If it is not possible to test for possible co-infection with chlamydia it may be appropriate to give a single 1 g dose of azithromycin (q.v.) as well by mouth. There is also a high risk of re-infection unless sexual partners are also seen and treated. Babies run a 30–50% risk of becoming infected at birth, and a 4% chance of developing of serious eye infection in the absence of prompt prophylaxis (as outlined in the monograph on eye drops). The presence of intracellular Gram-negative diplococci on a conjunctival Gram stain is virtually diagnostic. The eyes become increasingly purulent and inflamed, and sight can be put at risk if treatment is not started promptly. Untreated discharge from the eye can also cause cross infection. Generalised septicaemia can occur, and this can cause a destructive septic arthritis if early signs are not sought with diligence. Neonatal ophthalmia is a notifiable disease in the UK.

### Drug interactions

Never give ceftriaxone IV to any child who is being or has recently been given any IV fluid (such as TPN or Ringer lactate) that contains calcium – precipitation could be potentially lethal. Use cefotaxime instead.

### Treatment

**Neonatal gonococcal eye infection:** A single 125 mg IM dose was shown to be a simple and very effective treatment strategy in one African trial (use 40 mg/kg in any low birth weight baby). Consider giving oral azithromycin or erythromycin (q.v.) as well if there is a possibility of chlamydial co-infection.

**Other sepsis:** Give 50 mg/kg IM or, preferably, IV once a day for 7 days. Use with great caution in young babies with unconjugated jaundice. Use a 75 mg/kg dose for meningitis in babies over 4 weeks old.

### Supply and administration

250 mg vials cost £2.70. They contain 0.9 mmol of sodium. Dissolve the powder in this vial in 4–8 ml of water for injection to obtain a 50 mg/ml solution for IV administration. It is only necessary to give this slowly over an hour if the baby has a relatively high unconjugated bilirubin level. To make IM (but *not* IV) injection less painful dissolve the 250 mg of powder with 0.9 ml of plain 1% lidocaine hydrochloride to make a 250 mg/ml solution.

### References

- See the Cochrane review of gonococcal infection in pregnancy ©
- Laga M, Naamara W, Brunham RC, *et al.* Single-dose therapy of gonococcal ophthalmia neonatorum with ceftriaxone. *N Engl J Med* 1986;**315**:1382–5. [RCT]
- Lamb HM, Ormrod D, Scott LJ, *et al.* Ceftriaxone. *Drugs* 2002;**62**:1041–89. [SR]
- 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.
- 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 randomised non-inferiority study. *Lancet* 2005;**366**:308–13. [RCT]
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