CODEINE PHOSPHATE

Use

Codeine is an opioid analgesic frequently given by mouth to adults together with aspirin or paracetamol. Paracetamol on its own (q.v.) is more often used to provide oral analgesia in young children.

Pharmacology

Codeine was first isolated from the opioid juices left over after morphine had been extracted from poppy juice in 1832. The name chosen came from the Greek word *codeia* meaning a poppy capsule. Codeine is only a mild narcotic but it is probably as effective an antitussive (cough suppressant) as morphine. When given by mouth its analgesic effect starts to become apparent after 30 minutes and peaks at 2 hours. Absorption is as rapid but less complete after rectal administration, making a larger dose necessary. Few pharmacokinetic studies have yet been done in early infancy. Tissue levels exceed plasma levels (V_D ~ 3 l/kg). The drug is partly metabolised by the liver (morphine being one of the metabolites), and it is increasingly thought that metabolism to morphine probably explains much of the drug's analgesic effect. The extent to which this occurs seems to depend on which genetic variant of the CYP2D6 cytochrome P450 enzyme the child has inherited, making the exact analgesic effect of any given dose hard to predict except in child who has taken the drug before. Contrary to general belief it certainly seems to cause as much nausea, vomiting, constipation and ileus as a dose of morphine of similar analgesic potency. It also causes as much respiratory depression and hypotension (due to histamine release). Much is finally excreted after conjugation with glucuronic acid in the urine, making repeated, or high dose, administration hazardous where there is renal or liver failure. Little has been published relating to the use of codeine in babies less than three months old.

Excess medication can cause somnolence and respiratory depression, and death has been reported as a result of accidental ingestion. Some cough medicines contain quite a lot of codeine. Even 5 year old children have died after taking more than 5 mg/kg of codeine a day in this way. For this reason the British National Formulary strongly discourages the use of any cough mixture containing codeine in children less than one year old. Codeine is also an ingredient of many of the compound analgesic preparations routinely available in the UK (including a range of preparations that are available 'over the counter') even though it is a schedule 2 controlled drug - a fact that those travelling abroad need to bear in mind.

Codeine crosses the placenta but there is no evidence of teratogenicity. Tolerance develops with repeated usage and withdrawal symptoms have been documented, even in infancy. Heavy maternal usage in the period immediately before delivery can even, occasionally, cause neonatal symptoms of opiate withdrawal 1-2 days after delivery. Codeine, and its active metabolite morphine, are also excreted into breast milk. While the highest blood level usually achieved is less than a third of the lowest therapeutic blood level, a minority of babies inherit a gene that results in their metabolising very much more of the codeine into morphine, and there is one recent report where this caused death from opiate toxicity. The baby of any breast feeding mother taking codeine for more than 1–2 days ***must***, therefore, be monitored for lethargy and somnolence.

Treatment

Dose: Give 1 mg/kg by mouth, or IM, or 1.5 mg/kg rectally. Never give the drug IV because of the risk of anaphylactoid hypotension.

Timing: Never give a dose more than once every 6–8 hours in the first 3 months of life, or every 4–6 hours in children older than that, and never give repeat medication without looking for signs of respiratory depression.

Antidote

An overdose causes drowsiness, pinpoint pupils, hypotension and dangerous respiratory depression. Naloxone (q.v.) is a specific antidote for all the opiate drugs.

Supply

A sugar-free linctus containing 5 mg/ml of codeine phosphate is available on request (100 ml costs 90p). It can be further diluted if requested. The linctus can also be given rectally if oral treatment is not possible. An IM preparation is available, but it would probably more appropriate, in this situation, to give IV or IM morphine (q.v.). Staff need to be aware that some tablets of co-codamol, which is widely used as an analgesic after childbirth, contain as much as 30 mg of codeine as well as 500 mg of paracetamol.

References

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