

AMODIAQUINE

Use

Amodiaquine is an antimalarial that is generally effective against all strains of *Plasmodium falciparum* that are chloroquine sensitive (q.v.), and also against some strains that are not. Because toxicity can sometimes develop with long term use, the drug is now only used to treat specific episodes of overt infection.

History

The search for a drug that can prevent, rather than cure, infection with the malaria parasite has been long and complex. It began in 1917 with the testing of a range of compounds on deliberately infected patients with terminal paralytic syphilis, before it was shown, in 1924, that canaries could be used instead. Knowing that the plasmodia parasite takes up the dye methylene blue, work initially focused on quinoline/methylene blue hybrids, and clinical trials showed, within a year, that one such drug pamaquin could cure naturally acquired falciparum malaria. It took rather longer to realise that it worked by killing the sporozoites lurking in the liver, and not the merozoites liberated by cyclical liver-cell rupture into the blood (as quinine did). A range of 4- and 8-aminoquinolones were then studied during the second world war by the American Army's Malaria Research Programme before chloroquine, and then amodiaquine, came into widespread use in the late 1940s.

Pharmacology

Amodiaquine hydrochloride is a 4-aminoquinolone, that is structurally related to chloroquine. It is well absorbed when taken by mouth and rapidly converted by the liver to the active metabolite monodesmethylamodiaquine which is then excreted by the kidney in a relatively slow, and rather variable way, (the mean plasma half life being 2–3 days). Amodiaquine was developed by Parke-Davis and Company, and it was quite widely used in the 1960's after chloroquine-resistant strains of malaria started to become increasingly common. However, use declined very abruptly in 1986 once it was realised that sustained use could sometimes cause quite severe neutropenia and also, rather more rarely, liver toxicity. While amodiaquine is no longer used to *prevent* infection it has started to be used to *treat* infection once more, because there is a widespread belief that toxicity only occurs with sustained use. Time will tell whether this is actually true although, in the countries where amodiaquine is most widely used at present, such toxicity could well go unrecognised. There is no evidence that an overdose causes any of the life-threatening cardiovascular complications often seen after an overdose of chloroquine (although this may simply be because the drug has not yet been very widely used), but a serious overdose of amodiaquine can certainly cause seizures and a loss of consciousness. An attack of malaria in the last six months of pregnancy can seriously affect maternal health and jeopardise fetal survival, and treatment with amodiaquine, preferably with one dose of pyrimethamine (q.v.) and sulphadoxine (as Fansidar[®]) seems very safe, even though it can briefly exacerbate co-existent tiredness, dizziness and nausea. Little is known about the use during lactation, but there is very good evidence that use of the closely related drug chloroquine is extremely safe.

Treatment

During pregnancy: Give two 600 mg doses 24 hours apart and then one 300 mg dose. Co-treatment with a single 75 mg dose of pyrimethamine and 1.5 g of sulphadoxine on the first day minimises treatment failure.

During infancy: Give 10 mg/kg of amodiaquine base twice by mouth at daily intervals, and then one 5 mg/kg dose after a further 24 hours.

Supply

Amodiaquine is provided for oral administration as the hydrochloride, but the product is normally described in terms of the amount of amodiaquine base (260 mg of amodiaquine hydrochloride being equivalent to 200 mg of amodiaquine base). The drug is not currently marketed in the UK or the US, but it is available from Parke-Davis as a 200 mg tablet (Camoquine[®]) costing 65p that can be crushed, suspended in water, and the dose then given by spoon. A commercial suspension has also been supplied for research purposes.

References

See also the relevant Cochrane reviews ©

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