Quinine and Quinidine

Class:
Quinine and quinidine are both arylaminoalcohols.

Antiparasitic Activity:
Quinine acts primarily on the erythrocytic stage of human malarias with little parasiticidal effect on sporozoites, hepatic stages, or gametocytes of *P. falciparum*. The asexual stages of *P. ovale* are the most vulnerable to quinine, followed by *P. vivax*, *P. malariae* and then *P. falciparum*. Quinine has some gametocytocidal activity for *P. vivax* and *P. malariae*.

Mechanism of Action:
The mechanism of action is interference with the parasite’s ability to digest haemoglobin. Quinine and quinidine also inhibit the spontaneous formation of beta-haematin (haemozoin or malaria pigment) which is a toxic product of the digestion of haemoglobin by parasites.

Pharmacokinetics (quinine and quinidine):
Quinine is rapidly and completely absorbed. The clearance of quinine varies between 1.2-4 ml/min/kg and the mean elimination half-life is 10-12 hours. Clearance may be reduced in the elderly, smokers and in patients with malaria. Quinine is cleared primarily by hepatic metabolism. The systemic clearance of total drug and renal elimination (15-40%) is higher for quinidine (2.5-5 ml/min/kg) than quinine. (Tables 1 & 2).

Dosage:
Quinine:
In uncomplicated malaria, the standard oral dose of quinine is 10mg/kg of salt 8 hourly for 7 days for both children and adults.
In patients with previously untreated severe malaria an initial loading dose of quinine (as a dihydrochloride salt) or if unavailable, quinidine (as the gluconate), should be given.
Quinine is given for a minimum of 7 days, and an antimalarial antibiotic is added, if indicated, when the patient can tolerate oral treatment.

Quinidine:
In the USA, quinidine is used to treat severe falciparum malaria.
Quinidine should be given in a loading dose (10 mg/kg gluconate in 1 hour) followed by a maintenance infusion of 0.02 mg/kg/minute during the acute phase of severe infection. Conversion to oral quinidine can take place when it is tolerated.

Pregnancy:
Most cases of falciparum infection in pregnancy will be treated with quinine.
Pregnancy causes an increase in unbound (pharmacologically active) fractions of quinine.

Adverse Effects:
Headache, nausea, sweating vasodilatation and diarrhoea are common (15-50%) reactions to oral quinine and quinidine even when drug levels are in the therapeutic range. The most troublesome side effects are due to cinchonism, which includes reversible hearing loss. Quinine or quinidine-induced cardiotoxicity is the usual cause of death when either in overdoses. Quinine in the potential to cause reversible as well as permanent blindness in overdoses. Hyperinsulinaemic hypoglycaemia can occur in both children and adults.