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Pharmacology assignment

Classify the antimalarial agents and state the mechanism of action of every drug listed.

Answer

1. Chloroquine: chlorquine and other similar quinolones (e.g. hydroxychloroquine, quinine) become concentrated in parasite food vacuoles, preventing the polymerization of the hemeoglobin product, heme, into hemozoin and thus eliciting parasite toxicity due to the build-up of heme It is not active against liver stage parasites (and primaquine must be added for the radical cure of these species).Malarial parasites have a limited ability to synthesize amino acids, and rely upon amino acids obtained by the breakdown of host hemoglobin molecules in digestive vacuoles. Degradation of hemoglobin releases both amino acids as well as a toxic heme metabolite ferriprotoporphyrin IX, which is normally detoxified by a pH-dependent polymerization to an unreactive malarial pigment named hemozoin. When polymerization of ferriprotoporphyrin IX is inhibited, its increased concentration in the parasites food vacuole will cause oxidative damage to membranes and death of the parasite.
2. Quinine (& Quinidine) for Malaria: Its precise mechanism as an antimalarial is poorly understood. In *Plasmodium falciparum* quinine has been found to inhibit nucleic acid synthesis, protein synthesis, and glycolysis; it also binds with hemazoin in parasitized erythrocytes. Quinine is effective as a malarial suppressant and in control of overt clinical attacks. Its primary action is schizontocidal, no lethal effect is exerted on sporozoites or pre-erythrocitic tissue forms. Quinine blocks cardiac K & Na channels similar to quinidine.
3. Mefloquine: Unknown, chemically related to quinidine. Has strong blood schizonticidal activity against *P. falciparum* and *P. vivax*, but not against hepatic stages or gametocytes. It is the drug of choice for chemoprophylaxis against chloroquine-resistant strains of malaria.Recommended by the CDC for chemoprophylaxis in all malarious areas except those with no chloroquine resistance (where chloroquine is preferred) and some rural areas of SE Asia with a high prevalence of mefloquine resistance. As with chloroquine, eradication of *P. vivax* and *P. ovale* requires a course of primaquine.
4. Pyrimethamine + Sulfadoxine**:** They are folic acid antagonists. The rationale for the combination is a synergistic effect to inhibit folic acid synthesis, and a differential requirement between host and parasite for nucleic acid precursors involved in growth. This activity is highly selective against plasmodia and Toxoplasma gondii. Pyrimethamine is chemically related to trimethoprim. It acts slowly against erythrocytic forms of susceptible strains of all four human malaria species. It is not adequately gametocidal or effective against liver stages.
5. Artesunate & Artemether (Artemisinin analogs): it produces a free radical when it undergoes an iron-catalyzed cleavage of an endoperoxide bond in the parasite food vacuole. It is a rapidly acting blood schizonticide, with some activity against gametocytes, but no activity against the hepatic stages of the malarial parasite.