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Department: Nursing

Course title: Systemic Pharmacology in Nursing Practice

Assignment title: Chemotherapy of malarial parasite

Question

Classify the antimalarial agents and state the mechanism of action of each class of drug listed

Antimalarial agents are drugs effective in the treatment of malaria. Malaria is an infectious disease caused by the bite of an anopheles mosquito infected with certain protozoans.

Classification of antimalarial drugs

- Therapeutic classification
- Chemical classification

Therapeutic Classification

1. **Casual prophylaxis: (primary tissue schizonticides):** These drugs act on the primary tissue forms of the plasmodia which after growth within the liver, initiate the erythrocytic stage. By blocking this stage, further development of the infection can be theoretically prevented. Pyrimethamine and Primaquine have this activity.

Pyrimethamine: An antiparasitic drug used in the prevention and treatment of malaria.

Primaquine: May convert into electrophilic intermediates that act as oxidation – reduction mediators. This could contribute to antimalarial effect by generative reactive oxygen species or by interfering with mitochondrial electron transport in the parasite.

2. **Suppressives Prophylaxis:** These drugs suppress the erythrocytic phase and thus attack of malarial fever can be used as prophylactics.

Chloroquine: It is actively concentrated by sensitive intraerythrocytic plasmodia. Higher conc. is found in infected RBCs. By accumulating in the acidic vesicles of the parasite and because of its weakly basic nature, it

raises the vesicular pH and thereby interferes with degradation of haemoglobin by parasitic lysosomes.

Polymerization of toxic heme to nontoxic parasite hemozoin is inhibited by formation of chloroquine heme complex. Heme itself or its complex with chloroquine then damages the plasmodial membrane.

Proguanil: A medication indicated for prophylaxis and treatment of plasmodium falciparum malaria.

3. **Clinical cure: erythrocytic schizonticides** – These drugs act on the blood forms of the parasite and thereby terminate clinical attacks of malaria. These are the most important drugs in anti-malarial chemotherapy.

Fast acting high efficacy – Chloroquine, quinine, mefloquine, artemisinin

Slow acting low efficacy drugs – Pyrimethamine, sulfonamides, proguanil

4. **Radical curative:** These drugs act on the hypnozoites of *P. vivax* and *P. ovale* in the liver that cause relapse of symptoms on reactivation. Primaquine is the prototype drug; Pyrimethamine also has such activity.
5. **Gametocidal:** These drugs destroy the sexual forms of the parasite in the blood and thereby prevent transmission of the infection to the mosquito. Chloroquine and quinine have gametocytocidal activity against *P. vivax* and *P. malariae*, but not against *P. falciparum*. Primaquine has gametocytocidal activity against all plasmodia, including *P. falciparum*.

Chemical Classification

1. **4 – Aminoquinolines;** Chloroquine, amodiaquine, piperaquine

Chloroquine: Binds to and inhibits dna and polymerase; interferes with metabolism and hemoglobin utilization by parasites; inhibits prostaglandin effects. The parasite digests the human hemoglobin in order to get amino acid. Chloroquine enters parasite cell by simple diffusion. It then becomes protonated as the digestive vacuole is known to be acidic. Chloroquine inhibits polymerization of heme and accumulation of heme. Chloroquine binds to heme to form fp – chloroquine complex, which is highly toxic to the cell and disrupts membrane function. Action of the toxic compound results in cell lysis and ultimately parasite cell autodigestion.

2. **Quinoline** – Methanol; Mefloquine

Mefloquine: It is a very potent blood schizonticide with a long half – life. It

isthought to act by forming toxic hemem complexes that damage parasitic food vacuoles.

3. **Cinnchona alkaloid;** Quinine, Quinidine

Quinine: As an alkaloid, it is accumulated in the food vacuoles of P. species especially Plasmodium falciparum. It acts by inhibiting the hemozoin biocrystallization, thus facilitating an aggregation of cytotoxic heme. Quinine is less effective and more toxic as a blood schizonticidal agent than chloroquine; however, it is still very effective and widely used in the treatment of acute cases of severe P. falciparum.

4. **Biguanide;** Proguanil

Proguanil: It inhibits the malarial dihydrofolate reductase enzyme of sensitive plasmodia, causing inhibition of DNA synthesis and depletion of folate cofactors

5. **Diaminopyrimidine;** Pyrimethamine

Pyrimethamine: It is used in the treatment of uncomplicated malaria. It acts by inhibiting dihydrofolate reductase in the parasites thus preventing the biosynthesis of purines and pyrimidines, thereby halting the processes of DNA replication, cell division and reproduction.

6. **8 – Aminoquinoline;** Primaquine, tafenoquine

Primaquine: It is a highly active 8 – aminoquinolone that is effective against P. falciparum gametocytes but also acts on merozoites in the bloodstream and on hypnozoites. It is thought to block oxidative metabolism in plasmodia.

7. **Sulfonamides and sulfone;** Sulfadoxine, sulfamethopyrazine, dapsone

8. **Tetracyclines;** Tetracycline, doxycycline

9. **Sesquiterpine Lactones;** Artesunate, artemether, arteether

Artemisinin: These compounds contain endoperoxide bridge. Endoperoxide bridge interacts with heme in parasite. There is generation of highly reactive free radicals which damage parasite membrane by covalently binding to membrane proteins. They act rapidly killing blood stages of all plasmodium species and reducing the parasite biomass. Artemisinin are active against gametocytes, the parasite form that is infectious to mosquitoes and their use has been associated with reduced malaria transmission.

10. **Naphthoquinone;** Atovaquone

