**NAME; INEGBEDION OMONE**

**MATRIX NO; 17/MHS02/045**

**DEPARTMENT; NURSING**

**LEVEL; 300**

**COURSE TITTLE; PHARMACOLOGY**

**COURSE CODE; PHA326**

**QUESTION**

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

**ANSWER**

Antimalarial agents can be classified as follows

1. 4-AMINOQUINOLINES: Chloroquine, Amodiaquine, Piperaquine.
2. QUINOLINE-METHANOL: Mefloquine.
3. CINCHONA ALKALOID: Quinine, Quinidine.
4. BIGUANIDE: Proguanil (Chloroguanide), Chlorproguanil.
5. DIAMINOPYRIMIDINE: Pyrimethamine.
6. 8-AMINOQUINOLINES: Primaquine, Bulaquine.
7. SULFONAMIDES AND SULFONE: Sulfadoxine, Sulfamethopyrazine, Dapsone.
8. ANTIBIOTICS: Tetracycline, Doxycycline.
9. SESQUITERPINE LACTONES: Artesunate, Artemether,Arteether.
10. AMINO ALCOHOLS: Halofantrine, Lumefantrine.
11. NAPHTHYRIDINE: Pyronaridine.
12. NAPHTHOQUINONE: Atovaquone

And the mechanism of action is as followed

1. 4-AMINOQUINOLINES

chlorquine and other similar quinolones (e.g. hydroxychloroquine, quinine) inhibits the action of heme polymerase in malarial trophozoites, preventing the conversion of heme to hemazoin. Plasmodium species continue to accumulate toxic heme, killing the parasite. Chloroquine passively diffuses through cell membranes and into endosomes, lysosomes, and Golgi vesicles; where it becomes protonated, trapping the chloroquine in the organelle and raising the surrounding pH. The raised pH in endosomes, prevent virus particles from utilizing their activity for fusion and entry into the cell.

1. QUINOLINE-METHANOL

It is chemically related to quinidine. Has strong blood schizonticidal activity against P. falciparum and P.vivax, but not against hepatic stages or gametocytes. Mefloquine produces swelling of the Plasmodium falciparum food vacuoles. It may act by forming toxic complexes with free heme that damage membranes and interact with other plasmodial components.

1. CINCHONA ALKALOID

It is actively concentrated in the sensitive intra erythrocytic plasmodia by accumulating in the acidic vesicles of the parasite and the weakly basic nature. It raises the vesicular ph and thereby interfering with the degradation of hemoglobin by parasitic lysosomes. Polymerization of toxic heame to nontoxic parasite pigment hemozoin is inhibited by formation of the Quinine-heame complex. Heame itself or in complex with Quinine then damages the plasmodial membranes. Clumping of pigment and changes in parasite membranes follow: death.

1. BIGUANIDE

It is a prophylactic antimalarial drug, which works by stopping the malaria parasite, Plasmodium falciparum and Plasmodium vivax, from reproducing once it is in the red blood cells. It does this by inhibiting the enzyme, dihydrofolate reductase which is involved in the reproduction of the parasite.

1. DIAMINOPYRIMIDINE

Pyrimethamine interferes with the regeneration of tetrahydrofolic acid from dihydrofolate by competitively inhibiting the enzyme dihydrofolate reductase. Tetrahydrofolic acid is essential for DNA and RNA synthesis in many species, including protozoa.

1. 8-AMINOQUINOLINES

It eliminates tissue erythrocyte infection. Thereby, kit prevents the development of the erythrocytic forms of the parasite which is responsible for relapse in vivax and ovale malaria. Primaquine phosphate is also active against gametocyte of Plasmodium falciparum.

1. SULFONAMIDES AND SULFONE

Sulfadoxine is a sulfa drug, often used in combination with pyrimethamine to treat malaria. This medicine may also be used to prevent malaria in people who are living in, or will be traveling to, an area where there is a chance of getting malaria. Sulfadoxine targets Plasmodium dihydropteroate synthase and dihydrofolate reductase. Sulfa drugs or Sulfonamides are antimetabolites. They compete with para-aminobenzoic acid (PABA) for incorporation into folic acid. The action of sulfonamides exploits the difference between mammal cells and other kinds of cells in their folic acid metabolism. All cells require folic acid for growth. Folic acid (as a vitamin) diffuses or is transported into human cells. However, folic acid cannot cross bacterial (and certain protozoan) cell walls by diffusion or active transport. For this reason bacteria must synthesize folic acid from p-aminobenzoic acid.

1. ANTIBIOTICS

They inhibit the initiation of translation in variety of ways by binding to the 30S ribosomal subunit, which is made up of 16S-rRNA and 21 proteins. They inhibit the binding of aminoacyl-tRNA to the mRNA translation complex.

1. SESQUITERPINE LACTONES

The mechanism of action for Artesunate is thought to involve the cleavage of the endoperoxide bond. Though reaction with heame. This produces free radicals with alkylate parasitic proteins. It has been shown to inhibit an essential parasite calcium adenosine triphosphate enzyme.

1. AMINO ALCOHOLS

The mechanism of action of Halofantrine may be similar to that of chloroquine, quinine, and mefloquine; by forming toxic complexes with ferritoporphyrin IX that damage the membrane of the parasite.

1. NAPHTHYRIDIN

It is actively concentrated in the sensitive intra erythrocytic plasmodia by accumulating in the acidic vesicles of the parasite and the weakly basic nature. It raises the vesicular ph and thereby interfering with the degradation of hemoglobin by parasitic lysosomes. Polymerization of toxic heame to nontoxic parasite pigment hemozoin is inhibited by formation of the Pyronaridine-heame complex. Heame itself or in complex with Pyronaridine then damages the plasmodial membranes. Clumping of pigment and changes in parasite membranes follow: death.

1. NAPHTHOQUINONE

The mechanism of action against Pneumocystis carinii has not been fully elucidated. In Plasmodium species, the site of action appears to be the cytochrome bc1 complex (Complex III). Several metabolic enzymes are linked to the mitochondrial electron transport chain via ubiquinone. Inhibition of electron transport by atovaquone will result in indirect inhibition of these enzymes. The ultimate metabolic effects of such blockade may include inhibition of nucleic acid and ATP synthesis. Atovaquone also has been shown to have good in vitro activity against Toxoplasma gondii.