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COURSE TITLE: SYSTEMIC PHARMACOLOGY IN NURSING PRACTICE

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CHEMOTHERAPY OF MALARIAL PARASITES

Question

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

Antimalarial agents can be classified as follows

* 4-AMINOQUINOLINES
* QUINOLINE-METHANOL
* CINCHONAALKALOID
* BIGUANID
* DIAMINOPYRIMIDIN
* 8-AMINOQUINOLINE
* SULFONAMIDES AND SULFON
* ANTIBIOTICS
* SESQUITERPINE LACTONES
* AMINO ALCOHOLS
* NAPHTHYRIDINE
* NAPHTHOQUINONE
1. 4-AMINOQUINOLINES : Chloroquine, Amodiaquine, Piperaquine.

**MECHANISM OF ACTION**

The mechanism of action of 4-aminoquinolines is characterized by the concentration of the drug in the digestive vacuole of the intraerythrocytic parasite.

It is actively concentrated by sensitive intra-erythrocytic plasmodia by accumulating in the acididc vessels of the parasite and weakly basic nature it raises the vesicular pH and thereby interferes with degradation of haemoglobin by parasitic lysosomes

Polymerization of toxic haeme to non toxic parasite pigment hemozoin is inhibited by formation of chloroquine-heme complex.

1. QUINOLINE-METHANOL: Mefloquine

**MECHANISM OF ACTION**

Anti malarial agent which acts as a blood schizonticide. 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: Quinine, Quinidine.

**MECHANISM OF ACTION**

It is a weak base and gets concentrated in the acidic food vacoule of sensitive plasmodia and inhibits polymerization of haeme to hemozoin.

Levels of Free haeme builds up which is toxic or haeme-quinine complex damages parasite membranes and kills it.

1. BIGUANIDE: Proguanil(Chloroguanide), Chlorproguanil.

**MECHANISM OF ACTION**

Slow acting erythrocytic schizontocide. It is cyclized in the body to cycloguanile which inhibits plasmodial DHFRase in preference to the mammalian enzyme.

1. DIAMINOPYRIMIDINE : Pyrimethamine

**MECHANISM OF ACTION**

Pyrimethamine interferes with the generation 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 : Primaquine, Bulaquine

**MECHANISM OF ACTION**

Primaquine's mechanism of action may be acting by generating reactive oxygen species or by interfering with the electron transport in the parasite. Also, primaquine may bind to and alter the properties of protozoal DNA.

1. SULFONAMIDES AND SULFONE : Sulfadoxine, Sulfamethopyrazine, Dapsone.

**MECHANISM OF ACTION**

Sulfadoxine targets plasmodium dihydropteroatesynthase and dihyrofolatereductase. Sulfa drugs or Sulfonamides are anti-metabolites. They compete with Paraaminobenzoic acid (PABA) for incorporation into folic acid. The action of sulfonamides exploits the difference between mammal cells and other kind of cells in their folic acid metabolism.

1. ANTIBIOTICS : Tetracycline, Doxycycline

**MECHANISM OF ACTION**

Tetracycline passively diffuses through porin channels in the bacterial membrane and reversibly binds to the 30 ribosomal sub unit, preventing binding of RNA to the RNA-ribosome complex, and thus interfering with protein synthesis.

1. SESQUITERPINE LACTONES; Artesunate, Artemether, Arteethe

**MECHANISM OF ACTION**

The mechanism of artesunate is thought to involve cleavage of the endoperoxide bond through reaction with haeme. This produces free radicals which alkylate parasitic proteins. It has been shown to inhibit an essential parasite calciumadenosine triphosphtransferase, responsible for breaking down cytotoxic hematin.

1. AMINO ALCOHOLS: Halofantrine, Lumefantrine

**MECHANISM OF ACTION**

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

11: NAPHTHYRIDINE : Pyronaridine

**MECHANISM OF ACTION**

It has a mechanism of action similar to that of Chloroquine, namely it inhibits formation of B-hematin complex, inhibits gluathione dependent degradation of hematin and enhances hematin induced lysis of red blood cells.

12. NAPHTHOQUINONE: Atovaquone

**MECHANISM OF ACTION**

The mechanism of action against Pneumocystiscarinii has not been fully elucidated.In Plasmodium species,the site of action appears to be the cytochrome bc1 complex (ComplexIII). 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 acic an ATP synthesis. Atovaquone also has beeen shown to have good in vitro activity against Toxoplasma gondii.