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**DEPARTMENT: Nursing science**

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 Classify Antimalarial agents and state the mechanism of action of each of the drug .

**Classification and Their Mechanism of Actions**

**Chemical Classification**

**Sesquiterpine lactones (Artesunate, Artemether, Arteether):**

**Mechanism of action**

* It is a rapidly acting blood schizonticide, with some activity against the gametocytes, but no activity against the hepatic stages of the malaria parasite.
* Produces a free radical when it under goes an iron-catalyzed cleavage of an endoperoxide bond in the parasite food vacuole.

 **4-Aminoquinoline (**Chloroquine, Amodiaquine**):**

 **Mechanism of Action**

* It is actively concentrated by sensitive intra-erythrocytic plasmodia by accumulating in the acidic vesicles of the parasites and weakly basic in nature, it raises the PH of the vessel and thereby interfere with degradation of hemoglobin by parasite lysosome.
* Polymerization of toxic haeme to nontoxic parasite pigment Hemozoin is inhibited by formation of Chloroquine or Amodiaquine-Heme complex.

Haeme itself or its complex with Chloroquine or Amodiaquine then damages the plasmodia membranes, clumping of pigment and changes in parasitic membrane and then follow death.

 **8-Aminoquinoline (Primaquine, Tafenoquine)**

 **Mechanism of Action**

* It eliminates tissue erythrocytic 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 to plasmodium falciparum.

 **Sulfonamide and Sulfone (Sulfadoxine, Sulfamethopyrazine, Dapsone )**

**Mechanism of Action**

* They interfere with folic acid synthesis by preventing addition of para-aminobenzoic(PABA) into the folic acid molecule through competying for the enzyme, dihydropteroate synthase.

**Cinchona alkaloid (**Quinine, Quinidine)

Mechanism of Action

* 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 the schizontocidal, no lethal effect is exerted on sporozites or pre-erythrocytic tissue forms
* Quinine blocks cardiac K&Na channels similar to quinidine.

**Diaminopyrimidines (Pyrimethamine)**

**Mechanism of Action**

* It inhibits plasmodial hydrofolate reductase, reducing the production of folic acid required for nuclei and synthesis in the malaria parasite. It is used to treat acute malaria but not for prophylaxis.

**Antibiotics (Tetracyclins, Doxycycline)**

**Mechanism of Action**

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

**Biguanides(Proguanil, Chloroguanide)**

**Mechanism of Action**

* 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 enzymes, dihydrofolate reductase which is involved in the reproduction of the parasite.

**Amino Alcohols (Halofantrine, Lumefantrine)**

**Mechanism of Action**

* **I**t is actively concentrated in the sensitive intra erythcytic plasmodial by accumulating in the acidic vesicles of the parasite and the waaaaaeakly basic nature. It raises the vascular PH and thereby interfering with the degradation of hemoglobin by parasite lysosomes.
* Polymerization of toxics haeme to nontoxic parasite pigment hemozoin is inhibited by formation of the Lumenfantrinephaeme complex. Haeme itself or in complex with Lumenfantrine then damages the plasmodial membranes. Clumbing of pigment and changes in parasite membranes follow death.

**Naphthyridine** (Pyronaridine)

**Mechanism of Action**

* It is actively concentrated in the sensitive intra erythrocytic plasmodial 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 parasite lysosomes. Polymerization of toxics haeme to nontoxic parasite pigment hemozoin is inhibited by formation of the Pyronaridine-haeme complex. Haeme itself or in complex with Lumenfantrine then damages the plasmodial membranes. Clumbing of pigment and changes in parasite membranes follow death

**Naphthoquinone (Atovaquone)**

**Mechanism of Action**

* It possesses a novel model of action against Plasmodium falciparum through inhibition of the electron transport system at the level of cytochrome bc1 complex. Avotaquone also causes the collapse of the parasite mitochondrial potential in Plasmodium falciparum.