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Mini Review

A Review on Anti-Malarial Drugs

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Abstract

Malaria is death causing disease if not treated properly on time. Maleria is caused by a protozoan called as *Plasmodium parasite*. Newly identified anti-malarial drug is a fixed dose mixture of two effective anti-malarial components arterolane maleate and piperaquine phosphate. Arterolane does reductive breakage in the meal vacuaole by Fe^{2+} iron to develop free radical species which prevent "PfATP6", a Sarcoplasmic Reticulum Calcium ATPs. The main metabolic pathway is the oxidation of adamantate to arterolane.

Key words: antimalarial drugs; plasmodium vivax; allergic reactions

Introduction

Malaria disease is a death causing which caused by a parasite which belongs to phylum protozoa. This malaria parasite infects WBC present in human blood.

The word "mal aria" was used by H. Walpole in 1740 very first. The Term malaria is derived from an Italian word "mal aria" which connote "bad air".

This word "mal aria" was shortened to malaria century by C. Laveran in 20th.

There are five species of malaria parasite which is source malaria malaria.

Plasmodium falciparum, Plasmodium vivax, Plamodium malariae, Plasmodium ovale

Plasmodium knowlesi

Signs and Symptoms

1. Spleen enlargement
2. Diarrhea
3. Dry Cough
4. Vomiting
5. Nausea
6. Central headache.
7. Muscle aches (Fatigue, Pain)
8. Chills, Sweating
9. Flulike illness with systemic fever

Malarial infection in Bareilly region

Most of the area of Bareilly district covered by Tarai Region (Area nearest to rivers) due to The Holy Ganga River. Due to which this trai region contain wet land and this wet land favors the growth of different species of mosquitoes including female Anopheles, which play an important role to transmittance of malaria parasite; that is why malaria disease still a most dangerous disease in tarai region**.** A report printed in Times of India on dated October 5 ,2019 said in 2019 total 74749 cases of malaria was reported in duration of January 2019 to September 2019. According to the report 51% cases (37824) was reported only in Bareilly District.

Among these malaria cases in state 9690 were found to be a killer strain *Plasmodium falciparum*. Surprisingly around 83% cases were reported again from bareilly district with 8057 cases.

Medication of malaria

Antimalarial drugs play a vital role in preventing and treating malaria, a life-threatening disease caused by the Plasmodium parasite transmitted through the bite of infected mosquitoes. This review will assess the overall effectiveness, safety, and availability of antimalarial drugs.

- Quinine and related Agents
- Chloroquinine
- Amodiaquine
- Pyrimethamine
- Proguanil
- Sulphonamides
- Atovaquone
- Primaquine

- Mefloquine
- Doxycycline
- Clindamycin
- Primaquine

Chloroquine and Hydroxychloroquine

One of the most commonly used antimalarial drugs is chloroquine. It has been widely used for several decades and is known for its effectiveness against Plasmodium vivax and Plasmodium malariae. However, in recent years, resistance to chloroquine has emerged in many parts of the world, rendering it less effective in certain regions. This highlights the importance of continuous monitoring and surveillance of drug resistance patterns to ensure proper treatment. Chloroquine is an effective antimalarial drug which acts effectively against infection of malaria parasite. Chloroquine is most effective the erythtrocytic forms of plasmodium parasite. Thus, Chloroquine is an important drug for malaria treatment. Chloroquine is is an important medicine which was using around 1934. There is analog of Chloroquine which is known as hydroxylchloroquine. There is drawback of hydroxylchloroquine is banned in some countries like US, Uganda because malaria parasite built resistant against hydroxylchloroquine.

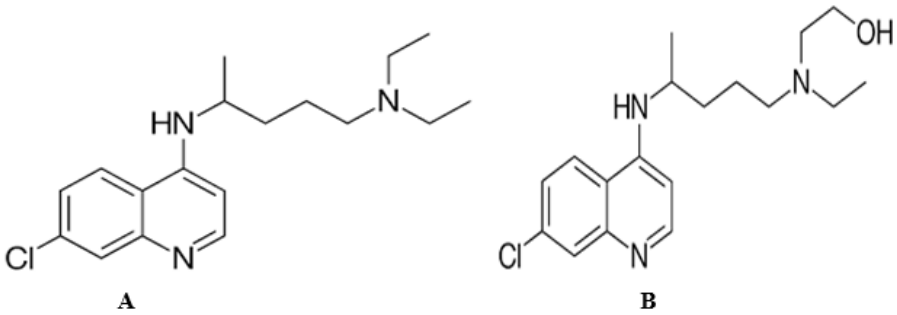

Figure 1: (A) Structure of Chloroquine; **(B)** Structure of hydroxychloroquine

Amodiaquine

Amodiaquine is medicine which is used as anti-malarial agent. It is quinoline which contain chloro group at 7th position and it also contain an amino group at 4th position.

Its molecular formula is $C_{20}H_{22}ClN_3O$

Its molecular weight is 355.9 g/mol.

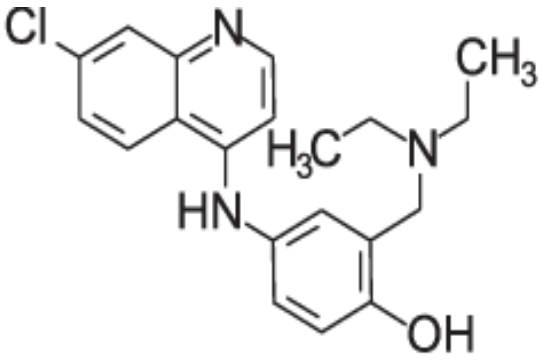

Figure 2: Structure of Amodiaquine

Primaquine

Another commonly used antimalarial drug is primaquine, which is crucial in the elimination of Plasmodium vivax and Plasmodium ovale. C acts against the dormant liver stage of the parasite, preventing relapses of these species. However, primaquine should be used with caution due to the risk of hemolysis in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

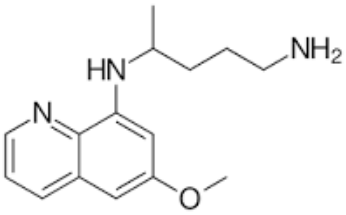

Figure 3: Structure of Primaquine

Anti-malarial resistance

The Anti-malarial resistance may define as "the capability of parasite to alive and reproduce even the absorption of drug even in equal or higher than the recommended dose of the drug."

Drug resistance can cause failure of treatment.

Prevention of Anti-malarial resistance

The Anti-malarial resistance can be prevented by two general methods

• It can prevent by spreading Malaria infection.

• It can also be prevented by transmission of resistant malaria parasite.

Combination therapy

The treatment of malaria cases in current practice is based on pattern of combination therapy. Combination therapy have many advantages like, it reduces treatment failure risk, it reduces resistance development in the parasite, it is more convenience and reduce side effects.

Artemisinin-based therapies (ACTs)

Artemisinin-based combination therapies (ACTs) have become the first-line treatment for uncomplicated malaria in many countries. ACTs combine an artemisinin derivative with a partner drug, such as mefloquine or lumefantrine, to provide rapid parasite clearance and prevent resistance development. These medications have shown high efficacy in treating malaria and have significantly contributed to reducing malaria-related morbidity and mortality.

Artemisinin has very important and effective pathway of action than other traditional methods of treatment. In an Artemisinin-based therapies another non-artemisinin-based therapy is combined to prevents enlargement of resistance to this drug. Artemisinin dependent therapies produce very fast reduction of biomass of parasite with reduction of malarial symptoms. There is no artemisinin resistance seen, however few resistance species are emerging.

Artemether-Lumefantrine Combination

Artemether-Lumefantrine Combination was the first combination of dose which contain temisinin derivatives.

Chemically Lumefantrine is an aryl amino alcohol. Lumefantrine works against all the parasite which cause infection to human including multi-drug resistance. Artemether-Lumefantrine commercially sold as tablets containing 80/480 mg respectively.

New antimalarial dose

As old drugs becoming unsuccessful against death causing malaria parasite as malaria parasite acquiring resistance to existing antimalarial drugs. New drugs will provide another option for malaria treatment.

Name of drug

A combination of Piperaquine phosphate and arterolane Maleate.

Description

Arterolane Maleate is a synthetic trioxalane compound. Its chemical name is cis adamantane-2-spiro-3'-8'- [[[(2'-amino-2' methylpropyl) amino] carbonyl] methyl] 1', 2', 4'-trioxaspiro [4.5] decane hydrogen maleate.

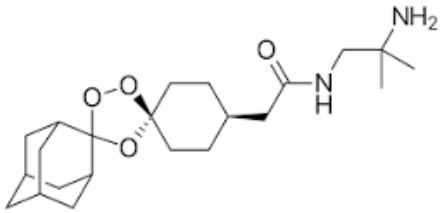

Figure 4: Structure of Arterolane Maleate

Properties of Aterolane

Arterolane is also known as RBx 1160 or OZ277. It is a substance being tasted and find important as anti-malarial drug. It is discovered by European and US scientists.

• Its molecular formula is $C_{22}H_{36}N_2O_4$

• Its molecular weight is 392.53224

• Its density is 202 g/cm^3

• Its boiling point is 572.161 °C at 760 mmHg

Piperaquine phosphate

It is another agent which use to malaria disease caused by malarial parasite.

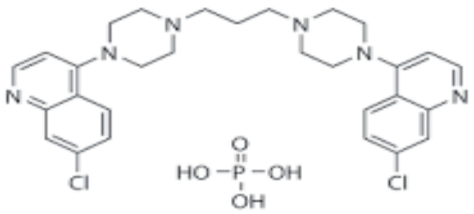

Figure 5: Structure of Piperaquine phosphate

Properties of Piperaquine **phosphate**

• Its molecular formula is C_{29} $H_{35}Cl_2N_6O_4P$

• Its molecular weight is 633.5058

• Its density is 202 g/cm^3

• Its boiling point is 721.161 °C at 760 mmHg

•Its vapour pressure is 1.21E-20 mmHg at 20 °C

In terms of safety, antimalarial drugs generally have an acceptable safety profile when used correctly and at appropriate doses. However, individuals may experience side effects such as gastrointestinal disturbances, headache, dizziness, and, rarely, life-threatening allergic reactions. Healthcare professionals should be aware of these adverse effects and carefully consider the risk-benefit ratio before prescribing antimalarial drugs, particularly in pregnant women, children, and individuals with underlying medical conditions.

Availability and accessibility of antimalarial drugs remain a significant challenge, particularly in resource-limited settings where malaria is endemic. Efforts to ensure equitable access to affordable and high-quality antimalarial drugs must continue to prevent the spread of malaria and minimize its impact on affected populations.

Conclusion

In conclusion, antimalarial drugs play a crucial role in the prevention and treatment of malaria. While some drugs face challenges due to emerging resistance, the development and use of new combination therapies have improved outcomes. The safety, efficacy, and availability of antimalarial drugs are essential considerations in the fight against malaria. Continued research and global collaborative efforts are necessary to combat this deadly disease comprehensively. The mixture of Arterolane and Piperaquine work as blood schizonticides with fast approval of parasitemia and many malarias associated symptoms, joined with avoidance of recrudescence. The mixture provides high medical effectiveness as assess by PCR accurated ACPR (Adequate Clinical and Parasitological Response), fever consent time and parasite removal time. Arterolane maleate and Piperaquine Phosphate were as well put up with as Artemether and Lumefantrine, and had an alike security profile. Arterolane maleate and Piperaquine phosphate is a artificial medicine and increase easier to produce with effective inevitability and consistency of materials.

Malaria still is a most dangerous disease in tarai region. And malaria parasite acquiring resistance against many recently used medicine so many efforts are needed to find such medicine which is not resistant to the parasite.

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