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Malaria A Silent Killer Disease: Causes, Prevention And Curative Action of Drugs and Herbs

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ABSTRACT: Malaria has been rated as the second leading killer disease in Africa. In order to cure and prevent malaria parasite, many drugs have been developed and used including orthodox medicine and herbal preparation. However, the malaria parasites have been reported to be resistant to many of these drugs. The use of unprescribed drugs and over dose has contributed to the problems of resistance by the malaria parasites. Increasing drug resistance to plasmodium falciparum with a resurgence of malaria infections in tropical area has effected changes in treatment of malaria in the last two decades. Since plasmodium falciparum is known to be the most serious form of malaria fever in Africa and particularly Nigeria, serious attention is being given to it. This paper therefore, examines critically the causes of malaria fever, the chemistry of drugs and herbs with advantages and disadvantages of herbs over drugs. It also looks at the curative action of anti-malaria drugs against malaria.

KEYWORDS: parasites, ailments, infection, anti-malaria, resistance.

I. INTRODUCTION

Malaria is a mosquito-borne infectious disease of human and other animals caused by parasitic protozoans belonging to the genius plasmodium. The disease results from the multiplication of plasmodium parasites within the red blood cells causing symptoms that typically include fever, fatigue, vomiting and headaches. In severe cases it can cause yellow skin, seizures, coma or death. It is wide spread in tropical and subtropical regions, including much of sub-sahara Africa, Asia and the America [1].

Five species of malaria can infect and be transmitted by human.In general, severe cases are largely caused by plasmodium vivax and plasmodium ovale[2]. Plasmodium malaria is generally a milder disease that is rarely fatal. Malaria parasites are members of the genus plasmodium (*Phylum Apicomplexa*). In human, malaria is caused by plasmodium ovale, plasmodium vivax and plasmodium knowlesi[3]. While plasmodium vivax is responsible for the largest number of malaria infections worldwide, infections by plasmodium falciparum account for about 90% of deaths from malaria[4]. Parasite plasmodium species also infect birds, reptiles, monkeys, chimpanzees and rodent[5]. There have been documented human infections, with several similar species of malaria. However with the exception of plasmodium knowlesi, these are mostly of limited public health importance [6].

This disease is transmitted most commonly by an infected female Anopheles mosquito. The mosquito bite introduces the parasites from the mosquito's saliva into a person's blood stream. The parasites travel to the liver where they mature and reproduce.The disease is transmitted by mosquito bites and the symptoms usually beginsten to fifteen days after being bitten. If not appropriately treated, people may have recurrences of the disease months later. In those who have recently survived an infection, re-infection typically causes milder symptoms. This partial resistance disappears one month to a year if the person has no continuing exposure to malaria.

Malaria is typically diagnosed by the microscope examination of blood using blood film or with antigen-based rapid diagnostic test [7].Malaria reoccurs after treatment for three reasons. Reoccurrence occurs when parasites are not cleared by treatment whereas; reinfection indicates complete clearance with new infection established from a separate infective mosquito bite, both can occur with any malaria parasite species. Relapse is specific to *P. vivax*and *P. ovale* and involves re-emergence of blood-stage parasite, from latent parasite (hypnozoites) in the liver.

Certain drugs and herbs have been developed to tackle different diseases, which vary with ranges of illness from physical to psychological illness. The recommended treatment for malaria using orthodox medicine is a combination of

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antimalarial medications that includes Quinine, Artemisinin, Mefloquine, Lumefantrine, Sulfadoxine/Pyrimethamine along with Doxycydline. If Arteminsinin is not available, it is recommended that in areas where the disease is common, malaria is confirmed if possible before treatment is started due to concerns of increasing drug resistance. Resistance has developed to several anti-malarial medications. For example, cholroquine resistance, *P.falciparum* has spread to most malarial areas and resistance to Artemisinin has become a problem in some part, of south-East Asia [8].

The recommended treatment for malaria using herbal preparation is the combination of Morinda Lucida (Oruwo), Nauclea Latifolia (Egbesi), Cymbvopogon Citratus (Kooko Oba), Carica Papaya leaves (ewe poopo), Moringa Oleifera (ewe igbale tabi ewe ille), Mongifera Indica (Mangoro), Garcinia Kola (Orogbo) and Psdidium guajava (guwafa).Another herbal preparation for malaria is yellow pawpaw leaves and bitter leaf plants.Malaria being a silent deadly disease and the parasite tends to be resistant to some of the available drugs makes it commonly associated with poverty and thus has a major negative effect on the economic development of any nation. Therefore this paper focuses on the causes of malaria and the curative action of antimalarial drugs against malaria.

II. THE CAUSES OF MALARIA

Malaria is usually transmitted by the bite of an infected female anopheles mosquito.Other modes of transmission include blood-borne transmission (blood or blood products transfusion, transplantation, needle-sharing among intravenous drug addicts, accidental nosocomial transmission) or congenital transmission may occur [9].

Malaria is a serious disease that causes a high fever and chills. It can be gotten from a bite of an infected mosquito [10]. Cases ofmalaria infections are rare in the United States of America. It is most often found in Africa, South Asia, Central America and South America.

In the case of mosquito-borne transmission, sporozoites, the infective plasmodial stage injected along with saliva into subcutaneous capillaries disappear from the blood within approximately forty-five minutes of bite and enter liver parenchimal cells (hepatocytes). Inside the hepatocytes, each sporozoite begins a phase of sexual reproduction resulting in the formation of a schizont which contains thousands of merosoites. The rupture of mature schizonts generates the liberation of merozoites into the blood stream. The hepatic phase of parasitic development lasts on average of between 5 days (plasmodium falciparum) and 15 days (plasmodium malariae). In case of plasmodium vivax and plasmodium ovale, infections, a proportion of parasites may remain dormant in hepatocytes as hypnozoites for several months up to 5 years.

Once in the blood stream, merozoites reach and invade red cells rapidly to start a process of sexual multiplication. Within the red blood cell, merozoites mature to trophozoites and schizonts, which then rupture liberating the new generation of merozoites to invade other red blood cells and thus continue the erythrocytic cycle. At the time of schizont rupture, the release of malaria parasites and erythrocytic material into the circulation induces the pathophysiology process of malaria and the onset of symptoms. The addition of the cytokine cascade is responsible for many of the symptoms and signs of malaria.

The recent increase in malaria infections frommosquito-borne mode may have resulted from poor advice from the WHO and National Health Polices failure in the tropical countries. Indiscriminate disposal of waste and improper drainage (which includes: abandoned reservoir covered and uncovered gutter as well as stagnant water) are also known to be contributory to the proliferation of mosquitoes that cause malaria morbidity [11,12]. In addition to being infected with malaria by mosquito bites. In very rare cases though, people can also get malaria if they come into contact with infected blood. For example, a developing foetus may get the disease from its mother. However, nobody can contract malaria just by being near to an infected person.

Malaria is spread when an infected anopheles mosquito bites a person. The mosquito becomes infected by biting an infected person and drawing blood that contains the parasite when that mosquito bites another person that person becomes infected too.

Most malaria infections cause symptoms like the flu, such as a high fever, chills and muscle pain. Symptoms tend to come and go in cycles. Some types can be deadly; blood tests are carried out to check the malaria parasite in the blood.

III. SYMPTOMS OF MALARIA

In the early stages, infection from *P. falciparum* is similar to infection from *P. vivax*, *P. malariae* and *P. ovale*. There may be no symptoms or symptoms that are less severe if a person is partially immune to malaria. The time from the initial malaria infection until symptoms appear (incubation period) typically ranges from: 9-14days for *P.falciparum,* 12-18days for *P.vivix* and *P. ovale*, 18-40 days for *P. malariae* while it is 11-12 days for *P. knowlesi*.

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Symptoms can appear in 7 days and the time between exposure and signs of illness may sometimes be as long as 8-10 months with P. vivax and P. ovale. The incubation period may be longer if the infected person takes some prevent medications (chemoprophylaxis) or because one has some immunity due to previous infection.

In the early stages, malaria symptoms are sometimes similar to those of many other infections caused by bacteria, viruses or parasites. Symptoms may include fever, chills, headache, sweats, fatigue, nausea and vomiting. Other common symptoms of malaria include: dry cough, muscle or back pain or both and enlarged spleen. In rare cases, malaria can lead to impaired function of the brain or spinal cord, seizures or loss of consciousness.

The classics symptom of malaria is cyclical occurrence of sudden coldness followed by rigor and then fever and sweating lasting four to six hours, occurring every two days in *P. vivax* and *P. ovale* infections, and every three days for *P. malariae. P. falciparum* can have recurrent fever every 36-48 hours or a less pronounced and almost continuous fever. For reasons that are poorly understood, but that may be related to high intracranial pressure.

Malaria has been found to cause cognitive impairment especially in children. Children with malaria frequently exhibit abnormal posting, a sign indicating severe brain damage. It causes widespread anemia during a period of rapid brain development and also the direct brain damage. This neurologic damage results from cerebral malaria which children are more vulnerable, cerebral malaria is also associated with retinal whitening which may be a useful clinical sign in distinguishing malaria from other causes of fever. Severe malaria is almost exclusively caused by *P. falciparum* infection, and usually arises 6-14 days after infection. Consequences of severe malaria include splenomegaly (enlarged spleen) severe headache, cerebral ischemia coma and death if untreated. Children and pregnant are most vulnerable.

IV. DRUGS AND HERBS

Mc Graw-hill concise dictionary of modern medicine (2002) define drugs as any chemical compound that may be used on or administered to human to help diagnose, treat, cure, mitigate, prevent disease or other abnormal conditions. Also, the American heritage dictionary of the English language, fourth edition copyright (2000) defines drug as a substance used in the diagnosis, treatment or prevention of a disease or as a compound of medication.Drugs are absorbed by the body and which changes or enhance a physical or psychological function. A drug can be a gas, a liquid or a solid; it can have a simple structure or a complicated one. Drugs have been used by humans for thousands of years to alleviate pain and illness.

Herbs are any plant with leaves, seeds or flowers used for flavouring food, medicine or perfume or parts of such a plant as used in cooking and in botanical use. By trial and error, people learned which herbs berries, roots and bark could be used for medicinal purpose. The knowledge about natural medicine was passed down from generation to generation without any understanding of how the herbs actually worked. Those who dispersed the herbs; medicine men and women, shamans and witchdoctors were important members of every civilization. However, the drugs available to them were just a small fraction of the drugs available to us today.

V. CURATIVE ACTION OF ANTI-MALARIA DRUGS

Anti-malaria medication are designed to prevent or cure malaria, such drugs may be used for some or all the following;

i. Treatment of malaria in individuals with suspected or confirmed infection.
ii. Prevention of infection in individuals, visiting a malaria endemic region who have no immunity
iii. Routing intermittent treatment of certain group in endemic regions (intermittent preventive therapy).

Some anti-malaria agents, particularly chloroquine and hydroxychloroquine are also used in treatment of rheumatoid arthritis and lupus associated arthritis. Current practice in treating cases of malaria is based on the concept of combination therapy, since this offers several advantages such as; reduced risk of treatment failure, reduced risk of development persistence, enhanced convenience and reduced side effect prompt parasitological confirmation by microscope is recommended in all patients suspected of malaria before treatment is started [13].Treatment solely on the basis of clinical suspicious should only be considered when a parasitological diagnosis is accessible.

VI. MEDICATIONS

It is always practical to consider anti-malaria drugs by chemical structure, since this is associated with important properties of each drug, such as the mechanism in action.

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A Quinine and related agents;

Quinine has a long history stretching from discovery of the cinchona tree, and the potential uses of the bark, to the current day and a collection of derivatives that are still frequently used in the prevention and treatment of malaria. Quinine is an alkaloid that acts as a blood schizontiadal and weak gametocyte against plasmodium species, especially plasmodium falciparum, it acts by inhibiting the hemozoin biocrystallization, thus facilitating an aggregation of cytoxic heme.

Quinine is less effective and more toxic as a blood schizoticida agent than chloroquine however; it is still very effective and widely used in the treatment of acute cases of severe plasmodium falciparum. It is especially useful in areas where there is high level of resistance to chloroquine, mefloquine and sulfa drugs combinations with pyrimethanine. Quinine is also used in post-exposure treatment of individuals returning from an area where malaria is endemic. The treatment regimen of quinine is complex and is determined largely by the parasites level of resistance and the reason for drug [14].

B Chloroquine:

Chloroquine was until recently the most widely used anti-malaria drug. It was the original prototype from which most methods of treatment are derived. It is now suggested that it is used in combination with other anti-malaria drugs to extend its effective usage. Chloroquine is a 4-aminoquinoline compound with a complicated and still concentration in the vacuole of the parasite, which due to its alkaline nature, raise the internal P^H. It controls the conversion of toxic heme to hemozoin by inhibiting the biocrystallization of hemozion, thus poisoning the parasite through excess level of toxicity. However, itching can occur, at intolerable level and cholorquine can be provocative factors of psorialisis [14].

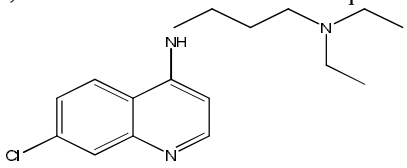

Figure 1. [Rs]-N-[7-Chloroquinoline-4-11]-N-diethyl-pentane-1-4-diamine or 4-aminoquinoline.

C Amodiaquine

Amodiaquine (trade names, Camoquine, flavoquine) is a 4-aminoquinoline compound related to chloroquine used as an anti-malaria and anti-inflammatory agent. Amodiaquine has been shown to be more effective than chloroquine in treating chloroquine-resitstant plasmodium-falciparum (CRPF) malaria infections and may afford more protection than chloroquine. It is generally well tolerated and widely available in Africa. Its use therefore, is probably more practicable in long term visitors and person who will reside in Africa.Amodiaquine is histamine N-methyltransferase inhibitor.

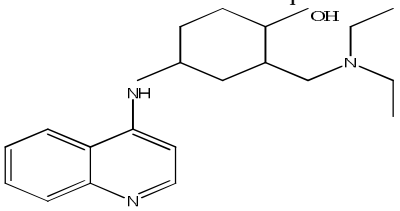

Figure 2: 4- (Chloroquinoline-4-amino)-2-diethyl amino)methyl-1-phenol

D Pyrimethamine

Pyrimethamine is used in the treatment of uncomplicated malaria cases. It is particularly useful in cases of chloroquine resistance plasmodium falciparum strain when combined with sulfadoxine. It acts by inhibiting dihydrofolate reductake in the parasite thus preventing the biosynthesis of purines and pyrimidines, thereby halting the processes of DNA synthesis, cell division and reproduction. It acts primarily on the schizonts during the erythrocytic phase, and nowadays it is only used in concert with a sulfonamide.

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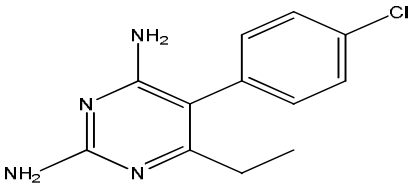

Figure 3: 5-[4-chloropheny]-6-ethyl-2,4-pyrimidine diamine]

Side effects: - pyrimethamine may deplete folic acid in humans resulting in hematologic side effects associated with folate deficiency.

E Proguanil

Proguanil (chloroguanide) is a biguanicle, a synthetic derivative of pyrimidine which was developed in 1945 by British anti-malaria research group. It has many mechanism of action but primarily it is medicated through conversion to the active metabolite cycloguanil pamoate. This inhibits the malaria dihydrofolate reluctance enzyme. However it is useful in prophylaxis when combined with atovaguione or choloroquine. It does not provide effective protection against resistance strains of *P.falciparum*when not used in combination with other anti-malaria drugs. There are very few side effects to proguanil with slight hairs loss and mouth ulcer being occasionally reported following prophylactic use proguanil hydrochloride is marketed as paludirine by Astrazeneca. [14].

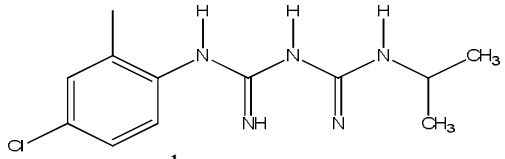

Figure 4: 1[4-chlorophenl]-2-[N[1]-propan-2-ylcar-carbamimidol guanidine]

F Atovaquone

Atovaquone is only available in combination with proguanil under the name malarone albert at a price higher than lariam. It is commonly used in prophylaxis by travelers and used to treat falciparum malaria in developed countries.

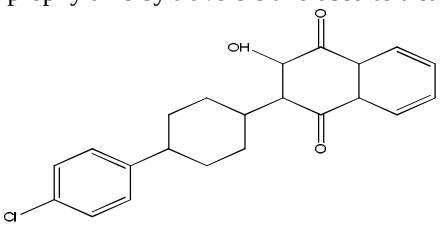

Figure 5: Trans-2-[4- [chlorophenyl] cyclohexyl)-3hydroxyl-1,4-napthalenedione

G Mefloquine

Mefloquine may not be taken to prevent malaria infections unless the malaria parasite in that area one is visiting is resistant to mefloquine. One should not take mefloquine if one already has a history of active or recent depression or other mental illness, seizures or some types of heart rhythm problems.

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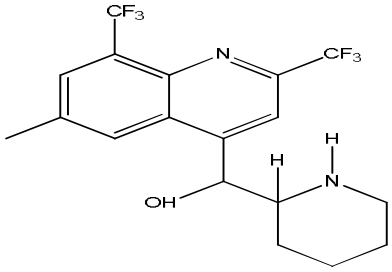

Figure 6: 2,8-bis(trifloromethyl) quinoline-4-yl)-(2-piperidy methanol)

VII. STATISTICS ON MALARIA INFECTIONS

Caraballo [15] and Federal Ministry of Health (2000) state that Nigeria is known for a high prevalence of malaria and it is a leading cause of morbidity and mortality in the Country. Available records show that at least 50% of the population of Nigeria suffers at least one episode of malaria each year and malaria accounts for over 45% of all out-Patients. In 2014 World Health Organization (WHO) reported that malaria caused an estimated number of 584,000 deaths (with an uncertainty range of 367,000 to 75,000), mostly among African children.

Non-immune travelers from malaria free areas are very vulnerable to the disease when they get infected. According to the estimates released in December, 2014, there were about 198 million cases of malaria in 2013 (with an uncertainty range of 124 million to 283 million) and an estimated 584,000 deaths (with an uncertainty range of 367,000 to 755,000). Most deaths occur among children living in Africa where a child dies every minute from malaria. Malaria mortality rates among children in Africa have been reduced by an estimated 58% since 2000 [15]. Approximately half of the world's population is at risk of malaria. Most malaria cases and deaths occur in sub-Saharan Africa. However, Asia, Latin-America and to a lesser extent the Middle East and parts of Europe are also affected. In 2014, 97 Countries and territories had ongoing malaria transmission. Early diagnosis and treatment of malaria reduces disease and prevent deaths. It also contributes to the reducing malaria transmission. The best available reatment particularly for *P.falciparum* malaria is Artemisinin-based combination Therapy (ACT).

VIII. PREVENTION OF MALARIA TRANSMISSION

Malaria is preventable and curable. Increased malaria prevention and control measures are dramatically reducing the malaria burden in many places.To prevent malaria transmission, vector control is the main way of reducing malaria transmission. Personal protection against mosquito bites represents the first line of defense for malaria prevention. Three forms of vector control are effective in wide range of circumstances:

- Use of insecticide-treated mosquito nets
- Indoor spraying with residual insecticide
- The use of antimalaria medicines.

IX. CONTRIBUTION OF WHO TO MALARIA ERADICATION

Malaria has been a priority for World Health Organization (WHO) since its founding in 1948. Control activities are coordinated by WHO Programme on Communicable Diseases (CDs). The four basic technical elements of WHO global control strategy are:

- Provision of early diagnosis and prompt treatment for the disease.
- Planning and implementation of selective and sustainable preventive measures.
- Early detection for the prevention or containment of epidemics.
- Strengthening local research capacities to promote regular assessment of malaria situation in particular the ecological, socio and economic determinants of the disease.

In 1992, WHO convened a ministerial conference on malaria in Amsterdam where a global malaria control strategy was endorsed. The conference was attended by health leaders from 102 countries and representatives of United Nations Bodies and Non-Governmental Organizations (NGOs).WHO planned to implement control programme in 90% of the

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countries affected by the disease not later than 1997. The target was to reduce mortality by at least 20% between 1995 and 2000.

X. CONCLUSION

Malaria is one of the deadliest diseases on the planet affecting about 50% of the world population. It is a leading cause of morbidity and mortality in the developing world. *P.falciparum*, a tiny parasite is the major cause of malaria and is possibly the major dangerous stow away in history. Malaria has become a major economic concern to some of the tropical and sub-tropical countries. A number of antimalarial drugs have been developed from plants as such or their semi-synthetic analogues. One of the major approaches to the discovery as well as development of new drugs from plants is to study the plants used locally for the treatment of a particular ailment. Most of the drugs used for malaria treatment are synthetic derivation of plant products. A good example is quinine, which is derived from the back of Cinchona tree. Likewise, Artemisinin is extracted from Artemisia annua and is very potent against malaria parasites. There is again an alarming situation of drug resistance against most of the antimalaria drugs. There are several plants that exhibit antimalaria activity better than the existing drugs. A systematic evaluation of these plant based leads to the need of time to develop safe, effective and affordable new antimalarial drug and the need to determine the active ingredient in these herbs, and subsequently determine the correct dosage.

Some of the preventive measures to guide against contracting malaria include:

- Use of insecticide-treated mosquito net
- Spray of insecticide in homes
- Clear the bushes around home of residence
- Put oil in any stagnant water around homes
- Ground them if the water content harboring the mosquito's eggs cannot released to flow away.

All these can simply make our environment healthy and conducive for lives and not be truncated by this deadly disease.

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