International Journal of Enhanced Research in Science, Technology & Engineering
ISSN: 2319-7463, Vol. 11 Issue 5, May-2022, Impact Factor: 7.957

# A Review on Drug Artemether as Antimalaria Agent

Anjita Singh[1]*, Chandra Kishore Tyagi[2]

[1,2]Sri Satya Sai University of Technology and Medical Science, Sehore (M.P)

**ABSTRACT**

**World Health Organization (WHO) in 2011, They generally recommended the parenteral administration of artesunate in preference to quinine as first-line treatment for people with severe malaria. Prior to this recommendation different countries, In Africa, They use artemether, an alternative artemisinin derivative. This study is used to assess the efficacy and safety of intramuscular artemether versus any other parenteral medication in the treatment of severe malaria in adults and children.**

**Keywords*: Artemether, quinine, parenteral.***

## INTRODUCTION

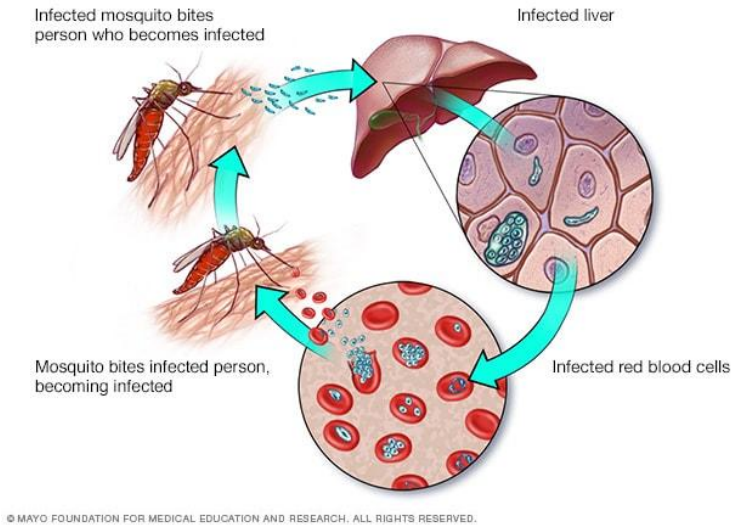
**Malaria: -**
Malaria is a disease caused by a parasite. The parasite is spread to humans through the bites of infected mosquitoes. People who have malaria usually feel very sick with a high fever and shaking chills.While the disease is uncommon in temperate climates, malaria is still common in tropical and subtropical countries[1]. Each year nearly 290 million people are infected with malaria, and more than Protective clothing, bed nets and insecticides can protect you while traveling. You also can take preventive medicine before, during and after a trip to a high-risk area. Many malaria parasites have developed resistance to common drugs used to treat the disease.[2,3]

**Symptoms of Malaria[5]: -**

- Fever
- Chills
- General feeling of discomfort
- Headache
- Nausea and vomiting
- Diarrhea
- Abdominal pain
- Muscle or joint pain
- Fatigue
- Rapid breathing
- Rapid heart rate
- Cough

Some people who have malaria experience cycles of malaria "attacks." An attack usually starts with shivering and chills, followed by a high fever, followed by sweating and a return to normal temperature. Malaria signs and symptoms typically begin within a few weeks after being bitten by an infected mosquito. However, some types of malaria parasites can lie dormant in your body for up to a year[6].

**Causes of malaria**[7]




**Malaria transmission cycle:**[8,9]
Malaria is caused by a single-celled parasite of the genus plasmodium. The parasite is transmitted to humans most commonly through mosquito bites.

- Uninfected mosquito. A mosquito becomes infected by feeding on a person who has malaria.
- Transmission of parasite. If this mosquito bites you in the future, it can transmit malaria parasites to you.
- In the liver. Once the parasites enter your body, they travel to your liver — where some types can lie dormant for as long as a year.
- Into the bloodstream. When the parasites mature, they leave the liver and infect your red blood cells. This is when people typically develop malaria symptoms.
- On to the next person. If an uninfected mosquito bites you at this point in the cycle, it will become infected with your malaria parasites and can spread them to the other people it bites.

**Other modes of transmission**[10]
Because the parasites that cause malaria affect red blood cells, people can also catch malaria from exposure to infected blood, including:

- From mother to unborn child
- Through blood transfusions
- By sharing needles used to inject drugs

**Risk factors**[11]
The greatest risk factor for developing malaria is to live in or to visit areas where the disease is common. These include the tropical and subtropical regions of:

- Sub-Saharan Africa
- South and Southeast Asia
- Pacific Islands
- Central America and northern South America

The degree of risk depends on local malaria control, seasonal changes in malaria rates and the precautions you take to prevent mosquito bites.

**Risks of more-severe disease**[12]
People at increased risk of serious disease include:

- Young children and infants
- Older adults

- Travelers coming from areas with no malaria
- Pregnant women and their unborn children

**Complications**[13]

Malaria can be fatal, particularly when caused by the plasmodium species common in Africa. The World Health Organization estimates that about 94% of all malaria deaths occur in Africa — most commonly in children under the age of 5.

**Malaria deaths are usually related to one or more serious complications, including:**

- Cerebral malaria. If parasite-filled blood cells block small blood vessels to your brain (cerebral malaria), swelling of your brain or brain damage may occur. Cerebral malaria may cause seizures and coma.
- Breathing problems. Accumulated fluid in your lungs (pulmonary edema) can make it difficult to breathe.
- Organ failure. Malaria can damage the kidneys or liver or cause the spleen to rupture. Any of these conditions can be life-threatening.
- Anemia. Malaria may result in not having enough red blood cells for an adequate supply of oxygen to your body's tissues (anemia).
- Low blood sugar. Severe forms of malaria can cause low blood sugar (hypoglycemia), as can quinine — a common medication used to combat malaria. Very low blood sugar can result in coma or death.

**Prevention**[14]

If you live in or are traveling to an area where malaria is common, take steps to avoid mosquito bites. Mosquitoes are most active between dusk and dawn. To protect yourself from mosquito bites, you should:

- Cover your skin. Wear pants and long-sleeved shirts. Tuck in your shirt, and tuck pant legs into socks.
- Apply insect repellent to skin. Use an insect repellent registered with the Environmental Protection Agency on any exposed skin. These include repellents that contain DEET, picaridin, IR3535, oil of lemon eucalyptus (OLE), para-menthane-3,8-diol (PMD) or 2-undecanone. Do not use a spray directly on your face. Do not use products with OLE or PMD on children under age 3.
- Apply repellent to clothing. Sprays containing permethrin are safe to apply to clothing.
- Sleep under a net. Bed nets, particularly those treated with insecticides, such as permethrin, help prevent mosquito bites while you are sleeping.

**Preventive medicine**[15,16]

If you'll be traveling to a location where malaria is common, talk to your doctor a few months ahead of time about whether you should take drugs before, during and after your trip to help protect you from malaria parasites. In general, the drugs taken to prevent malaria are the same drugs used to treat the disease. What drug you take depends on where and how long you are traveling and your own health.

**Vaccine**[17]

The World Health Organization has recommended a malaria vaccine for use in children who live in countries with high numbers of malaria cases.Researchers are continuing to develop and study malaria vaccines to prevent infection

**Artemether**[18,19]**: -**

Artemether is an antimalarial agent for the treatment of uncomplicated acute malaria. For enhanced efficacy, it is given in combination with lumefantrine. This combination therapy exerts its effects against Plasmodium spp. erythrocytic stages. It can be used to treat infections caused by P. falciparum and unidentified species of Plasmodium, including chloroquine-resistant infections.

This medicine is used to treat adults and kids with malaria. In this prescription, the two ingredients belong to a class of drugs known as antimalarials. Malaria is an infection caused by mosquito bites acquired in regions of the world where malaria is prevalent while travelling or living. Parasites of malaria enter the body and reside in tissues in the body, such as red blood cells or the liver. This drug is used to destroy the parasites of malaria that reside within red blood cells. In some cases, in order to kill the malaria parasites living in the liver, you will need to take a different drug (such as primaquine). Both treatments may be appropriate for a full cure and to prevent infection from returning (relapse). For the prevention of malaria, this substance is not used.

**Artemether Side Effects**[20]**:**

- Headache

- Dizziness
- Loss of appetite
- Weakness
- Fever
- Chills
- Abdominal pain
- Cough
- Trouble sleeping

**Some of the serious side effects of Artemether are[21]:**

- Rash
- Itching/ swelling
- Severe dizziness
- Trouble breathing
- If you have any of these serious symptoms immediately contact the doctor for further assistance. In any case, due to Artemether if you get any kind of reactions in the body try avoiding it.
- A doctor advised you to take the medicines by seeing the problems and the benefits of this medicine are greater than the side effects. Majority of the people who use this medicine don't show any side effects. Get medical help immediately if you get any serious Artemether side effects.

**Precautions[22]:**

Before taking Artemether talk with the doctor if you are allergic to it or any other medications. The product may contain some inactive ingredients which can cause some serious problems. Before using Artemether talk with the doctor if you are having any medical history such as:

- Kidney problems
- Liver problems
- Stomach disease
- Ulcers

**How to take Artemether[23]?**

Take this medicine orally, with food, just as your doctor has prescribed it. Usually, this drug is taken twice a day for 3 days with a meal (6 doses), or as instructed by your doctor. Take the first dose of food on the first day of therapy, followed 8 hours later by your second dose. Then you can take one dose in the morning and one dose in the evening per day for the next 2 days. With food or milk, infant formula, pudding, porridge, or broth, it is necessary to take every dose of this drug. Food helps function well with this drug. If you are not able to eat, tell your doctor. With food or milk, infant formula, pudding, porridge, or broth, it is necessary to take every dose of this drug. Food helps function well with this drug. If you are not able to eat, tell your doctor.

**Missed Dose[24]:**

- Missing one or two-dose of Artemether won't show any effect on the body. The skipped dose causes no problem. But with some medication, it won't work if you don't take the dosage on time. If you miss a dose some sudden chemical change may affect your body. In some cases, your doctor would advise you to take the prescribed medicine as soon as possible if you have missed the dose.

**Overdose[25]:**

- Overdose of a drug can be accidental. If you have taken more than the prescribed Artemether tablets there is a chance of getting a harmful effect on your body's functions. Overdose of a medicine can lead to some medical emergency.
- Interactions:
- Drug interactions can affect the working of the drugs or increase the risk of serious side effects. Not all potential drug interactions are included in this paper. Keep a list and share it with the doctor and pharmacist of all the medications you use (including prescription/nonprescription medicines and herbal products). Do not start, stop, or change the dosage of any drug without being treated by the doctor.
- Before the treatment with artemether/lumefantrine, be sure to tell your doctor about any drugs you take for malaria. Within one month of treatment with artemether/lumefantrine, certain antimalarial medications (such as halofantrine) should not be used. A severe (possibly fatal) association with drugs can occur in some cases.

**Storage[26]:**

- Direct contact with heat, air and light may damage your medicines. The exposure of medicine may cause some harmful effects. The medicine must be kept in a safe place and out of children's reach.
- Mainly the drug should be kept at room temperature between 68ºF and 77ºF (20ºC and 25ºC).
- Before taking Artemether consult your Doctor. In case if you face any problems or get anyside effects after taking Artemether rush immediately to your nearby hospital or consult your doctor for better treatment. Carry your medications always in your bag while travelling to avoid any immediate emergencies. Follow your prescription and follow your Doctor advice whenever you take Artemether.

**Artemether vs Artesunate[28]:**

| Artemether | Artesunate |
|---|---|
| Artemether is an antimalarial agent for the treatment of uncomplicated acute malaria. For enhanced efficacy, it is given in combination with lumefantrin. | Artesunate is indicated for the initial treatment of moderate malaria. Artesunate is recommended by the World Health Organization for first-line treatment of severe malaria. |
| This medicine is used to treat adults and kids with malaria. In this prescription, the two ingredients belong to a class of drugs known as antimalarials. | Artesunate is used for the treatment of malaria. |
| Some of the common side effects of Artemether are:<br>Headache<br>Dizziness<br>Loss of appetite<br>Weakness<br>Fever | Some of the common side effects of Artesunate are:<br>Loss of appetite<br>Dizziness<br>Nausea<br>Diarrhea<br>Hives<br>Rash |

## CONCLUSIONS

This review represents about malaria causes, side effects as well as treatment of malaria. In this review they gave detailing on the treatment of malaria by artemether with their different advantages as well as dosing of drug in treatment.

## REFERENCES

[1]. Miller, L. H., Ackerman, H. C., Su, X. Z. &Wellems, T. E. Malaria biology and disease
[2]. White, N. J. et al. Malaria. Lancet 383, 723–735 (2014).
[3]. Cowman, A. F., Healer, J., Marapana, D. & Marsh, K. Malaria: biology and disease. Cell 167, 610–624 (2016). References 1–3 comprehensively review malaria biology and the disease.
[4]. Baker, D. A. Malaria gametocytogenesis. Mol. Biochem. Parasitol. 172, 57–65 (2010).
[5]. Waters, A. P. Epigenetic roulette in blood stream Plasmodium: gambling on sex. PLoSPathog. 12, e1005353 (2016).
[6]. White, N. J. Determinants of relapse periodicity in Plasmodium vivax malaria. Malar. J. 10, 297 (2011).
[7]. Wassmer, S. C. et al. Investigating the pathogenesis of severe malaria: a multidisciplinary and cross-geographical approach. Am. J. Trop. Med. Hyg. 93, 42–56 (2015). Comprehensively reviews the causes of severe malaria and ongoing research efforts to understand malaria pathophysiology.
[8]. Wassmer, S. C. & Grau, G. E. Severe malaria: what's new on the pathogenesis front? Int. J. Parasitol. 47, 145–152 (2017).
[9]. World Health Organization. Severe malaria. Trop. Med. Int. Health 19 (Suppl. 1), 7–131 (2014).
[10]. Dondorp, A. M. & Day, N. P. The treatment of severe malaria. Trans. R. Soc. Trop. Med. Hyg. 101, 633–634 (2007).
[11]. Bernabeu, M. & Smith, J. D. EPCR and malaria severity: the center of a perfect storm. Trends Parasitol. 33, 295–308 (2017). Reviews the molecular basis of parasite sequestration in the tissues, which leads to the obstruction of the microvasculature and severe disease, and discusses the key role of EPCR in these processes.
[12]. Bhatt, S. et al. The effect of malaria control on Plasmodium falciparum in Africa between 2000 and 2015. Nature 526, 207–211 (2015). Attempts to identify the relative contribution of different antimalaria measures in reducing the number of malaria cases over the 2000–2015 period.
[13]. Mitchell, S. N. et al. Mosquito biology. Evolution of sexual traits influencing vectorial capacity in anopheline

mosquitoes. Science 347, 985–988 (2015).
[14]. Sinka, M. E. et al. The dominant Anopheles vectors of human malaria in Africa, Europe and the Middle East: occurrence data, distribution maps and bionomic precis. Parasit. Vectors 3, 117 (2010).
[15]. World Health Organization. Eliminating malaria: learning from the past, looking ahead. WHOhttp://www.path.org/publications/files/MCP_rbm_pi_rpt_8.pdf (2011).
[16]. World Health Organization. World malaria report 2015. WHOhttp://www.who.int/malaria/publications/world-malaria-report-2015/report/en/ (2015).
[17]. Florens, L. et al. A proteomic view of the Plasmodium falciparum life cycle. Nature 419, 520–526 (2002).
[18]. Gardner, M. J. et al. Genome sequence of the human malaria parasite Plasmodium falciparum. Nature 419, 498–511 (2002). Reports for the first time the P. falciparum genome, which has formed the basis for research into the molecular basis of pathogenesis and parasite biology; a modern-day understanding of the disease would not be possible without this groundbreaking work.
[19]. Winzeler, E. A. Advances in parasite genomics: from sequences to regulatory networks. PLoSPathog. 5, e1000649 (2009).
[20]. Gething, P. W. et al. Mapping Plasmodium falciparum mortality in Africa between 1990 and 2015. N. Engl. J. Med. 375, 2435–2445 (2016).
[21]. Maitland, K. Severe malaria in African children — the need for continuing investment. N. Engl. J. Med. 375, 2416–2417 (2016).
[22]. Miller, L. H., Mason, S. J., Clyde, D. F. &McGinniss, M. H. The resistance factor to Plasmodium vivax in blacks. The Duffy-blood-group genotype, FyFy. N. Engl. J. Med. 295, 302–304 (1976). Describes the discovery that led to a molecular understanding of why most Africans are resistant to infection by P. vivax, thereby explaining the limited penetration of P. vivax in Africa.
[23]. Mercereau-Puijalon, O. & Menard, D. Plasmodium vivax and the Duffy antigen: a paradigm revisited. Transfus. Clin. Biol. 17, 176–183 (2010).
[24]. Howes, R. E. et al. Plasmodium vivax transmission in Africa. PLoSNegl. Trop. Dis. 9, e0004222 (2015).
[25]. Sutherland, C. J. et al. Two nonrecombining sympatric forms of the human malaria parasite Plasmodium ovale occur globally. J. Infect. Dis. 201, 1544–1550 (2010).
[26]. Cox-Singh, J. et al. Plasmodium knowlesi malaria in humans is widely distributed and potentially life threatening. Clin. Infect. Dis. 46, 165–171 (2008).
[27]. Singh, B. et al. A large focus of naturally acquired Plasmodium knowlesi infections in human beings. Lancet 363, 1017–1024 (2004). Describes the discovery that P. knowlesi, which was previously thought to primarily infect macaques, accounted for over half of the cases of malaria in their study in the Kapit district (Malaysia). Demonstrates for the first time that P. knowlesi should be considered as an emerging infectious disease in humans. Whether transmission via mosquitoes was occurring from monkey to man or from man to man remained an open question.
[28]. Brock, P. M. et al. Plasmodium knowlesi transmission: integrating quantitative approaches from epidemiology and ecology to understand malaria as a zoonosis. Parasitology 143, 389–400 (2016).
[29]. Imwong, M., Nakeesathit, S., Day, N. P. & White, N. J. A review of mixed malaria species infections in anopheline mosquitoes. Malar. J. 10, 253 (2011).
[30]. Ginouves, M. et al. Frequency and distribution of mixed Plasmodium falciparum–vivax infections in French Guiana between 2000 and 2008. Malar. J. 14, 446 (2015).
[31]. Srisutham, S. et al. Four human Plasmodium species quantification using droplet digital PCR. PLoS ONE 12, e0175771 (2017).
[32]. Armed Forces Health Surveillance Branch. Update: malaria, U. S. Armed Forces, 2016. MSMR 24, 2–7 (2017).
[33]. IISS: International Institute for Strategic Studies. Armed Conflict Survey 2016 (IISS, 2016).
[34]. Mueller, I. et al. Natural acquisition of immunity to Plasmodium vivax: epidemiological observations and potential targets. Adv. Parasitol. 81, 77–131 (2013).
[35]. Ataide, R., Mayor, A. & Rogerson, S. J. Malaria, primigravidae, and antibodies: knowledge gained and future perspectives. Trends Parasitol. 30, 85–94 (2014).
[36]. Desai, M. et al. Epidemiology and burden of malaria in pregnancy. Lancet Infect. Dis. 7, 93–104 (2007).
[37]. McGready, R. et al. Adverse effects of falciparum and vivax malaria and the safety of antimalarial treatment in early pregnancy: a population-based study. Lancet Infect. Dis. 12, 388–396 (2012).
[38]. Cohen, C. et al. Increased prevalence of severe malaria in HIV-infected adults in South Africa. Clin. Infect. Dis. 41, 1631–1637 (2005).
[39]. Mulu, A. et al. Epidemiological and clinical correlates of malaria–helminth co-infections in southern Ethiopia. Malar. J. 12, 227 (2013).
[40]. Gwamaka, M. et al. Iron deficiency protects against severe Plasmodium falciparum malaria and death in young children. Clin. Infect. Dis. 54, 1137–1144 (2012).

[41]. Neuberger, A., Okebe, J., Yahav, D. & Paul, M. Oral iron supplements for children in malaria-endemic areas. Cochrane Database Syst. Rev. 2, CD006589 (2016).
[42]. Tilley, L., Straimer, J., Gnadig, N. F., Ralph, S. A. & Fidock, D. A. Artemisinin action and resistance in Plasmodium falciparum . Trends Parasitol. 32, 682–696 (2016). Comprehensively reviews the emerging threat of artemisinin resistance, covering what is known about the mechanism of action of the drug and the molecular basis of artemisinin resistance.
[43]. Woodrow, C. J. & White, N. J. The clinical impact of artemisinin resistance in Southeast Asia and the potential for future spread. FEMS Microbiol. Rev. 41, 34–48 (2017).
[44]. Menard, D. et al. A worldwide map of Plasmodium falciparum K13-propeller polymorphisms. N. Engl. J. Med. 374, 2453–2464 (2016).
[45]. Imwong, M. et al. The spread of artemisinin-resistant Plasmodium falciparum in the greater Mekong subregion: a molecular epidemiology observational study. Lancet Infect. Dis. 17, 491–497 (2017).
[46]. Paul, A. S., Egan, E. S. &Duraisingh, M. T. Host–parasite interactions that guide red blood cell invasion by malaria parasites. Curr. Opin. Hematol. 22, 220–226 (2015). Reviews the molecular basis of parasite invasion.
[47]. Lim, C. et al. Reticulocyte preference and stage development of Plasmodium vivax isolates. J. Infect. Dis. 214, 1081–1084 (2016).
[48]. Boddey, J. A. & Cowman, A. F. Plasmodium nesting: remaking the erythrocyte from the inside out. Annu. Rev. Microbiol. 67, 243–269 (2013).
[49]. Spillman, N. J., Beck, J. R. & Goldberg, D. E. Protein export into malaria parasite-infected erythrocytes: mechanisms and functional consequences. Annu. Rev. Biochem. 84, 813–841 (2015). Reviews the biology associated with red blood cell remodelling upon parasite invasion.
[50]. Phillips, M. A. in Neglected Diseases and Drug Discovery (eds Palmer, M. & Wells, T. N. C. ) 65–87 (RCS Publishing, 2011).
[51]. Istvan, E. S. et al. Validation of isoleucine utilization targets in Plasmodium falciparum . Proc. Natl Acad. Sci. USA 108, 1627–1632 (2011).
[52]. Wunderlich, J., Rohrbach, P. & Dalton, J. P. The malaria digestive vacuole. Front. Biosci. (Schol. Ed.) 4, 1424–1448 (2012).
[53]. Chugh, M. et al. Protein complex directs hemoglobin-to-hemozoin formation in Plasmodium falciparum . Proc. Natl Acad. Sci. USA 110, 5392–5397 (2013).
[54]. Sigala, P. A. & Goldberg, D. E. The peculiarities and paradoxes of Plasmodium heme metabolism. Annu. Rev. Microbiol. 68, 259–278 (2014).