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Epidemiologia

MALARIA: NARRATIVE REVIEW

Luisa Fernanda Rengifo Ávila	MD. Universidad del Valle.
Dayana Quiñones Chamorro	MD. Universidad Central del Valle del Cauca.
Juan Carlos Arias Valencia	MD. Universidad de Antioquia.
María Fernanda Rosero Chamorro	MD. Universidad de Manizales.
David Felipe Delgado Santacruz	MD. Universidad Nacional de Colombia.
Diana Carolina Becerra Becerra	MD. Universidad Industrial de Santander.
Angelica Natalia Piedrahita Rincón	MD. Fundación Universitaria Juan N. Corpas.
Michelle Denisse Lozano Colón	MD. Universidad del Magdalena.
Paula Andrea Rodríguez Mosquera	MD. Universidad Central del Valle.

ABSTRACT Malaria is a vector-borne tropical parasitic disease that occurs through the bite of a female Anopheles spp mosquito that transmits protozoa of the genus Plasmodium. P. vivax and P. falciparum are the most frequent species. The clinical presentation of the disease is a febrile syndrome accompanied by nonspecific symptoms. Diagnosis is based on tests for microscopic detection of the parasite (thick smear, blood smear) or rapid antigen diagnostic tests. Treatment will depend on the infecting species of plasmodium and whether it is a complicated disease. There are multiple tools for prevention such as the use of mosquito nets, repellents, chemoprevention, and vaccination. Various strategies have been proposed for its eradication, considering that it is a public health problem and represents a great burden of morbidity and mortality worldwide.

KEYWORDS : Elderly; malaria prevention; older travellers; systematic review; travel medicine.

INTRODUCTION

Malaria is a vector-borne tropical parasitic disease caused by the bite of a female Anopheles spp mosquito. Of the 120 existing species of Plasmodium, only 6 are known to infect humans regularly. P. vivax and P. falciparum are the most frequent species. P. malariae is rare and is found especially in sub-Saharan Africa. P. ovale, even rarer and comprises <1% of isolates. P knowlesi, morphologically like P. malariae, has only been identified by molecular methods in Malaysia, the Philippines, Myanmar, and Thailand.

Methods

This narrative review was based on a search strategy that was carried out in databases such as PubMed/Medline, Lilacs and Redalyc, EBSCO. The MeSH and DeCS thesauri were used. Articles such as clinical trials, systematic reviews, topic reviews between the years of 1999 and 2022 were included (Figure 1).

Pathophysiology

The life cycle of the malaria parasite involves two hosts. During a bite, a malaria-infected female mosquito of the genus Anopeheles spp inoculates sporozoites into the human host, these sporozoites infect liver cells, in which they mature into schizonts, which subsequently rupture and release merozoites, in the genera vivax and ovale there is a latent stage in the liver called hypnozoites that if not properly treated can cause relapses of the disease, after this hepatic replication, a replication also occurs in the red blood cells in an asexual manner. which releases even more merozoites from a schizogony. Some parasites in this erythrocyte cycle differentiate into gametocytes which represent the sexual stages of the parasite, the microgametocytes (male) and macrogametocytes (female) are ingested by the mosquito and there the sporogonic cycle occurs, in the stomach of the mosquito a fusion of These become ookinetes and later oocysts, which grow and break, releasing sporozoites again and repeating the cycle (6).

Clinical Manifestations

The initial symptoms of malaria are nonspecific, including paroxysmal attacks of fever, tachycardia, tachypnea, chills, diaphoresis, headache, anorexia, nausea, abdominal pain, myalgia, and arthralgia. Among the physical examination findings, it is common to find hepatosplenomegaly and signs of anemia, especially in children. P. falciparum malaria can progress if left untreated and be classified as complicated or severe malaria, which can lead to hypoglycemia, acidosis,

kidney failure, pulmonary edema, liver dysfunction, and hemolysis.

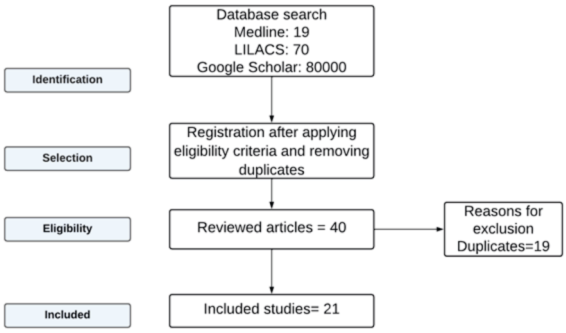

Figure 1. PRISMA.

Fever

Malaria should be suspected in all patients with fever (temperature > 37.5°C) and a history of stay in an endemic area (7). The acute attack begins with febrile episodes preceded by chills and followed by intense sweating, repeated every 24, 48 or 72 hours, which is why a pattern of fever behavior has been established. In P vivax infection, we speak of a benign or simple tertian fever, P. malariae quartan fever and P. falciparum malignant tertian or subtertian fever, this periodicity of the fever develops only if the patient is not treated (8).

Anemia And Jaundice

Anemia occurs due to the rupture of parasitized red blood cells, which in turn is also the cause of jaundice with hyperbilirubinemia, predominantly indirect due to the release of heme components. That is why it is one of the diagnoses to consider in patients with febrile syndrome that presents with jaundice (9).

Cerebral Malaria

It is an encephalopathy characterized by altered state of consciousness, delirium, seizures. Onset can be gradual or sudden after a seizure, risk groups for developing cerebral malaria include children, older adults, and HIV infection. In a study carried out in Kenya with 19,560 children with malaria, it was shown that around 48% of the cases presented neurological involvement (10).

Hypoglycemia

It is a common complication of severe malaria, this is secondary to decreased hepatic gluconeogenesis, hepatic glycogen consumption and increased glucose requirement by the parasite, it is worth mentioning that hyperinsulinemia is also produced using quinine (11).

Renal Insufficiency

Although its cause is unknown, it is believed to be related to erythrocyte sequestration that interferes with the flow and metabolism of the renal microcirculation, other factors include hypovolemia and hemolysis. Renal failure can manifest as acute tubular necrosis (12).

Pulmonary Edema

It is due to sequestration of parasitized red blood cells in the lungs and/or cytokine-induced leakage from the pulmonary vasculature, leading to adult respiratory distress syndrome, which is usually worsened by excessive administration of intravenous fluids (13).

Liver Dysfunction

It is not uncommon to find severe jaundice due to hemolysis, hepatocyte injury, and cholestasis in the setting of P. falciparum infection, with subsequent elevation of transaminases and bilirubins; this manifestation is more common among adults than among children (14).

Diagnosis

The diagnosis of malaria is established with consistent symptoms of malaria + a positive diagnostic test, within the diagnostic tests we have optical microscopy tests and rapid diagnostic tests (PDR). In most cases of symptomatic malaria, thick film and smear examination by a competent microbiologist will reveal malaria parasites. PDR can be used if there is no system to guarantee the quality of microscopy, these are antigenic tests for PfHRP2 detection, they can be useful for patients who have received incomplete antimalarial treatment, in whom blood slides can be negative. If the initial blood slide examination is negative in patients with manifestations consistent with complicated malaria, a series of blood slides should be examined at 6–12-hour intervals, or RDT should be performed. If the slide examination and PDR results are negative, malaria is highly unlikely and other causes of illness should be sought and treated (15).

Within the differential diagnosis of malaria, other etiological agents of acute febrile syndrome must be considered, among which rickettsiosis, typhoid fever, dengue, chikungunya, zika stand out. In addition, when presenting with jaundice, yellow fever must also be considered as possible causes. leptospirosis, hepatitis A, B, E, EBV and CMV (16).

Treatment

Uncomplicated malaria due to P. falciparum

The treatment of choice for uncomplicated malaria due to P falciparum is the use of the combined scheme based on artemisinin, Artemer 1.7 mg/kg/dose + lumefantrine 12 mg/kg/dose is an effective scheme that can be used in both children and adolescents. in adults, CONTRAINDICATED in the first trimester of pregnancy, it should be administered at 0, 8, 24, 48 and 60 hours and should not exceed more than 4 tablets per dose, its presentation for Colombia is 20 + 120 mg tablets respectively. In the case of pregnant women in the first trimester, the scheme of quinine sulfate + clindamycin for 7 days at doses of 10 mg/kg/dose + 10 mg/kg/dose, respectively, is recommended. Remember a maximum of 900 mg of clindamycin per dose, distributed every 8 hours (17).

Uncomplicated malaria due to P. vivax, P. ovale, P. malariae, P. knowlesi

The usefulness of the scheme of chloroquine 25 mg/kg/total dose and administered once a day for 3 days + primaquine 0.25 mg/kg/day for 14 days has been demonstrated; 30 mg of primaquine should not be exceeded per day. day. First-trimester pregnant women with chloroquine-resistant infection can be treated with quinine and use of primaquine should always be avoided (17).

Complicated Malaria

The efficacy of the IV artesunate treatment schedule for complicated malaria has been shown to be effective in children, adults, and pregnant women in all trimesters, given at a dose of 2.4 mg/kg/dose, spread over time 0, 12, 24, in case of clinical improvement, treatment is changed to artemether + lumefantrine, if the patient persists without improvement, IV artesunate can be given for up to 5 days and it is important to remember not to exceed 180 mg per dose, in children with less weight at 20 kg, the use of a higher dose of 3 mg/kg is recommended (17). Although IV artesunate monotherapy remains the treatment of choice, the emergence of resistance to it is a major concern, so combination with other active agents may protect against the development of such resistance to individual drugs (18).

Control, Elimination, And Eradication

Malaria control is considered as the reduction of the incidence and prevalence of the disease so that it does not represent a public health problem. Elimination refers to the reduction of

incidence and transmission to zero in humans in a defined geographic area, and eradication is the global elimination of human disease. Towards the year 2007 with the challenge of Bill and Melinda Gates there is an enthusiasm in creating measures and developing methods that can eradicate malaria. By 2015, the United Nations, with the support of the Bill and Melinda Gates Foundation, published a new framework for malaria eradication (19) and the WHO published a technical strategy for the elimination of P. vivax (20). If malaria elimination is to be achieved for the proposed goal by the year 2040, it will be necessary to create an infrastructure within the next 3 to 5 years, which entails challenges for which it is timely to reexamine the global strategy (21). Among the tools for the prevention of malaria infection are measures against mosquito bites, chemoprevention, and vaccination.

Avoid Mosquito Bites

Various clinical studies support the use of repellents and mosquito nets as an effective measure to prevent the bite of malaria-transmitting mosquitoes. In a study carried out in Bolivia with 4,008 participants, it is evident that people who sleep with a mosquito net treated with repellent and, in addition to that, use an insecticide, reduced the rates of malaria episodes due to P. vivax compared to those who only used placebo (19). A systematic review associated the use of long-acting insecticide-treated nets with a 44% reduction in the incidence of severe malaria episodes (20).

Chemoprevention

The use of drugs such as amodiaquine, pyrimethamine sulfadoxine and TMP-SMX have been shown to have a benefit in reducing malaria events and complicated malaria in special populations (children, pregnant women, and HIV patients). A systematic review shows that this seasonal preventive scheme prevented 75% of malaria episodes in school-age children (24). Its effectiveness was also seen in pregnant women. In patients with HIV, the use of TMP-SMX as chemoprophylaxis showed a reduction in morbidity and mortality rates due to malaria (21).

Vaccination

The RTS, S. Approved by the WHO in 2012, it consists of a recombinant fusion protein created from an antigen on the surface of the P. falciparum sporozoite. The results of the phase 3 clinical trial conducted with 15,459 children showed that the vaccine induced partial protection against malaria among children aged 5 to 17 years during a follow-up period of 48 months and demonstrated the benefit of the booster at 20 months (21).

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