Review Article

J Integral Sci, 2022, Volume 5, Issue 4, 19-21

Journal of Integral Sciences (JIS)

(An International Open Access Journal)

Available at www.jisciences.com ISSN: 2581-5679

World-changing malaria vaccine

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Received: 09 Nov 2022 Revised: 18 Nov 2022 Accepted: 15 Dec 2022

Abstract

Malaria is a life-threatening disease caused female Anopheles mosquitoesm, transmitted to people through the bites of infecton. It is preventable and curable. According to WAR-2021 (World Malaria Report), half the world's population lives at risk of malaria transmission in 87 countries and territories. The WHO African Region carries a is proportionately high share of the global malaria burden. Children under 5 accounted for about 80% of all malaria deaths in the Region. More than 260,000 African children under age 5 die from the disease annually. This review highlights the recent research in the development of the malaria vaccine.

Keywords: Malaria vaccine, Antimalaria, RTS, S Malaria vaccine.

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DOI: https://doi.org/10.37022/journal.v5i4.48

Produced and Published by

South Asian Academic Publications

Introduction

Malaria is a mosquito-borne infectious disease that affects humansand other animals. Theterm*malaria* was derived from the Italian word "*mala aria*", meaning foul air. It is a protozoal blood infection caused by a mosquito-borne apicomplexan parasite, which is transmitted to humans during the bite of an infected female*Anopheles*mosquito species. Symptoms of malaria include fever, tiredness, vomiting, and headaches. In severe cases, it may cause yellow skin, seizures, coma, and even death.

Malaria kills approximately 627,000 people a year worldwide and causes illness in hundreds of millions more, with most deaths occurring among children living in sub-Saharan Africa. Till now, no vaccine against malaria has been licensed for use.

Anti-malarials

Anti-malarials are antiparasitic chemotherapeutic drugs that are used to prevent and cure malaria. *Plasmodium falciparum, Plasmodiummalaria,Plasmodiumovale,* and *Plasmodium vivax* arethe four Plasmodium species that cause malaria **[1]**.The malaria is also caused due to the blood transfusion from the diseased person, contamination of food materials, and accumulation of waste water, and irregular cleanliness etc.

The malaria can be controlled by

- By avoiding contaminated food
- By maintaining proper hygienic conditions
- By maintaining cleanliness etc.

These are the different methods involved in the prevention of malaria.

Classification of Ant malarial Drugs [2]

Sl. No.	Derivatives	Example
1	Cinchona alkaloids	(-) Quinine; (+) Cinchonine; (-) Cinchonidine. Quinidine [(+) isomer (used as antiarrhythmic)]
2	7-Chloro-4-Amino Quinolines	Cholorquine; Amodiaquine; Hydroxychloroquine; Sontoquine; Amopyroquine
3	8-Amino Quinolines	Primaquine; Pamaquine; Pentaquine phosphate; Isopentaquine; Quinocide HCl.
4	Acridine derivatives (9-amino acridine derivatives)	Quinacrine; Acriquine
5	Biguanides	Proguanil; Chloro proguanil;

		Bromoguanil; Nitroguanil
6	Diamino pyrimidines	Pyrimethamine; Trimethoprim
7	Sulphonamides and Sulphones	Sulphadoxine; Sulphadiazine; Sulphamethoxazole; Sulphalene
8	Miscellaneous drugs	Halofantrine; Mefloquine; Dapsone; Artemether, Artemotil; Artesunate

2. Malaria Vaccine

The research on development of malaria vaccines has been started in 1960.Pre-erythrocytic vaccinesPre-erythrocytic vaccines (PEV) target antigens from *Plasmodium* sporozoite and liver stages, the clinically silent forms that initiate human infection after a mosquito inoculates sporozoites into skin. PEV are designed to induce antibodies against surface antigens that clear sporozoites from skin or bloodstream or block their invasion of hepatocytes, or T cell responses that attack infected hepatocytes [3].

RTS, S and CSP-based vaccines:

The first malaria gene to be cloned encodes the major surface antigen of sporozoites called circumsporozoite protein or CSP, which continues to be a major focus of vaccine development. RTS,S, the most advanced PEV, incorporates a *P. falciparum* CSP fragment comprising central repeat (hence "R") and C-terminal regions (containing T cell epitopes, hence "T") fused to hepatitis B surface antigen ("S"), or altogether "RTS". RTS is expressed in yeast that also carry hepatitis B "S" expression cassettes, and thus synthesize S and RTS polypeptides that spontaneously co-assemble into mixed lipoprotein particles (or "RTS,S") with the CSP fragment on their surface [4].

RTS,S formulated in GSK's proprietary AS01 adjuvant completed trials in adults, children, and young infants in sub-Saharan Africa. The phase III trial enrolled 15,459 children at 11 centers in seven African countries, and delivered 3 doses at 1-month intervals to coincide with the Extended Program for Immunization schedule, with a booster dose 18 months after the third dose.

Whole sporozoite vaccines

In 2010, the company Sanaria introduced a platform technology that entails harvesting PfSPZ from the salivary glands of aseptic mosquitoes infected by cultured laboratory parasites, followed by purification, vialing, and cryopreservation in liquid nitrogen vapor phase. PfSPZ are attenuated by different approaches to prepare the vaccine candidate product: radiation attenuation (called PfSPZ Vaccine), chemoattenuation achieved in vivo by concomitant administration of antimalarial drugs (called PfSPZ-CVac for chemoprophylaxis vaccination), or genetic attenuation by deletion of genes required to complete liver-stage development (called PfSPZ-GA1 for the first genetically attenuated PfSPZ candidate (NCT03163121)). PfSPZ Vaccine has required direct venous inoculation to confer sterile immunity against challenge with sporozoites.

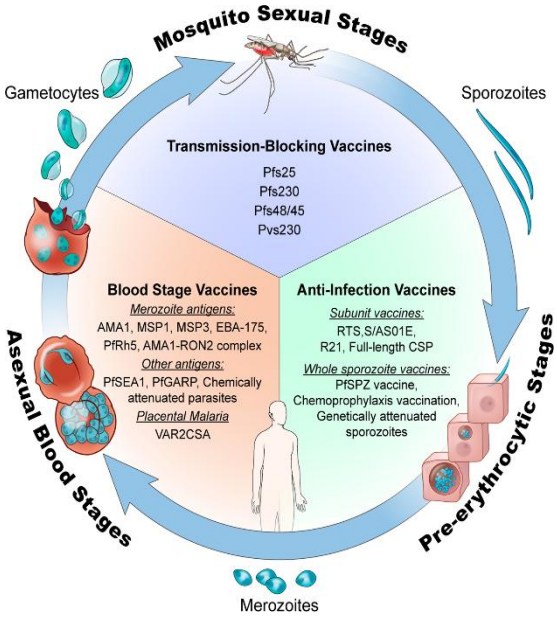
Blood-stage vaccines

BSV target the asexual parasite forms that undergo repeated multiplicative cycles in erythrocytes and cause disease and death. Cycle duration varies between malaria parasite species and determines the period between fevers, or periodicity: 1 day for *P. knowlesi*, 2 days for *P. falciparum, P. Vivax* and *P. ovale*, and 3 days for *P. malariae*. At the completion of each cycle, the brood of ~1–2 dozen progeny (called merozoites) egress from host erythrocytes and within seconds each merozoite has invaded a new erythrocyte to initiate another round of multiplication [5].

RTS,S Malaria vaccine

The World Health Organization (WHO) is recommended the use of the RTS,S/AS01 (RTS,S) malaria vaccine among African children in sub-Saharan Africa and other places with moderate to high *P. falciparum* malaria transmission. As per the pilot programme in Ghana, Kenya and Malawi where the positively tested people havemore than 900000 children since 2019 [10].

Vaccine types



Types of Antimalaria vaccines [11]

Potential targets for Vaccine development

- ✓ Direct anti-sporozite
- ✓ Anti-host erythrocyte
- ✓ Direct anti-hepatozoite
- ✓ Anti-gametocyte (6)

TS,S malaria vaccine candidate (Mosquirix™)

RTS,S/AS01,is also known as Mosquirix™. RTS,S, The vaccine was developed by PATH Malaria Vaccine Initiative (MVI) and GlaxoSmithKline (GSK). The WHO recommended large-scale pilot implementations of RTS, S in children 5 to 9 months of age of moderate-to-high parasite transmission [2].

Other malaria vaccines under development

R21/matrix-M

It was developed by the University of Oxford, the Kenya medical research institute, the Londonschool of hygiene and tropical medicine, Novavax the serum institute of India. It showed a great efficacy in its initial clinical trials with 77%. It was the first vaccine to meet the WHO goal of minimum 75% efficacy. It also contains M21 as an adjuvant which was used in the novavax covid-19 vaccine.

The phase II clinical trials were shown 77% efficacy with having more significant antibody levels than RTS,S vaccine. The phase III clinical trials are going on in four African countries.

PfSPZ vaccine

It was developed by Sanaria using radiation attenuated sporozoites to elicit immune response.The clinical trials are going on in countries like Africa, Europe and US with 80% volunteers. This vaccine candidate was fast track granted by the USFDA in September 2016. The phase III clinical trials are announced in Bioko on April 2019 [7].

SPf66 vaccine

It was a synthetic peptide which was developed by the Manuel Elkin Patarroyo team in Columbia. It was resulted with only 28% efficacy in South America and less or minimum efficacy in Africa. The circum-sporozoite protein also known as CSP was appeared to be promising enough to undergo clinical trials [8].

NYVAC-Pf7 vaccine

It is a multi-stage vaccine which was attempted to use a different technology of incorporating seven *p. Falciparum* antigenic genes. It was resulted in the poor antibody responses.

Conclusion

Malaria vaccine candidate's research is progressing in clinical trials. RTS, S was more advanced to develop a vaccine. Scientists are still under research in antigen discovery, and structural vaccinology of vaccine candidates. More development is required to combat the malaria especially in African regions to save hundreds of lives of children.

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