Experimental vaccine protects against multiple malaria strains

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Credit: CDC

An experimental malaria vaccine protected healthy subjects from infection with a malaria strain different from that contained in the vaccine, according to a study published today in the *Proceedings of the National Academy of Sciences* (*PNAS*). The research was conducted by scientists at the University of Maryland School of Medicine (UM SOM) and the National Institute of Allergy and Infectious Diseases (NIAID),

part of the National Institutes of Health (NIH).

The Phase 1 clinical trial is important because in places where malaria is common, there is usually more than one strain of malaria. To be effective in the real world, a vaccine must protect against more than one. The study's lead researcher, Kirsten E. Lyke, MD, associate professor of medicine at the UM SOM Center for Vaccine Development, said the vaccine's versatility was promising. "Our study shows that that this vaccine can protect against at least two strains of malaria," said Dr. Lyke, who has studied malaria for more than a decade. "We need to continue our research, but this is a fantastic finding."

Malaria is transmitted to humans through the bite of infected mosquitoes, which inject immature malaria parasites called sporozoites into a person's bloodstream. The parasites travel to the liver, where they mature, multiply and spread via the bloodstream throughout the body causing malaria symptoms including chills, fever, headache, nausea, sweating and fatigue. According to the World Health Organization, 212 million people were infected with malaria globally in 2015 and 429,000 people died, mostly young children in Africa. The species Plasmodium falciparum is the most common cause of malaria morbidity and mortality in Africa. In the United States, travel-related malaria is a concern for international tourists, aid workers and military personnel worldwide.

The PfSPZ Vaccine used in this study was developed by Sanaria Inc., of Rockville, Maryland. The vaccine contains weakened P. falciparum sporozoites that do not cause infection but are able to generate a protective immune response that protects against live malaria infection. Earlier research with the vaccine found it to be safe, well-tolerated and protective for more than a year when tested in healthy U.S. adults against a single Africa-derived malaria strain matched to the PfSPZ Vaccine.

The study enrolled 31 healthy adults ages 18 to 45 years, and was led by Dr. Lyke and Robert A. Seder, MD, chief of the Cellular Immunology Section of NIAID's Vaccine Research Center (VRC). Participants were assigned to receive three doses of the vaccine over several months by rapid intravenous injection.

Nineteen weeks after receiving the final dose of the test vaccine, participants who received the vaccine and a group of non-vaccinated volunteers were exposed in a controlled setting to bites from mosquitoes infected with the same strain of P. falciparum parasites (NF54, from Africa) that were used to manufacture the PfSPZ Vaccine.

Nine of the 14 participants (64 percent) who received the PfSPZ Vaccine demonstrated no evidence of malaria parasites; all six of the non-vaccinated participants who were challenged at the same time had malaria parasites in their blood.

Of the nine participants who showed no evidence of malaria, six participants were again exposed in a controlled setting to mosquito bites, this time from mosquitoes infected with a different strain of P. falciparum parasite, 33 weeks after the final immunization. In this group, 5 of the 6 participants (83 percent) were protected against malaria infection; none of the six participants who did not receive the vaccine and were challenged were protected. All participants who became infected with malaria immediately received medical treatment.

The research team found that the PfSPZ Vaccine activated T cells, a key component of the body's defenses against malaria, and induced antibody responses in all vaccine recipients. Vaccine-specific T-cell responses were comparable when measured against both of the malaria challenge strains, providing some insights into how the vaccine was mediating protection.

Ongoing research will determine whether protective efficacy can be improved by changes to the PfSPZ Vaccine dose and number of immunizations. Accordingly, a Phase II efficacy trial testing three different dosages in a three-dose vaccine regimen is now underway in 5- to 12-month-old infants in Western Kenya to assess safety and efficacy against natural infection.

More information: Attenuated PfSPZ Vaccine induces strain-transcending T cells and durable protection against heterologous controlled human malaria infection, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1615324114

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