RTS,S vaccine could favor the acquisition of natural immunity against malaria

13 August 2019

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The RTS,S malaria vaccine could enhance the production of protective antibodies upon subsequent parasite infection, according to a study led by the Barcelona Institute for Global Health (ISGlobal), an institution supported by "la Caixa." The results, published in *BMC Medicine*, identify the antigens (or protein fragments) that could be included in future, more effective multivalent vaccines.

Immunity to a pathogen can be acquired by natural exposure to the microorganism or through vaccination. The mechanisms underlying both types of immunity are not always the same, particularly in the case of parasites with complex life cycles, such as Plasmodium falciparum, that causes malaria. Over the last few years, ISGlobal researcher Carlota Dobaño and her team have been investigating the immune response induced by the RTS,S, the most advanced malaria vaccine that will be tested at large scale in sub-Saharan Africa this year.

In this study, the authors investigated how vaccination affects natural immunity to the parasite upon subsequent exposure. "To date, most studies had focused on evaluating vaccine-specific responses but not responses towards other parasite antigens," explains Gemma Moncunill, last author of the study. The RTS,S vaccine contains one single parasitic antigen: a fragment of the CSP protein.

The research team analysed serum samples obtained from 195 children, vaccinated or not, who made part of the phase III RTS,S clinical trial and were followed up during 12 months. 78 were from Kintampo, Ghana, a region with high malaria transmission, and 115 were from Manhiça, Mozambique, where transmission is low to moderate. They studied the levels and type of antibodies recognising a total of 38 P. falciparum antigens, including the CSP protein, before and after vaccination.

They found three patterns of antibody responses to these antigens: those that decrease after vaccination, those that are unchanged, and those that increase. Many antibodies in the first group are considered markers of parasite exposure and were associated with a higher malaria risk. Those in the third group were associated with protection—they reduced by half the risk of developing the disease. These protective antibodies mostly recognised antigens expressed by parasite stages that circulate in the blood and that infect red blood cells.

"We think that the partial efficacy of the vaccine allows low infection levels upon subsequent parasite exposure which in turn leads to the production of protective antibodies," explains Carlota Dobaño. "This effect would be observed especially in regions with low to moderate transmission levels," she adds. Importantly, these results identify antigens that could be included in future and more effective multivalent vaccines.

More information: Dobaño C, Ubillos I, Jairoce C, et al. RTS,S/AS01E immunization increases

antibody responses to vaccine unrelated Plasmodium falciparum antigens associated with protection against clinical malaria in African children: a case-control study. 2019 August 14. *BMC Med*. DOI: 10.1186/s12916-019-1378-6

Provided by Barcelona Institute for Global Health