

Abstract

This study is an evaluation of the acquisition of natural antibodies against specific *Plasmodium falciparum* antigens, and the protection they provide against clinical malaria. The data relate to blood samples collected 1993-94 during a randomized double-blinded placebo-controlled trial of the SPf66 vaccine against *Plasmodium falciparum* malaria in children in southern Tanzania. Altogether 586 children aged 1-5,99 years were included in the original trial. Only the data from 275 children of the placebo arm were used in this study, for whom baseline blood samples were available, and in each of whom incidence of clinical malaria was monitored over 434 days (62 weeks) through passive case detection (in a subgroup there was also active case detection). Antibody levels were measured (in the laboratory of Prof. G-P Corradin) in each of these samples against a range of short peptides derived from pre-erythrocytic or erythrocytic *Plasmodium falciparum* surface antigens. The present analyses use this information to explore associations between anti-parasitic antibodies and protection against clinical malaria.

Kaplan-Meier (KM) survival analysis of the age-related protection against clinical malaria showed a continuous increase of the median (malaria free days) with age ranging from 30 days in the one to two years old to 186 days in the five to six year old children.

In linear regression analyses of age and the logarithmic transformed antibody levels a significant age-related increase of IgG antibody levels could be shown for 17 out of 36 epitopes and for seven out of eight cytophilic IgG antibody levels.

To perform survival analysis of the cytophilic IgG subclasses IgG1 and IgG3, the children were divided into 50% with the higher antibody level and into 50% with the lower antibody level to the specific antigen. In seven out of eight times the median of malaria free days was higher in the "higher IgG antibody level" group. Only the results of the cytophilic IgG1 and IgG3 antibody levels against MR141A (MSP-2) were proven to be significant.

KM survival analyses of the antibody levels against 36 different epitopes showed on 32 occasions a positive association between the increase of antibody level and higher protection against clinical malaria. From these 32 epitopes nine could be proven to be significant within the sample size: five of the antibody levels were directed against genome based epitopes and four against MSP-2 epitopes. The coefficients for antibody levels were plotted against the previously calculated increase in median antibody levels. The epitopes LR149, LR171A, MR198 and MR219 (genome derived) and MR144A, B and C (MSP-2) showed the highest association between their antibody levels and protection and were therefore identified as the best potential vaccine candidates out of the 36 epitopes analysed.