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Ishih, A

Mount Kenya University

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Chloroquine efficacy in Plasmodium berghei NK65-infected ICR mice, with reference to the influence of initial parasite load and starting day of drug administration on the outcome of treatment.

Ishih A[1], Suzuki T, Muregi FW, Matsui K, Terada M.

Author information

- [1]Department of Parasitology, Hamamatsu University School of Medicine, Japan. aishih@hama-med.ac.jp

Abstract

We examined whether the initial number of parasites inoculated and the starting day of medication post-infection influenced the antimalarial efficacy of chloroquine (CQ) against Plasmodium berghei NK65 infection in ICR mice. Male ICR mice were inoculated intraperitoneally with 1 x 10(5), 1x10(6), 1 x 10(7), 1 x 10(8) P. berghei NK65-parasitized erythrocytes (pRBC). In the treated group, all mice received an oral dose of 20 mg/kg of CQ base for 4 days starting on day 0 after infection. From day 3, Giemsa-stained thin blood smears from tail vein blood were used to assess parasitemia. Mice in the untreated control in each group showed a progressive increase in parasitemia leading to death. Treatment of mice, inoculated with 1 x 10(5), 1 x 10(6) and 1 x 10(7) pRBC, with CQ showed a marked effect. All the mice survived during the experiment. During the observation period, malaria parasites could not be detected on microscopic examination. Conversely, mice inoculated with 1 x 10(8) pRBC showed little response to CQ treatment, and all mice showed a progressive increase in parasitemia and ultimately died. In another experiment, mice infected with 1 x 10(3) and 1x 10(5) pRBC were treated with an oral four-day dosage of 20 mg/kg of CQ base from days 2, 3 or 4 post-infection. Treatment of mice, inoculated with 1 x 10(3) pRBC, with CQ from days 2 and 3 showed a marked effect. All mice survived during the experiment. However, treatment from day 4 showed a limited derease in parasitemia and all the mice ultimately died. On the other hand, treatment from day 2 showed a marked effect against 1 x 10(5) P. berghei NK65-infected mice, but treatment from days 3 or 4 was only slightly effective and all the mice died with an increasing parasitemia. The present results indicate that in in vivo antimalarial drug-assay systems, several factors, sush as initial parasite load and starting time of treatment may influence the drug response in the host.

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