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Possible involvement of IFN-gamma in early mortality of Plasmodium berghei NK65-infected BALB/c mice after febrifugine treatment.

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Abstract

Parasitemia patterns, survival and cytokine levels of Plasmodium berghei NK65-infected BALB/c mice, treated orally with the alkaloidal mixture of febrifugine and isofebrifugine at a dose of 1 mg/kg twice a day for 4 consecutive days were monitored. Whereas the untreated mice showed a progressive increase in parasitemia and ultimate death, the alkaloid mixture-treated group showed a transient suppression of parasitemia during the course of treatment. However, the parasitemia increased on discontinuation of treatment, leading to earlier death of mice in the treated group than in the infected but untreated controls. Mice in the infected but untreated group displayed a significant elevation in serum IFN-gamma levels during the first week post-infection (pI) and from Day 14 pI, relative to the levels in the uninfected controls. In contrast, although mice in the alkaloid mixture-treated group displayed no significant elevation in serum IFN-gamma levels during the first week pI, they showed considerable levels on Day 14 pI. There were no significant differences in serum IL-4 levels among the groups. The titers of the parasite-specific IgG1, IgG2a, IgG2b and IgG3 were significantly elevated from Day 11 pI in both the treated and untreated groups. There was a significant difference in survival duration between the IFN-gamma^{-/-} mutant and BALB/c mice. IFN-gamma^{-/-} mutant mice showed a decrease in parasitemia levels while receiving medication, which was significantly lower than those of the treated BALB/c mice. The results of the present study suggest that although IFN-gamma is significant for protective immunity in mice with malaria infection, it may play an adverse role post-medication, causing earlier mortality of treated BALB/c mice.

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