O036

2-hour Oral Session

Iron deficiency increases mortality in experimental malaria

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Background: Iron deficiency is the most widespread nutrient deficiency worldwide, causing considerable development impairments in children. Iron deficiency has been proposed to protect against malaria morbidity and mortality and iron supplementation to children in malaria-endemic areas is controversial.

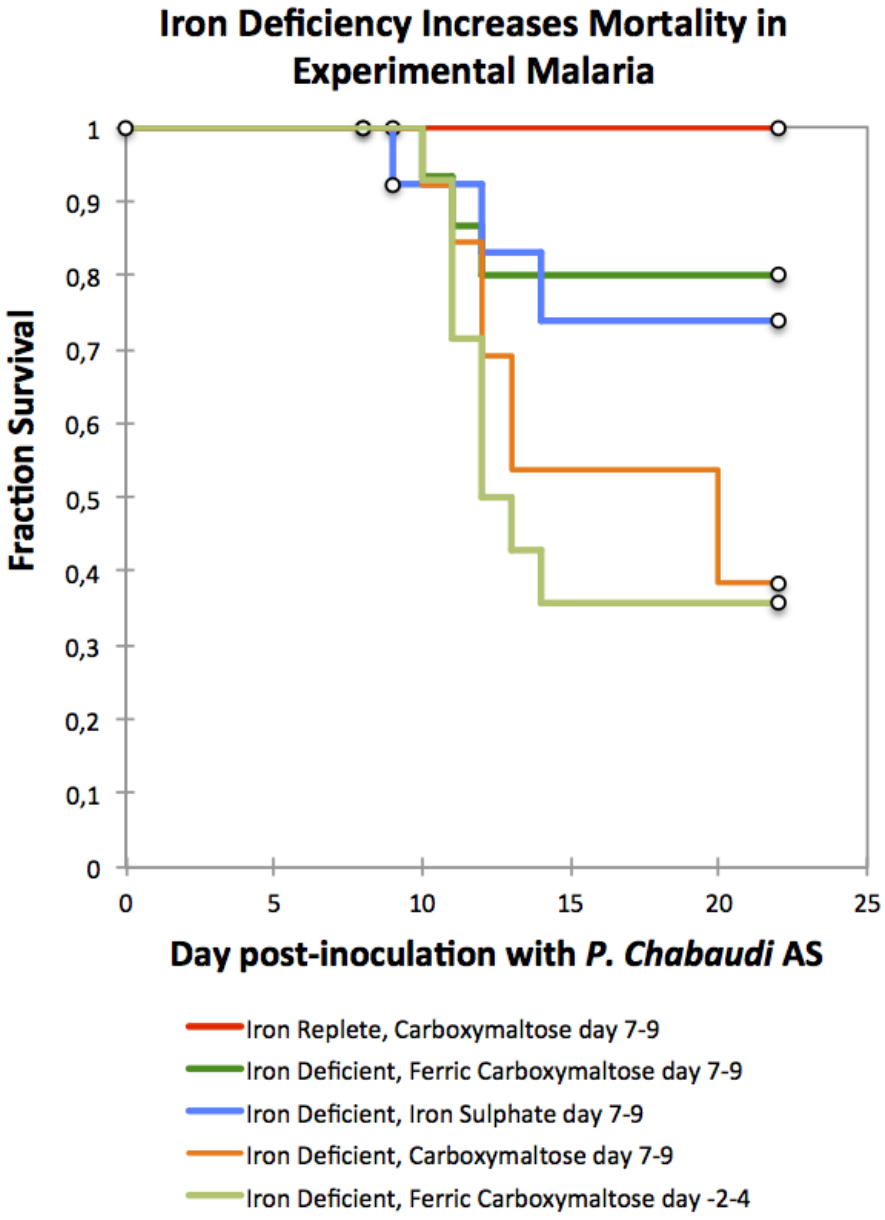
Objective: To investigate the effects of nutritional iron deficiency and the response to iron treatment on the course of infection in a non-lethal malaria model.

Methods: 3-week-old male A/J mice were placed on iron-deficient diet (n=58), and a control group was given standard diet (n=16). At the stage of iron deficiency anaemia, defined as a 20% drop in haemoglobin concentration, all mice were infected intraperitoneally with 10^4 *Plasmodium Chabaudi* AS. Subgroups of mice received a three-day course of either intravenous ferric carboxymaltose (FC), carboxymaltose (controls) or oral ferrous-sulphate at different times. Daily measurements of haemoglobin, reticulocytes, parasitaemia, weight and temperature were recorded. A humane endpoint of 30°C was used as proxy for death. Survival was analysed using log-rank test, while multivariate mixed-effects models were used to analyse continuous outcome measures.

Results: Iron deficiency resulted in a mortality of 34% in this otherwise non-lethal model of malaria. Thus, iron-deficient mice exhibited increased mortality compared to iron-replete mice ($p = 0.0005$). Iron treatment during the course of malaria appeared to have a positive impact on survival, however only treatment with intravenous FC reached statistically significance ($p = 0.046$). FC administered immediately prior to infection did not have a beneficial effect on survival. Finally, a tendency towards faster erythropoietic recovery in FC treated mice compared to ferrous sulphate-treated mice was observed. Two earlier pilot studies have confirmed these findings.

Conclusion: Our findings challenge the view that iron-deficiency protects against malaria and show the need for further trials of ferric carboxymaltose as an adjunctive treatment for severe malarial anaemia.

Conflict of interest: The study was supported by Vifor Pharma Int. Independence of researchers was secured through an intellectual property agreement.


Iron Deficiency Increases Mortality in Experimental Malaria
Fraction Survival
1
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0
0
5
10
15
20
25
Day post-inoculation with P. Chabaudi AS
Iron Replete, Carboxymaltose day 7-9
Iron Deficient, Ferric Carboxymaltose day 7-9
Iron Deficient, Iron Sulphate day 7-9
Iron Deficient, Carboxymaltose day 7-9
Iron Deficient, Ferric Carboxymaltose day -2-4