# Oral iron supplements for children in malaria-endemic areas (Review)

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[Intervention Review]

# Oral iron supplements for children in malaria-endemic areas

Joseph U Okebe[2], Dafna Yahav[3], Rana Shbita[3], Mical Paul[1]

[1]Infectious Diseases Unit, Sackler Faculty of Medicine, Tel Aviv, Israel. [2]Medical Research Council Unit, Banjul, Gambia. [3]Department of Medicine E, Beilinson Hospital, Rabin Medical Center, Petah Tikva, Israel

Contact address: Mical Paul, Infectious Diseases Unit, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, 49100, Israel. paulm@post.tau.ac.il. mica@zahav.net.il; MichalP2@clalit.org.il; paulm@post.tau.ac.il.

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## ABSTRACT

### Background

Iron-deficiency anaemia is common during childhood. Iron supplementation has been claimed to increase the risk of malaria.

### Objectives

To assess the effect of iron on malaria and deaths.

### Search methods

We searched *The Cochrane Library*, PUBMED, MEDLINE, LILACS; and trial registry databases, all up to June 2011. We scanned references of included trials.

### Selection criteria

Individually and cluster randomized controlled trials conducted in hypoendemic to holoendemic malaria regions and including children below 18 years of age. We included trials comparing orally administered iron, iron with antimalarial treatment, or iron with folic acid versus placebo or no treatment. Iron fortification was excluded. Antihelminthics could be administered to either group. Additional micronutrients had to be administered equally to both groups.

### Data collection and analysis

The primary outcomes were clinical (symptomatic) malaria, severe malaria, and death. Two authors independently selected the studies and extracted the data. We assessed heterogeneity and conducted subgroup analyses by the presence of anaemia at baseline, age, and malaria endemicity. We assessed risk of bias using domain-based evaluation. We performed a fixed-effect meta-analysis for all outcomes and random-effects meta-analysis for hematological outcomes. We adjusted analyses for cluster randomized trials.

### Main results

Seventy-one trials (45,353 children) were included. For clinical malaria, no significant difference between iron alone and placebo was detected, (risk ratio (RR) 0.99, 95% confidence intervals (CI) 0.90 to 1.09, 13 trials). The results were similar in the subgroups of non-anaemic children and children below 2 years of age. There was no significant difference in deaths in hyper- and holoendemic areas, risk difference +1.93 per 1000 children (95% CI -1.78 to 5.64, 13 trials, 17,898 children). Iron administered for treatment of anaemia resulted in a larger increase in haemoglobin than iron given for prevention, and the benefit was similar in hyper- or holoendemic and lower endemicity settings. Iron and folic acid supplementation resulted in mixed results for severe malaria. Overall, the risk for clinical

malaria was higher with iron or with iron plus folic acid in trials where services did not provide for malaria surveillance and treatment. Iron with antimalarial treatment significantly reduced malaria. Iron supplementation during an acute attack of malaria did not increase the risk for parasitological failure, (RR 0.96, 95% CI 0.74 to 1.24, three trials) or deaths.

**Authors' conclusions**

Iron alone or with antimalaria treatment does not increase the risk of clinical malaria or death when regular malaria surveillance and treatment services are provided. There is no need to screen for anaemia prior to iron supplementation.

## PLAIN LANGUAGE SUMMARY

**Iron supplements for children living in malaria-endemic countries**

Children commonly develop anaemia (low haemoglobin) after birth. Anaemia is associated with several ill effects, including hindering motor development and learning skills, and impaired immunity. Children are therefore commonly given iron supplements to prevent or treat anaemia. In countries where malaria is prevalent, it has been suggested that iron supplementation increases the risk of malaria and death. The high dose of iron which is given as medicine may result in free iron circulating in the blood and is made available to the malaria parasite, promoting its growth. We aimed to assess the effects of oral iron supplementation in children living in countries where malaria is prevalent.

Iron did not increase the risk of malaria, indicated by fever and the presence of parasites in the blood. There was no increased risk of death among children treated with iron. Although it is hypothesized that iron supplementation might harm children who do not have anaemia because of the iron overload, we did not find an increased risk for malaria among non-anaemic children. When iron was administered with folic acid (a vitamin necessary for DNA synthesis) one large trial suggested there was an increased risk of severe (lethal) malaria. When iron was administered in settings of poor malaria management there was an increased risk for malaria. Iron supplementation increased haemoglobin by about 1 g/dL in areas where malaria is highly prevalent. At the end of follow-up, which varied between two weeks and six months after the end of iron supplementation, the haemoglobin gain was smaller but still present at 0.4 g/dL. Iron did not increase the risk of respiratory infections or other infections. Children given iron visited medical clinics less than children given placebo, but the rate of hospitalization was similar. The children's weight and height at the end of treatment were similar. Iron did not adversely affect the rates of cure when it was given together with antimalarial treatment in the three trials that examined this issue.

Our conclusions are that iron supplementation (without folic acid) does not adversely affect children living in malaria-endemic areas. The evidence shown in our review is limited by the lack of trials examining the relevant outcomes and the limited information available, so that we were unable to fully analyse factors that could affect our results, such as the children's baseline level of haemoglobin. Based on our review, routine iron supplementation should not be withheld from children living in countries where malaria is prevalent.