Effect of iron supplementation on physical performance in children and adolescents: systematic review of randomized controlled trials
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CRD summary
This review evaluated the effect of iron supplementation on the physical performance of children and adolescents. The authors concluded that oral iron supplementation may have a positive effect on the post-exercise heart rate, blood lactate levels and treadmill endurance time. These conclusions have to be viewed with caution given the small number of studies and participants included.

Authors' objectives
To evaluate the effects of iron supplementation on the physical performance of children and adolescents.

Searching
MEDLINE, the Cochrane Controlled Trials Register, EMBASE, IBIDS and HealthSTAR were searched to March 2003. Only studies reported in the English language were included. The reference lists of relevant articles and reviews, the bibliographies of books, abstracts, and proceedings of international conferences were checked for additional studies. Donor agencies, experts in the field, and authors of recent iron supplementation trials were also contacted in order to identify additional or ongoing trials. Both published and unpublished trials were eligible.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies evaluating oral iron supplementation or iron-integrated milk or cereals were eligible. Non placebo-controlled trials were eligible only if iron was given parenterally. Studies using other micronutrients and drugs were eligible if iron administration was the only therapeutic difference between the study and control groups. Iron was administered orally in all included studies at doses ranging from 30 to 40 mg/day for 2 months up to 200 mg/day for 1 month.

Participants included in the review
The review was restricted to studies with children and adolescents (up to 18 years old). The participants in the included studies varied from students of 8 to 15 years of age from a school for underprivileged children in India (1 study), to 10- to 14-year-old children with haemoglobin levels above 90 g/L (1 study), to adolescent female athletes from the USA with serum ferritin below 20 ng/mL and haemoglobin levels above 120 g/L (1 study). The patients were followed up for 1 to 2 months.

Outcomes assessed in the review
Studies that assessed heart rate, treadmill endurance time, blood lactate levels or oxygen consumption during exercise were eligible for inclusion.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Validity was assessed, but the authors did not state how many reviewers performed the validity assessment. The authors considered the method of randomisation, adequacy of allocation concealment, blinding and the percentage of participants lost to follow-up.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. They stated that, when needed, authors were contacted for additional data. Data (mean and standard deviation) on heart rate in each group before and after exercise were used to calculate a weighted mean difference (WMD) and associated 95% confidence interval (CI).

Methods of synthesis
How were the studies combined?
A pooled WMD and 95% CI were calculated for the outcome heart rate using both fixed-effect and random-effects models. Other outcomes were discussed separately. Publication bias was assessed graphically using funnel plots and statistically by Egger's regression test and Begg's rank correlation test.

How were differences between studies investigated?
Differences in study outcomes were discussed in the text and presented in tabular format. For the outcome heart rate, statistical heterogeneity was calculated and visualised through a forest plot.

Results of the review
Three RCTs (106 participants) were included.

In all the included studies, the method of randomisation was not mentioned, allocation concealment was unclear and the percentage of patients lost at follow-up was below 3%. Two studies were double-blinded; the method of blinding was unclear in the third study.

Running performance.
At 5, 6 and 7 miles per hour running speeds, the pooled WMDs in heart rates after exercise between the iron and the placebo groups were -7.3 (95% CI: -19.6, 4.9, p=0.241), -6.6 (95% CI: -19.9, 6.6, p=0.327) and -8.0 (95% CI: -19.7, 3.7, p=0.182), respectively, suggesting no significant effect of iron supplementation. There was evidence of statistical heterogeneity for these outcomes (test for heterogeneity, p<0.001). After excluding a study with iron-deficient but non-anaemic participants, the WMDs were -13.1 (95% CI: -23.2, -3.1, p=0.01), -14.2 (95% CI: -22.3, -6.1, p=0.001) and -12.7 (95% CI: -23.5, 1.9, p=0.021), respectively, suggesting a significant positive effect of iron supplementation in terms of reducing heart rate after exercise. There was no evidence of publication bias on the funnel plot or when using the Egger's or Begg's methods.

Blood lactate.
One study found significantly lower levels of blood lactate in patients receiving 30- or 40-mg iron supplements in comparison with placebo both before (7.71 and 7.55 mg/dL versus 8.43 mg/dL) and after (14.36 and 14.35 mg/dL versus 16.48 mg/dL) exercise (p<0.05).

Oxygen consumption.
One study observed an increase in oxygen consumption in both the placebo and iron supplementation groups at 5, 6 and 7 miles per hour running speeds. The difference in oxygen consumption was not statistically significant between the treatment groups. Another study showed no significant differences in maximal or submaximal oxygen consumption among 5 patients treated with iron or placebo.

Treadmill endurance time.
Iron supplementation was associated with an improved endurance time (mean +0.57 minutes, range: +0.03 to +1.92), whereas a reduction was observed in patients receiving placebo (mean -0.67 minutes, range: -0.07 to -1.3).

Authors' conclusions
Iron supplementation may have a positive effect on the physical performance of children, as evaluated by the post-
exercise heart rate in anaemic patients, blood lactate levels and treadmill endurance time. Given the limited data
available, these findings have to be considered preliminary.

CRD commentary
This review had clearly stated inclusion criteria with respect to the study design, participants, intervention and
outcomes. Several relevant databases were searched and efforts were made to find further published and unpublished
studies, thereby reducing the potential for publication bias. Publication bias was assessed and there was no evidence of
any for the outcomes evaluated. Only studies reported in the English language were included, which might have
introduced language bias. It was not stated whether the study selection, data extraction and quality assessment processes
were performed in duplicate, therefore reviewer error and bias might have been introduced.

Statistical heterogeneity was assessed, although the test used was not stated clearly. The authors found significant
statistical heterogeneity for the outcome heart rate, therefore the decision to pool data for this outcome does not seem
to have been appropriate. The authors’ conclusions need to be taken cautiously given the small number of trials and
participants evaluated.

Implications of the review for practice and research
Practice: The authors did not state any implication for practice
Research: The authors stated that additional controlled trials evaluating the role of iron supplementation on physical
performance in children are needed, and that greater attention should be placed on the simultaneous measurement of
iron levels and their correlation with physical performance. The authors suggested that these studies should also take the
effect of infectious illnesses, malnutrition, and other micronutrients and vitamins on physical performance into account.

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