Review: iron treatment does not improve psychomotor development and cognitive function at 30 days in children with iron deficiency anaemia


QUESTION: In children <3 years of age with iron deficiency, does treatment with iron improve psychomotor development and cognitive function?

Data sources
Studies were identified by searching databases that included the Cochrane Library (2000 Issue 4), Medline (1966 to August 2000), EMBASE/Excerpta Medica (1980 to August 2000), and the Latin American Database (LILACS). Bibliographies of relevant articles were reviewed, key authors in this field were contacted for information on unpublished trials, and forward citation searches on relevant trials were performed within the Science Citation Index.

Study selection
Randomised controlled trials (RCTs) were selected if they compared iron (oral or intramuscular) with placebo or iron plus vitamin C with placebo plus vitamin C. Patients were children <3 years of age, and outcomes included psychomotor development or cognitive function.

Data extraction
2 reviewers independently extracted data on patient characteristics, key components of the intervention, quality of the study, and outcomes.

Main results
7 RCTs met the selection criteria: 5 RCTs examined the short term (within 30 days) and 2 trials the longer term effects (after 2 and 4 mo) of iron treatment. 4 RCTs (128 children) examining the short term effects of iron treatment were included in the meta-analysis. The iron treatment and placebo groups did not differ for short term effects of iron treatment assessed by changes in the Bayley Scales of Infant Development (table). Findings from the 2 RCTs that examined the longer term effects of iron treatment were reported separately. One RCT reported that the groups did not differ for the number of skills (assessed by the Denver Developmental Screening Test) gained after 2 months of iron treatment. The second RCT reported a greater improvement in the treatment group than in the control group, for change from baseline scores on the Bayley Scale Psychomotor Development Index (difference in mean increase from baseline score 18, 95% CI 10 to 27) and the Bayley Scale Motor Development Index (difference in mean increase from baseline score 19, CI 10 to 27).

Conclusions
In children <3 years of age with iron deficiency, treatment with iron does not improve psychomotor development and cognitive function within 30 days. Findings from longer term treatment are inconclusive.

COMMENTARY
The first 3 years of a child’s life represent one of the most important periods of a child’s development. Many factors in the environment influence this development, and as our tools for measuring brain function improve, we are becoming increasingly aware of how critical this period is.

Iron deficiency in the first 2 years of life is a common problem that has generated enormous study and some controversy in relation to the importance and prevention of this deficiency. The gathering evidence of the impact of iron deficiency on behaviour and cognitive processes has clearly heightened attention to this issue.

The review by Logan et al clearly illustrates how little we know about the impact of intervening in children with iron deficiency. 7 RCTs were found in the world literature: 5 RCTs defined short term effects and 2 longer term effects. The outcomes of the existing trials have relied primarily on the Bayley Scales of Infant Development, scales that may not be sensitive enough to identify important changes, especially over the short term. This lack of sensitivity is certainly the case for the study using the Denver Developmental Screening Test. The single longer term study using a more sensitive measure (Bayley Scales) showed dramatic benefits. The authors rightly note that this is not sufficient evidence to draw any conclusions but it is an important study.

Although further research is required, the early evidence that cognitive outcomes may be influenced by iron deficiency and that treatment of this deficiency results in improved outcomes should raise this issue as a concern to public health professionals and clinicians. The focus must be on prevention through proper nutrition counselling, effective screening, and when identified, introduction of treatment of known benefit. More effective and sensitive measures of brain function and development will be important to future clinical trials looking at outcomes of therapeutic interventions.

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Iron treatment v placebo for iron deficiency anaemia in children <3 years of age*

<table>
<thead>
<tr>
<th>Outcomes at 5 to 30 days after study entry</th>
<th>Number of studies</th>
<th>Weighted mean differences (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change from baseline in Bayley Scales MDI</td>
<td>4</td>
<td>-0.55 (−2.84 to 1.75)</td>
</tr>
<tr>
<td>Change from baseline in Bayley Scales PDI</td>
<td>4</td>
<td>-3.20 (−7.24 to 0.85)</td>
</tr>
</tbody>
</table>

*MIDI=Mental Developmental Index; PDI=Psychomotor Developmental Index.
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