Iron deficiency and infant gross motor development: linked randomized controlled trials of pre- and/or postnatal iron supplementation

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INTRODUCTION

- Motor development is a critical factor in child behavior and is associated with cognitive and social-emotional development (Angulo-Barroso et al., 2011; Hadders-Algra 2008; Piek et al., 2008; Murray et al., 2006).
- Iron deficiency (ID) in infancy is associated with poorer motor development: short and long-term effects on fine and gross motor development (Shafir et al., 2008, Gunnarsson et al., 2007, Shafir et al., 2006).
- Randomized controlled trials (RCTs) show positive effects of iron supplementation in infancy (Lind et al., 2004, Friel et al., 2003, Stoltzfus et al., 2001).
- No previous RCT considers effects of the timing of iron supplementation (pregnancy vs. infancy) on motor development.

AIM

To examine the effects of iron supplementation in pregnancy and/or infancy on infant gross motor development at 9 mo.

METHODS

- Design: RCT of iron supplementation in infancy linked to RCT of iron supplementation in pregnancy (Fig. 1).
- Sample: Participants from Hebei Province, China
- Inclusion criteria: Healthy full-term neonates with outcome for prenatal RCT and neonatal/6w developmental testing
- Exclusion criteria: Low cord ferritin suggestive of brain ID (< 35 µg/L) (Siddappa et al., 2004), Perinatal conditions (e.g. multiple birth, prematurity, maternal diabetes, birth complications)
- Assessment of motor development at 9 mo: Peabody Developmental Motor Scales 2nd ed. (PDMS-2)

RESULTS

Table 1. Sample characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo/placebo</th>
<th>Placebo/iron</th>
<th>Iron/placebo</th>
<th>Iron/iron</th>
<th>p-value1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at testing, mo</td>
<td>9.3 (0.4)</td>
<td>9.2 (0.4)</td>
<td>9.3 (0.4)</td>
<td>9.2 (0.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>Sex, % male</td>
<td>53</td>
<td>46</td>
<td>50</td>
<td>52</td>
<td>0.26</td>
</tr>
<tr>
<td>Birth weight, g</td>
<td>3372 (374)</td>
<td>3373 (387)</td>
<td>3324 (370)</td>
<td>3380 (351)</td>
<td>0.22</td>
</tr>
<tr>
<td>Gestational age, wk</td>
<td>39.7 (1.1)</td>
<td>39.7 (1.1)</td>
<td>39.7 (1.1)</td>
<td>39.7 (1.0)</td>
<td>0.83</td>
</tr>
<tr>
<td>9-month WAZ</td>
<td>1.03 (2.7)</td>
<td>0.80 (1.08)</td>
<td>0.92 (0.98)</td>
<td>0.96 (0.98)</td>
<td>0.23</td>
</tr>
<tr>
<td>ID2 at 9 months, %</td>
<td>68</td>
<td>60</td>
<td>68</td>
<td>68</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Values are Mean (SD) for continuous variables or % for categorical ones. *Anova or x². ID defined as ≥ 2 abnormal iron measures (MCV < 74 fl, ZPP/H > 69 µmol/mol heme, serum ferritin < 12 µg/L).

- Infants who received iron postnatally, regardless of whether or not their mothers received iron supplements in pregnancy, showed better PDMS-2 outcome compared to infants who did not receive iron postnatally (received iron only prenatally via maternal supplements or in neither time period) (Fig. 2).

DISCUSSION AND CONCLUSIONS

- Motor scores were higher with iron supplementation in infancy.
- Why only postnatal effect?
  - Rapid gross motor development in this period (6 w – 9 mo) may contribute to increase sensitivity to insufficient iron
- Insufficient external sources of iron in infancy appear to limit infant gross motor development.
- Poorer gross motor development may initiate cascading effects on cognitive and socio-emotional development
- The RCT design supports causal inferences.
- Iron supplementation in infancy, with or without iron supplementation in pregnancy, improved gross motor test scores at 9 mo.

Acknowledgments

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References

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Figure 1. Flowchart of study participation

Figure 2. PDMS-2 results by group

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