Effect of low-dose ferrous sulfate vs iron polysaccharide complex on hemoglobin concentration in young children with nutritional iron-deficiency anemia: a randomized clinical trial

Mitchell Goodwin, PharmD Candidate

BACKGROUND:

- As of 2010, over one billion people worldwide have iron-deficiency anemia
- 3% of children aged one to two years old in the United States have iron-deficiency anemia primarily from insufficient iron intake
- Current standard of care is ferrous sulfate, but iron polysaccharide complex is being used due to increased tolerability

OBJECTIVE

- This study aims to test the efficacy of iron polysaccharide complex against ferrous sulfate for the treatment of pediatric nutritional iron-deficiency anemia

METHODS

- Design
  - Double blind, randomized controlled trial over 12 weeks
- Inclusion Criteria
  - Age > 9 to < 48 months
  - Dietary history consistent with low iron intake
  - Moderate-severe IDA
- Exclusion Criteria
  - Iron deficiency anemia due to blood loss or other causes of anemia
  - Response to recent initiation of iron therapy
  - Evidence of malabsorption on history and/or physical exam
  - History of prior intravenous iron therapy
  - Significant co-existing illness resulting in chronic inflammation
  - High likelihood of suboptimal adherence
  - Inability to tolerate oral medications
  - Prematurity (< 30 weeks gestation)
  - Other factors at discretion of physician
- Primary Outcome Measure
  - Hemoglobin concentration
- Secondary Outcome Measures
  - Complete resolution of IDA
  - Successful administration
  - Median serum ferritin level
  - Mean total iron-binding capacity
- The primary analysis utilized linear mixed regression with intention-to-treat.
- Categorical outcomes were measured using the Chi-square test
- All tests were 2-sided with a significance level of 0.05.
- Adjustment for multiple comparisons of secondary end points was not performed.
- Inference about secondary outcomes should be interpreted as exploratory

RESULTS

- 80 patients were randomized
  - 59 patients completed the trial

        - 28 in ferrous sulfate group
            - 7 lost to follow-up, 3 discontinued study drug, and 2 withdrew from the study
        - 31 in iron polysaccharide complex group
            - 6 Lost to follow-up and 3 discontinued study drug
- Primary endpoint: Hemoglobin concentration
    - Ferrous sulfate group: increase of 4g/dL from baseline
    - Iron polysaccharide Complex group: increase of 3.4g/dL from baseline
    - A significant difference of 1.0g/dL (95% CI from 0.4g/dL to 1.6g/dL; P<0.001) was found in favor of ferrous sulfate
- Secondary endpoints
    - Complete resolution of IDA
        - A statistically significant difference of 22% (95% CI from 3% to 41%; P=0.04) in favor of ferrous sulfate
    - Successful administration
        - A statistically significant difference of 13% (95% CI from 1% to 25%; P=0.009) was found in favor of iron polysaccharide complex
    - Median serum ferritin level
        - A statistically significant difference of 10.2ng/mL (95% CI from 6.2ng/mL to 14.1ng/mL, P < 0.001) was found in favor of ferrous sulfate
    - Mean total iron-binding capacity
        - A significant difference of −50μg/dL (95% CI from −86μg/dL to −14μg/dL, P < 0.001) was found in favor of ferrous sulfate
- Author's Conclusion
    - The authors concluded that ferrous sulfate was superior to iron polysaccharide complex in the treatment of nutritional iron deficiency anemia.

STRENGTHS
- Compared current treatment plan to potential alternative
- Dosing for IDA appropriate with appropriate duration of treatment (Camaschella C. Iron-deficiency anemia. *N Engl J Med* 2015; 372:1832-1843)
- Appropriate statistical tests

LIMITATIONS
- Small sample size all from one center
- High dropout rate (~26%)
- One patient received the wrong study drug
- The 95% CI for the mean hemoglobin concentrations overlap
- The 95% CI for the change in hemoglobin goes below 1.0g/dL

CONCLUSION
- More studies are required to come to a conclusion. The drugs have shown similar efficacy, the limitations make the results and interpretation of results difficult, and a trial with a larger sample size is warranted

Reference: Powers J, Buchanan G, Adix L, Zhang S, Gao A, McCavit T. Effect of low-dose ferrous sulfate vs iron polysaccharide complex on hemoglobin concentration in young children with nutritional iron-deficiency anemia: a randomized trial. *JAMA* 2017 June; 317(22): 2297-2304