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April 29, 2019



Iron-ing Out the Wrinkles in Anemia Management

Clinical Question: Are newer oral iron formulations (iron polysaccharide complex or heme iron polypeptide) better than ferrous salts for iron deficiency anemia (IDA)?

Bottom Line: Newer iron formulations appear inferior to older ferrous salts. Ferrous salts improve hemoglobin up to 10-20g/L more and perhaps one in five more attaining IDA resolution at 3 months. Evidence that newer formulations have less adverse effects is inconsistent.

# Evidence:

- Randomized controlled trials. Differences statistically significant unless indicated.
  - General population adults:
    - 80 patients (92% female, mean age 39):<sup>1</sup> iron polysaccharide (Niferex<sup>™</sup>) versus ferrous fumarate, both ~150mg/day elemental iron. After 12 weeks:
      - Ferrous fumarate improved hemoglobin (28.4g/L) more than iron polysaccharide (6g/L), and had better serum ferritin, mean corpuscular volume, and transferrin saturation but more nausea (31% versus 3%).
    - 80 children (mean age 23 months):<sup>2</sup> Iron polysaccharide (NovaFerrum<sup>™</sup>) versus ferrous sulfate, both 3mg/kg/day elemental iron.
      - At 12 weeks, ferrous sulphate improved hemoglobin more (10g/L), resolved IDA (29% vs 6%, Number Needed to Treat=5), caused less diarrhea (35% versus 58%).
    - Smaller trials of adults (n=43)<sup>3</sup> and premature infants (n=32)<sup>4</sup>: iron polysaccharide and ferrous salts were no different in hemoglobin improvement after 4-6 weeks.
    - Subgroups:
      - Dialysis patients: At 6 months, ferrous salts no different from newer formulations on transferrin saturation<sup>5, 6</sup> or proportion of iron-replete patients.<sup>5</sup>
        - Ferritin ~ (160µg/L) better with ferrous sulfate than heme iron (Proferrin ES<sup>™</sup>).<sup>5</sup>

- Post-gastric bypass (n=14):<sup>7</sup> Ferrous sulfate improved hemoglobin after 8 weeks, but heme iron (Proferrin ES<sup>™</sup>) did not.
- Blood Donors (n=97):<sup>8</sup> and pregnant patients (n=90)<sup>9</sup>: Heme iron with ferrous fumarate (Hemofer<sup>™</sup>) no different from higher doses ferrous fumarate alone in achieving anemia outcomes; <sup>8,9</sup> ferrous fumarate alone caused more constipation (35% versus 14%).<sup>8</sup>

## Context:

- Multiple limitations including underpowered,<sup>2,4,6-9</sup> multiple outcomes,<sup>1-9</sup> nonintention-to-treat.<sup>1,2,5</sup>
- Approximate costs/month for 100mg elemental iron/day<sup>10</sup>: ferrous fumarate/sulphate (generics \$5-10), ferrous fumarate (Palafer<sup>™</sup> \$35), iron polysaccharide complexes (Feramax<sup>™</sup> \$35).
- To reduce iron-related gastrointestinal upset: lower dose<sup>11</sup>; use another ferrous salt (incidence of adverse effects: ferrous gluconate 30%, sulfate 32%, fumarate 47%);<sup>12</sup> alternate day dosing.<sup>13</sup>

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### Disclosures:

Authors do not have any conflicts of interest to declare

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