Short Study Protocol

Title:
Superiority of Liposomal Iron in Post-Sleeve Gastrectomy Iron Deficiency Anemia: A Prospective Randomized Comparative Study

Date: January 2025

Background and Rationale:
Sleeve gastrectomy (SG) is a common bariatric procedure but frequently leads to iron deficiency anemia (IDA) due to reduced gastric acid production, bypassed duodenal absorption sites, and dietary changes. Conventional oral iron (e.g., ferrous sulfate) is the standard treatment but often causes gastrointestinal side effects, leading to poor adherence. Liposomal iron encapsulates ferric pyrophosphate in phospholipids, potentially improving absorption, reducing side effects, and enhancing efficacy via alternative uptake pathways (e.g., M-cell transport). This study aims to compare low-dose liposomal iron with standard-dose conventional oral iron in SG patients with IDA.

Objectives:
- Primary: To compare the change in hemoglobin (Hb) levels from baseline to 6 months.
- Secondary: To evaluate changes in iron parameters (ferritin, transferrin saturation [TSAT], serum iron, total iron-binding capacity [TIBC], transferrin), erythrocyte indices (MCV, MCH, MCHC, RDW), reticulocyte parameters (count, percentage, Ret-He), hepcidin, hs-CRP; gastrointestinal tolerability (GSRS scale); treatment adherence; discontinuation rates; and quality of life (SF-36).

Hypothesis:
Low-dose liposomal iron will provide superior hematological improvement, better gastrointestinal tolerance, and higher adherence compared to standard-dose ferrous sulfate.

Study Design:
Prospective, randomized, parallel-group, open-label clinical trial.
- Duration: 6 months per participant.
- Allocation: 1:1 randomization (computer-generated blocks).
- Setting: Single-center (outpatient clinic, tertiary hospital).

Eligibility Criteria:
- Inclusion: Adults (≥18 years) who underwent SG ≥6 months prior; confirmed IDA (Hb <13 g/dL in males, <12 g/dL in females; ferritin <30 ng/mL or TSAT <20%); informed consent.
- Exclusion: Other causes of anemia (e.g., vitamin B12/folate deficiency, chronic disease); ongoing IV iron therapy; pregnancy/lactation; severe comorbidities; known allergy to iron preparations; active gastrointestinal bleeding.

Interventions:

- Arm 1 (Experimental - Low-Dose Liposomal Iron, LD Group): Oral liposomal iron providing 34 mg elemental iron daily for 6 months.
- Arm 2 (Active Comparator - Conventional Iron, CD Group): Oral ferrous sulfate providing 100 mg elemental iron daily for 6 months.
- Concomitant: All patients receive standard post-SG multivitamin supplementation; vitamin C encouraged with iron intake.

Outcome Measures:
- Primary: Change in Hb (g/dL) at 6 months vs. baseline.
- Secondary: Changes in ferritin, TSAT, serum iron, Ret-He, RDW, MCV, hepcidin, etc.; GSRS score; adherence (pill count/self-report); discontinuation rate; SF-36 score.
- Safety: Adverse events, particularly gastrointestinal symptoms.

Sample Size:
112 patients (56 per arm), based on expected Hb increase of 2.4 g/dL (LD) vs. 1.4 g/dL (CD) (SD 1.0 g/dL, $\alpha$=0.05, power=90%, 10% dropout).

Randomization and Blinding:
Central computerized randomization; open-label (no blinding due to different formulations).

Data Collection and Visits:
- Baseline: Screening, labs, GSRS/SF-36.
- Follow-up: Months 1, 3, 6 (labs, tolerability, adherence).

Statistical Analysis:
Intention-to-treat; primary outcome: ANCOVA adjusting for baseline Hb; secondary: t-tests/chi-square as appropriate; $p<0.05$ significant.

Ethical Considerations:
Approved by institutional ethics committee; informed consent; data confidentiality; monitoring for adverse events.

Funding and Sponsorship:
None