In Focus - Micronutrients and Obesity: iron deficiency & obesity.

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Background: double burden of malnutrition
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Coexistence of undernutrition with overweight/obesity, throughout the life course. At the individual, the double burden of malnutrition may manifest itself as two or more simultaneous forms — for example, obesity with iron deficiency.

Population

Household

Individual

- Environmental
- Behavioral
- Biological

Obesity and iron deficiency

• 1960s: Researchers observed a strong correlation between increased adiposita and decreased serum iron (sFe) y in children and adolescents.

• 1989: Body size was found to be associated with lower sFe and Tsat, but higher Hb and HCT, in US women.

• 2003: Overweight Israeli children and adolescents were 1.75 times more likely to have decreased sFe, than those of a normal weight.

• 2004: US overweight children and adolescents were two times more likely to be ID, than those of a normal weight.

• 2006: In Iranian children with obesity, ID was three times more prevalent compared to those of normal weight.

• 2010: Obese Mexican women and children had 2-4 times higher risk of ID compared to normal weight.

How it is all linked?

There are two possible mechanisms:

1) Hemodilution

2) Hepcidin
How it is all linked: hemodilution?

Greater blood volume in OW/OB individuals could be responsible for low iron status and increase iron requirements.
How it is all linked: Hepcidin?

- Hepcidin is the main regulator or iron status in our body.
- Iron status → regulates hepcidin secretion → iron absorption in the gut & storage at macrophages and liver.
- Hepcidin production: mainly in the liver, small amounts in adipose tissue.
- Other regulators of hepcidin: Inflammation, hypoxia.
- Adipose tissue → secretes pro-inflammatory cytokines → hepcidin expression.
High amounts of adipose tissue triggers chronic low grade inflammation (IL6), IL6 induces HEPcidIN expression which may reduce iron absorption in overweight/obese persons.

Fe–Tf, iron–transferrin complex
HJV, hemojuvelin
TFR2, transferrin receptor 2.
Objectives

To study iron metabolism in obesity using stable iron isotopes:

1) To identify if greater blood volume (hemodilution) is responsible for low iron status in overweight and obese (OW/OB) individuals.

2) To assess the difference in iron absorption in OW/OB compared to normal weight (NW) participants and to what extent can ascorbic acid enhance iron absorption.

3) To identify if the effect of OB on iron absorption is reversible by weight/fat loss.
Shift in the enrichment of $^{57}\text{Fe}$ and $^{58}\text{Fe}$ in natural $^{56}\text{Fe}$ in erythrocytes

**IV isotopes (systemic utilization)**
Labelled infusion (100 μg $^{58}\text{Fe}$)

**Oral isotopes (Absorption from diet)**
labelled test meal (2-6 mg $^{57}\text{Fe}$)

Blood sample after 14 days

Natural iron in the body ($^{56}\text{Fe}$)

Fe absorption + Fe utilization = Fe bioavailability
Methods: studies 1 and 2

In 62 healthy, non-anemic women in Switzerland we determined:

- Blood volume: the carbon monoxide (CO) rebreathing method.
- Body composition: dual energy X-ray absorptiometry (DXA).
- Hepcidin, iron and inflammatory status: Blood sample.
- Iron absorption: from 2 test meals using stable iron isotopes. The test meals consisted of bread with butter and honey, with or without ascorbic acid (+AA/-AA).
Methods: studies 1 and 2

VISIT 1
Blood volume

Day 0

VISIT 2
Test Meal Administration
G1: Fe57
G2: Fe58 + Vit C

VISIT 3
Test Meal Administration
G1: Fe58 + Vit C
G2: Fe57

Day 14
Day 15

VISIT 4
DXA (+/- 1 week)

2 weeks

VISIT 5
Blood sample

2 weeks

Day 30
Results: study 1

OW/OB participants had significantly higher blood and plasma volume compared to normal weight (** p<0.05; ***p<0.001).
Results: study 1

Circulating masses of hepcidin, sTfR and hemoglobin were higher in OW/OB that in NW participants (***(p<0.001).
Results: study 1

Total mass of serum iron was lower in OW/OB that in NW participants.
Results: study 2

Iron absorption in OW/OB participants was two-thirds that in NW participants (p=0.049).

The increase in absorption with ascorbic acid was 56% in NW and only 28% in OW/OB (p<0.05 compared to –AA).
Influence of vitamin C on iron absorption

Action of vitamin C

Action of inflammation

Brittenham G., Hematology, 2013
Methods: study 3

In 38 obese participants during weight loss induced by sleeve gastrectomy at 2 and 8 months in Mexico we determined:

- Body composition: dual energy X-ray absorptiometry (DXA).
- Iron absorption: stable isotopes (100μg 58Fe & 6 mg 57Fe)
- Hepcidin, iron and inflammatory status: Blood samples.
Bariatric Surgery

**VISIT 1**
Test Meal (6mg Fe57)
Infusion (100μg Fe58)
Administration
DXA
Blood Sample

2 months after bariatric surgery

**VISIT 2**
Blood sample

2 weeks

**VISIT 3**
Test Meal (6mg Fe57)
Infusion (100μg Fe58)
Administration
DXA
Blood Sample

8 months after bariatric surgery

**VISIT 4**
Blood sample

2 weeks
Results: study 3

Total **body fat** and **CRP** were significantly reduced 8 months after surgery compared to 2 months.
Results: study 3

IL6 and hepcidin were significantly reduced 8 months after surgery compared to 2 months.

Cepeda-Lopez et al. AJCN. 2016
Results: study 3

In subjects who were iron deficient at 2 months post surgery (n=17), iron absorption increased by 28% (from 9.7% to 12.4%) while there was no change in iron replete subjects (5.9% and 5.6%).

Cepeda-Lopez et al. AJCN. 2016
Summary of findings

• Overweight and obese subjects have increased Hb mass which increases iron requirements for erythropoiesis.

• Overweight and obese subjects have a reduction in iron absorption and the enhancing effect of ascorbic acid is blunted.

• The overweight body fails to fully downregulate hepcidin secretion even if iron stores are low.

• Increased blood/plasma volume leads to diluted serum iron and affects interpretation of iron biomarkers.
Why is this important?

Overweight and Obesity:

• Can worsen iron deficiency through an impairment of iron absorption, and greater catabolic losses of the nutrient.
• Can deplete iron concentrations, leading to deficiency (anemia).
• Can influence iron biomarkers.

Especially in developing and transition countries the current surge in OW/OB may significantly impair efforts to control iron deficiency in vulnerable population groups and new strategies are urgently needed.
THANK YOU!

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