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Original

Iron ($FeSo_4$) bioavailability in obese subjects submitted to bariatric surgery

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Abstract

Background: **Iron bioavailability in obese subjects after the ingestion of a nutritional supplement was the aim of this work.**

Methods: **Fourteen persons were studied before and after bariatric surgery after the ingestion of a nutritional formulation containing 25 mg iron, 25 g fiber and 800 mg calcium.**

Results: **The following ferremia values (median and minimum - maximum) were obtained before and after bariatric surgery, respectively: Fasting, 105 (70 - 364) µg/dL and 198 (38 - 617) µg/dL; 1 hour, 103 (63 - 305) µg/dL and 160 (11 - 207) µg/dL; 2 hours, 103 (62 - 150) µg/dL and 141 (10 - 412) µg/dL; 3 hours. 97 (63 - 190) µg/dL and 153 (6 - 270) µg/dL; 4 hours, 91 (58 - 163) µg/dL and 156 (40 - 251) µg/dL ($p>0.05$), with no association of serum iron levels with time. There was a difference in total triglycerides (95 ± 29 mg/dL and 60 ± 10 mg/dL) which were correlated with a decrease in serum ferritin levels (r = 0,926, p = 0.008), UIBC (r = 0.910, p = 0.01), total cholesterol (r = 0,918, p = 0.01) and LDL-c fraction (r = 0.830, p = 0.04), with an increase in HDL-c fraction (r = 0,807, p = 0.05).**

Conclusion: **Iron bioavailability in obese subjects was affected by the ingestion of the nutritional formulation containing calcium and fiber, a fact that may cause these patients to develop iron deficiency.**

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Key words: *Iron bioavailability. Nutritional formulation. Obese subjects. Bariatric surgery.*

BIODISPONIBILIDAD DE HIERRO ($FeSO_4$) DE LOS SUJETOS OBESOS SOMETIDOS A CIRUGÍA BARIÁTRICA

Resumen

Objetivo: **Obesos sometidos a cirugía bariátrica muestran la utilización de deterioro de hierro. Evaluar la biodisponibilidad del hierro en los obesos por el consumo de suplemento nutricional que contiene múltiples nutrientes antes y después de seis meses de la cirugía bariátrica.**

Material y Métodos: **El estudio incluyó a 14 voluntarios antes y después de la cirugía bariátrica que recibieron formulaciones que contienen múltiples nutrientes y medir las concentraciones séricas de hierro en ayunas y cada 1 hora después de la ingestión de formulaciones, con un total de cuatro horas.**

Resultados: **Ferremia por el consumo de entre dos formulaciones de pre-y post-operatorios fueron: El ayuno 104.50 (70,00-363,00) mg / dl y 198.00 (38.00 a 617.00) mg / dl, 103.00 horas (63,00 a 305,00) mg / dl y 160.00 (11,00-206,90) mg / dL, 2 horas 102.50 (62.00 a 150.00) mg / dL y 141.30 (10.00 a 412.20) mg / dl, 3 horas 97.00 (63.00 a 190.00) mg mg / dl y 153,00 (6,00 hasta 269,60) / dl , 4 horas 91,00 (58,00 a 163,00) mg / dl y 156.10 (40.00 a 250.50) mg / dl y no hubo asociación estadísticamente significativa entre los dos períodos para los niveles de hierro suero. Los valores de la zona de las curvas en el suero fueron 453,50 ± 202,80 mg / dl / hora, p = 0,000 y 579,00 ± 380,30 mg / dl / hora, p = 0,007 y fue estadísticamente diferente entre los dos períodos. La biodisponibilidad del hierro en soluciones que contienen múltiples nutrientes se vio afectada antes y después de seis meses de la cirugía bariátrica.**

Conclusión: **Se encontró que los niveles se redujeron ferremia con la cirugía, que puede poner en peligro estos pacientes presentaron deficiencia de hierro.**

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Palabras clave: *Disponibilidad de hierro. Formulaciones nutricionales. Personas con obesidad. Cirugía bariátrica.*

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Introduction

Iron bioavailability is defined by measuring the proportion of the total element offered by the oral route as part of the diet which is utilized for the maintenance of the normal functions of the organism including digestion and absorption. Iron absorption is influenced by the organic reserve and by the solubility of the element, which in turn is influenced by its valence and/or by the form of binding to other nutrients. Dietary factors tend to alter iron absorption as a function of the interactions among nutrients and proper absorption is important for the prevention and treatment of possible nutritional disorders[1,2].

Obese patients are characterized by a set of comorbidities associated with the accumulation of adipose tissue, including the presence of iron-deficiency anemia. In particular, iron deficiency is considered to be a severe disorder in patients submitted to bariatric surgery[3-4]. A possible factor triggering or precipitating iron deficiency is the interaction between the nutrients included in the formulation of the supplements offered to these patients[5,6]. Inadequate intake and intestinal malabsorption may also be considered to be a cause of iron deficiency, intimately related to the mechanical changes induced by bariatric surgery[3-7]. On this basis, it is imperative to study the mechanisms of iron absorption and regulation in these patients during the preoperative and postoperative periods.

Thus, the objective of the present study was to assess iron bioavailability in obese patients after the ingestion of a nutritional supplement containing multiple nutrients before and six months after bariatric surgery.

Methodology

Patients

The study was conducted on14 obese individuals of both genders aged 18 to 50 years, during the preoperative and postoperative period of bariatric surgery. Surgery was performed at the Center for the Treatment of Bariatric Surgery of the Discipline of Nutrology, University Hospital, Faculty of Medicine of Ribeir„o Preto (HCFMRP). The study was approved by the Research Ethics Committee of the Hospital, and the data were collected from November 2007 to December 2008.

Inclusion Criteria: Adult subjects aged 18 to 50 years with no diseases potentially interfering with absorptive capacity and giving informed consent to participate. Exclusion Criteria: Patients with anemia (hemoglobin level of less than 10.0 mg/dL), with chronic renal insufficiency, alcoholism, intestinal parasitic diseases, diabetes, and chronic diarrhea were excluded from the study.

Preparation and Composition of the Nutritional Supplement Formulation

The formulation was prepared at the Hospital Pharmacy of HCFMRP and placed in sealed pots containing 100 g powder. For use in the Metabolic Unit of HCFMRP, 100 g powder was diluted in 200 mL filtered water, transferred to a pot with a lid and stored in the refrigerator for 12 hours. The experimental assays involving the research subjects were started in the morning. The formulation of the nutritional supplement provided 25.0 mg elemental iron from heptahydrated ferrous sulfate, and its interaction with 800 mg calcium and 25 g fiber was determined. The formulation contained 38 additional nutrients, whose quality and quantity are listed in tables I and II.

Experimental Procedure

The nutritional formulation was prepared on the day preceding the experiment using aseptic techniques and stored in a refrigerator for 12 hours before being offered to the research subjects. The experiments conducted before and six months after surgery were started in the morning and lasted 5 hours. The volunteers were studied in the Metabolic Unit of HCFMRP, sitting on a reclining armchair. Water intake was permitted throughout the experiment. After an overnight fast of 12 hours, a blood sample was collected from each subject. Each patient then received the prepared multiple nutrient formulation containing 100 g powder in a final volume of 200 mL. Blood samples were obtained at 0, 1, 2, 3 and 4 hours[8,9].

Table I
Composition of the nutritional supplements administeree to obese patients

Components	*Formulation of the Nutritional Supplement*
Total Protein (g)	
Soy Protein Isolate	3.1
Total Carbohydrates (g)	
Maltodextrin	64.1
Fat (g)	
TCM	
Corn oil	1.0
Canola Oil	3.5
Soy Lectin	0.3
Minerals (g)	
Salt Mixture	3.0
Vitamins (g)	
Vitamin Mixture	1.0
Fiber (g)	
Partially hydrolyzed guar gum	25.0
Total (g)	100.0

[1]Dilution: 3.0 g salt mixture/100 g supplement

Table II
Composition of the salt mixture in the nutritional supplement formulation

Salts	*Value in 300 g of the salt mixture*	*Element*	*Quantity of the element in 300 g of the salt mixture*	*Quantity of the element in 1,000 kg[1]*	*Quantity of the element in 200 g[1]*
$FeSO_4.7H_20$	6.80 g	Iron	2500.00 mg	250.00 mg	50.0 mg
$MgCO_3$	8.00 g	Magnesium	2.29 g	115.00 mg	28.75 mg
KH_2PO_4	48.00 g	Phoshphorus	11.13 g	557.00 mg	139.25 mg
		Potassium	14.04 g	702.00 mg	175.5 mg
$ZnSO_4.7H_20$	0.316 g	Zinc	72.00 mg	3.60 mg	0.9 mg
KIO_3	0.024 g	Iodine	14.40 mg	0.72 mg	0.18 mg
$MnSO_4.H_20$	0.054 g	Manganese	17.64 mg	0.88 mg	0.22 mg
$CuSO_4.5H_20$	0.046 g	Copper	11.88 mg	0.59 mg	0.15 mg
NaCl	24,00 g	Sodium	9.22 g	461.00 mg	115.25 mg
		Chorine	14.24 g	712.00 mg	178.00 mg
$CaCO_3$	200.00 g	Calcium	80.00 g	8,00.00 mg	1,00.00 mg
Maltodextrin	12,76 g				
Total	300 g				

Protocol for the Study of the Response Curve of Serum Iron

For data comparison, the areas under the curve of ferremia concentration obtained from the five plasma concentrations (time 0 and 1, 2, 3 and 4 hours) and the sum of these values were calculated in addition to the difference between the concentrations obtained at each time point and at time 0[10].

Biochemical Evaluation of the Patients Determination of Serum Iron Levels after the Ingestion of the Nutritional Supplement Formulation

Serum samples were placed in demineralized Eppendorf tubes and stored frozen at -20 ºC until the time for analysis. Iron concentrations were determined by inductively coupled plasma mass spectrometry (ICP-MS) in the DRC mode according to the method of Palmer et al[11]., with the samples being diluted 1:20 with 0.5% HNO_3 diluent (v/v) + 0.005% TRITON X-100(v/v). Readings were then obtained with a Perkin Elmer ELAN DRC PLUS instrument equipped with a cyclonic chamber and coupled to a Meinhard nebulizer under conditions of optimization of gas flow of 0.60 mL/min, lens voltage of 6.00 A and radiofrequency power of 1100.00 W.

Table IV
Postoperative serum iron levels (µg/dL) as a function of time of ingestion of formulations for obese patients

Variable	*Preoperative* Median (range)	*Postoperative* Median (range)
Fasting	105 (70 - 364)	198 (38 - 617)
1 hour	103 (63 - 305)	160 (11 -207)
2 hours	103 (62 - 150)	141 (10 - 412)
3 hours	97 (63 - 190)	153 (6 - 270)
4 hours	91 (58 - 163)	156 (40 - 250)

Determination of Biochemical Indicators

The reference values adopted by HCFMRP for the laboratory tests studied are: serum iron, 35 to 150 µg/dL; ferritin, 28 to 397 ng/mL (men) and 6 to 159

Table IV
Values of the area under the curve for obese patients who ingested a formulation of nutritional supplementation before and after bariatric surgery

Patient	*Preoperative Curve (µg/dL/hour)*	*Postoperative Curve (µg/dL/hour)*
1	397.0	926
2	380.0	641
3	453.0	154
4	327.0	1050
5	908.0	180
6	550.0	875
7	260.0	228
8	353.0	
Mean	453.50	579.00
Standard Deviation	202.80	380.30
P value (Student	6.32	3.96
t-test	0.000	0.007

ng/mL (women); UIBC, 112 to 346 mg/dL; hemoglobin, 12 to 13 g/dL; albumin, 3 to 5.4 g/dL; total proteins, 6.4 to 8.2 g/dL; borderline range of total cholesterol, 200 to 239 mg/dL (lower: <200 mg/dL, increased: ≥ 240 mg/dL); desirable HDL cholesterol, ≥ 40 mg/dL; borderline range of LDL cholesterol, 130 a 159 mg/dL (lower: <130 mg/dL, increased: ≥ 160 mg/dL); borderline range of triglycerides, 150 to 199 mg/dL (lower: <150 mg/dL, increased, ≥ 200 mg/dL).

Statistical Analysis

Friedman's ANOVA was used to analyze the data regarding iron absorption before and after surgery at time 0 and from 1 to 4 hours of the experiment. The parametric Student t-test for two groups was used to compare the areas under the curve of serum iron levels obtained before and after surgery and at the 4 time points compared to the basal time (fasting value, t = 0). The paired Student t-test for independent samples was used to compare the biochemical parameters of the patients determined before and six months after surgery. Statistical analysis was performed with the aid of the Statistics 6.0 software (STATASOFT INC., Tulsa, OK)[12]. The level of significance was set at $p < 0.05$ in all analyses.

Results

Table III presents the serum iron levels of obese patients determined before and after bariatric surgery. The values are reported as median and range because the data did not present normal distribution. Table IV presents the area under the serum curves for the obese patients before and after bariatric surgery. The Student t-test showed that there was a significant difference between the two times, revealing a greater mobilization of circulating iron after the surgery.

Table V presents the pre- and postoperative values of the biochemical indicators of the patients, which were analyzed by the paired Student t-test. There was a difference in mean total triglyceride levels between times, with a significant reduction six months after the surgical procedure. Also, serum ferritin, UIBC, total cholesterol and LDL cholesterol levels were reduced after surgery, whereas HDL cholesterol was increased.

Discussion

Regarding nutrient interactions, it is known that excess amounts of one nutrient can worsen or improve the absorption of another, as is the case, for example, for iron and zinc or iron and vitamin C[3-5]. In the present study, after the ingestion of a nutritional supplement containing multiple nutrients, the mean value of the area under the curve for serum iron differed in relation to the curve obtained before the surgical procedure. However, on both occasions, iron absorption was low, possibly demonstrating that iron absorption from supplements may be negatively affected by several nutrients such as calcium, fiber and perhaps others not studied here. In addition, this may suggest a greater mobilization of body iron regarding the reduction of serum ferritin and UIBC after the surgical procedure.

Cook, Dassenko and Whittaker[13] assessed the effect of calcium salts commonly used as supplements on iron absorption when administered during the interval between meals and observed that calcium carbonate at the dose of 600 mg did not inhibit the absorption of ferrous sulfate (18 mg), at an iron/calcium proportion of 1:33). When the same assays were repeated using citrate and phosphate salts as a source of calcium at the same concentrations, iron absorption was reduced to 44% and 62%, respectively, showing that the type of salts used can also affect the bioavailability of minerals. Reddy and Cook[14] observed that different iron/cal-

Table V
Biochemical indicators of obese patients before and six months after bariatric surgery

Biochemical indicators	*Preoperative value Mean (SD)*	*Postoperative value Mean (SD)*	*p*	*Correlation (pared-Student t-test)*	*p*
Serum Iron, μg/dL	80 (25)	63 (14)	0.91	r = 0.647	0.16
Ferritin, ng/mL	160 (105)	122 (78)	0.91	r = 0.926	*0.008
UIBC, mg/dL	212 (65)	206 (49)	0.60	r = 0.910	*0.01
Hemoglobin, g/dL	13 (1,5)	13 (1,7)	0.79	r = -0.699	0.12
Albumin, g/dL	4 (0,2)	4 (0,2)	0.17	r = -0.208	0.69
Total Proteins, g/dL	6 (0,4)	7 (0,2)	0.86	r = -0.080	0.88
Cholesterol, mg/dL	173 (45)	153 (35)	0.52	r = 0.918	*0.01
HDL, mg/dL	40 (12)	46 (11)	0.95	r = 0.807	*0.05
LDL, mg/dL	114 (38)	96 (29)	0.91	r = 0.830	*0.04
Triglycerides mg/dL	95 (29)	60 (10)	*0.007	r = 0,768	0.07

*Statistically significant values ($p \leq 0.05$).

cium proportions (above 1:40) and the types of salt sources of the minerals interfere with the bioavailability of iron.

Yoon et al[15]. discussed the possibility of fiber acting on the human gastrointestinal tract by causing changes in the utilization of nutrients and showed that greater amounts of fiber (>20 g/day) can affect the bioavailability of minerals. The supplements studied here contained 25 g fiber that may have represented a factor capable of reducing iron absorption.

Rosa[3] observed an increase in ferremia in obese adults with the ingestion of 15 mg iron and zinc in the sulfate form before and after bariatric surgery, with no change in iron absorption at any time point (1, 2, 3 or 4 hours) compared to the basal concentration (time zero). The area under the curve did not differ between the preoperative and postoperative period. Brolin et al[16]. observed that 155 of 348 patients (47%) receiving vitamin and mineral supplements after bariatric surgery presented iron deficiency. Oral iron supplementation corrected iron deficiency in only 43% of them.

When monitoring patients before and after bariatric surgery, Vargas-Ruiz et al[17]. observed that 6.6% of them were anemic before surgery and that iron deficiency was detected in 40.0% and 54.5% of them 2 and 3 years after surgery, respectively. Anemia was observed in 46.6 % and 63.6 % of the patients after 2 and 3 years, respectively. Love & Billett[18] suggested that iron prophylaxis should be oral after bariatric surgery and should be associated with the presence of vitamin C. These patients also require lifelong monitoring of hematologic and iron parameters since iron deficiency and anemia may develop years after the surgery. When deficiency is detected and oral treatment is not sufficient, parenteral nutrition, blood transfusions or surgical interventions are necessary.

Surgical treatment has shown increasing success in combating the disease; however, iron deficiency may occur due to the reduction of enzymatic secretions, changes in gastric acidity and intolerance of red meat intake. An important physiological factor is the exclusion of the duodenal region of the small intestine, which is responsible for iron absorption. It has also been shown that changes in taste and rejection of certain foods are associated with reduced gastric capacity. These two factors may result in multiple nutritional deficiencies involving iron, calcium, zinc, copper and vitamins of the B, A, and D complex[18,19]. In conclusion, the iron availability in solutions containing multiple nutrients was impaired in obese patients both before and six months after bariatric surgery. Ferremia levels were reduced after surgery, a fact that may cause these patients to develop iron deficiency.

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