Efficacy evaluation of a medical food supplementation as prevention and therapy of nutritional deficiency in bariatric surgery

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ABSTRACT — OBJECTIVE: *Severe obesity represents a serious threat for public health for prevalence, incidence and economic burden. When changes in lifestyle, psychological behavioural therapies or specific medicines are not able to improve the clinical picture of patients, bariatric surgery represents the most effective treatment. However, these patients need a careful nutritional surveillance because they are exposed to the risk of nutritional deficit. Supplementations with multivitamin formulations, calcium citrate and vitamin D were performed by nutritionist in the past, to correct the deficits but the results were often ineffective. Recently, several foods for special medical purposes (FSMP) were developed for these cases. The aim of this study is to assess the efficacy of FSMP administration to avoid micronutrients deficiencies, particularly vitamin D and Iron, in post-surgery phase to a sample of patients undergoing bariatric surgery.*

PATIENTS AND METHODS: *52 patients undergoing bariatric surgery were enrolled. For each patient, starting from the third day after surgery, one sachet for day of FSMP, containing Vitamins (A, B1, B2, B3, B5, B6, B8, B9, B12, C, D, E, K) and minerals (Iron, zinc, copper, selenium) was administered for three months. Anthropometric parameters, complete blood count, blood levels of folic acid, calcium, parathormone, ferritin, iron serum, transferrin, vitamin B12 and vitamin D were recorded, both at the time of surgery (T0) and after 3 months of FSMP intake (T1).*

RESULTS: *All patients have shown a significative weight loss 3 months after surgery (T1), with reduction of BMI, body fat, white blood cell count, platelets and transferrin. Moreover, at T1, increases of medium corpuscular volume (MCV), iron and vitamin D were observed.*

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CONCLUSIONS: Study results highlight that the administration of this FSMP for three months in post-surgery phase of patients underwent bariatric surgery is useful to avoid micronutrients deficiencies, favouring a better adherence to the treatment.

KEYWORDS
Bariatric surgery, Malnutrition, Micronutrients, Obesity, Food for special medical purposes.

INTRODUCTION

According to World Health Organization (WHO) recent estimates, obesity prevalence has increased almost threefold from 1975 to 2016. Over a 1.9 billion adults is overweight and about 650 million of adults are obese, corresponding to 13% of adult population worldwide (11% of men and 15% of women)[1]. Obesity represents a serious threat for world public health in terms of prevalence, incidence and economic burden. In addition to its impact on health expenditure, obesity causes costs related to productivity reduction, affecting the global economic growth, an effect due to the loss of working days for illness, permanent disability and mortality[2]. Obesity treatment includes changes in lifestyle (diet and physical activity), psychological behavioural therapies and, if necessary, the use of specific medicines (Orlistat, Liraglutide, Naltrexone/Bupropion). When these strategies are not able to improve the clinical picture of patients with severe obesity, bariatric surgery represents one of the most effective measures[3]. The number of bariatric surgeries is increasing substantially, due to the increase of subjects affected by severe obesity and to the improvement of laparoscopic surgical techniques. Bariatric surgery represents the most effective approach to determine an important weight loss, reducing the risks of non-communicable diseases associated to obesity[4]. Since 2008, only in Italy, more than 97.000 bariatric surgery procedures were performed according to the National Register of Italian Society of Obesity Surgery and Metabolic Diseases (SICOB) data.

Patients undergoing these procedures need accurate nutritional surveillance because they are exposed to the risk of nutritional deficit related to a reduced food intake, taste and eating habits changes, non-compliance to dietary and supplementary recommendations and/or nutrients malabsorption. These complications are more frequent after malabsorptive or mixed procedures than after restrictive ones and can deteriorate a deficit condition already present before the surgery.

Nutritional deficiencies may occur with a wide range of clinical manifestations, depending on specific nutrients/micronutrients involved, severity and duration of deficiency[5]. One of the most frequent and urgent problems after bariatric surgery is the deficiency of vitamins and/or minerals. Prevention, identification and deficit treatment are fundamental in the follow-up of post-bariatric patients[6]. In order to detect most common deficits of micronutrients as thiamine (vitamin B1), folic acid (vitamin B9), cobalamin (vitamin B12), iron and vitamin D[7], periodic evaluations should be performed[8,9]. In the past, to correct these deficits, supplementations with multivitamin formulations, calcium citrate and vitamin D were performed but the results were repeatedly ineffective. Currently, in order to prevent these deficits immediately after bariatric surgery, several kinds of specific food supplements with vitamins and or minerals are administered to the patients. However, these supplementations are subject to dosage limits imposed by law. Due to the prohibition[10] to cross the threshold of 150% of daily intake for single nutrient, frequently, these treatments result insufficient, especially in cases of micronutrient deficits already present before surgery[11-13]. For vitamin D, calcium, iron and vitamin B12, frequently, a further specific supplementation is needed[14].

This additional supplementation can cause a reduction of the adherence to prescription, with the risk that patient can follow partially the therapy. In these cases, deficits persist or even can get worse[15]. The onset of nutritional deficits is influenced by factors related to the surgery technique, but also by other clinical, socio-economical and psychological situations that interfere with the adherence to dietetic prescription and to vitamins and minerals supplementation post-surgery[16].

Several foods for special medical purposes (FSMP) are produced in order to improve the efficacy of a nutritional intervention. These FSMP are specifically developed for situations that need vitamins and minerals in doses higher than specific food supplements, for use under medical supervision. FSMP intake can help to counteract more efficiently the onset of micronutrients deficits improving therapy compliance.

The aim of this study is to assess the capability of a FSMP, containing Vitamins (A, B1, B2, B3, B5, B6, B8, B9, B12, C, D, E, K) and minerals (Iron, zinc, copper, selenium), to prevent micronutrients deficiencies, in particular iron and vitamin D, in post-surgery phase of patients undergoing bariatric surgery enrolled in 5 Italian centres.

PATIENTS AND METHODS

A multicentre study involving patients undergone bariatric surgery in 5 centres from January to March 2017 was carried out. All patients enrolled for this study were selected following the inclusion and exclusion criteria of SICOB guidelines[4] for bariatric surgery. Patients with BMI > 40 kg/m^2 without comorbidities or with BMI > 35 kg/m^2 but <40 kg/m^2 in presence of comorbidities classically associated to obesity as type 2 diabetes, dyslipidaemia, PCOS, female infertility, hyperuricemia, cardiopathies, pulmonary embolism, stroke, hypertension, neoplasms or asthma etc were involved. On the contrary, pa-

tients with psychotic disorders, severe depression, eating disorders, absence of a period of identifiable medical management, drugs dependencies and/or alcohol abuse problems, diseases threatening in life in the short term, patients unable to participate in prolonged medical follow-up, patients unable to care for themselves and have no adequate family or social support were excluded by this study.

Patients can be subjected to different surgical interventions: gastric bypass (GBP), gastric bypass with single anastomosis (OAGB), gastric banding (LAP) or Sleeve Gastrectomy (SG).

For each patient enrolled, starting from the third day after surgery, one sachet for day of FSMP (Bariatrifast, BIOITALIA S.r.l., Italy), containing 65 mg of iron, 500 µg of vitamin D (7000 IU) and other micronutrients (vitamins A, B1, B2, B3, B5, B6, B8, B9, B12, C, E, K, Iron, zinc, copper, and selenium), was administered. Anthropometric parameters (weight, height and BMI), complete blood count (CBC), blood levels of folic acid, calcium, parathormone, ferritin, iron serum, transferrin, vitamin B12 and vitamin D were recorded, both at the time of surgery (T0) and after 3 months of FSMP intake (T1). All subjects involved provided written Informed Consent Form before participation, according to the Declaration of Helsinki.

Primary outcome of this study was to avoid iron and vitamin D deficiencies caused by bariatric surgery[7,17]. The prevention of other micronutrients deficiencies is the secondary outcome.

Statistical analysis

Differences between T0 and T1 for demographic variables were analysed using One-way ANOVA test. T-paired test was used to identify significative differences between T0 and T1 data.

Only variables with significative difference from T0 to T1 were considered for ANOVA analysis for repeated measures Group (GBP, OAGB, LAP, SG) x Time (Evaluation from T0 to T1). ANOVA test for repeated measures was used, considering the variable Group (type of surgery) x Time (times of evaluation T0 and T1), to evaluate, at T1, effects potentially correlated to the type of surgery performed. Significative interactions were analysed subsequently with One-way ANOVA test and Post-hoc. For Post-hoc analysis LSD correction were used for multiple comparisons. All results with a significative level of $p<0.05$ were reported. For One-way ANOVA analysis and for repeated measures were reported respectively Eta-squared (η^2) and partial Eta-squared (η_p^2).

The effect due to small, medium and large sample size corresponds respectively to 0.01, 0.09 and 0.25.

RESULTS

52 patients were included in this study, 13 males and 39 females, with average age of 44 years with an average Body Mass Index (BMI) of 44 kg/m^2; 18 subjected

Table I. Clinical parameters of patients at T0 and T1.

Parameters	T0 (mean ± SD) N= 52	T1 (mean ± SD) N= 52	T-*paired* test
Weight (kg)	120.34 ± 28.95	99.21 ± 24.38	$p<0.001$
BMI (kg/m^2)	44.22 ± 8.84	35.67 ± 9.40	$p<0.001$
Lean body mass (%)	58.89 ± 13.06	58.76 ± 11.14	n.s.
Fat body mass (%)	51.70 ± 10.37	40.22 ± 11.81	$p<0.001$
Phase angle	5.84 ± 1.02	5.48 ± 1.42	n.s.
TBW (%)	43.24 ± 9.36	43.81 ± 8.60	n.s.
WBC (x109/L)	8.0 ± 2.36	7.25 ± 1.58	$p<0.01$
RBC (x1012/L)	4.89 ± 0.46	4.79 ± 0.42	n.s.
HB (g/dL)	13.65 ± 1.04	13.65 ± 1.04	n.s.
HCT (%)	41.94 ± 3.50	41.58 ± 2.81	n.s.
MCV (fL)	85.98 ± 6.23	87.30 ± 6.12	$p<0.01$
Platelets (x10^3/µL)	273.78 ± 80.43	249.58 ± 62.67	$p<0.001$
Folic Acid (ng/mL)	7.67 ± 4.04	7.10 ± 4.39	n.s.
Calcium (mg/dL)	8.35 ± 2.63	8.62 ± 2.18	n.s.
Ferritin (µg/L)	176.95 ± 115.03	148.01 ± 174.71	n.s.
PHT (pg/mL)	51.22 ± 25.81	47.87 ± 18.86	n.s.
Iron serum (µg/dL)	57.63 ± 31.77	67.76 ± 28.54	$p<0.05$
Transferrin (mg/dL)	286.96 ± 63.66	243.47 ± 38.86	$p<0.001$
Vitamin B12 (pg/mL)	429.04 ± 164.62	394.33 ± 141.43	n.s.
Vitamin D (ng/mL)	29.18 ± 26.68	36.89 ± 29.84	$p<0.05$

HB: Hemoglobin; HCT: Hematocrit; MCV: Medium Corpuscular Volume; PHT: Parathormone; RBC: Red Blood Cells; TBW: Total Body Water; WBC: White Blood Cells;

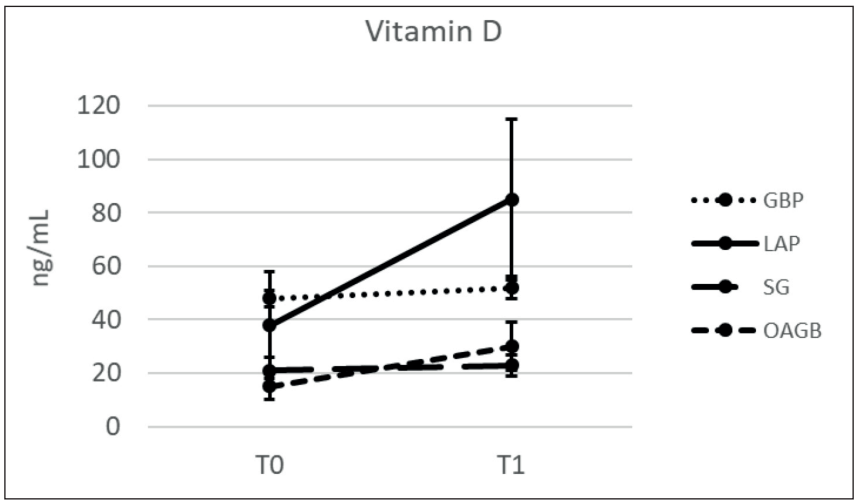

Figure 1. Vitamin D levels at the time of surgery (T0) and after 3 months (T1) in bariatric surgery procedure groups. (GBP: Gastric Bypass; OAGB: One-Anastomosis Gastric Bypass; SG: Sleeve Gastrectomy).

to gastric bypass (GBP), 4 to gastric bypass with single anastomosis (OAGB), 5 to gastric banding (LAP) and 25 to Sleeve Gastrectomy (SG). As reported in Table 1, all patients have shown at T1, increases of iron and vitamin D. Moreover, an increase of medium corpuscular volume (MCV) was observed. Significative weight losses at 3 months after surgery (T1), with reduction of BMI, body fat, white blood cell count, platelets and transferrin were reported.

Interestingly, a significative interaction Group x Time was observed for vitamin D dosage ($F(3.48)= 4.58$, $\eta_p^2= 0.22$, $p<0.01$). The groups have shown significative differences at T0 and T1 ($F(3.51)= 3.84$, $\eta^2= 0.19$, $p<0.02$) and ($F(3.51)= 11.11$, $\eta^2=0.41$, $p<0.001$), respectively. As reported in Figure 1, GBP group had higher vitamin D levels at T0 in comparison to SG and OAGB groups (p's<0.05) and LAP group have shown greatest level of vitamin D at T1 if compared to the other groups (p's<0.01), while SG group had a lower level of vitamin D at T1 than GBP.

For BMI, ANOVA analysis Group x Time have also shown a significative interaction (Figure 2) ($F(3.48)=4.06$, $\eta_p^2= 20.03$, $p<0.05$). The main effects for Time resulted significative ($F(1.3)= 64.75$, $\eta_p^2=57.4$, $p<0.001$), but not the effects for Group. One-way ANOVA analysis has shown that, at T0, groups never differ, but reports significative differences at T1 ($F(3.51)= 3.20$, $\eta^2= 0.17$, $p<0.05$), with OAGB group that have shown lower levels for BMI Index in comparison to the other groups (p's<0.02).

A significative interaction Group x Time was observed also for transferrin levels (Figure 3) ($F(3.48)= 2.96$, $\eta_p^2= 0.16$, $p<0.05$). Once again, main effects for Time ($F(1.48)=27.95$, $\eta_p^2=0.37$, $p<0.001$) but not for Group were reported. The interaction was explained considering that groups have shown a reduction of transferrin levels from T0 to T1 ($F(3.51)$, $\eta^2= 0.16$, $p<0.05$), with OAGB and SG groups that reported greater reduction from T0 to T1 in comparison to the GBP group (p's<0.05). No other interaction was observed.

DISCUSSION

Bariatric surgery procedures modify the physiology of gastrointestinal tract impairing nutrients absorption. These treatments can induce nutritional deficits which are frequently added to deficits already pres-

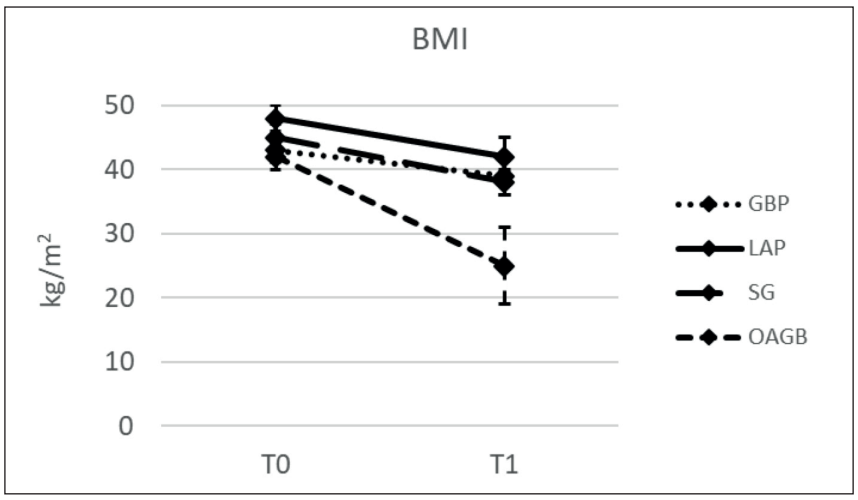

Figure 2. BMI values at the time of surgery (T0) and after 3 months (T1) in bariatric surgery procedure groups. (BMI: Body Mass Index; GBP: Gastric Bypass; OAGB: One-Anastomosis Gastric Bypass; SG: Sleeve Gastrectomy).

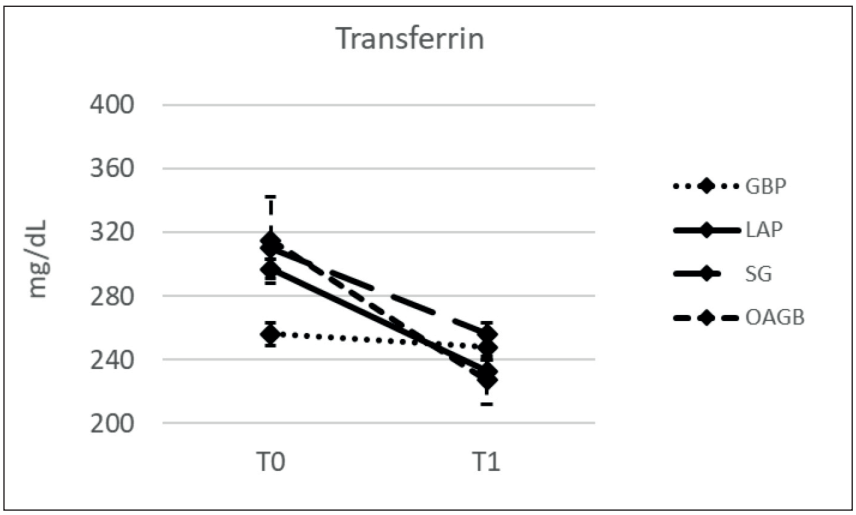

Figure 3. Transferrin levels at the time of surgery (T0) and after 3 months (T1) in bariatric surgery procedure groups. (GBP: Gastric Bypass; OAGB: One-Anastomosis Gastric Bypass; SG: Sleeve Gastrectomy).

ent, considering the high incidence of malnutrition in obese patients especially for micronutrients[13,18].

Nutritional deficit risk needs an accurate follow-up, repeated over time in patients subjected to bariatric surgery procedures.

To counteract the onset of deficits, and/or to correct them if already present, micronutrients supplements can be administered immediately after the bariatric surgery, continuing at least until to weight stabilization. Considering data obtained, thanks to this FSMP, already in the first three months, it was possible to compensate micronutrients deficits hardly manageable with other supplements favouring a better patient adherence to the treatment. As reported in this paper, this FSMP was able to increase of MCV and iron already 3 months after surgery. Also, vitamin D, frequently lacking before surgery, resulted increased at T1 without additional supplementations. These data confirm the ability of this FSMP to improve patient quality of life lightening the impact of post-surgical treatments and favouring a better adherence to treatment. Indeed, thanks to this FSMP, a reduction of post-surgical treatment duration is possible, limiting the need of food supplements to only one product. According to current guidelines, patients undergoing bariatric surgery should supplement their nutrition after intervention for about one year. Data shown in this paper, instead, highlight great results already after three months allowing to predict a more rapid weight stabilization than current food supplements [19].

Particularly, deepening these aspects emerges that among these patients, subjects undergone to LAP benefited more of FSMP treatment regarding vitamin D values. This evidence can be correlated to this surgery procedure, exclusively restrictive, and to the short observational period[14]. The transferrin level also shows a different effect of FSMP between groups. Patients subject to GBP procedure tend to maintain stable transferrin levels (in a normal range), while in patients subject to LAP, SG and OAGB, transferrin levels tend to decrease in the time. Our data seem to indicate that FSMP is effective to improve micronutrients absorption in patients subjected to bariatric surgery.

CONCLUSIONS

In the study was highlighted how the administration of this FSMP, containing Vitamins (A, B1, B2, B3, B5, B6, B8, B9, B12, C, D, E, K) and minerals (Iron, zinc, copper, selenium) favours a better adherence to the treatment during the first three months after surgery. Furthemore, it restored the levels of iron and vitamin D. In the following period, until the weight stabilization, the administration of specific supplements for bariatric surgery is recommended if the clinical conditions of the patients allow[6]. The limit of this study is the short duration of observation. Indeed, this study does not allow to evaluate the effectiveness of long-term supplementation with FSMP in correcting malnutrition risk associated with bariatric surgery procedures. Moreover, further studies should be performed to highlight the utility and tolerability of this FSMP for the improvement of malnutrition status antecedent to bariatric surgery.

Conflicts of interest:
The authors report no conflict of interest.

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