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The Effect of Laparoscopic Sleeve Gastrectomy on Vitamin D, Calcium and Fat Metabolism

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Abstract

Background: Obesity defined as a body mass index more than 30 kilogram for every square meters of body surface area, is a growing worldwide disease effecting 1 in 10 adults, with rates as high as 40% in the United States. This study aimed to detect the effect of sleeve gastrectomy on vitamin D, Calcium, Cholesterol and Triglyceride homeostasis with early detection of abnormalities

Patients and methods: This prospective case series study was carried out on 40 morbidly obese patients at the surgical departments in Kasr Al-ainy and Sayed Galal Hospitals. These patients underwent the standard laparoscopic sleeve gastrectomy with pre-operative and post-operative assessment of vitamin D, Calcium, Cholesterol & micronutrient deficiencies at three and six months postoperatively.

Results: Pre-operatively, vitamin D deficiency was found in 24(60%) of patients and 18 (45%) patients had hypocalcemia. Post-operative vitamin D deficiency at 3 months was found in 30(75%) patients, 23 (57.5%) patients had hypocalcemia. Post-operative vitamin D deficiency at 6months was found in 34 (85%) patients and 31(77.5%) patients had hypocalcemia. decrease in the level of total cholesterol, triglyceride and LDL and increase in the HDL at 6 months than at 3 months and pre operatively.

Conclusion: There was a highly statistically significant decrease in the levels of vitamin D and serum calcium together with a highly statistically significant improvement of serum lipid profile at 3 and 6 months post-operatively than the preoperative levels

Keywords: Laparoscopic Sleeve Gastrectomy; Vitamin D; Calcium; Fat Metabolism.

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INTRODUCTION

As obesity continues to be one of the greatest health struggles of our time, bariatric surgery is a valuable therapeutic tool for both the treatment of morbid obesity and associated co-morbid conditions. Regardless of the procedure performed, there are nutritional deficiencies that can occur both pre and postoperatively, and pose a challenge to patient and clinician alike. This study will review the nutritional risks of bariatric surgery and will also touch on the evaluation and prevention of these problems [1].

Studies of bariatric surgery patients presenting for surgery have found significant deficiencies of nutrients. For example, in retrospective study of 379 morbidly obese patients, 68.1 % of the patients were deficient in vitamin D, 39 % were low in iron, 22 % had low hemoglobin, 8.4 % had low ferritin, and 29 % were deficient in thiamine. In a comparison of pre and postoperative nutritional levels in 100 patients, the following deficiency rates before surgery: Vitamin A – 11%, Vitamin B12 – 13%, Vitamin D – 40%, Zinc – 30%, Iron – 16%, Ferritin – 9%, Selenium 58% and Folate 6%. For some nutrients such as vitamin D and Selenium, the nutrient levels were significantly changed before surgery than they were one year after surgery [2].

Researchers looking at individual nutrients have found deficiencies of vitamin D, thiamine, vitamin C and others. Thus, overall we can clear paint a picture of the morbidly obese patient as having a high incidence of nutritional deficiency [3].

Deficiencies left untreated can cause acute or chronic problems that can be serious if not addressed. While it may not be cost effective or practical to broadly assess nutritional status prior to surgery, it is becoming increasingly common to check not only for anemia, but also for common treatable problems such as vitamin D or thiamine deficiency [4].

Other disorders, including small intestinal bacterial overgrowth, can promote micronutrient deficiencies, especially in patients with diabetes mellitus. Recognition of the clinical presentations of micronutrient deficiencies is important, both to enable early intervention and to minimize long-term adverse effects [3].

There is very limited data available on the impact of the vertical sleeve gastrectomy (SG) on micronutrient status. Most literature refers to SG as a purely restrictive procedure (since it is limited to surgical alteration of the stomach), which may give the impression that there should be minimal impact on vitamins and minerals – similar to gastric banding. However, the position statement from the ASMBS notes that, "The mechanisms of weight loss and improvement in comorbidities seen after SG might be related to gastric resection, neuro-hormonal changes related to gastric restriction or gastric emptying, or some other unidentified factor or factors." Because vitamin and mineral status can be adversely impacted in the absence of malabsorption, it is not surprising that even the limited available data begins to indicate some challenges [5].

Dyslipidemia is common feature in obes e patient and major risk factor for development of atherosclerosis and then heart related diseases [6].

Bariatric surgery has proven to be an effective treatment against obesity related comorbidities achieving high rate of remission in disease such as type 2 DM or arterial hypertension among others [7].

In these cases of dyslipidemia, studies have shown acceptable short term outcome after bariatric surgery reaching more than 85% of resolution in one year [8].

Due to its greater efficiency and low complication rate LSG has become more widely accepted as a definitive treatment for morbidly obese patients [9].

Hyperlipidemia is widely recognized as major co-morbidity in severe obese patients. So now a day's bariatric surgeries are increasingly focused on lipid profile in the drive to potentially reduce cardiovascular related disease [10].

PATIENTS AND METHODS

This prospective case series study was carried out on 40 morbidly obese patients at the surgical departments in Kasr Al-ainy and Sayed Galal Hospitals from May 2018 to March 2019.

All patients were subjected to full clinical preoperative evaluation as well as investigations. Patients' demographics including: age, gender, BMI were recorded. Clinical evaluation aimed at assessment of degree of obesity and detection of different complications of morbid obesity like hypertension, Diabetes mellitus, obstructive sleep apnea & skeletal problems.

Methods of the study:

These patients underwent sleeve gastrectomy operation by the standard technique. Preoperative (immediately before surgery) & postoperative (3 & 6 months) assessment of the serum levels of vitamin D, Calcium, Cholesterol and Triglyceride was done.

Informed consent was obtained from all patients included in the study.

Preoperative investigations:

Laboratory investigations: CBC, FBS, Renal function tests: Urea & creatinine, Liver function tests: ALT, AST, Albumin, Bilirubin (total & direct) and coagulation profile. Serum levels of vitamin D, Calcium, Cholesterol and Triglyceride was done and repeated at 3 and 6 months postoperatively.

Imaging: CXR, Abdominal ultrasound.

Cardiac assessment: ECG & Echocardiography.

Respiratory function tests.

Upper GI endoscopy if the patient complains of manifestations of GERD.

Preoperative Diet:

All patients are required to start a Liquid Diet 2 weeks before their surgery date. Following this diet will not only jump start weight loss but will also help reduce the size of the liver making the procedure easier to perform and thus more successful. During this time it is important to include a protein shake multiple times daily to help ensure good nutritional status prior to surgery. Aim for a goal of 60-80 grams of protein per day obtained from the protein shake. It would also be beneficial to add a general multivitamin and calcium supplement as a safety net in meeting basic nutrient needs. While swallow form of supplements will be acceptable long-term, initially chewable forms are recommended for optimal digestion and absorption.

Intervention in details: Operative technique

The procedure was done under general anesthesia with oro-tracheal intubation the patient was placed in the supine position. Elastic compression stockings were placed on the legs. Prophylactic antibiotics, Ampicillin and ceftriaxone intravenously were administrated.

Laparoscopic technique began with CO2 insufflation by using Veress needle until the working pressure reached 14 mm Hg. The insufflation site was Palmers point, 1 inch below the left costal margin in the midclavicular line.

The operation was carried out using 5 ports. The first trocar for the optic was placed slightly above and to the left of the umbilicus using a 10 mm port. We used 30 degree optic. After entering abdominal cavity, the position of Veress needle was inspected for the possible organ injury. Two 12 mm port were placed in both right and left hypochondria in the midclavicular line as the surgeon's working ports and another 5 mm or 10 mm according to the liver size in the epigastrium for the liver

retraction. A fifth 5 mm port was placed in left anterior axillary line for the assistance

In steep reverse Trendelenburg position, dissection began with opening of the greater omentum using a sealing device (Harmonic: an ultrasonic dissector Ethicon Endosurgery, Cincinnati, OH, USA or Ligasure (Auto suture Bariatric Covidien) along the greater curvature of the stomach. The dissection continued proximally to the gastroesophageal junction and the left crus. The short gastric vessels were sealed carefully and care was taken to avoid injury to the spleen. The left crus was completely freed of any attachments to avoid leaving a posterior pouch when constructing the sleeve in this region and completed distally to approximately 3-6 cm proximal to the pylorus. The dissection was completed by freeing any posterior attachments of the stomach to the pancreas.

Once the dissection completed, a 36 Fr bougie was introduced orally by the anesthesiologist through the esophagus and inside the stomach. The surgeon then guided it along the lesser curvature and into the pyloric channel and duodenal bulb. The greater curvature of stomach was transected by a linear stapler (Echelon 60 Endopath Stapler and Cutter. 60 mm: 1 green, 2 gold and 2 blue, Ethicon, Cincinnati, OH) or (Covidien Endopath Stapler: 1 green and 4 blue) from antrum starting about 3-6 cm proximal to pylorus till angle of His.

All patients were given antibiotic (third generation cephalosporin), proton pump inhibitor, analgesic and chemical and physical thrombo-prophylaxis. Multivitamins and micronutrient supplementation were administered in the usual doses. Patients were examined preoperatively and throughout a 6 month follow-up period (preoperative, 3 and 6 months postoperatively) in the department and obesity and metabolic surgery clinic. Furthermore, short- and long-term results with regard to BMI, weight, %EWL and important laboratory parameters (Hemoglobin level, iron level, Vitamin B12, Calcium, Vitamin D, Zinc level, Copper level & Albumin level, Lipid profile).

Follow up and Outcome parameters:

All patients were followed up for early post-operative complications (30 days) like Bleeding, Leaks, Infections and VTE. Patients were reviewed at 1, 3, 6 and 12 months postoperative for % EWL, control of preoperative comorbidities and manifestations of vitamin and micronutrients deficiencies (hair loss, teeth problems, edema, Anemia etc.) **Postoperative Medications & Supplementation:**

Ceftriaxone 1 g Vial: Once daily for 48 hours (Intravenous or Intramuscular). Proton Pump Inhibitor tab: 40 mg twice daily for 6 months. Multivitamin and mineral supplement should include; Iron, Selenium, Copper: 2 mg (minimum), Zinc (ratio of 8-15 mg zinc for each 1 mg, Multivitamin and mineral supplement (chewable tab): Once daily for 6 months then according to the results of the routine follow up laboratory investigations. Iron: 45 to 60 mg daily (100 mg daily for menstruating women) 200 mg ferrous sulphate, 210 mg ferrous fumarate or 300 mg ferrous gluconate daily . Vitamin B12: Intramuscular injections of 1mg vitamin B12 once weekly in the first month then monthly for 5 months. Calcium: calcium citrate is the preferable form: 500-600 mg of calcium three times per day. Vitamin D: 20 mcg (800 IU) vitamin D per day. Protein Powder without fat or carbohydrates: once daily. Prophylactic anticoagulation to prevent thromboembolic disease: 40 Units vial subcutaneous for 2 weeks after the operation.

Statistical analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric. Also qualitative variables were presented as number and percentages. The comparison between groups regarding qualitative data was done by using **Chi-square test**. The comparison between more than two related groups regarding quantitative data and parametric distribution was done by using **Repeated Measures ANOVA test** followed by post hoc analysis using **Bonferoni test.** The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P-value > 0.05: Non significant (NS), P-value < 0.05: Significant (S), P-value < 0.01: Highly significant (HS).

RESULTS

This study was conducted on 40 morbidly obese patients presenting to the bariatric and metabolic surgery clinic in the Cairo university hospital (Kasr Alaini School of medicine and Sayed Galal Hospital). Out of these 40 morbidly obese patients, 29 were females (72.5%) and 11 were males (27.5%). The mean age was 34.38 ± 7.7. The mean body mass index (BMI) was 47.74 ± 5.65 kg/m^2. Table (1)

Table 1: Demographic data of the studied cases.

Sex	Female	29 (72.5%)
	Male	11 (27.5%)
Age	Mean ± SD	34.38 ± 7.7
	Range	20 – 54
BMI	Mean ± SD	47.74 ± 5.65
	Range	38 – 60

Table 2: Comparison between level of calcium and Vitamin D pre, 3 months and 6 months follow up.

	Preoperative		3 months		6 months		ANOVA test	
	mean	range	mean	range	mean	range	P-value	Sig.
Ca	8.50 ± 0.8	6 – 10.5	8.20 ± 0.7	6.5 – 10	7.70 ± 0.7	6.5 – 9.5	0.000	HS
Vit. D	27 ± 11	10 – 67	23.1 ± 9	7 – 54	19.3± 9	6 – 48	P-value	Sig.
							0.000	HS

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

The previous table shows that there was highly statistically significant decrease in the level of calcium at 6 months than 3 months and pre operative.

The previous table shows that there was highly statistically significant decrease in the level of vitamin D at 6 months than 3 months and pre operatively.

Table 3: Lipid profile pre-operative, 3 months and 6 months postoperatively.

	Pre		3 months		6 months		Repeated measures ANOVA test
	Mean (SD)	range	Mean (SD)	range	Mean (SD)	range	P-value
Total cholesterol	216.55 ± 10.35	200 – 235	183.03 ± 7	173 – 196	173.85 ± 7	159 – 194	0.000
TG	174.3 ± 29.04	121 – 220	112.05 ± 23.29	72 – 149	91.15 ± 19	65 – 115	0.000
HDL	39.83 ± 3.44	31 – 45	44 ± 3.63	35 – 53	45 ± 3	37 – 54	0.000
LDL	141.88 ± 9.58	124 – 169	116.58 ± 7.26	102 – 132	110.58 ± 7	94 – 132	0.000

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant. The previous table shows that there was highly statistically significant decrease in the level of total cholesterol, triglyceride and LDL and increase in the HDL at 6 months than at 3 months and pre operatively.

DISCUSSION

Our study was conducted on 40 morbidly obese patients presenting to the bariatric and metabolic surgery clinic in the Cairo university hospital (Kasr Alaini and Sayed Galal Hospitals). Out of these 40 morbidly obese patients, 29 were females (72.5%) and 11 were males (27.5%). The mean age was 34.38 ± 7.7. The mean body mass index (BMI) was 47.74 ± 5.65 kg/m^2.

Energy-dense diets often consumed by obese individuals do not indicate nutrient adequacy. Sanchez et al[11] performed an analysis on the diets of candidates preparing for bariatric surgery, finding mean energy intake to be 2801 ± 970 kcal/d, composed of 93.5 ± 28.6 g/d of protein (13.9% ± 3.3% calories), 101.8 ± 49.7 g/d of fat (32.5% ± 8.2% calories), and 386.4 ± 144.7 g/d of carbohydrates (55.0% ± 91.0% calories)**[11].**

Extreme variability in results occurred due to an outlier reporting an intake of >7000 kcal/d and another reporting an intake of 1000 kcal/d. Per this diet analysis, dietary intakes of iron, calcium, and vitamin D were below the recommended dietary allowance, while other vitamins and minerals met recommendations (zinc, copper, folic acid, vitamin B12, and phosphorus) **[12].**

Of the 40 patients evaluated in our study, 7 patients had 1 preoperative micronutrient deficiency (17.5 %), 9 patients had 2 preoperative micronutrient deficiency (22.5 %), 8 patients had 3 preoperative micronutrient deficiency (20 %), 2 patients had 4 preoperative micronutrient deficiency (5 %) and 2 patients had 5 preoperative micronutrient deficiency (5 %). Overall 27 patients included in our study (67.5%) had at least one micronutrient deficiency prior to surgery.

Our results were comparable to recent literature that showed that candidates of bariatric surgery had multiple micronutrient deficiencies before surgery. A cross-sectional study from a group in Baltimore, Maryland, found that nearly 40% of 58 candidates for bariatric surgery had multiple micronutrient deficiencies**[13].**

In another study by Degan and colleagues showed that out of 103 patients evaluated, 67% had at least 1 micronutrient deficiency despite more than adequate macronutrient intake. They also conducted an analysis of the diets among their candidates for bariatric surgery. Despite high energy and macronutrient intake, most micronutrients evaluated did not meet recommendations. Dietary intake of iron, calcium, folic acid, vitamin B12, and vitamin B1 were below the dietary reference intakes for 46%, 48%, 58%, 14%, and 34% of the study population, respectively, indicating poor diet quality**[12].**

Regardless of inadequate intake, biochemical markers did not show a high prevalence for deficiency except for vitamin D, as seen in the majority of candidates (83%). However, 59% of the population was taking supplements, which may have improved its baseline micro-nutrition. Better nutrition status in folic acid and vitamin B12 was seen among participants who reported the use of supplementation, suggesting a role for preoperative supplementation with this population. Unfortunately, data were lacking regarding the exact type and duration of supplements used **[14].**

The most common preoperative deficiencies in these candidates for bariatric surgery are in folate, vitamin B12, iron, and vitamin

D. Other vitamins and minerals may prove to be less than optimal as well; however, they have not been well studied to date[15].

The prevalence of preoperative vitamin and micronutrient deficiency in our study was as follows: 24 (12 deficiency and 12 insufficiency) of the 40 patients (60%) had vitamin D deficiency, 18 of the 40 patients (45%) had hypocalcemia.

According to ASMBS 2008 nutrition guidelines, deficiency of folic acid, vitamin A, vitamin E, vitamin K and zinc was uncommon in patients prior to surgery and preoperative assessment of copper and selenium was not recommended[14].

Also another important study on 2014 by Lefebvre and colleagues[16] showed that the preoperative values of fasting plasma glucose, insulin, lipid profile, 25hydroxy vitamin D, parathyroid hormone, thyroid-stimulating hormone, calcium, phosphate, albumin, magnesium, total proteins, liver function tests, iron, ferritin, folate, vitamin A, vitamin B12, selenium, and zinc were evaluated in 267 Caucasian outpatients (74.2% women, aged 40.5 ± 12.6 years) who were considering bariatric surgery. The determinants of nutrient variability were analyzed by linear regression for nutrients with a prevalence of deficiency > 10%, i.e., serum25 (OH) D, iron, phosphate, magnesium and vitamin A[16].

Assessment of different micronutrient deficiencies:

Papamargaritis et al evaluated serum trace element concentrations obtained by inductively coupled plasma-mass spectrometry (ICP-MS) method in 437 patients (82% women, median preoperative body-mass index 46.7 kg/m2 [interquartile range 42–51]) undergoing either gastric banding (22.7%), sleeve gastrectomy(20.1%), or gastric bypass (57.3%) procedures. Trace element data were available for patients preoperatively (n = 44); and 3 (n = 208), 6 (n = 174), 12 (n = 122), 18 (n = 39), 24 (n = 44) and 36 months (n = 14) post-operatively. All patients were recommended to take a multivitamin-mineral supplement after surgery [17].

In our study 30 (8 deficiency and 22 insufficiency) of the 40 patients (75%) and 34 (18 deficiency and 16 insufficiency) of the 40 patients (85%) showed reduced vitamin D levels at 3 and 6 months respectively.

The aim of the systematic review of observational studies that was conducted by Chakhtoura and his colleagues was to review 25-hydroxyvitamin D [25(OH) D] status pre and post bariatric surgery, describe the dose response of vitamin D supplementation, and assess the effect of the surgical procedure on 25(OH)D level following supplementation[18].

The increase in post-operative 25(OH) D levels tended to parallel increments in vitamin D supplementation dose but varied widely across studies[19].

An increase in 25(OH) D level by 9–13 ng/ml was achieved when vitamin D deficiency was corrected using vitamin D replacement doses of 1100–7100 IU/day, in addition to the usual maintenance equivalent daily dose of 400–2000 IU (total equivalent daily dose 1500–9100 IU)[20].

There was no difference in mean 25(OH) D level following supplementation between mal-absorptive/combination procedures and restrictive procedures[21].

In our study 23 of the 40 patients (57.5%) and 31 of the 40 patients (77.5%) showed hypocalcemia at 3 and 6 months respectively.

In a study conducted by the Academic Medical Center, USA. the prevalence of postoperative hypocalcemia and identify clinical predisposing factors. Retrospective analysis of 999 patients undergoing bariatric surgery. patients with revision surgeries were excluded. Hypocalcemia was defined as the lowest recorded serum calcium occurring at least 2 weeks post-operatively[22].

Patients fulfilled the criteria above. After correction for serum albumin concentration, 36 patients had serum calcium ≤8.9 mg/dl. Mean serum calcium was 8.1 ± 0.6 mg/dl. The prevalence was 1.9 % in the RYGB group, 9.3 % in the sleeve gastrectomy (SG) group, and 10 % in the BPD-DS group. In all three surgical types, patients with hypocalcemia had significantly lower serum albumin and serum 25 (OH) vitamin D concentrations when compared to their normo-calcemic counterparts ($P < 0.01$). Peterson et al.[13] the presence of renal insufficiency and vitamin D deficiency was associated with the highest risk of developing hypocalcemia after surgery. Pre-operative renal insufficiency increased the odds of developing hypocalcemia by 20-fold [23].

The higher prevalence of hypocalcaemia in our study may be attributed to the late timing of assessment (3m, 6m) postoperatively.

Therefore, major risk factors for vitamin D deficiency include season, latitude, altitude, skin pigmentation, and general sunlight exposure as well as the angle of the sun[24].

Because of this, vitamin D deficiency is prevalent in countries with limited sun exposure, leading to 40.4% of Europeans being vitamin D deficient, peaking in winter season, and being highest among individuals with darker skin pigmentation. Insufficient vitamin D has been associated with greater risk of infection, autoimmunity, cancer, and chronic disease in addition to poor bone mineralization[25].

The main purpose of this study was to investigate further the effect of LSG on hyperlipidemia. This study showed that LSG resolved or improved lipid profile in a majority of patients. The main obesity related metabolic risk factors of CVS involve low serum HDL cholesterol level with increased level of TG and LDL level. During the 6th postoperative months, significant

change in lipid profile had been reported specially an increase of HDL cholesterol, decrease in TG level and LDL cholesterol. Similar results were obtained by team of Zhang et al[26] as in our study**.** Low level of HDL cholesterol and high TG are the main risk factor for cardiovascular disease in obese patient[26]**.** Regarding the cardiovascular risk the observed increased HDL and decrease TG level are fairly positive prognostic factor[27]**.**

Similar results were obtained by Vidal et al.[28] with a significant improvement of lipid profile following LSG**.**

In this study 6 month after LSG we observed not only decreased total cholesterol, decrease TG and LDL cholesterol but also increase in HDL cholesterol.

CONCLUSION

There was a highly statistically significant decrease in the levels of vitamin D, serum calcium at 3 and 6 months post-operatively than the preoperative levels. Also, there was a highly statistically significant improvement of serum lipid profile at 3 months and 6 months post-operatively than the preoperative levels in the form of decrease in total cholesterol, triglyceride and LDL cholesterol and increase in HDL cholesterol.

Although, the results of this study were comparable to other recently published studies, the short term follow up period after the operation and the relatively low number of patients included represented potential limitation of this study.

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