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Original Article

Evaluation of changes in vitamin B12, ferritin, folic acid, and thyroid hormone levels after sleeve gastrectomy

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Abstract

Aim: The aim of this study was to evaluate the changes in vitamin B12, ferritin, folic acid, and thyroid hormone levels in patients with morbid obesity after laparoscopic sleeve gastrectomy (LSG).

Material and Methods: A total of 85 patients who underwent LSG operation with the diagnosis of morbid obesity were included in the study. Levels of vitamin B12, ferritin, folic acid, and thyroid-stimulating hormone (TSH), free triiodothyronine (fT3), and free thyroxine (fT4) hormone were measured using the chemiluminescence method. Pre- and postoperative levels of thyroid hormones, vitamin B12, ferritin, folic acid, and BMI values were evaluated.

Results: The mean BMI decreased from 45.44 ± 3.8 kg/m2 to 39.38 ± 3.69 kg/m2 ($p<0.001$). The mean TSH, fT3, vitamin B12, folic acid, and ferritin levels were statistically significant lower at six months postoperatively than preoperative levels, while the mean fT4 levels were found to be significantly higher ($p<0.001$). Preoperative and 6thmonth postoperative ferritin levels were significantly lower in female patients than male patients ($p<0.001$). There was a negative correlation between age with preoperative TSH and fT3 levels. There was a positive correlation between age and preoperative and 6thmonth postoperative folic acid levels.

Conclusion: Remodeling of the gastrointestinal system and endocrine alterations after LSG may result in changes in the levels of nutritional parameters such as thyroid hormone, vitamin B12, folic acid, and ferritin. Therefore, based on our study findings, we consider that the nutritional status of patients after bariatric surgery should be monitored particularly in long-term and nutritionally supported, if necessary.

Keywords: Thyroid-Stimulating Hormone; Vitamin B12; Ferritin; Gastrectomy.

INTRODUCTION

Obesity is a chronic disease characterized by excessive accumulation of body fat as a result of interaction between environmental and genetic factors. In the world, obesity is the second leading common cause of preventable death after cigarette smoking. Numerous factors contributing to the disease formation which increase the difficulties in understanding the etiology of the disease. In addition to genetic and environmental factors, nutritional and cultural differences play an important role in the development of obesity (1).

Adipocyte hypertrophy during the course of the disease leads to hypoxia, inflammation and oxidative stress which increase morbidity and mortality of this complex endocrine and metabolic disease (2,3). Functioning of adipose tissue as an endocrine organ results in metabolic changes in many organs and may lead to changes in plasma levels of various hormones and vitamins in obese patients (4).

Clinical trials have demonstrated that morbid obesity is associated with abnormal thyroid functions and shows a positive correlation with plasma thyroid-stimulating hormone (TSH) levels (5).

Changes in thyroid hormone levels can be observed after weight loss due to hypothalamic-pituitary-adipose (HPA) axis interaction. Leptin is secreted by adipocytes and has a major role in the body weight regulation by maintaining a balance between the food intake and expenditure of energy. Several studies have shown that the reduction in leptin level after weight loss leads to a decrease in serum TSH, free thyroxine (fT4), and free triiodothyronine (fT3) levels (6). Comparison of changes in vitamin B12, folic acid, and ferritin levels following laparoscopic sleeve gastrectomy (LSG) may be used to assess nutritional status. Bariatric surgery is currently the most effective treatment option for prevention of obesity-related diseases, weight loss, and long-term maintenance. Anatomic changes in the gastrointestinal tract after bariatric surgery, restrictive

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and inadequate nutrient intake may lead to deficiencies of some vitamins and trace elements. After LSG, rapid transit of nutrients in the gastrointestinal tract, intrinsic factor deficiency and decreased hydrochloric acid production are responsible for the deficiency of these vitamins (7).

In the present study, we aimed to evaluate the changes in thyroid hormone levels, vitamin B12, folic acid, and ferritin levels in obese patients after LSG operation.

MATERIALS AND METHODS

A total of 85 patients who underwent LSG with the diagnosis of morbid obesity were included in the study. The data of the patients who were operated at Antalya Education and Research Hospital, General Surgery Clinic were collected retrospectively. The study was approved by the Antalya Education and Research Hospital Ethics Committee and conducted in accordance with the Declaration of Helsinki. All study participants provided a written informed consent before the study.

In the medical history of 85 patients included in the study, there were no thyroid disease and thyroid hormone replacement therapy, and thyroid hormone levels were normal before the operation. Vitamin B12, folic acid, and ferritin levels were within normal ranges preoperatively. Data including age, sex, comorbidities (i.e., hypertension, diabetes, hyperlipidemia, and arthritis) and body mass index (BMI) were recorded. Additional thyroid hormone and vitamin supplementation were not given after LSG. The body mass index (BMI) was calculated preoperatively and at six month postoperatively. Blood sera were separated and levels of vitamin B12, ferritin, folic acid and TSH, fT4, fT3 hormones were measured using the chemiluminescence method. The correlation between the changes in thyroid hormone, vitamin B12, folic acid, and ferritin levels with age, sex, and BMI were.

The inclusion criteria were a primary diagnosis of morbid obesity, primary treatment of LSG for morbid obesity, patients with no history of thyroid disease and hormone therapy and age ≥18 years. The exclusion criteria were previous bariatric surgery, history of mental impairment, history of thyroid disease and hormone therapy, drug or alcohol addiction, recent major vascular event, and/or malignancy.

Surgical Procedure

All LSG operations were performed by a single bariatric surgery team in our general surgery clinic using a single technique in which a longitudinal resection from the angle of his to 5 cm to the pylorus was performed via a 36Fr boogie inserted along the lesser curve.

Measurements

The Ferritin, folic acid, vitamin B12, TSH, fT3, and fT4 levels were measured by Beckman Coulter DxI800 (Beckman Coulter Inc., USA) using the chemiluminescence method. Daily calibration and control of the tests were routinely performed. The inter- and intra-assay coefficients of variation (CV) of the tests were less than 10%.

Statistical Analysis

Statistical analysis was performed using the PS Imago software package (IBM SPSS Statistics Version 23; SPSS Inc., Chicago, IL, USA). The variables were investigated using Shapiro-Wilks test to determine whether or not they were normally distributed. Descriptive analysis was presented using frequencies, percentages, mean and standard deviation values. If the variables were normally distributed, the Student's t-test was used to compare the parameters. On the other hand, if the variables were not distributed normally, the Mann-Whitney U test was preferred. For the difference between the two dependent measurements, the Paired t-Test was used if the data was distributed normally, whereas if it was not distributed normally, the Wilcoxon Test was used. Correlation between numerical variables was investigated by Spearman Correlation Test. P values less than or equal to 0.05 were considered statistically significant .

RESULTS

Among 85 patients who underwent LSG operation with the diagnosis of morbid obesity, 68 were females (80%) and 17 were males (20%). The mean age of female patients was 39.9 ± 9.57 (range: 24 to 62) years and the mean age of male patients was 41.94 ± 13.9 (range: 19 to 63) years.

The mean BMI value (39.38 ± 3.69 kg/m2) was statistically significantly lower at six months postoperatively than preoperative BMI values (45.44 ± 3.8 kg/m2) ($p<0.001$). The mean TSH level was 2.32 ± 2.36 uIU/mL preoperatively and significantly decreased to 1.52 ± 0.85 uIU/mL at six months after bariatric surgery ($p <0.001$). The mean fT4 level was 0.88 ± 0.13 ng/dL preoperatively and significantly increased to 0.93 ± 0.16 ng/dL at six months following bariatric surgery ($p=0.024$). The mean fT3 level was 3.54 ± 0.56 pg/mL preoperatively and significantly decreased to 3.28 ± 0.49 pg/mL at six months after bariatric surgery ($p<0.001$).

The mean vitamin B12 was 293.34 ± 191.25 pg/mL preoperatively and significantly decreased to 222.61 ± 113.64 pg/mL at six months after bariatric surgery ($p<0.001$). The mean folic acid level was 8.52 ± 4.51 ng/mL preoperatively and significantly decreased to 7.01 ± 3.44 ng/mL at six months of surgery ($p<0.001$). The mean ferritin was 71.25 ± 115.12 ng/mL preoperatively and significantly decreased to 48.31 ± 62.74 ng/mL at six month of bariatric surgery ($p=0.003$) (Table 1).

The mean postoperative 6th month TSH, fT3, vitamin B12, folic acid ,and ferritin levels were statistically significantly lower than preoperative levels, while the mean fT4 level was found to be significantly higher ($p<0.001$). All measured parameters were within normal ranges.

In addition, there was a negative correlation between preoperative TSH ($p=0.026$, $r=-0.241$) and preoperative fT3 ($p=0.002$, $r=-0.331$) with age. There was, however, a positive correlation between preoperative ($p=0.001$, $r=0.354$) and 6thmonth postoperative ($p=0.001$, $r=0.366$) folic acid levels with age. Preoperative and 6thmonth postoperative

ferritin levels in female patients were statistically significantly lower than male patients (p<0.001). There was no difference among other parameters in terms of sex. There was a positive correlation between BMI and fT3 levels (p=0.036, r=0.228).

Table 1. Alterations of BMI, thyroid hormone and nutritional parameters of patients who underwent laparoscopic sleeve gastrectomy: Comparison between post-operative and 6 months post-operative

	Preoperative mean±SD	6 months post-operativ mean±SD	p value
BMI (kg/m2)	45.44 ± 3.8	39.38 ± 3.69	<0.001#
TSH (uIU/mL)	2.32 ±2.36	1.52 ± 0.85	<0.001*
fT4 (ng/dL)	0.88 ±0.13	0.93 ± 0.16	0.024*
fT3 (pg/mL)	3.54 ±0.56	3.28 ±0.49	<0.001*
Vitamin B12 (pg/mL)	293.34 ± 191.25	222.61 ± 113.64	<0.001*
Folic acid (ng/mL)	8.52 ± 4.51	7.01 ± 3.44	<0.001*
Ferritin (ng/mL)	71.25 ± 115.12	48.31 ± 62.74	0.003*

Data presented as mean±standart deviation
BMI: Body mass index; TSH: Thyroid-stimulating hormone; fT4: free thyroxine; fT3: free triiodothyronine
 # Paired t test, *Wilcoxon Signed Rank Test, p<0.05

DISCUSSION

Obesity is a chronic disease characterized by changes in plasma concentration and secretion pattern of many hormones and vitamins, accompanied by serious endocrine and metabolic diseases. In obesity, positive energy balance leads adipocyte hypertrophy and increased body fat ratio. A positive correlation between adiposity parameters and TSH and fT3 has been shown in several studies. Ren et al. suggested that dysfunction of adipose tissue is the main factor responsible for changes in the homeostasis of thyroid hormones, which is borne out by the observation that weight loss reverses or mitigates these changes (8).

This is thought to be caused by the effect of obesity on hypothalamus-pituitary-thyroid axis and deiodinase functions. Several mechanisms have been proposed, among which are those related to the adaptive process to increase energy expenditure, the influence of leptin, changes in the activity of deiodinases, the presence of central or peripheral resistance to thyroid hormones, the chronic low grade inflammation, and the presence of insulin resistance. Thyroid hormones are maintained by a complex mechanism which provides continuous feedback. The maintenance of the serum fT3 level within the normal range is achieved by the interaction of various genetic, physiological, pathological and environmental factors (9). In obese patients, leptin provide thyrotropin-releasing hormone (TRH) synthesis in paraventricular hypothalamic nucleus (direct route) and arcuate nucleus (indirect route). Subsequently, secretion of TSH is stimulated in pituitary gland and thyroid hormone levels are increased in obese patients (10). Several studies have shown a positive correlation between serum TSH concentrations and leptin in obese individuals (11). Leptin also affects thyroid hormone metabolism by regulating the activity of deiodinase enzyme in different tissues, such as the liver and kidney. Animal and human studies have demonstrated a positive relationship between leptin and D1 deiodinase enzyme expression and/or activity in the white adipose tissue (12,13). In a study, Bakiner et al. compared thyroid hormone levels in control, overweight, obese and morbid obese patients. They found no difference in TSH concentrations between groups, but found a positive correlation between TSH and BMI in the male patients (14). Knudsen et al. reported a negative correlation between BMI and fT4 in the study of 4082 obese patients (15). Similarly, in our study, after six months of LSG with significant weight loss, TSH, and fT3 levels were statistically significantly lower and fT4 levels were significantly higher than preoperative levels.

Different bariatric procedures such as laparoscopic Roux-en-Y gastric bypass (LRYGB), biliopancreatic diversion (BPD), and laparoscopic adjustable gastric banding (LAGB), showing that fT4 remained unchanged, while TSH and fT3 levels were often decreased after these surgical procedures. The inflammatory adipokines may also alter the activity of deiodinases. The decrease in these adipokines together with the body fat ratio causes a decrease in thyroid function (16).

Another cause of thyroid hormone depletion in obese patients after LSG is reduced insulin resistance. The insulin resistance in obesity seems to contribute to the D2 deiodinase activity reduction in thyrotrophic cells, leading to tissue hypothyroidism and subsequent increase in TSH synthesis (9).

Some of trace element deficiencies occur after all bariatric surgery types due to gastrointestinal tract modification. After surgery, restrictive diets, malnutrition and kidnapping effect of adipose tissue on the circulating vitamins are implicated. LSG has been considered to have lower postsurgical vitamin deficiencies prevalence than gastric bypass (GBP). Nonetheless, LSG is also associated with a more rapid passage of food through the gastrointestinal tract and decreased intrinsic factor and hydrochloric acid production, both potentially contributing to the development of trace and vitamin deficiencies. In particular, vitamin D deficiency was common, despite nutritional support. Restrictive nutrition, deterioration of gastric acid secretion, impaired absorption, and changes in the nutritional habits often lead to deficiencies of folic acid, copper, ferritin, vitamin B12, B1, and B6 after LSG operation. Nutritional deficiencies usually arise in the first year after surgery. In LSG-operated patients, iron deficiency is probably due to an impaired transformation of iron from meals to an absorbable form by hydrochloric acid in the stomach, as its secretion is reduced by this kind of surgery. Theoretically, it is thought to be that there would be no vitamin B12 deficiency for months or

even years due to hepatic storage, although few studies have shown an increase in the prevalence of vitamin B12 deficiency in the first year after surgery. This is thought to be due to decreased stomach acidity, decreased intrinsic factor secretion from parietal cells, and intolerance to meat and milk intake (17). In our clinic, the ferritin and vitamin B12 levels were found to be significantly lower in patients who were followed up after LSG. These patients did not receive supplementary vitamin B12 and iron. Even ıf nutritional parameters were still within normal limits, it is suggested that vitamins and nutritional supplements should be given after surgery.

Thiamine deficiency has been reported to be observed in up to 49% of patients after gastric bypass, although only few cases have been reported after LSG (18). Nutritional support for vitamin D and B12 deficiency after bariatric surgery has been suggested, while iron and folic acid deficiencies have been reported to be rarely observed. Pellitero et al. reported that 23% of patients had anemia, 16.5% of folic acid deficiency, 6.9% of vitamin B12 deficiency and 73% of vitamin D deficiency after LSG operation (19). The authors found that nutritional deficiencies were usually evident within the first two years after surgery and improved during the five-year follow-up duration. Insufficient consumption of carbohydrates and fat-rich nutrients such as cholesterol, trans-fatty acids, and saturated fats and reduced absorption from the gastrointestinal tract are responsible for nutritional deficiencies.

CONCLUSION

In conclusion, in our study, 6th month postoperative TSH, fT3, vitamin B12, folic acid and ferritin levels significantly decreased, compared to preoperative levels. However, nutritional parameters and thyroid hormone levels were found to be within normal ranges at six months of surgery. Additional vitamin or thyroid hormone therapy was not given in any patient. In the light of existing studies in the literature, and based on our study findings, we consider that patients undergoing bariatric surgery should be followed in the long-term and nutritionally supported after surgery in case of clinical necessity.

Competing interests: The authors declare that they have no competing interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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