Effect of sleeve gastrectomy on thyroid-stimulating hormone levels in morbidly obese patients with normal thyroid function

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Abstract. – OBJECTIVE: There are many studies, which demonstrate that morbid obesity is associated with an increase in Thyroid Stimulating Hormone (TSH) levels. However, the effect of Laparoscopic Sleeve Gastrectomy (LSG) procedure on postoperative TSH levels is not clear. This study aims to evaluate the effect of weight loss after LSG procedure on TSH levels in euthyroid patients with morbid obesity.

PATIENTS AND METHODS: 159 Euthyroid patients who applied for an LSG procedure (93.7% female, with a mean age of 34.18±10.01 years, BMI 43.2±6.82 kg/m²) were retrospectively analyzed for the study. The parameters used in the analysis were their serum free T3 levels (fT3), free T4 levels (fT4), and TSH levels preoperatively and at 6 months after surgery. The postoperative correlation between TSH and BMI (Body Mass Index), % EWL (Percent Excess Weight Loss), and % TWL (Total Weight Loss) levels were evaluated.

RESULTS: Mean BMI change from 43.2±6.82 kg/m² to 30.48±5.63 kg/m² (*p*<0.001), 6 months after LSG, was associated with a mean reduction in the TSH from 2.27±1.09 µU/dL to 1.61±0.99 µU/dL; *p*<0.001). Serum fT3 levels (3.23±0.42 ng/dL at baseline and 3.21±0.48 ng/dL at 6 months after surgery; *p*=0.409) remained steady. Serum fT4 levels (1.21±0.18 µU/dL at baseline and 1.43±0.20 µU/dL at 6 months after LSG; *p*<0.001) increased. Change in TSH was significantly correlated with change in BMI at 6 months after surgery (r=0.200, *p*=0.015). However, the decrease in TSH following LSG procedure did not correlate with % EWL (r=-0.114, *p*=0.159) and % TWL (r=-0.100, *p*=0.209).

CONCLUSIONS: After the LSG procedure, there was a significant decrease in TSH levels and a significant increase in fT4 levels, but no change was seen in fT3 levels. While this decrease in TSH levels showed a positive correlation with BMI, no statistically significant correlation was found with % EWL and % TWL.

Key Words:
Obesity, Sleeve gastrectomy, Thyroid function, TSH, Weight loss.

Introduction

Obesity has become one of the most critical public health problems in economically developed and developing countries in the world[1]. It causes metabolic disorders that increase the risk of mortality and morbidity in adulthood. Furthermore, obesity contributes significantly to the pathogenesis of diabetes mellitus, cardiovascular disease, hyperlipidemia, obstructive sleep apnea, and hypertension pathogenesis[2].

Obesity is associated with high TSH levels. Clinical studies have shown a positive correlation between obesity and plasma TSH levels. Furthermore, weight loss in these patients is associated with changes in serum TSH and thyroid hormone levels[3]. However, the relationship between adipose tissue and thyroid function has not been fully understood. There are various adipokines that act on thyroid functions and are associated with the hypothalamic-pituitary and adipose tissue axis[4]. In particular, changes in thyroid hormone levels following weight loss can be partially explained by a decrease in serum leptin levels, as seen frequently after weight loss[5].

Bariatric surgery is a well-established treatment option for morbid obesity as it provides a significant improvement in effective weight loss and accompanying comorbidities[6]. LSG has become an increasingly popular bariatric surgical procedure; especially since it is technically easy to apply, and its long-term results are at least as effective as other methods[7].

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There are clinical studies focusing on the effect of surgical weight loss on thyroid hormone levels, following different bariatric procedures such as laparoscopic Roux-en-Y gastric bypass (LRYGB), biliopancreatic diversion (BPD), and laparoscopic adjustable gastric band (LAGB)[8]. However, there are not many clinical studies showing the effect of weight loss on thyroid hormone levels after the LSG procedure.

This study aims to investigate the effect of weight loss after LSG on free fT3, fT4, and TSH levels in morbidly obese euthyroid patients.

Patients and Methods

Study Design and Participants

We conducted a retrospective, observational study evaluating patients with normal preoperative thyroid function, who underwent LSG operation due to morbid obesity (BMI≥40 kg/m^2 or BMI≥35 kg/m^2, and Type 2 diabetes, hypertension, sleep apnea, metabolic syndrome) in Pamukkale University Hospital, between June 2018-March 2019. The data were taken retrospectively from the routinely collected data recorded in the hospital database. Exclusion criteria were: patients with thyroid gland disease, patients receiving antithyroid drugs and thyroid hormone replacement therapy, patients whose TSH and free fT4 values before the operation were not in the normal range (TSH <0.27 µU/mL or > 4.2 µU/mL, sT4 <0.97 ng/dL or > 1 (65 ng/dL), or patients using amiodarone or any lithium medication. During the study period, after exclusion criteria were applied to 250 patients who underwent LSG in our institution; 159 patients were included to the final analysis.

Clinical Parameters Evaluated

Age, gender, body weight and height, BMI, fasting serum-free thyroxine (fT4), free triiodothyronine (fT3), and TSH levels were measured in the morning before the operation and at the 6th month postoperatively. The Chemiluminescence immunoassay method was used to identify serum hormones. Weight loss results were recorded as the percentage of excess weight loss (% EWL), percentage of total weight loss (TWL%), and changes in BMI. BMI was calculated as kg/m^2.

% EWL was calculated as: [(preoperative weight (kg)-current weight (kg))/preoperative weight(kg) – ideal weight(kg))]*100.

The ideal weight was calculated separately for women and men according to the Devine formula.

For males: 50 + (2.3) * ((Height (cm) – 152.4)/2.54)

For females: 45.5 + (2.3) * ((Height (cm) – 152.4)/2.54)

% TWL was calculated as: [preoperative weight (kg)-current weight (kg)]/[preoperative weight (kg)]*100

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences, version 25.0 (IBM Corp., Armonk, NY, USA) program. Preoperative and postoperative data were compared using an paired sample *t*-test, Mann Whitney U test, and repeated measures ANOVA test. The correlation among the variables was evaluated by the Pearson analysis of variance test. A *p*-value of <0.05 was considered as statistically significant.

Results

Baseline Population Characteristics

As seen in Table I, the mean age of the 159 patients is 34.18 years (SD = 10.01), their mean height is 164.3 cm (SD = 8.96), their mean weight is 116.91 kg (SD = 22.54), their mean preoperative BMI is 43.2 kg/m^2 (SD = 6.82). 93.7% of the patients included in the study were female (n = 125) and 6.3% (n = 34) were male.

Table I. Descriptive statistics about Preoperative demographic variables.

Variables	Mean ± SD	Median (min-max)
Age	34.18 ± 10.01	34 (18-64)
Height (cm)	164.3 ± 8.96	163 (144-197)
Weight (kg)	116.91 ± 22.54	113 (82-192)
BMI (kg/m^2)	43.2 ± 6.82	42 (32-67)

Table II. Comparison of BMI, % EWL, % TWL with 1st month, 3rd month and 6th month values.

		N	Mean ± SD	F	*p*
BMI (kg/m^2)	1st month	159	38.25 ± 6.25	67.381	< 0.001
	3rd month	159	34.13 ± 6.01		
	6th month	159	30.48 ± 5.63		
% EWL	1st month	159	24.10 ± 7.06	110.644	< 0.001
	3rd month	159	44.43 ± 11.70		
	6th month	159	61.97 ± 15.94		
% TWL	1st month	159	11.47 ± 2.49	142.476	< 0.001
	3rd month	159	21.11 ± 3.60		
	6th month	159	29.54 ± 5.28		

F = ANOVA test.

Weight Loss at 6 Months After Bariatric Surgery

As it is shown in Table II, BMI, % EWL, % TWL values were compared according to the 1st month, 3rd month, and 6th month values. The mean BMI value decreased from 43.2±6.82 kg/m^2 to 30.48 ± 5.63 kg/m^2 in the 6th month after LSG, and BMI values showed a statistically significant difference as compared to 1st month, 3rd month, and 6th month. ($F = 31.098$, $p<0.001$). % EWL values showed a statistically significant difference compared to 1st month, 3rd month, and 6th month ($F = 110.644$, $p <0.001$). % TWL showed a statistically significant difference compared to 1st month, 3rd month, and 6th month ($F = 142.476$, $p <0.001$).

TSH Variation at 6 months After Bariatric Surgery

As shown in Table III, fT3, fT4, TSH values were compared according to preop and postop measurements. Serum fT3 levels were 3.23 ± 0.42 µU/dL at baseline and 3.21 ± 0.48 µU/dL at 6 months following surgery ($p = 0.409$). fT3 values did not show a statistically significant difference compared to preop and postop values ($Z = -0.826$, $p = 0.409$). Serum fT4 levels were 1.21 ± 0.18 µU/dL at baseline and 1.43 ± 0.20 µU/dL at 6 months following LSG ($p<0.001$). fT4 values were found to be statistically significantly higher in postoperative compared to preoperative period ($t = -9.423$ $p<0.001$). Baseline serum TSH level was 2.27 ± 1.09 µU/dL, and it decreased significantly to 1.61 ± 0.99 µU/dL at 6 months after LSG was performed ($p<0.001$). TSH values were found to be significantly lower in postoperative period as compared to preoperative ($t = -7.007$ $p <0.001$).

As seen in Table IV, a statistically significant positive relationship was found between fT3 values and fT4 values ($r = 0.421$ $p<0.001$). A statistically significant negative relationship was found between fT3 value and TSH values ($r = -0.267$ $p = 0.001$).

A statistically significant, negative relationship was found between fT3 values and BMI values ($r = -0.304$ $p = 0.010$). Change in TSH was significantly correlated with change in BMI at 6 months after surgery ($r = 0.200$ $p = 0.015$). However, the decrease in TSH levels following LSG did not correlate with % EWL ($r = -0.114$, $p = 0.159$) and % TWL ($r = -0.100$, $p = 0.209$).

As seen in Figure 1, fT4 measurements showed a statistically significant effect between the preoperative and postoperative values ($p<0.001$). TSH measurements also showed a statistically significant effect between the preoperative and postoperative measurements ($p<0.001$).

Table III. Comparison of fT3, fT4, TSH preop, and postop values.

		N	Mean ± SD	*t*	*p*
fT3	Preoperative	159	3.23 ±0.42	-0.826	0.409
	Postopoperative	159	3.21 ± 0.48		
fT4	Preoperative	159	1.21 ± 0.18	-9.423	< **0.001**
	Postoperative	159	1.43 ± 0.20		
TSH	Preoperative	159	2.27 ± 1.09	-7.007	< **0.001**
	Postoperative	159	1.61 ± 0.99		
BMI	Preoperative	159	38.25 ± 6.25	-7.898	< **0.001**
	Postoperative	159	30.48 ± 5.63		

Table IV. Correlation results between Postop fT3, fT4, TSH, % EWL, and % TWL values.

		fT3	fT4	TSH	% EWL	% TWL	BMI
fT3	r	1					
fT4	r	.421**	1				
	p	< **0.001**					
TSH	r	-.267**	-.369**	1			
	p	**0.001**	< **0.001**				
%EWL	r	.294**	.269**	-0.114	1		
	p	< **0.001**	**0.001**	0.156			
%TWL	r	.218**	.244**	-0.100	.779**	1	
	p	**0.006**	**0.002**	0.209	< **0.001**		
BMI	r	-.304*	-.255*	0.200	-.795**	-.569**	1
	p	**0.010**	**0.033**	**0.015**	< **0.001**	< **0.001**	

Correlation is significant at 0.05 level (Pearson correlation test), **Correlation is significant at 0.01 level (Pearson correlation test).

Discussion

It is well known that thyroid hormone (TH) levels are related to body weight[9]. In hyperthyroidism, excessive thyroid hormone, weight loss, increased lipolysis, and a hypermetabolic state occurs[10]. Conversely, hypothyroidism is associated with hypometabolism characterized by low thyroid hormone levels, weight gain, and decreased lipolysis[11]. TH stimulates both lipogenesis and lipolysis, but when TH levels rise, the net effect results in fat loss[12]. Thyroid hormones play a role in regulating basal metabolism and thermogenesis and have a significant effect on body weight[13]. A negative correlation has been demonstrated between BMI and thyroid hormone values[14].

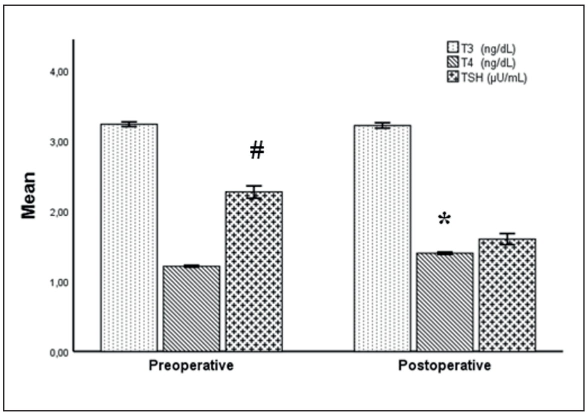

Figure 1. Comparison of fT3, fT4, TSH with Preoperative and Postoperative Levels (**p* <0.05; #*p* <0.05 statistically significant effect).

Bariatric surgery, which is widely used in the treatment of morbid obesity, provides effective weight loss, increased quality of life, and reduction in mortality due to its assistance in the improvement of obesity-related comorbidities[15]. We think that this metabolic recovery caused by bariatric surgery has a positive effect on thyroid hormones.

TSH levels decrease significantly with weight loss after bariatric surgery, and the need for thyroid hormone decreases after weight loss[16,17]. Fazylov et al[18] evaluated the effect of RYGB in 20 morbidly obese patients with hypothyroidism who were receiving thyroid replacement therapy. The authors showed that there was a decrease in postoperative L-thyroxine levels as an indicator of improvement in thyroid gland function, and hypothyroidism improved in 25% of the patients. However, there was no improvement in patients with autoimmune thyroid disease. In our study, it was shown that there was a statistically significant increase in fT4 and a statistically significant decrease in TSH levels at the 6th month after LSG; however, no change in fT3 levels was observed. Gokosmanoglu et al[19] in a study they conducted concluded that a mechanism similar to insulin resistance, caused by obesity, creates thyroid hormone resistance, increases the TSH levels, and therefore, thyroid hormone hemostasis is regulated after weight loss.

The decrease in adipose tissue after bariatric surgery causes changes in plasma fT3, fT4, and TSH levels. Nannipieri et al[20] conducted a study where they investigated the effect of adipocytes on TSH and thyroid hormone levels. They showed that obese patients had a decreased thyroid hormone gene expression (especially TSH receptor) in subcutaneous and visceral adipose tissue.

Neves et al[21] included 949 euthyroid patients in the 12th month after bariatric surgery; they found a significant decrease in TSH levels of patients with young age, high preoperative baseline BMI, and high weight. Abu-Ghanem et al[22] observed at the end of the 6th and 12th months after LSG that there was no significant decrease in TSH levels, and that there was no change in fT4 levels, and the decrease in TSH was not related to % EWL. Yang et al[17] found that there was a significant decrease in TSH levels 12 months after LSG; while the fT3 and fT4 levels remained stable. Furthermore, in the same study, the decrease in this TSH level correlated with BMI; however, it did not correlate with % EWL and TWL. In another study performed after RYGB and LSG with 129 obese patients, it was found that there was a significant decrease in TSH levels after 12 months. Moreover, in the same study, there was no change in fT4 levels, and a decrease in TSH was correlated with EBMIL (Excess BMI Loss)[23]. In the first meta-analysis evaluating the effect of bariatric surgery on thyroid function in euthyroid obese patients, postoperative fT3, T3, and TSH levels showed a reduction; while fT4, T4, and rT3 (reverse T3) concentrations did not change significantly compared to the preoperative condition[16]. In our study, TSH levels decreased in a statistically significant manner at 6th month after LSG; while the serum fT4 levels increased statistically, and there was no significant change in serum fT3 levels. Furthermore, it was found that the decrease in TSH level correlated with BMI, and it did not correlate with % EWL and % TWL.

Although, as in our study and other studies, a relationship has been indicated between bariatric surgery and the replacement of thyroid hormones, the cause of this condition is not yet fully understood, and can be partially explained by some mechanisms. The first and most popular mechanism is related to adipose tissue and adipokines (especially leptin). Produced by adipocytes and secreted from adipose tissue, leptin increases TSH and fT3 secretion with a stimulating effect on thyroid activity. Therefore, decreased leptin levels following surgery-related weight and adipose tissue loss may cause a decrease in TSH concentration[24,25]. Since the pathophysiological mechanisms and endocrine adaptations of morbid obesity have great heterogeneity; the thyroid axis shows excessive activation after obesity treatment, and as a result, TSH decreases[26].

Dall'Asta et al[27], in their study involving 258 patients who underwent LAGB, found that TSH levels did not change at 6 and 24 months after surgery, despite a marked increase in fT4 levels. The study also showed a decrease in fT3 and fT3: fT4 values. They thought that these changes might have been due to a reduced activity of iodothyronine deiodinase type 1 (D1) and type 2 (D2). In other words, not having a significant change in TSH, it shows that the increase in fT4 is the result of changes in deiodinase activity in favor of the decrease in peripheral conversion to fT3.

Ghrelin levels decrease following LSG and RYGB; however, they do not change after LAGB[28]. Removal of the gastric fundus lowers the level of ghrelin, and therefore, TSH levels can be affected by surgical procedures. In LAGB surgery, the stomach fundus remains in place, and the ghrelin levels do not change. In other words, different types of surgery lead to different hormonal profile changes. From this point of view, it can be thought that the decrease of ghrelin levels may be effective on the decrease in TSH levels. This effect occurs due to weight loss, as well as due to the effect of surgery, causing hormonal changes (an effect similar to diabetes remission)[29].

Our study has certain limitations. First, we evaluated the fT3, fT4, and TSH values once in the 6th month after surgery (before and after surgery). Repeated measurements could have been made at 12th and 24th month, as well as during longer periods. Although exclusion criteria, such as drug use and thyroid diseases were applied, TSH levels may also be affected by factors other than the effect of weight loss after bariatric surgery. For example, TSH values show seasonal changes, and they decrease during the summer and increase during the winter. Annual changes in TSH secretion may affect the results[30]. Thyroid function tests were evaluated 6 months after bariatric surgery in our study. Considering that other studies include the results of 6, 12, and 24 months; we can state that this topic requires more comprehensive studies. Moreover, studies with a larger number of patients, as well as long-term studies are needed. However, our research also has its strengths. Our number of patients is satisfactory as compared to previous studies in this topic. The effects of restrictive or malabsorptive bariatric surgery procedures on weight loss and hormonal levels may differ. In our study, all patients were subjected to a uniform bariatric surgical procedure at the same center and by the same team. Compared to other investigations, while only TSH levels were examined, in our study, additionally fT3, fT4, and TSH levels were examined as well.

From a clinical point of view, our research emphasizes that the TSH levels of morbidly obese patients tend to normalize after bariatric surgery. This indicates that caution should be exercised when interpreting TSH levels in patients with morbid obesity. This study will contribute to the existing evidence regarding changes in thyroid hormones in obesity. Obesity has previously been observed to impair thyroid function, and this study shows that weight loss regains this deterioration after bariatric surgery.

Changes in the thyroid function following bariatric surgery is a common phenomenon. However, the results differed from each other, and this may be partly due to the different types of surgery performed. The most studied type of bariatric surgery related to thyroid hormone changes was laparoscopic Roux-en-Y gastric bypass and biliopancreatic diversion.

Another point that should not be forgotten is that morbidly obese patients with different preoperative thyroid hormone levels may respond differently to bariatric surgery. However, most of the previous researches have focused only on specific thyroid dysfunctions. For obese patients with normal thyroid function, our results showed an increase in fT4 levels and a decrease in TSH, with no change in fT3 level following bariatric surgery.

In light of the current evidence, we believe that thyroid hormone deficiency is a consequence rather than a cause of obesity. Thus, postoperative follow-up alone is sufficient for most bariatric surgery patients with thyroid dysfunction, and they no longer need thyroid hormone therapy. It is essential to note that some other studies support this finding.

Conclusions

Shortly, in morbidly obese patients with normal thyroid function, a significant decrease in TSH levels, and a significant increase in fT4 levels were detected at 6 months after LSG, but no change was observed in fT3 levels. While this decrease in TSH levels showed a positive correlation with BMI, no statistically significant correlation was found with % EWL and % TWL. Although the mechanism responsible for these changes after bariatric surgery is interpreted as decreased adipose tissue, ghrelin, and leptin levels; extensive studies are needed for a better understanding.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the Ethical Standards of the University of Pamukkale Research Committee (Ethical Committee Application Number: 60116787-020/26600), and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Authors' Contribution

A – research concept and design: Mustafa Atabey, Muhammed Rasid Aykota. B – collection and/or assembly of data: Muhammed Rasid Aykota. C – data analysis and interpretation: Muhammed Rasid Aykota. D – writing the article: Mustafa Atabey, Muhammed Rasid Aykota. E – critical revision of the article: Mustafa Atabey. F – final approval of article: Mustafa Atabey, Muhammed Rasid Aykota.

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