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Thesis
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Effect of Laparoscopic Sleeve Gastrectomy on Clinical Hypothyroidism in Morbidly Obese Patients

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Abstract

Background: Laparoscopic sleeve gastrectomy (LSG) has an increase in popularity as a definitive bariatric operation. The purpose of this study was to evaluate excess weight loss (EWL) and the change in thyroxin (T4) requirement in morbidly obese patients with clinical hypothyroidism after LSG.

Methods: Between June 2012 and June 2015, 33 morbidly obese patients candidate for laparoscopic sleeve gastrectomy were enrolled in a prospective comparative study at Ain Shams University Hospitals, Egypt, and Muhayl National Hospital, Saudi Arabia. The patients were assigned to either Group A (13 patients) with clinical hypothyroidism on thyroxin treatment or Group B (20 patients) with euthyroid as control group. We compared postoperative EWL between two groups and preoperative and postoperative thyroxin requirements in Group A at one-year follow up.

Results: There was no significant difference in excess weight loss at 3,6 and 12 months after surgery between two groups, the dose of L-thyroxin was highly significantly decreased from 130.76 ± 49.11(mcg/d) to 69.23 ± 67.81(mcg/d) in 10/13 patients (77%), with complete resolution in 5/13(38.5%), and 5 patients (38.5%) had 40% median reduction of their thyroxin requirements range (16.5%-62.5%), while 3/13 patients (23%) continued on the same preoperative thyroxin dose. The mean change and percentage change in T4 requirement for all of Group A were 61.53 ± 48.53 mcg (range: 0-150 mcg) and 54.34 ± 42.12% (range: 0-100%), respectively.

Conclusion: .Improvement of clinical hypothyroidism after laparoscopic sleeve gastrectomy was evidenced by a reduction in T4 requirement with comparable weight loss to euthyroid patients at short-term follow up.

Introduction

Hypothyroidism is associated with marked changes in energy expenditure and increased body weight. Weight gain may occur despite normalization of thyroid stimulating hormone (TSH) and thyroxin (T4) by replacement therapy with failure to return to premorbid weight [1].

Obesity may induce a state of thyroid hormone resistance in the peripheral tissues similar to diabetes. As a result, obesity leads to increased thyroid hormone requirements, which may induce or worsen an existing thyroid insufficiency [2].

LSG has gained much popularity throughout the world and was recently approved as a valid alternative bariatric procedure, with significant improvement of different obesity associated comorbidities like diabetes; hypertension has been well documented after LSG [3].

Improved thyroid status has been reported among obese patients following other bariatric surgical procedures [4-12], while few studies have been published on the effect of LSG on thyroid status [13-15].

The aim of our study was to evaluate weight loss and to assess the change in thyroxin (T4) requirement in obese patients with clinical hypothyroidism after LSG.

Materials and Methods

Study design: This is a prospective comparative study which was done between June 2012 and June 2015, with 33 patients candidate for laparoscopic sleeve gastrectomy for obesity enrolled and divided into two groups: Group A (13 patients) with clinical hypothyroidism on thyroxin treatment and Group B (20 patients) with euthyroid as control group.

Study population: All patients diagnosed with clinical hypothyroidism and morbid obesity by past thyroid function tests and already on thyroid replacement therapy referred from department of internal medicine were included, with exclusion of patients with subclinical status. Patients with a body mass index (BMI)>40 kg/m^2 or >35 kg/m^2 in association with comorbid diseases were considered as candidates for surgery in both groups. Patients were operated upon in two different hospitals: Ain Shams University Hospitals, Egypt, and Muhayl National Hospital, Saudi Arabia. Eligible patients had to provide written informed consent for surgery. Baseline characteristics (age, sex, weight, and BMI) were collected for each patient. Routine preoperative upper GIT endoscopy, pelviabdominal US, and thyroid function tests were done for all patients. Surgical Techniques. All operations were done by one surgeon at Ain Shams University Hospitals, Egypt, and Muhayl National Hospital, Saudi Arabia. For prophylaxis against thromboembolic complications, all patients were given low molecular weight heparin. Pneumatic intermittent pressure stocking is used intraoperatively and continued postoperatively till the patient is fully ambulant. The patient was put in supine, reverse trendelenburg head-up position by 30 degrees with legs apart and surgeon standing between patient's legs with assistant to patient's left and cameraman on patient's

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right; five ports were used: one 10 mm to the left of the umbilicus for camera, one epigastric 5 mm for self-assistant, two working 12/15 mm at both midclavicular line for gastrolysis and stapling retaining laparoscopic liver retractor, and one 5 mm at left anterior axillary line for gastrolysis from a point 3 cm from the pylorus up to the angle of His using either ultrasonic shears or a bipolar sealing device (LigaSure). The left crus was completely exposed up to the medial border. A sleeve was created over a 36F gastric calibration tube with sequential firings of different color reloads according to the stomach thickness excluding all gastric fundus. Methylene blue test was done at the end without oversewing the staple line with drain left at gastric bed.

Postoperative follow up

The patients were seen at 1-week and then 1, 3, 6 and 12 month visits; routine nutritional screening and thyroid function tests were obtained at 3, 6 and 12 months to adjust T4 dose in Group A in consultation with the endocrinologist; and change in T4 requirement was compared at 12 months. Part of the follow up was done offshore by electronic mail or message especially the last follow up of the Saudi patients. Weight and EWL were recorded and compared between both groups at 3, 6 and 12 months. Improvement of hypothyroidism (IH) was defined either by a reduction in dosage necessary to maintain the TSH in the normal range or resolution of hypothyroidism by normalization of TSH, T3, and T4 without any thyroid hormone replacement. Patients with the same preoperative and postoperative thyroxin requirements were considered to have unchanged hypothyroidism (UH).

Statistical analysis

Required data were collected and tabulated and then statistically analyzed. Analysis of data was done using IBM SPSS software (statistical program for social science version 21). Data analysis was performed by the usual methods of descriptive statistics frequencies and percentages for discrete variables and average, median, and standard deviations for continuous variables. The homogeneity of the data between the two groups was tested by the chi-square test for discrete variables and the t-test for independent data for continuous variables. The results were significant (S) with $P<0.05$ and highly significant (HS) with $P<0.01$. $P \geq 0.05$ values were regarded as non-significant (NS).

Results

Enrolled patients

Between June 2012 and June 2015, 33 obese patients candidate for laparoscopic sleeve gastrectomy were enrolled in our study. The patients were assigned to either Group A (13 patients) with clinical hypothyroidism on thyroxin treatment or Group B (20 patients) with euthyroid as control group.

Between the two groups, the sex distribution, the mean age, BMI, and weight confirmed the homogeneity of the sample as shown in Table 1.

Postoperative excess weight loss

There was no significant difference in excess weight loss at 3, 6 and 12 months after surgery between the two groups as shown in Table 2.

Change in thyroxin requirements in group A

The dose of L-thyroxin was significantly decreased (0.0031) from 130.76 ± 49.11(mcg/d) to 69.23 ± 67.81(mcg/d) in 10/13 patients (77%), with complete resolution in 5/13(38.5%), and 5 patients (38.5%) reduced dose, while 3/13 patients (23%) continued on the same preoperative thyroxin dose.

The mean change and percentage change in T4 requirement for all of Group A were 61.53 ± 48.53 mcg (range: 0-150 mcg) and 54.34 ± 42.12% (range: 0-100%), respectively.

The mean change and percentage change in T4 requirement for the subgroup of improved hypothyroidism (IH) were 80 ± 38.72 mcg (range: 25-150 mcg) and 70.65 ± 32.95% (range: 16.5-100%), respectively

Five patients (38.5%) had 40% median reduction of their thyroxin requirements range (16.5%-62.5%). Tables 3 and 4 show changes in T4 requirement in Group A at 1 year.

Comparison between two subgroups of group A

IH and UH. Group A included 13 patients, with ten (10/13) patients (77%) having improvement in postoperative dose (IH) and3/13 patients (23%) continuing on the same preoperative thyroxin dose (UH).

There was no significant difference regarding age, sex, preoperative BMI, thyroxin dose, duration of hypothyroidism, and postoperative EWL between the two subgroups (IH and UH) (Table 5).

Variables	Group A (13)	Group B (20)	P value
Sex(F/M)	10/3	16/4	NS
Age	33.30 ± 9.96	33.45 ± 9.15	NS
Weight	128.15 ± 24.02	122.05 ± 23.69	NS
BMI	49.39 ± 6.56	45.07 ± 7.29	NS

Table 1: Demographic data in the study groups (Data presented in mean ± SD).

EWL (%)	Group A	Group B	P value
3 months	33.2% ± 6.05	34.1% ± 7.13	0.41 NS
6 months	52.14% ± 9.53	49.05 ± 8.45	0.34 NS
12 months	70.23% ± 16.89	72.55% ± 15.9	0.36 NS

Table 2: Comparison of EWL% between two groups (Data presented in mean ± SD).

	Dose
Preoperative thyroxin dose (mcg/d)	130.76 ± 49.11
Postoperative thyroxin dose (mcg/d)	69.23 ± 67.81
Whole change in thyroxin dose (mcg/d)	61.53 ± 48.53
Whole reduction percentage in thyroxin dose	54.34 ± 42.12%
Change in thyroxin dose (mcg/d) in subgroup of IH	80 ± 38.72 mcg
Whole reduction percentage in thyroxin dose in subgroup of IH	70.65 ± 32.95%

Table 3: Change in T4 requirement in Group A at 1 year; data are presented in mean ± SD, IH (improved hypothyroidism).

	Preoperative Dose	Postoperative Dose	Change in thyroxin dose	Percentage of dose reduction
1	100	0	100	100
2	100	0	100	100
3	75	0	75	100
4	50	0	50	100
5	150	0	150	100
6	200	75	125	62.5
7	100	50	50	50
8	125	75	50	40
9	150	125	25	16.5
10	200	125	75	37.5
11	100	100	0	0
12	150	150	0	0
13	200	200	0	0

Table 4: Change in T4 requirement individually in Group Aat 1 year; data are presented in mean ± SD. Thyroxin dose in mcg/d.

	Improved hypothyroidism (IH)	Unchanged hypothyroidism (UH)	P value
Number(percentage)	10/13(77%)	3/13(23%)	
Age (yrs)	31	34	**NS**
Sex(F/M)	8/2	2/1	**NS**
PreoperativeBMI (Kg/m^2)	52	48	**NS**
Preoperative thyroxin dose	125 ± 50	150 ± 50	**NS**
Durationof hypothyroidism(yrs)	8	7	NS
EWL (%) at 1 year	72 ± 17.18%	70 ± 11.13%	NS

Table 5: Comparison between two subgroups of Group A: IH and UH (Data presented in mean ± SD).

Discussion

Insidious hypothyroidism in patients undergoing major surgery can produce severe derangements of normal physiology, including depression of myocardial function and decreased hypoxic and ventilatory responses. Therefore, hypothyroid patients should be given thyroid replacement and be brought into the euthyroid range before major surgery [16].

Hypothyroidism is one of the most common endocrinologic disorders associated with weight gain, with continued weight gain despite normal thyroid function tests; these patients rarely return to their premorbid weight. It has been hypothesized that elevated TSH concentrations stimulate pre adipocyte differentiation, thus inducing adipogenesis [17].

As stated by Reinehr, fat tissue could affect thyroid hormones in a number of ways. First, leptin, an adipocyte-derived hormone, stimulates hypothalamic thyrotropin-releasing hormone (TRH) gene expression. Second, there is a change in deiodinase activity in central and/or peripheral tissue. Third, there is hormone resistance in obese subjects as a result of a euthyroid T3 receptor decrease. Fourth, a partially bioinactive TSH protein in obese subjects has been speculated [18].

Different authors proved decrease in TSH level after bariatric surgery in euthyroid, subclinical hypothyroidism and clinical hypothyroidism.

Abu-Ghanem et al. [15] found significant decrease in TSH with no change in FT4 in patients after LSG compared to results seen after LRYGB by Moulin et al. and Chikunguwoet al. in euthyroid patients [8,9].

Status of subclinical hypothyroidism (SCH) in which there are mildly elevated serum thyrotropin (TSH) and normal levels of free thyroxin (fT4) is usually asymptomatic and found to be present in up to 25% of obese patients during routine preoperative screening [13].

Complete resolution of subclinical hypothyroidism after LRYGB found by Moulin et al. and Chikunguwoet al. and after LSG found by Ruiz-Tovar et al. suggests that, in morbidly obese subjects, SCH is just a consequence of the abnormal fat accumulation and not a real hypothyroid state, indicating that obesity causes TSH elevation rather than the reverse unless thyroid autoimmunity is positive [19].

In our study we found no significant difference in excess weight loss at 3,6 and 12 months after surgery between two groups, so treated hypothyroidism appears not to be a determining factor in the outcome of obese patients regarding postoperative weight loss.

Similar results were reported by Szomstein et al. in which they compared two matched groups of patients: one with clinical hypothyroid and the other with euthyroid, and they revealed no difference in weight loss at 3 and 9 months after LRYGB [1].

In our study the dose of L-thyroxin was highly significantly decreased (0.0031) from 130.76 ± 49.11 (mcg/d) to 69.23 ± 67.81(mcg/d) in 10/13 patients (77%), with complete resolution in 5/13(38.5%); 5 patients (38.5%) had reduction of dose, while 3/13 patients (23%) continued on the same preoperative thyroxin dose.

The mean change and percentage change in T4 requirement for all of Group A were 61.53 ± 48.53 mcg (range: 0-150 mcg) and 54.34 ± 42.12% (range: 0-100%), respectively.

The mean change and percentage change in T4 requirement for the subgroup of improved hypothyroidism (IH) were 80 ± 38.72 mcg (range: 25-150 mcg) and 70.65 ± 32.95% (range: 16.5-100%), respectively.

Five patients (38.5%) had 40% median reduction of their thyroxin requirements range (16.5-62.5%).

The supplemental T4 dose was gradually reduced, and serial TSH assays were continued until the TSH value reached a mid-normal range (i.e., 2.0-3.0 mIU/L; normal 0.3-5.5 mIU/L).

There was no significant difference regarding age, sex, preoperative BMI, thyroxin dose, duration of hypothyroidism, and postoperative EWL between patients who reduced or stopped thyroxin and patients who continued on the same preoperative dose.

In study by Aggarwal [14], the absolute mean change percentage in T4 requirement was 42.07% (12-100%) after LSG in 68.4% of hypothyroid patients with dose reduction, while 31.6% patients remained with the same preoperative dose with whole mean change percentage 28.78% (range 0-100%).

Fazylov et al. [4] have shown a decrease in postoperative L-thyroxine dosage after LRYGB for morbid obese patient with clinical hypothyroidismin 35% of patients (25% complete resolution and 10% reduction in dose) in dose unchanged in 40% of patients and worsened in 25% of patients with thyroid autoimmune disease.

Raftopoulos' series [5] reported that post-LRYGB hypothyroidism improved and thyroxine requirements were reduced in 10 of the 23 patients (43.5%). Two of the 23 patients (8.7%) had complete resolution and the remaining 8 patients (34.8%) had reduction (14%-50%, median 33%) of their thyroxine requirements; 13 of the 23 patients (56.5%) had no change in their thyroxine requirements.

In study by Janković et al. [20], which included 44 patients with clinical hypothyroidism and 32 with subclinical hypothyroidism, they found normalization of the TSH levels after weight loss by bariatric surgery; they did not specify the type of surgery or change in thyroxin requirements.

The exact mechanism of improvement of thyroid dysfunction status after bariatric surgery related not only to weight loss but also to the hormonal change after LSG, LRYGB as hypothesized by different studies in which the level of TSH reduction was not directly correlated to the EWL [4,8,15].

A reduction in leptin levels following the weight loss induced by bariatric surgery would lead to a reduction in this TSH secretion [21].

A recently published paper has shown that circulating ghrelin levels significantly correlated with TSH levels [22]. Since ghrelin levels were shown to be suppressed following LRYGB and LSG but not after LAGB, these procedures which exclude fundus may have an added effect in improving thyroid function over weight loss alone [23] and this may explain why in Dall'Asta et al.'s study, in patients undergoing LAGB, TSH levels did not change 6-24 months following the operation [7].

Limitations of our study are small sample size and short term follow up. Many issues still needed to be elucidated at larger studies including weight loss at long-term follow up and the exact mechanism leading to a decrease in TSH following bariatric surgery.

Conclusion

Improvement of clinical hypothyroidism after laparoscopic sleeve gastrectomy was evidenced by a reduction in T4 requirement with comparable weight loss to euthyroid patients at short-term follow up.

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