



Dietary Iodine Absorption is not Influenced by Malabsorptive Bariatric Surgery

M. Michalaki · S. Volonakis · I. Mamali ·
F. Kalfarentzos · A. G. Vagenakis · K. B. Markou

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Abstract

Background Bariatric surgery is accompanied by malabsorption of protein, carbohydrates, fats, vitamins, and trace elements. Iodine is essential to the synthesis of thyroid hormones. The aim of this study was to estimate the daily iodine intake in severely obese patients before and after bariatric surgery.

Methods Thirty-five severely obese patients (obese group) with a BMI of $51.3 \pm 8.3 \text{ kg/m}^2$ were studied before, 3 months, and 6 months after bariatric surgery. Eleven out of 35 patients were subjected to gastric bypass operation Roux-en-Y and 24 were subjected to a variant of biliopancreatic diversion with long limb procedure. The patients did not use any iodine supplements and no iodine antiseptics were administered during the operation. The messmates of the patients, following a similar diet (control group) with a BMI of $31.2 \pm 10.7 \text{ kg/m}^2$, were also studied. Serum T_3 , T_4 , TSH, thyroid peroxidase antibodies, urinary iodine excretion (UIE) in a spot urine, and thyroid volume were measured in all subjects, at baseline and at 3- and 6-month follow-up in the obese group.

Results UIE at baseline was similar in obese and control group (median (min-max), 129.5 (24.9–462) vs. 138.9 (30.8–381) $\mu\text{g/L}$, ns). In the obese group, a transient increase of UIE was observed 3 months after the operation and returned to baseline levels 6-months postsurgery.

Conclusions The UIE is not reduced after malabsorptive bariatric surgery, although all stomach, duodenum, and a

substantial part of jejunum were bypassed. It appears that iodine is absorbed sufficiently along the remaining gastrointestinal tract.

Keywords Urinary iodine excretion · Bariatric surgery · Intestinal iodine absorption · Thyroid function · Obesity

Introduction

According to the National Health and Nutrition Examination survey, in the US in 2009–2010, the age-adjusted prevalence of grade 3 obesity in adults was 6.3 % [1]. Nowadays, bariatric surgery is considered an effective and safe intervention of severe obesity, and nearly 130,000 operations have been performed annually in the last decade in the US [2]. Bariatric operations, especially those with a malabsorptive component, result to malnutrition of proteins, carbohydrates, fats, vitamins, and trace elements such as iron and calcium [3]. Iodine is a trace element essential to the synthesis of thyroid hormones. Absorption of dietary iodine takes place in the small intestine and is the first step in iodide (I^-) utilization. Iodide is actively transported via the Na^+/I^- symporter (NIS) from the plasma into the thyroid for thyroid hormone biosynthesis and into other tissues such as lactating breast, which subsequently supplies I^- to the newborn via the milk [4]. Only a limited number of studies have been carried out, mainly conducted on animals, concerning iodine absorption from the gastrointestinal tract.

There are no available analytical techniques to directly measure an individual's daily iodine status. Urinary iodine excretion (UIE) reflects dietary iodine intake within the past few days. In general, as a clinical biomarker, UIE is not useful in classifying the intake sufficiency or deficiency in an individual, but rather to define the risk of a population. UIE measurement in 24-h urine collection is preferred, but iodine

M. Michalaki · S. Volonakis · I. Mamali · A. G. Vagenakis ·
K. B. Markou (✉)

Division of Endocrinology, Department of Internal Medicine,
University of Patras Medical School, Thisseos 6, Ovia,
Patras 26500, Greece
e-mail: markoukonst@upatras.gr

F. Kalfarentzos
Division of Nutritional Support and Morbid Obesity, Department of
Surgery, University of Patras Medical School, Patras, Greece

excretion could also be expressed in spot urine samples in population groups with very low inter- and intraindividual variation.

The aim of this study was to estimate the iodine daily intake, using UIE measurements, in individuals with severe obesity at baseline and after bariatric surgery in which several parts of intestine were bypassed.

Materials and Methods

Patients-Study Design

We studied 35 consecutive patients with severe obesity, candidates for bariatric surgery from the surgical department of our hospital. The severely obese patients (obese group) aged 40.7 ± 9.2 years, with a BMI of $51.3 \pm 8.3 \text{ kg/m}^2$, were studied before (baseline), 3 months, and 6 months after the bariatric surgery. Prior to and following surgery, the patients did not receive any iodine supplement, and no iodine antiseptics were used during the operation. Eleven out of the 35 patients were subjected to gastric bypass operation Roux-en-Y (RYGBP) and 24 were subjected to a variant of biliopancreatic diversion with long-limb (BPD-LL) procedure [5]. The 35 partners/messmates (control group) who lived in the same house and followed similar daily diet aged 43.4 ± 8.6 years and BMI $31.2 \pm 10.7 \text{ kg/m}^2$ were also studied. All participants were euthyroid and had negative thyroid peroxidase antibodies (TPO-abs). Serum T_3 , T_4 , TSH, TPO-abs, and UIE in a spot urine sample and thyroid volume were measured at baseline for all participants. In the obese group, T_3 , T_4 , TSH, UIE, creatinine clearance (eGFR), and thyroid volume were measured also at 3- and 6-months postsurgery. The eGFR was calculated by the modification of diet in renal disease (MDRD 6) formula. Thyroid volume was estimated by ultrasonography, according to the formula $d1 \times d2 \times d3/2$ [6]. Postoperatively, the patients received a very low calorie diet of approximately 800 kcal/day for up to 6 months.

Types of Bariatric Surgery

The types of applied bariatric surgery have been described elsewhere [7]. In brief, the RYGBP procedure included a small gastric pouch of $15 \pm 5 \text{ ml}$, a biliopancreatic limb of 50 cm, and an alimentary limb of 150 cm. The BPD-LL was a variant of BPD and was the procedure of choice for the super-obese patients ($\text{BMI} > 50 \text{ kg/m}^2$). The main outcomes of the BPD-LL procedure were a gastric pouch of 60 ml, a common limb of 100 cm, an alimentary limb that was almost always equal to 400 cm, and the remainder of the small intestine as the biliopancreatic limb [5]. Cholecystectomy was performed during every bariatric procedure, with the addition of appendectomy in the BPD-LL procedure.

Assays

Serum T_3 , T_4 , TSH, and thyroid peroxidase antibodies were measured by chemiluminescence immunoassays (E170 Module for Modular Analytics; Roche Diagnostics GmbH, Mannheim, Germany). Reference range; T_3 : 0.8–2.0 mg/ml, T_4 : 5.1–14.1 $\mu\text{g/dl}$, TSH: 0.270–4.2 $\mu\text{IU/ml}$, and TPO-abs: $< 34 \text{ IU/ml}$. The samples were assayed in a single large batch. The intrarun and interrune coefficients of variance were 1.5–3.1 and 1.3–1.7 % for T_3 , 1.1–3.0 and 3.7–4.5 % for T_4 , and 3.4–4.2 and 3.3–7.2 % for TSH, respectively. UIE was measured by the spectrophotometric method (Sandell–Kolthoff reaction, after digestion with ammonium persulfate at 90–100 °C for 1 h) [8]. Our laboratory is verified by the Ensuring the Quality of Urinary Iodine Procedures (EQUIP).

Statistics

Values of UIE are expressed as median (min-max) and all the rest values as mean \pm SD. Statistical significance was set at a p value of < 0.05 . The normality of parameters distribution was checked by One-Sample Kolmogorov–Smirnov test. If the parameters distributions were normal, parametric tests were used. Comparisons between control and obese group at

Table 1 Comparison between control and obese group at baseline

	Control group	Obese group	<i>p</i>
<i>n</i>	35	35	
Age (years)	40.7 ± 9.2	43.4 ± 8.6	ns
BMI (kg/m^2), mean \pm SD	31.2 ± 10.7	50.7 ± 8.5	< 0.001
UIE ($\mu\text{g/l}$), median (min-max)	138.9 (30.8–381)	129.5 (24.9–462)	ns
TSH ($\mu\text{IU/ml}$), mean \pm SD	1.47 ± 0.94	2.02 ± 0.97	< 0.01
T_3 (ng/ml), mean \pm SD	1.3 ± 0.21	1.36 ± 0.28	ns
T_4 ($\mu\text{g/dl}$), mean \pm SD	8.55 ± 1.52	8.92 ± 1.57	ns
V thyroid (ml^3), mean \pm SD	$1,0847 \pm 6,039$	$10,467 \pm 4,817$	ns

Data were analyzed by independent samples *t* test

ns Not significant

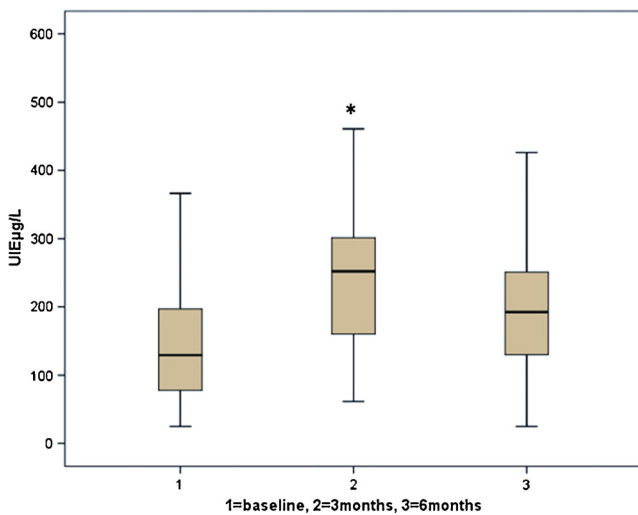


Fig. 1 In obese group, UIE transiently increased 3-months postnalabsorptive bariatric surgery

baseline were analyzed by independent samples *t* test. Variation of UIE, thyroid hormones, thyroid volume, and eGFR in obese group at baseline, 3 months, and 6 months postbariatric surgery was analyzed by ANOVA for repeated measurements and Bonferroni test for post hoc comparisons. Data were analyzed by IBM SPSS statistics 21.

Results

BMI in the obese group was higher than in the control group (Table 1). Body weight was substantially reduced in the obese group at 3- and 6-months postsurgery (ANOVA for repeated measurements, *p*<0.001; baseline: 149.6±30.4 vs. 3 months: 115.6±22.5 kg, *p*<0.001; baseline: 149.6±30.4 vs. 6 months: 99.65±20.2 kg, *p*<0.001; 3 months: 115.6±22.5 vs. 6 months: 99.65±20.2 kg, *p*<0.001).

Table 3 Variation of thyroid function tests and volume in obese group at baseline, 3 months, and 6 months postbariatric surgery

	Baseline	3 months	6 months	<i>p</i>
T3 (ng/ml)	1.36±0.28 ^a	1.15±0.26	1.16±0.2	<0.001
T4 (µg/dl)	8.93±1.57	8.41±1.47	8.38±1.51	ns
TSH (µIU/ml)	2.02±0.97	2.17±1.25	2.4±1.06	ns
V thyroid (ml ³)	10,467±4,817	8,382±2,867	7,614±2,886 ^b	<0.05

Values are expressed as mean ± SD. Data were analyzed by ANOVA for repeated measurements and Bonferroni test for post hoc analysis

^aT3 at baseline is significantly higher than 3 and 6 months

^bV thyroid at 6 months is significantly lower than baseline

UIE Measurements

Before bariatric surgery, UIE was similar in obese and control groups (obese group 129.5 (24.9–462) vs. control group 138.9 (30.8–381) µg/l, ns; Table 1). In all subjects of the entire obese group, a transient increase of UIE was observed at the 3-month follow-up compared to baseline and the 6-month values (ANOVA for repeated measurements, *p*<0.01, post hoc analysis by Bonferroni test, 3 months: 252.05 (61.4–461) µg/l vs. baseline 129.5 (24.9–462), *p*<0.01; 3 months: 252.05 (61.4–461) vs. 6 months: 192.25 (24.9–500.6) µg/l, *p*<0.05) and returned to baseline levels 6 months after the surgery (6 months: 192.25 (24.9–500.6) vs. baseline: 129.5 (24.9–462), µg/l, ns; Fig. 1 and Table 2). Similar variation of UIE was observed in the BPD-LL and RYGBP subgroups (Table 2).

Thyroid Function Tests

Mean TSH levels were higher in the obese group compared to controls (obese group 2.02±0.97 vs. control group 1.47±0.94 µIU/ml; *p*<0.01), whereas T₃, T₄, and thyroid volume did not differ (Table 1). In the obese group, the preoperative

Table 2 UIE in obese group and BPD-LL and RYGBP subgroups, at baseline, 3 months, and 6 months postbariatric surgery

UIE (µg/l) median (min-max)	Baseline	3 months	6 months	<i>p</i>
Obese group (<i>n</i> =35)	129.5 (24.9–462)	252.05 (61.4–461) ^a	192.25 (24.9–500.6)	<0.01
BPD-LL subgroup (<i>n</i> =24)	128.9 (45.5–462)	238.7 (61.4–460) ^b	183.1 (24.9–500.6)	<0.01
RYGBP subgroup (<i>n</i> =11)	136.3 (24.9–366.3)	280.6 (94–461) ^c	255.2 (67.1–426.1)	<0.05

Values are expressed as median (min-max). Data were analyzed by ANOVA for repeated measurements and Bonferroni test for post hoc analysis

^aUIE at 3 months is significantly higher than baseline and 6 months

^bUIE at 3 months is significantly higher than 6 months

^cUIE at 3 months is significantly higher than baseline

serum T₃ concentration and thyroid volume were higher than 3- and 6-months postsurgery, whereas T₄ and TSH and eGFR did not differ (Table 3).

Discussion

In the present study, we observed that UIE did not decrease 3- and 6-months postmalabsorptive bariatric procedures, indicating that the remaining gastrointestinal tract is capable of sufficiently absorbing the daily iodine intake. Surprisingly, the UIE increased 3 months after surgery and returned to baseline values 6 months later, despite the reduced postsurgery daily calorie intake and the subsequent lower dietary iodine intake with foods.

Few studies, mainly in animals, have thus far examined the physiology of intestinal absorption of iodine. Studies in rats in the 60s suggested that iodine is passively absorbed in the small bowel [9]. In humans, it has been reported that iodide is an important component of intestinal iodine excretion [10]. New insights into the iodine physiology rose with the discovery of NIS to the thyroid gland [11]. NIS was located in many extrathyroidal human tissues thereafter, such as in the lactating mammary gland, gastric mucosa, and salivary gland [12]. NIS activity in thyroidal cells is inhibited by excess iodide known as “Wolff–Chaikoff effect” [13, 14]. The transport of iodide via NIS in thyroidal cells is Na⁺-dependent [11] and inhibited by perchlorate (ClO₄⁻) [4]. The molecular basis of intestinal I⁻ absorption remains unknown and little is known on the regulation of intestinal NIS protein. Recently, Nicola et al. have found that NIS is functionally expressed in the apical surface of the brush border of intestinal enterocytes in rodents and mediates the active iodide transport from lumen to the bloodstream [4]. However, immunohistochemical studies in the human small intestine failed to locate NIS perhaps due to methodological differences [15]. The rodent intestinal NIS is also regulated by dietary iodide. Diet enriched with iodine reduced the expression and activity of intestinal NIS protein at posttranscriptional level in a dose-dependent manner and decreased the intestinal iodine absorption [4, 16]. Another candidate for intestinal iodine absorption could be the Na⁺/multivitamin transporter (SMVT), which is universally expressed in all human tissues, including intestine. A recent study in cell cultures has shown that Na⁺-coupled I⁻ uptake is carried via SMVT, and it is proposed that it is a complementary pathway for iodide absorption to the small intestine [17].

The unexpected finding of the transient increase of UIE 3 months after malabsorptive bariatric surgery is not readily explained, especially in the face of the reduced functional intestine. We hypothesize that the numerous surgical anatomic rearrangements of the gut structure modified the secretion of the gut hormones [3], the enterohepatic circulation physiology [18], and the flora [19, 20] of the gastrointestinal tract in the

early postsurgical period. This may transiently affect the environment of the intestinal lumen and consequently the regulation of NIS. The subsequent normalization of UIE at 6-months postsurgery might be a result of the reset of iodine kinetic model between thyroid, serum, urine, and feces. Further studies are needed to clarify this issue.

We found that mean TSH levels were higher in the obese group at baseline compared to controls, whereas T₃ and T₄ were not different. It is known that higher values and enhanced diurnal variation of TSH are observed in obese subjects [21, 22]. The rise of TSH in obesity could be in part explained by the central stimulatory effect of higher leptin levels that occurred in obese subjects on hypothalamic TRH neurons [23]. In contrast, weight loss either by a very low calorie diet or RYGBP bariatric procedure is accompanied by a fall of serum leptin, TSH, and T₃ [24, 25]. Our patients who received a very low calorie diet for up to 6-months postsurgery and lost substantial weight had a decrease in serum T₃ at this time point, whereas serum TSH remained unchanged until the end of the observational period.

Thyroid volume gradually decreased postoperatively accompanying the weight loss and the lean body mass. Lean body mass is linearly related to thyroid volume [26].

Our study has a number of limitations. First of all, further studies are needed which include a larger sample size. Additionally, patients who underwent RGYB should be separated from those who underwent BPD-LL. Finally, lean controls should be included in order to clarify potential discrepancies in iodine levels based upon BMI.

To conclude, the urinary iodine excretion in humans is not reduced after malabsorptive bariatric surgery, although all stomach, duodenum, and a substantial part of jejunum were bypassed. It seems that iodine is sufficiently absorbed along the remaining gastrointestinal tract.

Conflict of Interest Michalaki M., Volonakis S., Mamali I., Kalfarentzos F., Vagenakis A.G., and Markou K.B. have no conflict of interest.

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