SURGERY FOR OBESITY AND RELATED DISEASES

Surgery for Obesity and Related Diseases 13 (2017) 227–233

Original article

Improvement of anthropometric and biochemical, but not of vitamin A, status in adolescents who undergo Roux-en-Y gastric bypass: a 1-year follow up study

Jacqueline Souza Silva, Ph.D.[a], Gabriela Villaça Chaves, Ph.D[b,*], Ana Paula Stenzel, M.D.[a], Silvia Elaine Pereira, Ph.D.[a], Carlos José Saboya, Ph.D.[c], Andréa Ramalho, Ph.D.[d]

[a]Center for Research on Micronutrients, Institute of Nutrition, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
[b]National Cancer Institute, Rio de Janeiro, Brazil
[c]Surgical Clinic, Center for Research on Micronutrients, Institute of Nutrition, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
[d]Department of Social and Applied Nutrition, Center for Research on Micronutrients, Institute of Nutrition, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil

Received July 12, 2016; accepted September 5, 2016

Abstract

Background: The aim of this study was to describe anthropometric, biochemical, co-morbidity, and vitamin A nutritional status in severely obese adolescents before and 30, 180, and 365 days after Roux-en-Y gastric bypass (RYGB).
Setting: Federal University of Rio de Janeiro, Rio de Janeiro, Brazil.
Methods: Sixty-four adolescents (15–19 years old) with a body mass index $\geq$40 kg/m^2 were enrolled in a prospective follow-up study. Vitamin A status was evaluated before surgery (T0), and 30 (T30), 180 (T180), and 365 (T365) days after surgery, applying biochemical and functional indicators. Anthropometric measures, lipid profile, glycemia, and basal insulin also were assessed. No patients were lost during follow-up.
Results: Before surgery, 26.6% of the sample group experienced vitamin A deficiency (VAD). Serum retinol levels dropped significantly 30 days after surgery and then returned to basal levels. There was a significant increase in the prevalence of β-carotene deficiency and night blindness throughout the postsurgery period. A significant reduction in blood glucose, insulin resistance, lipid profile, and anthropometric parameters was observed.
Conclusion: The finding that oral daily supplementation with 5000 IU retinol acetate failed to reverse VAD and night blindness after RYGB is highly significant. We recommend assessment of VAD and night blindness in extremely obese adolescents before and after RYGB. We further recommend monitoring for an additional 180 days (for VAD) and 365 days (for night blindness) after surgery, with particular attention to daily supplementation needs. (Surg Obes Relat Dis 2017;13:227–233.)

Keywords: Bariatric surgery; Vitamin A; Nutritional status

Severe obesity is the fastest-growing subgroup of obesity in youth worldwide. In the United States, the percentage of obese adolescents aged 12 to 19 years increased from 5% to 21% from 1998 to 2012 [1]. Adolescents with morbid obesity are at higher risk of developing chronic, noncommunicable diseases, which are the leading cause of

This study received a grant from Fundação de Amparo a Pesquisa do Rio de Janeiro.

*Correspondence: Gabriela Villaça Chaves, Ph.D., Rua General Ribeiro da Costa, 90/604, Leme, Rio de Janeiro, Brazil.
E-mail: gabrielavc@gmail.com

http://dx.doi.org/10.1016/j.soard.2016.09.002
1550-7289/

mortality in the general population in developed and developing countries [2]. In Brazil, these diseases account for approximately 70% of mortality [3]. Thus, the control of obesity in this age group is critical.

Clinical treatment usually is ineffective in cases of extreme obesity, and bariatric surgery, as part of a multidisciplinary treatment approach, is justified as the only way of controlling such obesity in the medium and long term [4]. Roux-en-Y gastric bypass (RYGB) commonly is used to control extreme obesity in adolescents [4,5]. RYGB is a combined restrictive and malabsorptive technique that generally leads to evident benefits to the quality of life of obese patients [6] and is considered to be a safe and effective surgical procedure for extremely obese adolescents [4].

However, despite the long-term loss of excess weight and improvement in related diseases [7,8], metabolic disorders stemming from the surgical procedure may lead to micronutrient deficiencies as a result of the significant drop in digestive enzymes and loss of nutrient absorption sites that result from the reduction of the gastric reservoir and subsequent hypochlorhydria associated with total removal of the duodenum and proximal jejunum. This promotes deficiencies in nutrients [6], including vitamin A [9].

Although RYGB has been associated with deficiencies in fat-soluble vitamins, there is no published data on the vitamin A nutritional status of adolescents who have undergone bariatric surgery. Vitamin A acts on immunologic activity, reproduction, growth, development, sexual maturation, visual acuity, cellular proliferation, and differentiation, among other functions. It is essential in adolescence, which is a biological moment of intense nutritional demand [10].

Currently there is no recommended daily allowance after bariatric surgery in adolescence. However, there is evidence suggesting that commonly consumed supplements containing 5000 IU are not effective in preventing night blindness (NB) and increased deficiency during RYGB postoperative periods in adults [11–13].

The aim of this study, therefore, was to describe the anthropometric, biochemical, co-morbidity, and vitamin A nutritional status in severely obese adolescents before and 30, 180, and 365 days after RYGB.

Methods

This was a prospective, longitudinal study with a sample group of extremely obese adolescents, who were evaluated in the preoperative period (T0) and 30 (T30), 180 (T180), and 365 (T365) days after RYGB. The sample group consisted of all adolescents who were treated and subsequently deemed eligible for surgery at a private hospital in Rio de Janeiro, Brazil. The group included males and females with a body mass index (BMI) $\geq$40 kg/m² who were between the ages of 15 and 19 years, on the basis of the World Health Organization (WHO) classification for adolescents and given the recommendation that RYGB surgery in severely obese adolescents should respect the minimum age of 14 and 15 years for girls and boys, respectively, due to peak bone mass constitution [14].

Exclusion criteria included patients who had already undergone prior restrictive and malabsorptive surgery, preoperative use of multivitamins and lipid-lowering drugs, postoperative use of other multivitamins in addition to those prescribed, pregnant or lactating females, cancer, and malabsorptive illnesses. There was no loss of participants during the follow-up period, and all participants completed the 365 days of accompaniment.

We collected data between January 2011 and July 2013. The study was approved by the University Hospital research ethics committee (Research Protocol No. 011/06 - CEP). Patients were included via written consent from their legal guardians in the form of an obligatory term of informed consent. Among the requirements listed in the document was a commitment to taking the daily 5000 IU retinol acetate oral supplementation that is routine protocol at the private hospital after RYGB. The technique used for RYGB was the long-limbed procedure.

Patients underwent clinical, anthropometric, and biochemical evaluations before and after surgery. Adherence to the supplementation regimen was evaluated through self-reporting, which included information regarding supplementation-specific issues, such as acceptance, reports on days and quantities taken, interruption of use, and clinical complications.

Weight, height, and waist circumference (WC) were used as anthropometric indicators, and trained specialists took measurements in duplicate. Weight and height values were used to calculate BMI, and BMI values $\geq$40 kg/m² indicated extreme or severe obesity [14].

To assess vitamin A status, a 5 mL blood sample was obtained by vein puncture of patients after a 12-hour fast to determine the serum levels of retinol and β-carotene. High-performance liquid chromatography–ultra violet was used for retinol and β-carotene quantification. Serum values of retinol were compared with the normality cutoffs proposed by WHO (International Vitamin A Consultative Group/WHO) [15], which are classified in .35 μmol/L intervals. Thus, vitamin A deficiency according to serum retinol levels was classified as severe ($<$.35 μmol/L), moderate ($\geq$.35–$<$.70 μmol/L) and mild ($\geq$.70–$<$1.05 μmol/L). In the study presented here, a serum retinol value $\geq$1.05 μmol/L was considered as adequate and $<$1.05 μmol/L was the cutoff used to indicate vitamin A deficiency (VAD). As suggested by Sauberlich et al. [16], the cutoff to indicate inadequacy of serum values of carotenoids was $\leq$40 μg/dL.

For functional evaluation, we evaluated for NB using a standardized interview by WHO [17], which has been validated for morbidly obese patients with the gold standard assessment of hepatic liver stores of vitamin A, as described by Pereira et al. [18]. NB interviews included the following questions: (1) Do you have difficulty in seeing during the day? (2) Do you have difficulty in seeing in poor light or at night? (3) Do you have NB?

Other laboratory tests were performed for assessment of the following lipid profile and biochemical parameters: cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, glycemia, and basal insulin. Insulin resistance (IR) was determined using the homeostasis model assessment (HOMA) index method [19] through the calculation of HOMA-IR = insulinemia after fasting (mU/L)/ glycemia after fasting (mmol/L)/22.5.

Diagnosis of systemic arterial hypertension was determined by a physician, according to the V Brazilian Guidelines of Arterial Hypertension guideline [20], which is in accordance with the American Heart Association's current guideline for arterial hypertension diagnosis and management.

RYGB was performed laparoscopically by creating a small (20–30 mL), vertically oriented gastric pouch immediately distal to the gastroesophageal junction. The jejunum was divided 25 to 50 cm distal to the ligament of Treitz and a Roux limb of 75 to 150 cm was created, which was anastomosed to the gastric pouch using a hand-sewn technique, resulting in a 1 cm gastrojejunal stoma. A jejunojejunostomy was performed in a stapled side-to-side fashion to complete the Roux-en-Y reconstruction.

Statistical analysis was performed using Statistical Package for Social Sciences for Windows, version 20.0, with a significance level of 5%. Measures of central tendency and dispersion were calculated with the means and standard deviation values of the continuous variables. The distribution of the referred values was identified as normal. Associations between the categorical variables were performed using the χ^2 test. The 1-way repeated measures analysis of variance test was used to evaluate the behavior of continuous variables during the follow-up period. The Bonferroni correction was used to identify which intervals were significantly different for each group. Cochrane Q tests and McNemar post hoc tests were used to compare differences in categorical variables within the follow-up period.

Results

The sample group consisted of 64 teenagers, of whom 65.6% were female and 34.4% were male. Mean age was 16.94 ± 1.46 years, ranging from 15 to 19 years.

Before surgery, 26.6% of the sample group had serum retinol levels below the <1.05 μmol/L cutoff point. After dividing them into class intervals to identify the severity of VAD, 18.8% were borderline deficient and 7.8% were moderately deficient at T0. After RYGB, the prevalence of VAD increased, with a larger number of adolescents classified as experiencing more severe deficiency (Fig. 1).

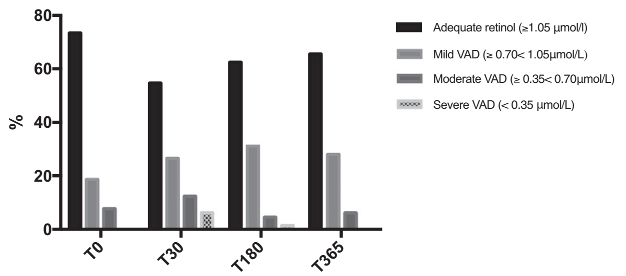

Fig. 1. Frequency of vitamin A deficiency (VAD) before and after Roux-en-Y gastric bypass. T0, preoperative; T30, 30 days postoperative; T180, 180 days postoperative; T365, 365 days postoperative.

There was no significant association between adequacy of retinol or β-carotene serum levels and the prevalence of NB after surgery for most of the study period (χ^2 test; $P > .05$), even though the frequency of NB increased from 10 (T0) to 33 patients (T30) among those with adequate serum retinol before RYGB, whereas NB frequency at T30 among patients with VAD at T0 remained unchanged (n = 4) ($\chi^2 = 11.11$; $P < .001$).

Serum retinol levels dropped significantly 30 days after surgery and then returned to basal levels. There was a significant decrease of serum β-carotene levels 30 days after RYGB, which remained unchanged throughout the study period (Table 1).

By separating the groups according to retinol adequacy before RYGB, we found an intriguing result—those with adequate retinol serum levels at T0 experienced an abrupt drop at T30, with a nonsignificant increase in subsequent evaluations (T180 and T365). On the contrary, those with retinol deficiency at T0 demonstrated a significant increase in serum levels at T30, with further decreases at T180 and T365 (Table 2). At T365, serum levels of retinol comparison demonstrated no statistical difference between the 2 groups (Student's t test, $P = .253$).

Adherence to the supplementation routine was 100% at T30 and 71.4% at T180 and T365. One of the main reasons reported for not taking the supplement daily was forgetfulness. There were no reports of gastrointestinal problems or complaints related to hypervitaminosis during follow-up.

In terms of other biochemical parameters evaluated, there was a significant reduction in blood glucose, triglycerides, and low-density cholesterol throughout the study period compared with T0. HOMA-IR demonstrated a significant reduction 180 days after RYGB. High-density cholesterol dropped 30 days after surgery and returned to basal levels at 365 days. With regard to anthropometric parameters, both BMI and WC remained significantly reduced throughout the evaluation period (see Table 1).

The prevalence of hypertension also demonstrated a significant drop, from 65.6% (T0) to 15.6% (T365) (Cochrane Q test; $P < .001$) (Fig. 2).

Assessing the adequacy of serum retinol and β-carotene according to the existing cutoffs, we observed that there

Table 1
Changes in vitamin A status and biochemical and anthropometric parameters before and after Roux-en-Y gastric bypass

Variables	T0	T30	T180	T365	*P* value*
Retinol (μmol/L)	1.51†±.14	1.13‡±.58	1.21†±.49	1.24†±.50	.020
β-carotene	35.11†±25.05	20.50‡±12.83	22.82‡±14.88	22.26‡±12.87	.003
Glucose (mg/dL)	96.90†±15.02	90.48‡±11.44	87.40‡±10.49	87.50‡±7.06	< .001
HOMA-IR	3.57†±1.64	4.40†±12.51	1.25‡±.56	1.56‡±1.2	< .001
Triglycerides (mmol/L)	129.50†±52.52	89.56‡±32.63	79.39§±20.64	102.25‡±37.72	< .001
LDL cholesterol (mmol/L)	123.00†±33.44	101.59‡±26.00	98.15‡±28.68	100.15‡±26.56	< .001
HDL cholesterol (mmol/L)	46.54†±9.97	41.26‡±10.75	48.09†±8.14	46.62†‡±8.96	0.005
Body mass index (kg/m^2)	45.79†±7.15	40.52‡±6.35	30.22§±4.90	27.60¶±4.45	< .001
Waist circumference (cm)	124.25†±13.73	114.25‡±14.95	95.10§±12.51	86.85¶±9.55	< .001

HOMA-IR = homeostasis model assessment index-insulin resistance;; LDL = low-density lipoprotein; T0, T30, T180 and T365 = before and 30, 180, and 365 days after RYGB; HDL = high-density lipoprotein.
Values with the same footnote (†, ‡, §, and ¶) are not significantly different from each other (Bonferroni test, *P* value < .05).
*Two-way analysis of variance for repeated measures test within each variable (time effect).

was no statistical difference in the prevalence of VAD after RYGB. However, there was a significant increase in the prevalence of β-carotene deficiency and NB throughout the postsurgery period (Table 3).

Discussion

Vitamin A plays an important role in several human functions and is essential in adolescence, especially during the biological moment of intense nutritional demand. Among other functions, vitamin A acts on growth and development [10]. Adolescents are not considered a population at risk of VAD, and little research has been conducted on VAD in this age group. Ours is the first study to assess vitamin A nutritional status using biochemical and functional indicators in extremely obese adolescents before and after RYGB.

The VAD rate at T0 was 26.6% according to the indicator serum retinol, with a mean of 1.51 ± .14 μmol/L. This percentage rate of deficiency is higher than that found by De Souza et al. [21], who assessed overweight 10- to 17-year-olds and found 12.6% of the sample group to be deficient in retinol. Ramalho et al. [22], who evaluated vitamin A nutritional status in 574 children and teenagers in the 7 to 17 age group, found inadequate serum retinol concentrations in 10.3% of them, with a mean of 1.66 ± .61 μmol/L. It is important to point out that these studies [22,23] addressed sample groups of predominantly healthy and overweight BMI ranges, whereas we focused on extreme obesity.

We also found 65.6% of the sample group to be deficient in β-carotene, according to the β-carotene at T0 indicator. β-carotene is considered the most potent retinol precursor and a powerful free radical scavenger [24,25]. The drop in β-carotene serum levels probably can be explained by the increased oxidative stress to which severely obese individuals are exposed, resulting in the greater demand for antioxidant nutrients [9]. Furthermore, it has been postulated that in a retinol-deficiency setting, the increase in β-carotene conversion to retinol may explain the higher rate of β-carotene deficiency compared with retinol deficiency [18].

The high rates of retinol and β-carotene deficiency reinforce the importance of ensuring that there is adequate serum retinol to preserve the function of β-carotene as an antioxidant. This function becomes even more prominent in

Table 2
Response of the serum retinol levels (μmol/L) according to retinol adequacy before Roux-en-Y gastric bypass

Group	Time	Mean ± SD	*P* value*	*P* value†
Adequate retinol ≥1.05 μmol/L (n = 47)	T0	1.76‡±.57	.04	.001
	T30	1.07§±.55		
	T180	1.14§±.42		
	T365	1.27§±.48		
Inadequate retinol <1.05 μmol/L (n = 17)	T0	0.82‡±.14	.01	
	T30	1.33§±.62		
	T180	1.40§±.62		
	T365	1.19§±.59		

SD = standard deviation.
For all variables with the same footnote symbol (‡ or §), the difference between the means is not statistically significant.
*The 2-way repeated measures analysis of variance test within each group (time effect).
†The 2-way repeated measures analysis of variance test between the 2 groups (interaction effect = group × time).

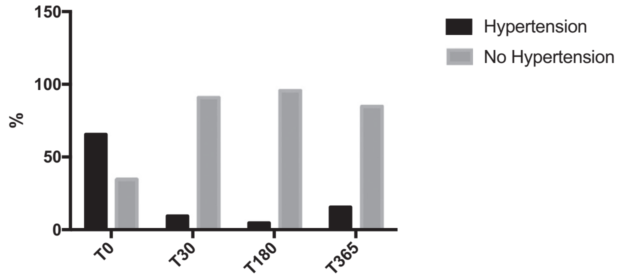

Fig 2. Frequency of hypertension before and after Roux-en-Y gastric bypass (in days).

Table 3
Comparison of adequacy of vitamin A status before and after Roux-en-Y gastric bypass

	T0		T30		T180		T365		*P* value*
	Adequate n (%)	Inadequate n (%)	Adequate n (%)	Inadequate n (%)	Adequate n (%)	Inadequate n (%)	Adequate n (%)	Inadequate n (%)	
Serum retinol	47 (73.4)	17 (26.6)	35 (54.7)	29 (45.3)	40 (62.5)	24 (37.5)	42 (65.6)	22 (34.4)	.189
Serum β-carotene	22 (34.3)	42 (65.6)	7 (10.9)	57 (89.1)	12 (18.8)	52 (81.3)	8 (12.5)	56 (87.5)	.002
Night blindness	50 (78.1)	14 (21.9)	27 (42.2)	37 (57.8)	35 (54.7)	29 (45.3)	28 (43.8)	36 (56.3)	< .001

T0, T30, T180, and T365 = before and 30, 180, and 365 days after Roux-en-Y gastric bypass.

*Cochrane *Q* test; the McNemar post hoc test demonstrated significant differences for β-carotene and night blindness frequencies comparing T0 to T30, T180, and T365.

severely obese individuals because obesity can be associated with increased oxidative stress and chronic inflammation, which in turn causes increased demand for antioxidant nutrients. Additional factors to consider are the anatomic changes after surgery and the high nutritional demand of adolescents [25].

NB is the first functional manifestation of VAD and is characterized by a change from the usual pattern of vision in dim lighting or at night and by difficulty in adapting to shifts from lit environments to darkness [26]. NB was demonstrated in 21.9% of the sample group at T0, and this percentage was similar to that found in classic risk groups in Brazil [11] and in morbidly obese adults undergoing bariatric surgery [18]. These results are worrisome and demand further attention to this population group in terms of meeting nutritional vitamin A needs even before bariatric surgery.

The lack of association between NB and serum retinol or β-carotene levels is expected because it is a functional marker of vitamin A status and is useful in detecting deficiency at the subclinical stage, when there is no alteration in biochemical indicators. Pereira et al. [18] reported 40.8% of adequate retinol serum levels among class III obese patients reporting NB before undergoing RYGB. In our study, the increased frequency of NB observed at T30 among those who underwent RYGB and presented with adequate serum retinol at T0 can be assumed to be an early subclinical manifestation that occurred before biochemical signs of deficiency.

Despite significant improvement in biochemical and anthropometric measures and the drop in hypertension rates after surgery, VAD frequency remained high. At T30, some patients developed severe VAD and β-carotene deficiency rose to 89.1%. Considering the follow-up period as a whole, there was a significant drop in serum retinol and β-carotene levels and a progressive increase in the frequency of NB, even with 5000 IU doses of retinol acetate being administered orally on a daily basis. Thus, functional assessment of VAD through the standardized WHO interview [17], which was validated for obese adult individuals by Pereira et al. [18], can be recommended for this population for early detection of VAD.

Some factors seem to contribute to the occurrence and/or aggravation of VAD in individuals with morbid obesity during the postoperative stages of RYGB. The anatomical changes of the gastrointestinal tract caused by RYGB may aggravate VAD because of the diet administered for the first 30 days after surgery, the main purpose of which is to let the stomach rest and rehydrate to lower the likelihood of postoperative complications. This diet regimen results in a lower intake of protein and lipids and consequently fewer dietary sources of vitamin A, a fat-soluble vitamin. In addition, a significant drop in vitamin A absorption occurs during the postoperative period because of the lack of proteins and lipids resulting from the malabsorptive component due to the removal of the main site of vitamin A absorption [11]. The low intake of iron and zinc also may play a part in VAD because of the involvement these nutrients have in vitamin A absorption and transport [26].

Mechanick et al. [27] recommends that adult patients receive vitamin A supplementation of 5000 to 10,000 IU per day. However, it is important to underscore that, to date, there is no recommended dosage for vitamin A supplementation for adolescents who have undergone bariatric surgery. A randomized clinical trial comparing adults who received routine retinol acetate supplementation containing 5000 IU, 10,000 IU, or 10,000 IU daily plus 50,000 IU of retinol intramuscularly monthly concluded that a supplementation protocol containing a daily oral dose of 10,000 IU seems to be the most appropriate in the postoperative period of RYGB [13].

The different behavior of serum retinol according to the nutritional status of vitamin A at T0 deserves attention. It is well known that serum retinol concentration is constant and does not always change in response to an intervention until total body stores are depleted. This lack of response is due partly to retinol's homeostatic control over a wide range of liver reserves. After supplementation, however, if liver stores are low, serum retinol concentration increases markedly [28]. This is our interpretation for the serum retinol behavior among patients with VAD at T0. Moreover, the behavior of retinol serum levels after T30 was similar in both groups. We hypothesized that, despite the factors that could explain the decline in serum retinol after

RYGB, which occurred in the group with adequate retinol before surgery, VAD patients experienced the expected rapid serum response that occurs as a result of a supplementation.

In assessing the effect of surgery on evaluated biochemical parameters (lipid and glycemic profile) and on hypertension, we found a significant improvement in these parameters after RYGB. HOMA-IR demonstrated significant reduction after 180 days of RYGB. The rise in HOMA-IR at T30 may be due to physiologic insulin resistance after major surgery. The prevalence of hypertension also demonstrated a significant drop compared with T0. In terms of anthropometric parameters, both BMI and WC decreased significantly in all evaluated periods. Similar results were obtained in a recent study by Inge et al. [7] and suggest that adolescents can lose a clinically significant amount of weight after bariatric surgery.

This study has limitations, including the lack of groups receiving different amounts of vitamin A, which may be helpful to determine which supplementary dose is sufficient to prevent VAD in adolescents undergoing bariatric surgery. However, the prescribed dose in this study was the dose routinely recommended for adults after RYGB.

Despite our small sample, reflecting a single-institutional experience, this is the first cohort study evaluating the profile of the nutritional status of vitamin A in adolescents who underwent RYGB and will be important for the required intervention studies that could propose new types of management of the nutritional status of vitamin A in this group. Furthermore, a multicenter study involving a large number of patients would be valuable in understanding whether specific conditions could predict VAD after RYGB, such as age, sex, race, BMI, and initial vitamin A status because our sample size prevented us from performing a logistic regression analysis.

Conclusion

Vitamin A nutritional status was inadequate in obese adolescents before and after of RYGB. Factors that might contribute to this include severe dietary restrictions, such as restriction on food sources of vitamin A and lipids; the removal of small intestine in RYGB, thereby eliminating the main vitamin A absorption site; and the concurrent deficiency of other nutrient. The finding that 5000 IU retinol acetate supplementation administered orally on a daily basis failed to reverse VAD and NB after RYGB is significant and suggests the need to establish new supplementation protocols for this segment of the population. We recommend assessment of VAD and NB in extremely obese adolescents before and after RYGB and recommend that these patients be monitored for an additional 180 (VAD) and 365 days (NB) after surgery, with particular attention to daily supplementation needs.

Disclosure

The authors have no commercial associations that might be a conflict of interest in relation to this article.

References

[1] Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States. JAMA 2014;311(8):806–14.

[2] Kelishadi R. Childhood overweight, obesity, and the metabolic syndrome in developing countries. Epidemiol Rev 2007;(29):62–76.

[3] Ministério da Saúde, Brasília-DF. *Plano de ações estratégicas para o enfrentamento das doenças crônicas não transmissíveis (DCNT) no Brasil 2011–2022*. Brazil: Ministério da Saúde; 2011.

[4] Nijhawan S, Martinez T, Wittgrove AC. Laparoscopic gastric bypass for the adolescent patient: long-term results. Obes Surg 2012;22(9):1445–9.

[5] Inge TH, Jenkins TM, Zeller M, et al. Baseline BMI is a strong predictor of nadir BMI after adolescent gastric bypass. J Pediatr 2010;156(1):103–8.

[6] Lawson ML, Kirk S, Mitchell T, et al. One-year outcomes of Roux-en-Y gastric bypass for morbidly obese adolescents: a multicenter study from the Pediatric Bariatric Study Group. J Pediatr Surg 2006;41(1):137–43.

[7] Inge TH, Courcoulas AP, Jenkins TM, Michalsky MP, Helmrath MA, Brandt ML, et al. Weight loss and health status 3 years after bariatric surgery in adolescents. N Engl J Med 2016;374(2):113–23.

[8] Ogden CL, Carroll MD, Curtin LR, Lamb MM, Flegal KM. Prevalence of high body mass index in US children and adolescents, 2007-2008. JAMA 2010;303(3):242–9.

[9] Xanthakos SA. Nutritional deficiencies in obesity and after bariatric surgery. Pediatr Clin North Am 2009;56(5):1105–21.

[10] Ramalho A. Fome oculta e doenças crônicas. São Paulo (Brazil): Editora Atheneu; 2014.

[11] Malinowski SS. Nutrition and metabolic complications of bariatric surgery. Am J Med Sci 2006;331(4):219–25.

[12] Shankar P, Boylan M, Sriram K. Micronutrient deficiencies after bariatric surgery. Nutrition 2010;26(11–12):1031–7.

[13] Pereira S, Saboya CJ, Ramalho A. Impact of different protocols of nutritional supplements on the status of vitamin A in class III obese patients after Roux-en-Y gastric bypass. Obes Surg 2013;23(8):1244–51.

[14] Freedman DS, Serdula MK, Srinivasan SR, Berenson GS. Relation of circumferences and skinfold thicknesses to lipid and insulin concentrations in children and adolescents: the Bogalusa Heart Study. Am J Clin Nutr 1999;69(2):308–17.

[15] Inge TH, Zeller M, Harmon C, et al. Teen-longitudinal assessment of bariatric surgery: methodological features of the first prospective multicenter study of adolescent bariatric surgery. J Pediatr Surg 2007;42(11):1969–71.

[16] Sauberlich HE, Hodges RE, Wallace DL, et al. Vitamin A metabolism and requirements in the human studied with the use of labeled retinal. Vitam Horm 1974;32:251–75.

[17] World Health Organization. *Global prevalence of vitamin A. Indicators for assessing vitamin A deficiency and their application in monitoring and evaluating intervention programmers. Micronutrient Series, WHO/NUT. 10*. Geneva (Switzerland): World Health Organization; 1996.

[18] Pereira SE, Saboya C, Saunders C, Ramalho A. Serum levels and liver store of retinol and their association with night blindness in individuals with class III obesity. Obes Surg 2012;22(4):602–8.

[19] Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28(7):412–9.

[20] Sociedade Brasileira de Cardiologia. V diretrizes Brasileiras de hipertensão arterial. São Paulo (Brazil): Sociedade Brasileira de Cardiologia; 2006.
[21] De Souza VSL, Veiga VG, Ramalho A. Association of serum concentrations of retinol and carotenoids with overweight in children and adolescents. Nutrition 2007;23(5):392–7.
[22] Ramalho A, Saunders C, Natalizi DA. Níveis séricos de retinol em escolares de 7 a 17 anos no município do Rio de Janeiro. Rev Nut 2004;17(4):461–8.
[23] Mecocci P, Polidori MC, Troiano L, et al. Plasma antioxidants and longevity: a study on healthy centenarians. Free Radic Biol Med 2000;28(8):1243–8.
[24] D'Ambrosio DN, Clugston RD, Blaner WS. Vitamin A metabolism: an update. Nutrients 2011;(3):63–103.
[25] Matsuoka H. Endothelial dysfunction associated with oxidative stress in human. Diabetes Res Clin Pract 2001;54(2):S65–S72.
[26] Ramalho A. Fome oculta: diagnóstico, tratamento e prevenção. São Paulo (Brazil): Atheneu; 2009.
[27] Mechanick JI, Kushner RF, Sugerman HJ, et al. American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery medical guidelines for clinical practice for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient. Surg Obes Relat Dis 2008;4(Suppl 5):S109–84.
[28] Tanumihardjo SA. Vitamin A: biomarkers of nutrition for development. Am J Clin Nutr 2011;94(Suppl):658 S–65 S.