METABOLISM CLINICAL AND EXPERIMENTAL XX (2015) XXX–XXX

Available online at www.sciencedirect.com

Metabolism

www.metabolismjournal.com

Hypovitaminosis D in bariatric surgery: A systematic review of observational studies

Marlene Toufic Chakhtoura [a,b,*], Nancy N. Nakhoul [b,c], Khaled Shawwa [b], Christos Mantzoros [d], Ghada A. El Hajj Fuleihan [a]

[a] Division of Endocrinology, Calcium Metabolism and Osteoporosis Program, WHO Collaborating Center for Metabolic Bone Disorders, American University of Beirut Medical Center, Beirut, Lebanon
[b] Scholars in HeAlth Research Program (SHARP), American University of Beirut Medical Center, Beirut, Lebanon
[c] Division of Endocrinology, American University of Beirut Medical Center, Beirut, Lebanon
[d] Division of Endocrinology, Diabetes and Metabolism, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

ARTICLE INFO

Article history:
Received 21 February 2015
Accepted 12 December 2015

Keywords:
Obesity
Bariatric surgery
Vitamin D deficiency
Vitamin D dose
Predictor

ABSTRACT

Background. Obesity is a public health problem that carries global and substantial social and economic burden. Relative to non-surgical interventions, bariatric surgery has the most substantial and lasting impact on weight loss. However, it leads to a number of nutritional deficiencies requiring long term supplementation.

Objectives. The aims of this paper are to review 25-hydroxyvitamin D [25(OH)D] status pre and post bariatric surgery, describe the dose response of vitamin D supplementation, and assess the effect of the surgical procedure on 25(OH)D level following supplementation.

Methods. We searched Medline, PubMed, the Cochrane Library and EMBASE, for relevant observational studies published in English, from 2000 to April 2015. The identified references were reviewed, in duplicate and independently, by two reviewers.

Results. We identified 51 eligible observational studies assessing 25(OH)D status pre and/or post bariatric surgery. Mean pre-surgery 25(OH)D level was below 30 ng/ml in 29 studies, and 17 of these studies showed mean 25(OH)D levels ≤20 ng/ml. Mean 25(OH)D levels remained below 30 ng/ml following bariatric surgery, despite various vitamin D replacement regimens, with only few exceptions. The increase in post-operative 25(OH)D levels tended to parallel increments in vitamin D supplementation dose but varied widely across studies. An increase in 25(OH)D level by 9–13 ng/ml was achieved when vitamin D deficiency was corrected using vitamin D replacement doses of 1100–7100 IU/day, in addition to the usual maintenance equivalent daily dose of 400–2000 IU (total equivalent daily dose 1500–9100 IU). There was no difference in mean 25(OH)D level following supplementation between malabsorptive/combination procedures and restrictive procedures.

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; AACE, American Association of Clinical Endocrinologists; AGB, Adjustable gastric banding; BMI, body mass index; BPD, biliopancreatic diversion; GBP, Gastric Bypass; LAGB, laparoscopic adjustable gastric banding; LSG, laparoscopic sleeve gastrectomy; QCT, quantitative computed tomography; RYGB, Roux-en-Y gastric bypass; SG, Sleeve Gastrectomy; vBMD, volumetric bone mineral density.

* *Corresponding author at:* Calcium Metabolism and Osteoporosis Program, WHO Collaborating Center for Metabolic Bone Disorders, American University of Beirut Medical Center, Beirut, Lebanon, P.O. Box: 113-6044/C8. Tel.: +961 1 737868.
E-mail address: mc39@aub.edu.lb (M.T. Chakhtoura).

http://dx.doi.org/10.1016/j.metabol.2015.12.004
0026-0495/

Please cite this article as: Chakhtoura MT, et al, Hypovitaminosis D in bariatric surgery: A systematic review of observational studies, Metabolism (2015), http://dx.doi.org/10.1016/j.metabol.2015.12.004

Conclusion. Hypovitaminosisis D persists in obese patients undergoing bariatric surgery, despite various vitamin D supplementation regimens. Further research is needed to determine the optimal vitamin D dose to reach desirable 25(OH)D levels in this population, and to demonstrate whether this dose varies according to the surgical procedure.

1. Introduction

The obesity epidemic is a worldwide public health problem [1–3]. Its overall prevalence reached about 35% in 2009–2010 among US adults, with a mean body mass index (BMI) of 28.7 kg/m^2 (95% CI, 28.4–29.0) [4]. The prevalence of grades 2 and 3 obesity (BMI ≥ 35 and ≥40 kg/m^2, respectively) reached 15.4% during the same time period, according to NHANES data [5,6]. While in the US the percent change was greater in the earlier years, before 2000, compared to the most recent years [5,6], the prevalence of obesity is still increasing in developing countries [1]. Obesity is a risk factor for several non-communicable diseases, including cardiovascular, metabolic, pulmonary, gastrointestinal, orthopedic, neurologic and psychological complications [7]. Therefore, obesity carries a significant socio-economic burden [1,8], accounting for 0.7%–2.8% of healthcare expenditure of various countries [9]. Obesity is one the major global health targets set by the WHO in its 2013 World Health Assembly [8].

While medical therapy has limited effectiveness [10], ample evidence supports the efficacy of surgical intervention to treat this morbid condition [11,12]. Indeed, bariatric surgery results in a significant and sustained weight loss [13], a substantial reduction in cardiovascular risk factors [14], an improvement in diabetes control [15–17] and a decrease in mortality [18,19].

However, bariatric surgery leads to various nutritional and vitamin deficiencies, including vitamin D and others, requiring adequate follow up postoperatively [20,21]. Vitamin D deficiency in the bariatric surgery population is multifactorial, some factors being related to obesity, and might not resolve completely after surgery, and others may be related to the type of the surgical procedure and/or its consequences. The inverse relation between BMI and serum 25-hydroxyvitamin D [25(OH)D] level has been demonstrated in the large Framingham [22] and NHANES III [23] studies and confirmed in a meta-analysis of multiple cohorts, using Mendelian randomization [24]. In the latter analysis, an increasing BMI allele score (combining a battery of 12 BMI SNPs) was significantly associated with lower 25(OH)D level [24]. Decreased sun exposure, altered dietary habits, and lack of intake of adequate amounts of various minerals and vitamins in obese individuals are all contributing factors [25,26]. Furthermore, obese individuals have decreased bioavailability of vitamin D, secondary to its sequestration in subcutaneous and visceral fat, despite normal vitamin D cutaneous synthesis and gastrointestinal absorption, compared to lean control subjects [27]. Compared to lean subjects, obese individuals have decreased expression of the vitamin D metabolizing enzymes, 25-hydroxylase and 1α-hydroxylase in cutaneous and visceral adipose tissues [28]. A decrease in the activity of the hepatic 25-hydroxylase activity has been previously described, and may be secondary to non-alcoholic fatty liver disease [29]. Volumetric dilution, rather than sequestration, has been suggested to explain the low 25(OH)D level in obese. Therefore, it was proposed to adjust daily vitamin D supplementation according to body weight, in order to be able to reach desirable levels [30]. This would require supplementation of 70–80 IU/kg body weight to reach 30 ng/ml, or 30–40 IU/kg body weight to reach 20 ng/ml [30]. The role of obesity-associated inflammation on vitamin D level has been also suggested and needs to be further elucidated [31]. The surgical procedure per se affects 25(OH)D status. In malabsorptive procedures, fat malabsorption is a major contributor to deficiencies in liposoluble vitamins, secondary to bypass of primary absorption sites in the small intestine (duodenum, jejunum and ileum) and impaired digestion [32,33]. In fact, duodenal surgical bypass decreases cholecystokinin secretion, which results in a reduction in the secretion of the pancreatic lipolytic enzymes and alteration in biliary salts, leading to problems in fat digestion, and thus steatorrhea [34]. Following both, malabsorptive and restrictive procedures, dietary intolerance with reduced intake of dairy products, vomiting, and non-adherence to supplement recommendations worsen 25(OH)D status further [32,33]. Finally, secondary hyperparathyroidism may be a contributory factor resulting in increased 25(OH)D hydroxylation, therefore decreasing 25(OH)D level [35].

The recommended 25(OH)D desirable level in the general population has been a matter of intense debate [36]. While the Institute Of Medicine (IOM) recommends a target of 20 ng/ml [37], the Endocrine Society aims at a higher level of 30 ng/ml [38]. Both societies based their recommendations on evidence related to musculo-skeletal outcomes. Despite the controversy around the desirable 25(OH)D cutoffs, it has been demonstrated that low 25(OH)D levels in bariatric surgery patients result in skeletal complications, including bone loss [39,40]; the latter has been recently confirmed using quantitative computed tomography (QCT), which assesses volumetric bone mineral density (vBMD) [41,42]. Furthermore, in addition to the classically described secondary hyperparathyroidism [43,44], several cases of osteomalacia have been reported following malabsorptive weight loss surgeries [45–47].

The aims of this paper are to review 25(OH)D status pre and post bariatric surgery, describe the dose response of vitamin D supplementation in this specific population, and assess the effect of the surgical procedure on 25(OH)D level following supplementation.

2. Materials and Methods

2.1. Literature Search

We searched the following databases: Medline, PubMed, the Cochrane Library, and EMBASE. The search timeframe was 2000–April 2015, since the accuracy of vitamin D assays has improved in the last decade, following the introduction of the International Quality Assessment Scheme for Vitamin D