

Persistently Elevated Vitamin D without Hypercalcemia: Possible Relation to GLP1 Agonist for Weight Loss?

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Introduction

- Elevated vitamin D levels in the absence of hypercalcemia presents an unusual diagnostic dilemma
- Thus far, an association between use of GLP-1 agonist and elevated vitamin D has not been established
- Vitamin D (25-hydroxy-vitamin D or 25(OH)D₃) levels are typically decreased in obese individuals. However, vitamin D levels are responsive to changes in weight
- Research supports the notion that dietary weight loss causes elevated levels of circulating vitamin D. Conversely, surgical weight loss via bariatric surgery typically results in transient increases in levels of vitamin D followed by overall decreasing levels¹
- Since the 2021 approval of semaglutide for weight loss in overweight people with a weight-related condition², prescriptions of GLP-1 agonists (Ozempic, Mounjaro, Rybelsus, and Wegovy) for the indication of weight loss have increased 2,082%³
- We describe a case of an individual with persistently elevated vitamin D levels in the absence of hypercalcemia thought to be caused by both excessive tanning and significant weight loss on a GLP-1 agonist
- We expect that as GLP-1 agonists increase in popularity, this clinical finding will present with increasing frequency

Case Description

- A 49 year old female with a past medical history of nephrolithiasis (calcium oxalate, calcium phosphate), pre-diabetes and hypertension was found to have a mildly elevated vitamin D (25(OH)D₃ level to 65ng/mL (normal range 30-60ng/mL). Her other lab testing at this time showed:
 - A1C 5.7%
 - Creatinine 1.35
 - Calcium 9.6mg/dL
 - PTH 27.3pg/mL
 - Phosphorous 3.8mg/dL
 - Other testing (specifically serum chemistry, liver function testing, lipid profile, and basic blood count were all within normal limits)
- She denied taking vitamin D supplements and had stopped taking a multivitamin 3 weeks prior to lab testing. She had also been participating in a lifestyle program for weight loss for about 3 months
- Two weeks after the initial lab results, she began semaglutide therapy to address her obesity, hypertension and pre-diabetes
- Repeat testing occurred two and a half weeks after her initial results, showing a 25(OH)D₃ level of 74ng/mL
- Prior 25(OH)D₃₃ testing in 2016 and 2010 was normal

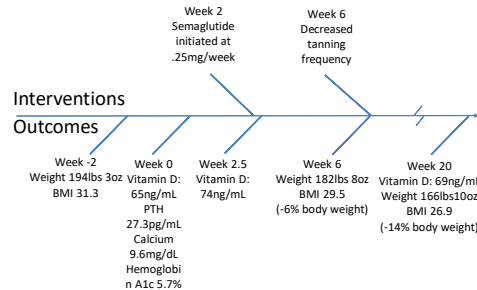
Clinical Update 1.0

- Six weeks after her initial lab results, she was seen in clinic to assess these elevated levels and her progress on semaglutide. At this time she self-reported a 9 pound weight loss since beginning semaglutide
- Regarding her vitamin D levels, she denied drinking milk or taking any Vitamin D supplementation. She reported eating fish once a week. She used a tanning bed 1-2x weekly.
- Recommendation was made to cease tanning and repeat testing in 1-2 months

Clinical Update 2.0

- Four and a half months after her initial elevated vitamin D level, our patient re-presented for follow up. Her 25(OH)D₃ level continued to be elevated at 69ng/mL
- She had initially decreased her tanning frequency to weekly and at the time of follow up had not tanned in 3 weeks. She had also continued to refrain from vitamin D supplementation
- According to our weight records, she had lost approximately 30 lbs (14% of her body weight) since two weeks prior to initiating semaglutide

Timeline



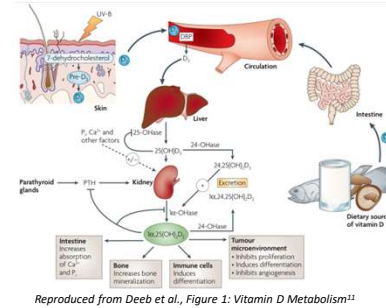
Differential Diagnosis of Elevated Vitamin D without Hypercalcemia

- Excessive supplementation (either over the counter or prescribed)
- Excessive tanning/sunlight exposure
- If applicable, weight loss

Discussion

- Exposure to UV light results in the generation of vitamin D₃. Once in the liver, vitamin D₃ is hydroxylated to 25(OH)D₃, also known as 25-hydroxyvitamin D. In the kidneys 25(OH)D₃ is hydroxylated once again to the physiologically active calcitriol 1,25(OH)₂D₃ or 25-dihydroxy vitamin D
- 25-hydroxyvitamin D is the typical form of vitamin D measured clinically to detect deficiency
- The differential for elevated vitamin D in the absence of hypercalcemia is relatively limited
- The half-life of vitamin D₃ is long, approximately 2 months,⁴ whereas the half-life of 25(OH)D₃ is estimated to be 15 days⁵
- Our patient's initial elevation in vitamin D was likely reflective of tanning bed use; however, its continued elevation was likely caused by her significant weight loss on semaglutide

Overview of Vitamin D Metabolism



Weight Loss

- Although use of GLP-1s has not yet been associated with elevated vitamin D levels, dietary weight loss is known to increase vitamin D levels¹
- Vitamin D is thought to be stored primarily in liver, adiposity, and muscle. The mechanism of weight loss induced vitamin D increases is thought to be due to loss of sequestration in adiposity
- Weight loss due to diet and exercise has been shown to be correlated with increases in serum 25(OH)D₃ in a dose-dependent fashion in multiple studies.^{6,7} One study showed that decreases in total body weight of <5%, 5-9.9%, 10-14.9%, and >15% over 12 months resulted in an increase in vitamin 25(OH)D₃ concentrations of 2.1, 2.7, 3.3, and 7.7 ng/mL, respectively⁶
- In one case report, the combined effect of vitamin D supplementation in addition to a 16% loss in total body weight over five months due to a low-carbohydrate diet resulted in a 25(OH)D₃ level of >150ng/dL, calcium of 12.9mg/dL in the setting of symptoms of intractable emesis⁸

Tanning Beds

- Tanning beds have been shown to increase 25(OH)D₃. In one study, just 4 sessions of exposure to UV-B treatment resulted in an increase in 25(OH)D₃ by 24.8nM (about 9.9ng/mL).⁹
- These results are likely transient, as one study showing that 8 weeks after ceasing UV exposure levels dropped back to their initial values¹⁰

Conclusions

- Vitamin D elevations can lead to hypercalcemia and resultant symptoms.
- As we expect use of GLP-1 agonists for the indication of weight loss to continue to increase, we will see more weight loss related vitamin D elevations
- More information is needed though awareness of the association between significant weight loss and elevated vitamin D levels and prudence regarding vitamin D supplementation in patients on GLP-1 agonists for weight loss is reasonable

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