Hypervitaminosis D in a woman: a diagnostic conundrum

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Introduction

Majority of hypervitaminosis D cases in literature are related to prescribing or manufacturing errors and increased use of over the counter multivitamins, rarely leading to vitamin D toxicity. Various studies have suggested that the use of oral contraceptives containing oestrogen is related. In one study, after adjusting 43 variables, the use of oestrogen containing contraceptive was associated with a 20% higher vitamin D status.



A 48 year-old lady was referred to Endocrinology clinic in November 2016 with symptoms of tiredness and lethargy for two months. GP had arranged routine bloods, which were quite unremarkable, apart from an incidental finding of raised Vitamin D:258nmol/L(NR: 50-150). She had depression and was otherwise fit & well. She was on Citalopram and combined oral contraceptive pill (Microgynon). She denied any excessive sun exposure. She didn't drink any milk, only drank orange juice. She had been taking multivitamins in 2016, but stopped it in summer time. Examination was unremarkable.



Investigation and Management

Investigations revealed normal full blood count, bone, kiney, liver function, inflammatory markers, thyroid, parathyroid hormones, Vitamin B12, Folate, Ferritin, HbA1c, angiotensin converting enzyme, lipid profile and renal ultrasound. Urine calcium excretion was 2.4mmol/24h (NR:2.5 – 7.5). Dual-Energy-X-ray-Absorptiometry (DEXA) showed moderately low spine density with moderate fracture risk. Vitamin D remained persistently high from 220-258 nmol/L from June 2016 to March 2017.

Hypervitaminosis D secondary to oestrogen-containing-contraceptivepill was suspected; we changed Microgynon (ethinylestradiol with levonorgestrel) to progesterone only pill (Desogestrel) in March 2017. Repeat Vitamin D in October 2017 was normal(134nmol/L). Recent Vitamin D was also normal(104nmol/L) in April 2018.

Conclusions:

The majority of hypervitaminosis D cases in literature are related to prescribing or manufacturing errors and increased use of over the counter multivitamins, rarely leading to vitamin D toxicity. One of the known culprits is the oestrogen-containing-contraceptive-pill. An American study in 2016 (1662 women) showed 20% increase in vitamin D levels in women using oestrogen-containing-contraception-pill. Although there is a clear link, the biological pathway behind this association is not well understood; possibly, changes in the metabolism of vitamin D in women taking oestrogen-containing-contraception-pill and rarely leading to toxic levels, unlike our patient who reached toxic levels and subsequently reverted back to normal

References:

Oestrogen-containing contraceptive pills increase vitamins D levels, study finds.

Mayor, S. BMJ. 2016 Aug 7; 354:i4345.

Use of Estrogen-Containing Contraception Is Associated With Increased Concentrations of 25-Hydroxy Vitamin D.

Harmon QE, Umbach DM, Baird DD. J Clin Endocrinol Metab. 2016 Sep; 101(9):3370-7

Effect of combined oral contraceptive use on serum 25-hydroxy vitamin D levels and ultrasound parameters in patients with polycystic ovarian syndrome.

Namli Kalem M, Hizli D, Kamalak Z, Kösüs A, Kösüs N, Turhan N, Kafali H. Gynecol Endocrinol. 2016;32(4):281-4

Plasma levels of 25-hydroxyvitamin D3 and in vivo markers of cytochrome P450 3A activity in Swedesand Koreans: effects of a genetic polymorphism and oral contraceptives

Nylén H, Björkhem-Bergman L, Ekström L, Roh HK, Bertilsson L, Eliasson E, Lindh JD, Diczfalusy U Basic Clin Pharmacol Toxicol. 2014Oct;115(4):355-71

Increased plasma concentrations of vitamin D metabolites and vitamin Dbinding protein in women using hormonal contraceptives: a cross sectional study

Møller UK, Streym SV, Jenson LT, Mosekilde L, Schoenmakers I, Nigdikar S, Rejnmark L. Nutrients. 2013 Sep 5;5(9):3470-80

Effect of hormonal contraception on levels of vitamins in the body

Hronek M, Poljaková G. Ceska Gynekol. 2004 Sep; 69(5):397-401. Review.Czech

