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A Word of Caution When Prescribing High-Dose Vitamin D

There has been a significant amount of research investigating the potential benefits of vitamin D supplementation. It is well supported that vitamin D supplementation can reduce risk of fractures and falls. Additionally, there is research proposing vitamin D supplementation is associated with decreased cardiovascular mortality, diabetes, risk of infection, and multiple cancers.[1] With the increase in interest of vitamin D, the amount spent on vitamin D supplements in the US alone has substantially increased from $40 million dollars in 2001 to $600 million in 2011.[2] In addition, various formulations and doses are now being used to achieve vitamin D sufficiency.

There is no clear consensus on the safest and most effective regimen to achieve adequate serum 25-hydroxyvitamin D levels. This may be due to large inter-individual variability in response to supplementation. Both intermittent high-dose regimens and daily low-dose regimens seem to show similar efficacy in achieving sufficiency.[2] A popular concept to decrease nonadherence and achieve sufficiency quickly involves using a loading dose followed by a daily maintenance dose. However, the maximum safe bolus is unclear. One of the most popular doses currently is once-weekly 50,000 IU of ergocalciferol (D2). While this has gained popularity for its ease of use and fast results, we have seen several cases of vitamin D toxicity and related complications as a result of prescriber error, prescriber and pharmacy communication error, and long-term use of high-dose vitamin D.

One such case involved an 82-year-old white woman who presented with nausea and vomiting and was found to have hypercalcemia (14.1 mg/dL). Upon further history and work-up it was discovered that the patient had accidentally been taking 50,000 IU of ergocalciferol twice daily. How did this happen? A prescription was inaccurately written for 50 IU twice daily. While we think this was intended to be 500 IU twice daily, the script was interpreted by the pharmacy as 50,000 IU twice daily. Her total 25-hydroxyvitamin D level at the time of diagnosis was 338 ng/mL. The time to toxicity was 5 months. In another case, a 74-year-old obese woman presented with calciphylaxis. She did not have any underlying renal disease, which is often the case with calciphylaxis. Besides her obesity, her only other risk factor was the fact that she had been on 50,000 IU of vitamin D weekly for the past 4 years. While her calcium was only mildly elevated (10.8 mg/dL) and her serum 25-hydroxyvitamin D was only 43 ng/mL, it is believed that her long-term high-dose vitamin D supplementation played a role, as it has been shown to be a risk factor in calciphylaxis.[3]

With the increase in vitamin D prescribing comes potential for error. Because there is no clear consensus on recommendations for supplementation and monitoring, prescribers are using a variety of approaches to try and achieve vitamin D sufficiency. With the increased use of high-dose vitamin D for bolusing, there is potential that these medications could 1) be taken incorrectly or 2) accidently become a chronic medication. Additionally, higher doses of vitamin D are now being sold over the counter, which could lead to patients taking excessive amounts on their own. Occasionally it is not the fault of patients or prescribers, but pharmaceutical companies. There have been cases of manufacturing errors leading to higher-than-advertised doses of vitamin D in supplements.[4,5]

This is just a reminder that supplements are not totally benign. Exercise caution when prescribing high-dose vitamin D. We would not recommend refilling prescriptions for high-dose vitamin D without rechecking a serum 25-hydroxyvitamin D level. It is not meant to be a chronic maintenance dose. Finally, patient education on the various doses may be the most important way to prevent unnecessary or excess supplementation.

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