Optimal Vitamin D Dosage in Multiple Sclerosis Patients with Vitamin D Deficiency

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Abstract

Our pilot study compared the efficacy of two different doses of vitamin D3 in raising serum vitamin D levels to a level greater than 50 ng/ml. Patients were randomized into two groups with one group taking vitamin D3 5,000 IU/daily and the other taking vitamin D3 50,000 IU/weekly. Twenty-nine patients successfully completed our study; 12 in the 5,000 IU/daily group and 11 in the 50,000 IU/weekly group. We administered post-study surveys to assess patient compliance, UV exposure, and barriers to treatment. Our results showed no significant difference in efficacy between the two groups and suboptimal efficacy overall with only 58% of the 5,000 IU/daily patients and 54% of the 50,000 IU/weekly patients achieving goal vitamin D levels of > 50ng/ml. The major weaknesses of our study were a small sample size and a large difference in average follow up interval between the two groups. Further studies are warranted to explore the obstacles to successful vitamin D repletion.

Methods

At our MS Center, we recruited 29 patients with MS and vitamin D deficiency defined as serum vitamin D levels ≤ 30 ng/ml. This threshold is based upon data which shows that a level less than 30 ng/ml is associated with an increased risk for conversion to clinically definite MS or MS relapse in patients with MS 1. Patients recruited included those with RRMS and SPMS. Patients were randomized to receive vitamin D3 5,000 IU daily or vitamin D3 50,000 IU weekly. We chose vitamin D3 over vitamin D2 based on data indicating that vitamin D3 may be 2.3x more effective than vitamin D2 at increasing plasma levels of vitamin D 1. We measured serum total vitamin D at the beginning of the study and at the patient’s next follow up visit. Post-study surveys were administered to all patients who completed the study to assess medication compliance, UV exposure, and barriers to treatment.

Results

There were no significant differences in the baseline characteristics of either groups indicating successful pre-study randomization. We used the t-test and chi-squared test for statistical analysis and found no significant difference between the two supplementation groups in regards to follow up serum vitamin D level, rate of change in the level of vitamin D, or percentage of patients who achieved a serum vitamin D level of > 50 ng/ml.

Conclusions

Our pilot study showed no significant difference in serum vitamin D levels in MS patients with vitamin D deficiency taking 5,000 IU vitamin D3 daily or 50,000 IU vitamin D3 weekly. We recommend that MS patients with vitamin D levels <30 ng/ml be supplemented with either 5,000 IU vitamin D3 daily or 50,000 IU vitamin D3 weekly based on patient preference in regards to daily vs weekly dosing. MS patients should likely benefit from higher doses of vitamin D given the excellent safety profile of vitamin D and the inverse relationship between serum vitamin D levels and MS development and disease progression.

References

1. Vieth R. A prospective cohort study concluded that vitamin D has a therapeutic, dose dependent effect with each 4 ng/ml increase in serum vitamin D resulting in a 12% reduction in risk of relapse in patients with relapsing-remitting multiple sclerosis (RRMS) 4. It is hypothesized that vitamin D exerts this therapeutic effect by modulating several types of immune cells that express vitamin D receptors and decreasing inflammation 4. Based on these findings, many clinicians have begun supplementing MS patients with vitamin D. Current MS drug dosages indicate the optimal dose for vitamin D supplementation in MS. There is also ambiguity in the literature about what level serum vitamin D levels clinicians should target.

In order to gain more information about what constitutes an effective vitamin D supplementation protocol in MS patients with vitamin D deficiency we conducted a randomized prospective study to compare the efficacy of two dosage regimens: 5,000 IU vitamin D3 daily vs 50,000 IU vitamin D3 weekly.

Discussion

In clinical studies, vitamin D has demonstrated a dose dependent linear effect on raising serum vitamin D levels. One study showed that in patients with normal absorptive capacity, for every 100 units of vitamin D given daily, serum 25(OH)D increased by approximately 0.7 to 1.8 ng/ml. This would predict an increase in 25(OH)D levels of 1.8 ng/ml/rise in serum vitamin D. Our study included patients with MS in various states of urinary 25(OH)D levels (at least 35 ng/ml in our 5,000 IU daily group and a 50 ng/ml rise in our 50,000 IU weekly group). However, in our study the average rise in serum vitamin D levels in our 50,000 IU group was 60 ng/ml/seem in the 5,000 IU weekly group. One possible reason for this difference is that vitamin D metabolism may differ between MS patients and the general population. This could also explain the increased risk for conversion to MS in the first place. On the other hand, patients with MS may not be getting outside as much depending on the degree of disability. Therefore, higher doses of vitamin D supplementation may be needed to see the same pharmacologic effect noted in the general population.

Our study showed no significant difference in serum vitamin D levels in MS patients with vitamin D deficiency taking 5,000 IU vitamin D3 daily vs 50,000 IU vitamin D3 weekly. Additionally, both supplementation regimens demonstrated suboptimal efficacy with only 58% of the patients in the 5,000 IU group and 54% of the patients in the 50,000 IU group reaching our primary outcome of obtaining levels > 50 ng/ml. Given these findings, we recommend that the choice of supplementation be based on patient preference for a specific dosing interval, daily vs weekly, rather than-persuaded efficacy of one regimen over the other.

Our study had several limitations. Firstly, our sample size was small and it is possible that with a larger sample size we would have detected a significant difference in efficacy between the two regimens. Secondly, of this small sample size, 25% of the patients enrolled dropped out further decreasing power. Thirdly, the second measurement of vitamin D levels were checked at different times with an average difference of at least 50 days between the two groups. This confounds how we look at the rate of change in vitamin D levels. Nonetheless, we believe our study was a successful pilot study that demonstrated some of the challenges in the clinical setting regarding vitamin D supplementation in patients with MS.

In conclusion, how best to supplement vitamin D and which goal serum level to target remains elusive. However, it is becoming increasingly clear that targeting serum levels of at least 50 ng/ml may be important for immune modulation. Moreover, the potential therapeutic benefits of Vitamin D outweigh the potential side effects of over supplementation, consisting of hypercalcemia, hypercalciuria and renal calculi. These side effects serve as relatively benign early warnings and have only been documented in patients with a serum vitamin D > 300 ng/ml.