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Full Length Research Paper

Oral or Intramuscular Vitamin D Replacement?

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Vitamin D deficiency has been shown to be extremely common condition even in sunny climate. We conducted a retrospective analysis on 123 cases to compare oral versus intramuscular cholecalciferol replacement in cases of vitamin D deficiency as well as different doses of intramuscular supplement as assessed by serum levels of total 25 hydroxy vitamin D3. There was a significant increase in vitamin D level after therapy in all regimens (oral, intramuscular 300,000 IU and 600,000 IU). However, the difference in percent change in vitamin D level as a result of therapy was not significant between the 3 groups.

Keywords: Vitamin D deficiency, replacement, cholecalciferol, intramuscular, oral.

INTRODUCTION

Vitamin D deficiency has gained a lot of importance beyond that of calcium metabolism, recently, its involvement has been extended to other (extra-skeletal) disease areas, such as cancer, cardiovascular diseases, energy metabolism and autoimmune diseases (Balvers et al., 2015).

All adults aged 50–70 and 70+ year require at least 600 and 800 IU/d, respectively, of vitamin D. Whether 600 and 800 IU/d of vitamin D are enough to provide all of the potential nonskeletal health benefits associated with vitamin D is not known at this time (Holick et al., 2011).

In cases of vitamin D deficiency replacement can be oral with 50,000 IU of vitamin D2 or vitamin D3 once a week for 8 weeks. (Holick et al., 2011) or intramuscular 300,000 IU (Nugent et al., 2010) or 600,000 IU (Diamond et al., 2005)

The aim of our study is to compare different method of vitamin D replacement, oral, intramuscular 300,000 IU and 600,000 IU

METHODS

The study includes 129 cases with vitamin D deficiency. Medical nurses in our institute. They were assigned to three regimens of vitamin D replacement therapy; cholecalciferol 50,000 IU weekly for 6-8 weeks, annual 300 IU, and annually 600 IU. Serum 25- hydroxyl vitamin D3 was measured only once around 3 months after replacement. Table 1 summarizes the baseline characteristics of the participants according to regimen of replacement therapy.

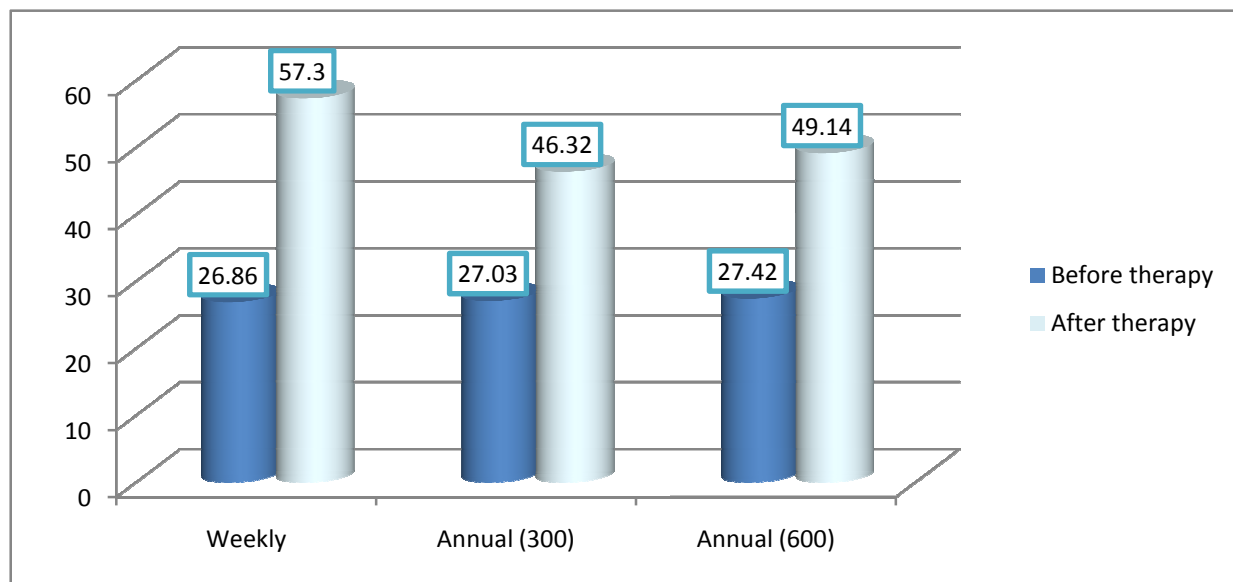
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Table 1. Baseline characteristics of the participants, according to regimen of vitamin D replacement

	Weekly (n=46)	Annual (300) (n=52)	Annual (600) (n=25)	Total (n=123)
Age (years)	24-51	33-47	29-49	24-51
Sex				
Males (%)	2 (4.3)	2 (3.8)	3 (12.0)	7 (5.7)
Females (%)	44 (95.7)	50 (96.2)	22 (88.0)	116 (94.3)
Vitamin D <25 ng/mL before therapy (%)	24 (52.2)	23 (44.2)	14 (56.0)	61 (49.6)

Table 2. Comparison between vitamin level before and after vitamin D replacement therapy according to regimen of replacement

Vitamin D replacement therapy	Before therapy Mean±SD	After therapy Mean±SD	p-value
Weekly	26.86±14.45	57.30±31.06	<0.001
Annual (300 IU)	27.03±14.10	46.32±24.37	<0.001
Annual (600 IU)	27.42±15.07	49.14±32.80	0.001

**Figure 1.** Comparison between vitamin level before and after vitamin D replacement therapy according to regimen of replacement

RESULTS

The study includes 129 cases with vitamin D deficiency. Follow up results of vitamin D were unavailable for 6 cases. Thus, the results described only 123 cases. They were assigned to three regimens of vitamin D replacement therapy; cholecalciferol 50,000 weekly for 6-8 weeks, annual 300 IU, and annual 600 IU. Table 2 and figure 1 present the results of vitamin D level before and after therapy in the three different groups of therapy.

It is evident that there was a significant increase of vitamin D level after therapy in all of the three compared regimens. Figure 2, shows that the percent change of vitamin D level as a result of vitamin D replacement therapy ranged between 113% for those treated with annual regimen of a dose of 300 IU to 168.6% for those treated with weekly regimen. However, the difference between percent change in vitamin D level as a result of therapy was not significant between the three regimens, $p=0.348$.

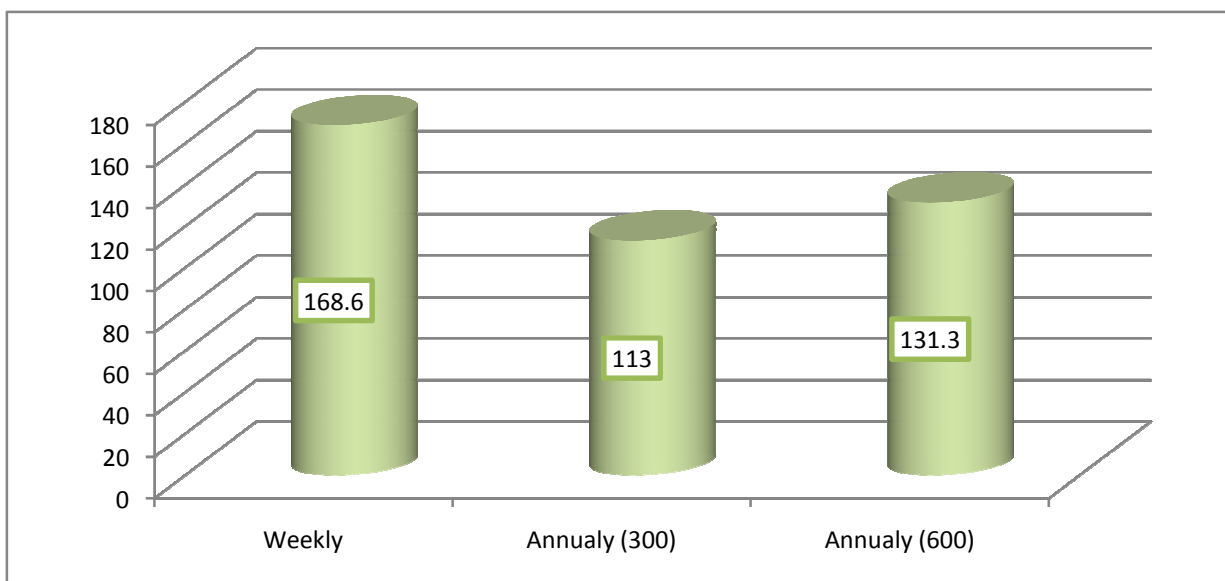


Figure 2. Comparison between different regimens of vitamin D replacement therapy regarding percent change in the vitamin D level.

DISCUSSION

Vitamin D deficiency is now recognized as a pandemic. The major cause of vitamin D deficiency is the lack of appreciation that sun exposure in moderation is the major source of vitamin D for most humans. Very few foods naturally contain vitamin D, and foods that are fortified with vitamin D are often inadequate (Holick et al, 2008). Vitamin D is a hormone, not a vitamin. The skin is responsible for producing vitamin D. During exposure to sunlight, ultraviolet radiation penetrates into the epidermis and photolyzes provitamin D3 to previtamin D3. Previtamin D3 can either isomerize to vitamin D3 or be photolyzed to lymisterol and tachysterol. Vitamin D is also sensitive to sunlight and is photolyzed to 5, 6-transvitamin D3, suprasterol I, and suprasterol II. Once formed, vitamin D3 enters the circulation and is sequentially metabolized to 25-hydroxyvitamin D3 and 1,25-dihydroxyvitamin D3 (1,25-[OH]₂-D3) (Holick et al, 1987). However, with changing life style nowadays, we have observed vitamin D deficiency in a sunny climate in which Lack of exposure to sunlight, outdoor activities under the sun are major contributor that (Bener et al., 2009). serum 25 hydroxyvitamin D (25(OH)D) concentration of 30 ng/mL (75 nmol/L) should be a minimum goal to achieve in older adults (Judge et al., 2014).

Vitamin D deficiency has gained a lot of importance beyond that of calcium metabolism, recently, its involvement has been extended to other (extra-skeletal) disease areas, such as cancer, cardiovascular diseases, energy metabolism and autoimmune diseases (Balvers et al., 2015). Vitamin D improve cognitive function and

behavior in some brain disorders such as attention deficit hyperactivity disorder, bipolar disorder, schizophrenia, and impulsive behavior. (Patrick et al., 2015). The increasingly reported association of vitamin D deficiency is of a great interest for rheumatologist, vitamin D deficiency is associated with a higher disease activity in systemic lupus erythematosus (Yap et al., 2015) and rheumatoid arthritis (Raczkiwicz et al., 2015)

Vitamin D replacement should be done to achieve serum 25 hydroxyvitamin D (25(OH)D) concentration of 30 ng/mL (75 nmol/L) and replacement can be orally or intramuscular as mentioned before.

In our current study we aim to compare which way is better oral or parenteral replacement and we get the following results it is evident that there was a significant increase of vitamin D level after therapy in all of the three compared regimens. However, the difference between percent change in vitamin D level as a result of therapy was not significant between the three regimens, $p=0.348$.

Our result is similar to other studies looking at that outcome of oral versus intramuscular supplementation, as in comparing single intramuscular 600,000IU with oral, regardless of the route of administration, the oral formulation displayed a rapid serum bioavailability and is therefore initially more effective in increasing 25(OH) D serum levels than the equivalent intramuscular dose, but the latter produced a sustained and gradual increase during the 4-month observation period (Cipriani et al., 2013).

Other trial also showed that there were no significant differences in terms of the type of supplementation received, although oral supplementation showed a better trend of increment during the observation period

compared to the intramuscular administration (Falasca et al., 2014)

Also another trial showed the same result that both regimens were considerably effective, safe and practical in treating hypovitaminosis D. Although it revealed superiority of oral route, at least at early short time (Zabihyeganeh et al., 2013)

On the other hand, another trial showed that intramuscular application seems to be more efficient because of serum 25 (OH)D levels increased linearly and all patients reached the optimal level of vitamin D at 12th week. In Oral group, presumably because of gastrointestinal factors levels began to decrease after 6 weeks. (Tellioglu et al., 2012)

Given the potential harmful effects reported in trials that used huge doses. However, these studies, even though randomized, double-blind, and placebo controlled, lack important information concerning, for example, the distribution of risk factors for falls in the 2 arms (cognitive impairment, drug use, units of alcohol consumed, and so on); moreover, the mechanism leading to an increased fracture incidence immediately after vitamin D administration still remains obscure. Therefore, further studies are needed to definitively solve this issue (Cipriani et al., 2013).

Our study has few limitations, Small sample size, retrospective design, Measurement of vitamin D level only once and short follow up period.

In conclusion, there was a significant increase of vitamin D level after therapy in all of the three compared regimens oral or intramuscular. However, the difference between percent changes in vitamin D level as a result of therapy was not significant between the three regimens. A future study in a prospective design with longer follow-up duration and toxicity monitoring is warranted. We prefer the weekly oral route for rapid rise in vitamin D level and awaiting for further study to address that issue of increased fracture risk with high dosage regimens.

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