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Original Article

Orthopaedics Section

Comparing the Effectiveness of Oral versus Intramuscular Vitamin D Supplementation in Adults with Fracture around Hip and Vitamin D Deficiency

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ABSTRACT

Introduction: Cholecalciferol plays vital role in bone mineralisation. Major circulating and storage form of vitamin D is 25-hydroxycholecalciferol {25(OH)D3} which is formed in the liver after 25-hydroxylation. It is also the form of vitamin D that is measured in blood tests to detect deficiency of vitamin D. There is scarcity of literature to support the best therapy at the lowest effective dose that is practicable, cost efficient and devoid of probable side effects. Oral medication compliance is a major stumbling block to replenishing vitamin D levels in the body. Vitamin D administered intramuscularly (i.m.) may be able to overcome this limitation.

Aim: To compare the effectiveness of oral versus intramuscular vitamin D in adults with fracture around hip and vitamin D deficiency.

Materials and Methods: This prospective interventional study was conducted in Orthopaedics Ward in Mahatma Gandhi Institute of Medical Sciences, Jaipur, Rajasthan, India, from January 2020 to June 2021. Total 60 male and female, above 18 years, with fractures around the hip and vitamin D levels less 30 ng/mL were included in the study. In group O (n=30) patient received oral vitamin D supplementation of 60000 IU once a week for six weeks. In group I (n=30) patient received single dose of 600000 IU vitamin D injection (i.m.). Follow-up of patients was done at baseline, six weeks and 12 weeeks for serum values of vitamin D, calcium, alkaline phosphatase and parathyroid hormone levels. Bivariate analytical techniques has been used to measure the improvement of group I with group O.

Results: The mean age in group I was 60.40±16.38 years and in group O was 59.47±15.17 years (p-value=0.82). There were total 31 females, 13 in group I and 18 in group O. No significant difference was observed among the groups in vitamin D level at the baseline, {group I: 13.84±3.54 ng/mL; group O: 16.45±6.3 ng/mL, p-value=0.053}. At six weeks, the mean value of the vitamin D significantly increased in both groups (p-value=0.001; group I: 40.94±4.67 ng/mL and group O: 33.64±9.89 ng/mL). At the 12th week, the mean value of the vitamin D was significantly higher in group I (44.52±7.09 ng/mL) compared to group O (24.65±10.92 ng/mL), p-value <0.001. The vitamin D mean was significantly raised with the time in group I and group O at six weeks and still remained increased at 12 weeks in group I but not in group O.

Conclusion: The present study concluded that although both administration routes are effective and appear to be safe, intramuscular application is more effective in increasing 25(OH)D levels and sustaining it for a longer period of time as compared to oral dose.

Keywords: Bone metabolism, Cholecalciferol, Effective dose, Osteoporosis

INTRODUCTION

Vitamin D plays a very significant role in bone metabolism and mineralisation. It is a fat soluble vitamin, leads to its effects by acting on vitamin D receptors [1]. Lesser mineralisation of bones leads to rickets and osteomalacia [2]. It has a preventive role in various diseases like in cancer, infection, autoimmune illness, cardiovascular diseases and diabetes mellitus, among other non skeletal disorders [3].

The high prevalence of hypovitaminosis D among pregnant women and children is a major concern. Weather changes has also reflected changes in vitamin D levels [4]. In large cities, air pollution probably also plays a role [5]. Urban subjects are found to be more deficient in vitamin D [6]. One-fifth of them also have indications of parathyroid hyperactivity, as measured by Parathyroid Hormone (PTH) levels in the blood [7]. Their hypovitaminosis D is caused by a lack of sunlight exposure and skin pigmentation [8]. There are studies which have shown decreased levels of vitamin D in neonates, healthy school girls, hospital staff and pregnant women in North India [5,8-10].

In most of the studies, the criteria used for defining hypovitaminosis (vitamin D deficiency) is serum 25(OH)D level below 50 nmol/L [9-11]. Various vitamin D deficiency and insufficiency diseases have been highlighted [12]. In adults, this can lead to decreased mineralisation that is osteomalacia. Decreased levels also leads to increased incidences of hip fractures muscle weakness thus affecting the mobility and functional ability of the person [13,14]. Prevention of such eventualities is feasible by adequate sunlight exposure, food fortification and supplementation of vitamin D for at risk population as a cost-effective measure in prevention of hip and other geriatric fractures. There is need for optimising vitamin D levels in cases of osteoporosis patients given antiresorptives (bisphosphonate) and anabolic (teriparatide) drugs [15]. Active vitamin D works in tandem with two additional hormones to maintain calcium and phosphate homeostasis and PTH [16].

Physicians in India are currently prescribing a 1500 mg cholecalciferol sachet to be taken once a week for one to eight weeks for overt or occult vitamin D insufficiency [17].

Its short-term and long-term effects on serum 25(OH)D levels in Asian Indians, however, have not been well investigated. There is a scarcity of scientific literature to support the best therapy at the lowest effective dose, that is practicable, cost-efficient and devoid of probable side effects. Persistence is very low with oral vitamin D supplementation [18]. Oral medication compliance is

a major stumbling block to replenishing vitamin D levels in the body. Vitamin D administered intramuscularly (i.m.) may be able to overcome this limitation. Vitamin D i.m. injections are regularly available in the market in two values (3 lac and 6 lac IU). Parenteral route (intramuscular) of administration of vitamin D has lead to effective increase in vitamin D levels but this cannot be administered without monitoring serum levels [19].

Supplementation, either oral or intramuscular, is a more realistic and easier way to receive enough vitamin D. However, no study comparing intramuscular injection and oral vitamin D dosage in Indian people has been conducted. Hence, present study was conducted to evaluate the efficacy and tolerability of oral cholecalciferol (60,000 IU) versus i.m. cholecalciferol (600,000 IU) in correcting vitamin D deficiency with fracture around hip.

MATERIALS AND METHODS

This prospective interventional study was conducted among patients, admitted to Orthopaedics Ward in Mahatma Gandhi Institute of Medical Sciences, Jaipur, Rajasthan, India, from January 2020 to June 2021. The study was permitted by Institutional Ethics Committee (MGMCH/IEC/JPR/2020/100).

Inclusion criteria: All males and females above 18 years of age, with hip fractures and vitamin D levels less than 30 ng/mL were included in the study [2].

Exclusion criteria: The patients taking Hormone Replacement Therapy (HRT) or anticonvulsants, with chronic debilitating illness {Chronic Obstructive Pulmonary Disease (COPD), cancer, Acquired Immune Deficiency Syndrome (AIDS), Congestive Heart Failure (CHF)}, renal disease (creatinine level >1.5 mg/dL), liver disease (bilirubin >2 mg/dL), malabsorption syndrome and patients with gastrectomy/steroid dependency were excluded from the study.

Sample size calculation: For sample size calculation, power was taken as 80%, from similar previous study by Gupta N et al., where they have used 40 samples, 20 in each arms with power 80% and level of significance 5% [20]. In present study, 10 more samples in each group 30 (total n=60) were taken.

A total 60 patients were divided equally into two groups (30 patients each group). Randomisation was done by chit in box method.

- **Group O (n=30):** Received oral vitamin D supplementation of 60,000 IU once a week for six weeks.
- **Group I (n=30):** Received i.m. vitamin D supplementation with a single dose of 6,00,000 IU vitamin D injection.

Study Procedure

A 10 mL of fasting blood samples were collected for measurement of serum vitamin D, serum calcium (albumin-adjusted) and serum PTH, Alkaline Phosphatase (ALP) levels.

1. Serum 25(OH)D level was determined by radioimmunoassay method [19].
   - Vitamin D deficiency: <10 ng/mL
   - Insufficiency: 10-29 ng/mL
   - Optimal: ≥30 ng/mL
2. Serum PTH was determined by chemiluminescence method. Reference range for serum PTH, 1.1-6.8 pmol/L
3. Serum calcium was measured with the enzymatic method using automated spectrophotometer the reference range for serum calcium is 2.20-2.60 mmol/L [21].

Follow-up was done for oral vitamin D, intramuscular vitamin D, PTH level and calcium at baseline, at six weeks and at 12 weeks.

STATISTICAL ANALYSIS

Continuous data were summarised in the form of mean and their standard deviation. Difference in change in means of two groups were analysed using student's t-test (difference in differential analysis). Intragroup analysis of means at multiple time duration was analysed using Analysis of Variance (ANOVA). Count data were expressed in form of proportions. Difference among proportions were analysed using Chi-square test. The level of significance was kept 95% for all statistical analysis. Statistical Package for Social Sciences (SPSS) software version 14.0 (Inc.,Chicago, IL, USA) was used for all analytics works.

RESULTS

The groups were comparable according to age and sex demographics. Mean age in group I was 60.40±16.38 years and in group O was 59.47±15.17 years (p-value=0.82). There were total 31 females, 13 in group I and 18 in group O [Table/Fig-1]. In present study, 52 (86.67%) were found to be vitamin D deficient and 8 (13.33%) were vitamin D insufficient.

Variable	Group I (n=30) n (%)	Group O (n=30) n (%)	Total (N=60) n (%)	p-value*
Gender				
Male	17 (56.67%)	12 (40%)	29 (48.33%)	0.301
Female	13 (43.33%)	18 (60%)	31 (51.67%)	
Age (in years)	60.40±16.38	59.47±15.17	59.93±15.66	0.82

[Table/Fig-1]: Age and gender wise distribution across the study groups.
*Chi-square test for categorical variable; two sample independent t-test for continuous variable

At baseline, no significant difference was observed between the groups for vitamin D (p-value=0.053). At sixth week, the mean value of the vitamin D increased in both groups. Mean value was significantly higher in group I (40.94±4.67 ng/mL) as compared to group O (33.64±9.89 ng/mL) (p-value=0.001). At 12th week, the mean value of the vitamin D was significantly higher in group I (44.52±7.09 ng/mL) as compared to group O (24.65±10.92 ng/mL) with p-value <0.001 [Table/Fig-2].

Vitamin D	Group I (Mean±SD)	Group O (Mean±SD)	p-value*
At baseline	13.84±3.54	16.45±6.3	0.053
6th week	40.94±4.67	33.64±9.89	0.001
12th week	44.52±7.09	24.65±10.92	<0.001

[Table/Fig-2]: Difference in vitamin D (ng/mL) values over time between two groups.
*Two sample independent test

Statistically no significant difference was observed in the calcium level at baseline, sixth week and 12th week during follow-up between the groups as shown in [Table/Fig-3].

The [Table/Fig-4] shows the difference in ALP values over time between two groups. Baseline values in the two groups were comparable. At sixth week, the mean value of the ALP decreased from the baseline in both the group I and group O. No significant difference was observed between the groups at 6th week (p-value=0.506) and 12th weeks (p-value=0.495).

Calcium levels (mg/dL)	Group I (Mean±SD)	Group O (Mean±SD)	p-value*
At baseline	9.11±0.87	9.34±0.75	0.271
6th week	9.03±0.69	9.02±0.55	0.957
12th week	9.43±0.37	9.31±0.47	0.279

[Table/Fig-3]: Difference in calcium levels (mg/dL) over time between two groups.
*Two sample independent test is used

Alkaline phosphatase (mg/dL)	Group I (Mean±SD)	Group O (Mean±SD)	p-value*
At baseline	181.30±53.80	171.63±40.96	0.437
6th week	162.75±37.93	169.60±41.33	0.506
12th week	151.97±36.63	158.40±35.90	0.495

[Table/Fig-4]: Difference in ALP values over time between two groups.
*Two sample independent test is used

The [Table/Fig-5] depicts the difference in PTH values over time between two groups. No Significant changes were observed in the serum PTH levels at baseline (p-value=0.170). At sixth week, the mean value of the PTH decreased from the baseline in both the group I and group O. No significant difference was observed between the groups at 6th week (p-value=0.801) and 12th week (p-value=0.371).

Parathyroid hormone (mg/dL)	Group I	Group O	p-values*
	Mean±SD	Mean±SD	
At baseline	46.89±18.97	54.79±24.71	0.170
6th week	32.93±15.92	34.10±19.72	0.801
12 week	20.01±10.20	22.88±14.13	0.371

[Table/Fig-5]: Difference in PTH values over time between two groups.
*two sample independent test is used

DISCUSSION

In present study, 86.67 % were found to be vitamin D deficient and 13.33% were Vitamin D insufficient according to Holick MF (Global Prospective 2013) [2].

Zhang D et al., did the study on 527 patients, 71% of the patients with fracture had low vitamin D levels [22]. In a study by Hershkovitz A et al., 92.6% of the patients had lower cholecalciferol levels, in which 78.2% were vitamin D deficient and 14.4% were vitamin D insufficient. 6.8% of the patients had optimal vitamin D level. Cholecalciferol deficiency was found in 20.3% of the patients [23].

The vitamin D mean value was significantly raised with the time in group I and group O at 6th weeks and still remained increased at 12th weeks in group I but not in group O which implied better results in vitamin D level in group I, as compared to group O. Billoo A et al., and Hashemipour S et al., have done similar studies comparing two different routes for Vitamin D supplementation and found similar results [24,25].

Previous studies by Gupta N et al., Robertson DS et al., and Lakkireddy M et al., reported similar observations regarding the safety, efficacy and acceptability of a single dose of vitamin D versus oral vitamin D [20,26,27]. Vitamin D (cholecalciferol) was found to be helpful in both oral and injectable forms. The vitamin D value at 6th weeks increased for both groups 40.94±4.67 ng/mL for group I and 33.64±9.89 ng/mL for group O as compared to their baseline values which were 13.84±3.54 ng/mL and 16.45±6.3 ng/mL for group I and group O respectively.

Although, the results after administration of injectable form were statistically significant as at 12th weeks vitamin D values sustained and showed increase in injectable group compared to group O as evident from the values 44.52±7.09 ng/mL for group I and 24.65±10.92 ng/mL for group O. There were no negative side effects, and both treatment options were well tolerated.

Significant changes were observed in the serum calcium levels from baseline within the groups which declined at 6th weeks followed by rise at 12th weeks. Statistically no significant difference was observed in the mean calcium levels between both the groups at 12th weeks. These observations were similar with studies conducted by Mittal H et al., [28]. They investigated the non inferiority of a lower therapeutic dose (3,00,000 IU) of vitamin D for boosting blood 25(OH)D levels when compared to a conventional dose (600,000 IU) [28]. They discovered hypercalcemia in two children at 4th weeks (one in each group) and three children at 12th weeks (one in group 1 and two in group 2). It was concluded that initially calcium level were decreased initially and then increased.

Difference was observed in the serum ALP from baseline within the groups. The mean serum ALP which in both the groups decreased at 6th and 12th weeks. Statistically no significant difference was observed in the mean ALP levels between both the groups at 12th weeks. This was similar to the outcome of the study conducted by Mittal H et al., both the groups demonstrated significant (p-value <0.05) and comparable fall in the serum alkaline phosphatase levels at 12th weeks [28].

Vitamin D deficiency have been observed to often have raised serum PTH levels. The mean serum PTH respectively in the group I and group O which showed a significant decrease in the levels at 6th weeks and 12th weeks. Statistically no significant difference was observed in the mean PTH levels between both the groups at 12 weeks. The PTH values were higher than normal range in many patients and may be attributed to higher ages of the subjects. This finding is consistent with that reported by Haden ST et al., where it was observed that both the study groups demonstrated significant (p-value <0.05) and comparable fall in the serum parathormone levels at 12 weeks. Relative change {ratio of geometric mean (95% CI)} in serum PTH, 12th weeks after therapy, were 0.98 (0.7-1.47) [29]. Choi HK et al., assessed the efficacy and safety of high dose vitamin D3 after intramuscular injection and found that decreased levels of PTH in the vitamin D3 group when compared to control group [30]. Haden ST et al., also observed that in both the groups, efficacious PTH suppression were observed. A single intramuscular dose of vitamin D3 had no meaningful effect on PTH. It was concluded that both the groups showed statistically significant suppression of PTH from baseline [29].

Reduced vitamin D levels may also have a role in the occurrence of hip fractures in these older people, especially if they also have osteoporosis, as suggested by the data. These studies demonstrated that calcium and vitamin D supplementation is safe and induced a moderate reduction in femoral neck bone loss associated with a substantial reduction of the risk of hip fracture in elderly ambulatory women. Previous research by Sanfelix-Genovés J et al., and Diez A et al., has shown that oral vitamin D replacement has a low rate of compliance [31,32]. Pearce SH and Cheetham TD, suggested an i.m. dose of 300,000 IU cholecalciferol once a month for three months followed by the same dose once or twice a year in patients with severe malabsorption [33]. The pharmacokinetics of i.m. D3 delivery, as well as the lack of 25(OH)D level variations after i.m. treatment, makes it a good therapeutic choice for people who have obesity, malabsorption, or compliance issues as suggested by Vieth R [34]. Kaur P et al., found that excessive doses and injudicious usage of the parenteral route, on the other hand, may be linked to problems including hypercalcemia, hypercalciuria and vitamin D toxicity [35].

Limitation(s)

Outcome of hip fractures could not be taken into consideration on oral versus intramuscular vitamin D injection.

CONCLUSION(S)

Present study established an association between hypovitaminosis D and intramuscular injection of vitamin D. It was concluded that although both administration routes are effective and appear to be safe, intramuscular application is more effective in increasing 25(OH) D levels and sustaining it for a longer period of time as compared to oral dose. Identifying and treating these patients early with vitamin D for osteomalacia and anti osteoporotic regimens for osteoporosis will improve the bone, muscle and overall health thereby reducing falls and fractures. Studies on larger scale are needed to be carried out to set the inferences on right dosage of vitamin D.

REFERENCES

[1] Moore DD, Kato S, Xie W, Mangelsdorf DJ, Schmidt DR, Xiao R, et al. International Union of Pharmacology. LXII. The NR1H and NR1I receptors: Constitutive androstane receptor, pregnene X receptor, farnesoid X receptor alpha, farnesoid X receptor beta, liver X receptor alpha, liver X receptor beta, and vitamin D receptor. Pharmacol Rev. 2006;58(4):742-59.
[2] Holick MF. Vitamin D: A D-lightful vitamin for health. Endocrinol Metab. 2012;27:255e67.

[3] Choi HS, Kim KA, Lim CY, Rhee SY, Hwang YC, Kim KM, et al. Low serum vitamin D is associated with high risk of diabetes in Korean adults. J Nutr. 2011;141:1524e8.
[4] Amrein, K, Scherkl M, Hoffmann M. Vitamin D deficiency 2.0: An update on the current status worldwide. Eur J Clin Nutr. 2020;74:1498-1513.
[5] Agarwal KS, Mughal MZ, Upadhyay P. The impact of atmospheric pollution on vitamin D status of infants and toddlers in Delhi India. Arch Dis Child. 2002;87:111-13.
[6] Harinarayan CV, Ramalakshmi T, Prasad UV. High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. Am J Clin Nutr. 2007;85:1062-67.
[7] Vupputuri MR, Goswami R, Gupta N, Ray D, Tandon N, Kumar N. Prevalence and functional significance of 25-hydroxyvitamin D deficiency and vitamin D receptor gene polymorphisms in Asian Indians. Am J Clin Nutr. 2006;83:1411-19.
[8] Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. Am J Clin Nutr. 2000;72:472-75.
[9] Sachan A, Gupta R, Das V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. Am J Clin Nutr. 2005;81:1060-64.
[10] Puri S, Marwaha RK, Agarwal N. Vitamin D status of apparently healthy schoolgirls from two different socioeconomic strata in Delhi: Relation to nutrition and lifestyle. Br J Nutr. 2008;99:876-82.
[11] Arya V, Bhambri R, Godbole MM, Mithal A. Vitamin D status and its relationship with bone mineral density in healthy Asian Indians. Osteoporos Int. 2004;15:56-61.
[12] Norman AW. From vitamin D to hormone D: Fundamentals of the vitamin D endocrine system essential for good health. Am J Clin Nutr. 2008; 88(2):491S-99.
[13] Lips P. Fortification of food with vitamin D is a reasonable approach to fracture prophylaxis. Ned Tijdschr Geneeskd. 2006;150(21):1180.
[14] Sandmann A, Amling M, Barvencik F, König HH, Bleibler F. Economic evaluation of vitamin D and calcium food fortification for fracture prevention in Germany. Public Health Nutr. 2017;20(10):1874-83.
[15] Management of osteoporosis in postmenopausal women: 2010 position statement of The North American Menopause Society. Menopause. 2010;17(1):25-54.
[16] Shimada T, Hasegawa H, Yamazaki Y, Muto T, Hino R, Takeuchi Y, et al. FGF-23 is a potent regulator of vitamin D metabolism and phosphate homeostasis. J Bone Miner Res. 2004;19:429-35.
[17] Sahu M, Bhatia V, Aggarwal A, Rawat V, Saxena P, Pandey A, et al. Vitamin D deficiency in rural girls and pregnant women despite abundant sunshine in northern India. Clin Endocrinol (Oxf). 2009;70(5):680-84.
[18] Giusti A, Barone A, Razzano M, Oliveri M, Pizzonia M, Palummeri E, et al. Persistence with calcium and vitamin D in elderly patients after hip fracture. J Bone Miner Metab. 2009;27(1):95-100.
[19] Tellioglu A, Basaran S, Guzel R, Seydaoglu G. Efficacy and safety of high dose intramuscular or oral cholecalciferol in vitamin D deficient/insufficient elderly. Maturitas. 2012;72(4):332-38.
[20] Gupta N, Farooqui KJ, Batra CM, Marwaha RK, Mithal A. Effect of oral versus intramuscular Vitamin D replacement in apparently healthy adults with Vitamin D deficiency. Indian J Endocrinol Metab. 2017;21(1):131-36.
[21] Jorde R, Bønaa KH, Sundsfjord J. Primary hyperparathyroidism detected in a health screening: The Tromsø study. J Clin Epidemiol. 2000;53(11):1164-69.
[22] Zhang D, Seo DH, Choi HS, Park HS, Chung YS, Lim SK. Effects of Single QVitamin D3 Injection (200,000 Units) on Serum Fibroblast Growth Factor 23 and Sclerostin Levels in Subjects with Vitamin D Deficiency. Endocrinol Metab. 2017;32:451-59.
[23] Hershkovitz A, Maydan G, Ben Joseph R, Nissan R. Vitamin D levels in post-acute hip fractured patients and their association with rehabilitation outcomes. Disabil Rehabil. 202120:01-08.
[24] Billoo A, Murtaza G, Memon MA, Khaskheli SA. Comparison of oral versus injectable vitamin-D for the treatment of nutritional vitamin-D deficiency rickets. Journal of the College of Physicians and Surgeons Pakistan. 2009;19(7):428-31.
[25] Hashemipour S, Sarukhani MR, Asef zadeh S, Ghazi AA, Mehrtash B, Ahmadian Yazdi MH. Effect of different doses of parenteral vitamin D3 on serum 25 (OH) D concentrations. DARO. 2009;17:26-29.
[26] Robertson DS, Jenkins T, Murtha YM, Della R. Effectiveness of vitamin D therapy in orthopaedic trauma patients. J Orthop Trauma. 2015;29(11):e451-e453.
[27] Lakkireddy M, Karra M, Patnala C. Efficiency of vitamin D supplementation in patients with mechanical low back ache. J Clin Orthop Trauma. 2019;10(6):1101-10.
[28] Mittal H, Rai S, Shah D, Madhu SV. 300,000 IU or 600,000 IU of Oral Vitamin D3 for Treatment of Nutritional Rickets: A Randomized Controlled Trial. Indian Pediatr. 2014;51(15): 259-61.
[29] Haden ST, Brown EM, Hurwitz S, Scott J, El-Hajj Fuleihan G. The effects of age and gender on parathyroid hormone dynamics. Clin Endocrinol (Oxf). 2000;52:329-38.
[30] Choi HK, Chung YS, Choi YJ, Seo DH, Lim SK. Efficacy and safety of vitamin D3 B.O.N intramuscular injection in Korean adults with vitamin D deficiency. Osteoporos Sarcopenia. 2016;2:228-237.
[31] Sanfelix-Genovés J, Gil-Guillén VF, Orozco-Beltran D, Giner-Ruiz V, Pertusa-Martínez S, Reig-Moya B, et al. Determinant factors of osteoporosis patients' reported therapeutic adherence to calcium and/or Vitamin D supplements: A cross-sectional, observational study of postmenopausal women. Drugs Aging. 2009;26:861-69.
[32] Díez A, Carbonell C, Calaf J, Caloto MT, Nocea G. Observational study of treatment compliance in women initiating antiresorptive therapy with or without calcium and Vitamin D supplements in Spain. Menopause. 2012;19:89-95.
[33] Pearce SH, Cheetham TD. Diagnosis and management of Vitamin D deficiency. BMJ. 2010;340:b5664.
[34] Vieth R. Why the minimum desirable serum 25-hydroxyvitamin D level should be 75 nmol/L (30 ng/ml). Best Pract Res Clin Endocrinol Metab. 2011;25:681-91.
[35] Kaur P, Mishra SK, Mithal A. Vitamin D toxicity resulting from overzealous correction of Vitamin D deficiency. Clin Endocrinol (Oxf). 2015;83:327-31.

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