ABSTRACT

Background: There are various scientific studies in literature which have pointed high prevalence of Vitamin D deficiency in elderly Indian population but there is no study which has shown that adequate Vitamin D supplementation can improve the bone and muscle health or increase the bone mineral density (BMD) in this age group. Aims and Objectives: (1) The primary objective of this study was to evaluate the role of Vitamin D supplementation in the improvement of BMD in elderly Indian population. (2) The secondary objective is to observe the change in serum Vitamin D levels by oral supplementation of Vitamin D in this age group. Materials and Methods: This is a randomized controlled study of total 80 elderly subjects. All subjects had Vitamin D levels <20 ng/ml, they were randomly allocated to one of the two groups as follows: Both groups were given calcium (500 mg) as a routine supplement for 6 months. Study Group I (n = 40): In this group along with calcium, the subjects were given 60,000 IU of Vitamin D as oral nano solution once weekly for 6 months. Placebo Group II (n = 40): In this group, no additional Vitamin D supplementation was given. Both groups were given calcium (500 mg) as a routine supplement for 6 months. Elderly subjects were followed up at 3 months, 6 months, 12 months, and at 18 months period with BMD and serum Vitamin D levels evaluated at each follow-up visit. BMD evaluation was done by dual-energy X-ray absorptiometry. A T-score was used for the evaluation of BMD. According to the World Health Organization, a T-score of –1.0 or above is normal bone density, a T-score between –1.0 and –2.5 means you have low bone density or osteopenia. A T-score of –2.5 or below is a diagnosis of osteoporosis. The data were analyzed using Statistical Package for the Social Sciences version 15.0. Results: Age of subjects ranged from 60 to 78 years. Maximum number of people were of 66–70 years (41.3%). Majority of them were female (n = 51; 63.7%). Female-to-male ratio was 1.75:1. At baseline, mean T-score values were −2.93 ± 0.24 in Group I and −2.89 ± 0.19 in Group II. At baseline, mean Vitamin D levels were 12.55 ± 2.35 ng/ml and 11.88 ± 2.39 ng/ml, respectively, in Groups I and II. At 6 months, mean T-score values were −1.47 ± 1.27 in Group I and −2.30 ± 0.67 in Group II. On evaluating the data statistically, the difference between two groups was found to be significant (P < 0.001). The mean Vitamin D levels were 26.44 ± 7.25 ng/ml and 13.58 ± 2.26 ng/ml, respectively, in Groups I and II. Thus, mean levels were higher in Group I as compared to that in Group II and this difference significant statistically too (P < 0.001). Conclusion: This study concludes that appropriate supplementation of Vitamin D helps in speedy improvement of BMD in elderly population. It also shows that Vitamin D oral supplementation helped to improvise as well as normalize the Vitamin D status among elderly. Hence, it is suggested through this study that Vitamin D supplementation is highly recommended in the elderly to improve their bone and muscle health.

KEY WORDS: Bone Mineral Density; Vitamin D; T-score
INTRODUCTION

Elderly population (65 years and older) of the world has been increasing over the years. In 2010, an estimated 524 million people were aged 65 years or older globally, representing 8% of the world’s population.[1] By 2050, this number is expected to nearly triple to about 1.5 billion individuals aged 65 years or older.[1] The world’s population percentage for people over 65 years will double from about 11% to 22%.[2]

Aging in humans as in other living being is an irreversible process characterized by anatomical, biochemical, and physiological changes in all the functional systems. There are significant changes in the musculoskeletal system as well causing loss of muscle mass, bone mass, and bone strength.[3] This causes gradual and severe weakening of bone and if unchecked can lead to increased risk of osteoporosis and fragility fractures. The Indian elderly population is especially prone to weakening of bone as their physiological and chronological age increases. This age-related osteopenia and osteoporosis increase the risk for falls and fractures, making older individuals more susceptible to the development of mobility limitations or severe disabilities that ultimately affect their capacity for independence.[4]

The correct assessment of physiological bone strength is measurement of bone mineral density (BMD) by dual-energy X-ray absorptiometry (DEXA). The gold standard for measuring bone material properties in clinical practice is axial DEXA measurement from femur and spine.[3]

The positive role of Vitamin D supplementation in increasing bone strength and hence decreasing risk of fractures is well known.[5-7] The association between Vitamin D supplementation and its impact on BMD rise Vitamin D is rarely studied in detail in elderly Indian population. The present study was planned to find out correlation between Vitamin D levels and rise in BMD and also to clearly define the role of Vitamin D supplementation in elderly Indian population.

This is the first Indian study which has carefully analyzed these important associations through a well-defined randomized controlled trial (RCT) in elderly people.

MATERIALS AND METHODS

This prospective randomized controlled study on elderly people was carried out at the Department of Physiology, Era’s Lucknow Medical College, Lucknow, from January 2018 to June 2019 (18 months). The study proposal was submitted to the Institutional Ethics Committee (IEC) of the medical college and appropriate ethical clearance was obtained.

Research Design

This was a prospective randomized controlled study.

Study Population

Normal elderly population comprising staff and relatives of Era Medical College.

Randomization Method

Computer-generated random tables.

Sample Size Calculation

In a study by Dawson-Hughes et al.,[8] 6-month Vitamin D intervention has shown BMD changes in total body to be +0.06 ± 1.83 and −1.09 ± 1.71 in the placebo group, thus showing a difference between two groups to be 1.15 with a pooled standard deviation of 1.8. We also targeted a similar change. The sample size has been calculated using the following formula:

$$n = \left[ \frac{16\sigma^2}{d^2} \right] + 1$$

where, $\sigma$ is the pooled standard deviation and $d$ is the mean difference between two groups. Thus, in the present study, $\sigma = 1.8$ and $d = 1.15$. Putting these values in formula, we get the equation

$$n = \left[ \frac{16 (1.8^2)}{(1.15^2)} \right] + 1$$

$$= \left[ (16*2.45) \right] + 1$$

$$= 39.2 + 1 \sim 40$$

that is, 40 samples in each group.

Inclusion Criteria

The following criteria were included in the study:

1. Normal elderly population aged >60 years (male and female both)
2. Having Vitamin D levels <20 ng/ml.

Exclusion Criteria

The following criteria were excluded from the study:

1. Subjects with secondary osteoporosis, tumors, or infection
2. Subjects unable to come for follow-up visits.

Methods

The study proposal was submitted to the IEC of the Era Medical College, Lucknow, and appropriate ethical permission and clearance for the study were obtained.

All elderly subjects (age >60 years M/F) were collected from the staff of Era Medical College and their relatives fulfilling the study criteria were subjected to the following:
Group allocation

Allocation of subjects into two groups –

After explaining the details of procedures and obtaining written informed consent including a detailed consent for blood test, the patients were allocated alternately to one of the two groups through computerized random number generation.

History Taking and Examination

Dietary habits, duration of sun exposure, and milk intake of the patients were evaluated by dietary recall method.

Investigations

Investigations as required and when feasible:
1. Routine hemogram
2. Biochemical profile including fasting blood sugar, liver function tests, and renal function tests
3. Serum Vitamin D and calcium levels
4. BMD
   - Hip region – including trochanter, femoral neck, and intertrochanteric regions

Procedure

Hematological and biochemical assessment was done using automated analyzer. BMD was measured using DEXA scan at the hip region and the lumbar spine. The DEXA machine used was Osteodoctor manufactured by GE Healthcare Inc., USA. Hip BMD included trochanter, femoral neck, and intertrochanteric regions; lumbar spine BMD included lumbar vertebrae L1-L4. T-scores were obtained. The reference value of T and Z scores was entered in the DXA machine with software for the Asian reference value.

Group Allocation

All the subjects having Vitamin D levels <20 ng/ml were randomly allocated to one of the two groups as follows [Table 1]:

- Both groups were given calcium (500 mg) as a routine supplement for 6 months. They were randomly allocated to one of the two groups as follows:

**Study Group I (n = 40)**

In this group along with calcium, the subjects were given 60,000 IU of Vitamin D as oral nano solution once weekly for 6 months.

**Placebo Group II (n = 40)**

In this group, no additional Vitamin D supplementation was given.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (n=40)</th>
<th>Group II (n=40)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>T-score</td>
<td>–2.92</td>
<td>0.24</td>
<td>–2.89</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>12.51</td>
<td>2.32</td>
<td>11.89</td>
</tr>
</tbody>
</table>

Follow-up [Figure 1]

- Subjects were called for follow-up at 6 months, 12 months, and 18 months
- BMD measurements were recorded at all the follow-up intervals
- Vitamin D levels were assessed again and recorded at follow-up intervals.

A T-score was used for evaluation of BMD. T-score shows how much the bone density of subject is higher or lower than the bone density of a healthy 30-year old adult. According to the World Health Organization, a T-score of –1.0 or above is normal bone density, a T-score between –1.0 and –2.5 means that the subject has low bone density or osteopenia. A T-score of –2.5 or below is a diagnosis of severe bone weakness or osteoporosis.[9] The lower a person’s T-score, the lower the bone density.

Statistical Analysis

The data were analyzed using Statistical Package for the Social Sciences version 15.0. Proportional data were compared using Chi-square test whereas mean differences were compared using Student’s “t”-test. Within-group change was studied using paired “t”-test. The confidence level of the study is kept at 95%, hence, “P” < 0.05 was considered statistically significant.

RESULTS

Age of subjects ranged from 60 to 78 years. Maximum number of persons were of 66–70 years (41.3%). There were 40 females and 40 males. At baseline, mean T-score values were –2.92 ± 0.24 in Group I and –2.89 ± 0.19 in Group II. On evaluating the data statistically, the difference between two groups was not found to be significant (P = 0.442). At baseline, mean Vitamin D levels were 12.51 ± 2.32 ng/ml and 11.89 ± 2.38 ng/ml, respectively, in Groups I and II. Although mean levels were higher in Group I as compared to that in Group II, yet this difference was not found to be significant (P = 0.207).

At 18 months, mean T-score values were –1.47 ± 1.27 in Group I and –2.30 ± 0.67 in Group II. On evaluating the data...
statistically, the difference between two groups was found to be significant \((P < 0.001)\). The mean Vitamin D levels were 26.44 ± 7.25 ng/ml and 13.58 ± 2.26 ng/ml, respectively, in Groups I and II. Thus, mean levels were higher in Group I as compared to that in Group II and this difference significant statistically too \((P < 0.001)\) [Table 1].

At baseline, in both the groups, none of the patients had Vitamin D levels in normal range. There were 35 (87.5%) patients with insufficiency and 5 (12.5%) patients with deficiency in both the groups [Table 2]. Statistically, the Vitamin D status was perfectly matched between two groups \((P = 1)\).

At 18 months, mean T-score values were –1.11 ± 0.27 in Group I and –2.30 ± 0.67 in Group II. On evaluating the data statistically, the difference between two groups was found to be significant \((P < 0.001)\). At 18 months, mean Vitamin D levels were 36.44 ± 7.25 ng/ml and 13.58 ± 2.26 ng/ml, respectively, in Groups I and II. Thus, mean levels were higher in Group I as compared to that in Group II and this difference significant statistically too \((P < 0.001)\) [Table 3].

No adverse effect/complication due to Vitamin D supplementation was noted during the entire course of study.

**DISCUSSION**

The present study examined whether addition of Vitamin D as a supplement helps in improvement of BMD in elderly Indian population. With increasing life expectancy and increasing focus on the health and well-being of the elderly, the focus has shifted to understanding the physiology of musculoskeletal aging and to maintain a healthy physiological bone strength to enable the elderly to lead an independent life.\(^{10,11}\) Evidence has shown that supplementation of Vitamin D, 400 IU daily has a positive impact on total hip BMD\(^{10}\) as well as overall improvement in musculoskeletal system health.\(^{12}\) However, clinical evidence regarding usefulness of Vitamin D supplementation among elderly Indian population is scarce and limited. Hence, the present study was carried out with an
aim to assess the prevalent Vitamin D levels in healthy elderly subjects and to correlate them with BMD values and to assess the role of Vitamin D supplementation in improvement or increase in BMD values. RCT is the best design to evaluate the efficacy of an intervention to be measured prospectively. In our study, elderly subjects were randomly allocated to one of the two groups, a total of 40 (50%) received Vitamin D supplementation along with standard calcium dosage for the elderly and comprised Group I or case group of study while remaining 40 (50%) did not receive any additional Vitamin D treatment and comprised the placebo group or Group II of the study. The two groups were matched for age and gender. Age of subjects enrolled in the study ranged from 60 to 78 years. Overall, the mean age of patients was 67.29 ± 3.76 years. In the present study, all the subjects at baseline had T-scores <−2.5 indicative of osteoporosis. Mean baseline Vitamin D levels in both the groups were 12.55 ± 2.35 ng/ml and 11.88 ± 2.39 ng/ml, respectively. Vitamin D levels were in insufficiency and deficiency categories in 87.5–12.5% of patients in both the groups, thus showing a perfect matching of baseline profile of two groups. After 18 months, the change in T-scores was 30% higher in Vitamin D supplemented group as compared to that in the other group. We also evaluated the impact of addition of oral Vitamin D supplementation on the serum Vitamin D levels, at the end of 18 months, nearly 100% of subjects in the supplementation group and 65% in the placebo group had achieved normal Vitamin D levels. This summarizes that adequate Vitamin D supplementation leads to overall improvement in bone health in elderly population.

Compared to the present study, Dawson-Hughes et al. in their study included the elderly above 65 years of age and reported the mean age of their patients above 70 years. In another study, Grados et al. reported the mean age of their subjects to be 75 years. Mukaiyama et al. reported the mean age of their subjects as 69.4 years. However, Larsen et al. in their study had mean age of patients lesser than ours (61.1 ± 7.6 years). In general, age >65 years is considered to be the age at which the decline in dermal capacity to produce Vitamin D reaches to its nadir. However, this decline is not simultaneous and happens gradually. In the present study, we defined the elderly as 60 years and using a purposive sampling selected only those patients who had Vitamin D levels lesser than normal range. Difference in mean age of patients in different series might be reflective of the average life expectancy in different environments. In India, the average life expectancy is relatively lesser, the average age of the elderly in the present study is slightly lesser. The present study showed a female preponderance with 63.7% of patients being female. The prevalence of osteoporosis is much higher in women in India as compared to men. In different intervention studies too, the female preponderance was dominant. Dawson-Hughes et al. in their study had a male-female ratio of 0.83. On the other hand, Gardos et al. and Mukaiyama et al. conducted their study in an exclusive female sample only. The findings of the present study are close to the observations made by Dawson-Hughes et al. who showed that at the end of 1 year, the % difference of change between the case and placebo groups is 22% which is slightly similar to 30% difference studied in the present study. The variation in response to treatment in different studies could probably be due to difference in profile of subjects in different studies. The present study was carried out in a tropical country where natural source of Vitamin D is available in plenty whereas most of the previous studies have been carried out in Western countries where exposure to sun is relatively lesser. Dietary differences might also contribute for the difference in outcome of study. The differences in results of different studies must also be considered in view of difference in baseline Vitamin D levels. In the present study, both the groups did not have Vitamin D levels in normal range (mean Vitamin D levels 12.55 ± 2.35 ng/ml and 11.88 ± 2.39 ng/ml, respectively, in the supplemented and placebo groups, respectively). However, Dawson-Hughes et al. in their study reported the initial 1,25-OH Vitamin D levels to be 33.3 ± 13.6 ng/ml and 33.0 ± 16.3 ng/ml, respectively, in the placebo and supplemented groups. In another study, Grados et al. included only those cases having Vitamin D levels <12 ng/ml. These differences in initial Vitamin D levels definitely might have an impact on the outcome. One of the biggest strengths of this study is that we evaluated the outcome in qualitative terms; at the end of our study, only 5% of patients in the supplemented group had BMD in osteoporotic range as compared to 35% of patients in the placebo group (difference of 30%). On reviewing the literature, we did not come across any study evaluating the outcome in qualitative terms. Another strength of this study is that we also evaluated the direct impact of addition of oral Vitamin D supplementation and lifestyle recommendations on the serum Vitamin D levels. At the start of study, Vitamin D levels were in insufficiency and deficiency category in all the subjects in both the groups, which is in concordance with earlier Indian studies showing the high prevalence of Vitamin D deficiency in elderly age groups, young females, as well as in people of high socioeconomic strata. However, at the end of 18 months, nearly 100% of subjects in the supplementation group and 65% in the placebo group had achieved normal Vitamin D levels. The change from Vitamin D deficiency/insufficiency to normalcy in the supplemented group could be viewed as an effect of adequate Vitamin D supplementation, however, the positive change in Vitamin D status in the placebo group could be attributed to the universal recommendation of adequate sun exposure and intake of diets rich in calcium and Vitamin D. Lifestyle and dietary factors might play an important role in determining the extent of change in Vitamin D status. This is very important in general elderly population in India who are inherently deficient in Vitamin D. Two limitations of the present study were length of study and sample size, due to which the long-term impact of Vitamin D supplementation

731 National Journal of Physiology, Pharmacy and Pharmacology 2021 Vol 11 Issue 07
in terms of rate of change in BMD could not be studied. In the absence of long-term follow-up and small sample size, the present study is not in a position to assess the benefit of adding Vitamin D supplementation in terms of fracture risk. Hence, further studies are recommended to be carried out for a longer follow-up duration and in a larger sample size.

CONCLUSION

On the basis of the present study, it can be concluded that supplementation of Vitamin D helped in improving the BMD levels, thus helping in increased bone formation and resultant bone strength. This study also highlights the increasing prevalence of Vitamin D deficiency among elderly population in India. Hence, Vitamin D supplementation helped to improvise the Vitamin D status among the elderly. Vitamin D supplementation is recommended in elderly population for the prevention of osteoporosis, maintenance of good musculoskeletal health, and in prevention of fractures.

ACKNOWLEDGMENTS

The authors are grateful to all the non-faculty staff members of Era Medical College and their relatives for their willful participation in this study.

REFERENCES

5. Epstein S. The problem of low levels of Vitamin D and osteoporosis: Use of combination therapy with alendronic acid and calcitriol (Vitamin D3). Drugs Aging 2006;23:617-25.

How to cite this article: Mishra P, Trivedi V, Srivastava D. A study on change in bone mineral density with Vitamin D supplementation in elderly Indian population. Natl J Physiol Pharm Pharmacol 2021;11(07):727-732.

Source of Support: Nil, Conflicts of Interest: None declared.