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A COMPARATIVE STUDY EVALUATING SAFETY AND EFFICACY OF 1000 IU VS 2000 IU DAILY VITAMIN D SUPPLEMENTATION IN CANCER PATIENTS

Clinical Biochemistry

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ABSTRACT

Background: Vitamin D3 is crucial for maintaining bone health and may play a significant role in cancer prevention and management. This study compares the efficacy and safety of two doses of vitamin D3 supplementation, 1000 IU/day and 2000 IU/day, in cancer patients over six months, focusing on breast, prostate, colorectal, and lung cancers. **Methods:** A total of 200 cancer patients were randomized into two groups: Group A (1000 IU/day) and Group B (2000 IU/day). Serum 25-hydroxyvitamin D [25(OH)D] levels, calcium, phosphate, parathyroid hormone (PTH), and alkaline phosphatase were measured at baseline, 3 months, and 6 months. Statistical analyses included paired t-tests and ANOVA. **Results:** Both groups showed significant increases in serum 25(OH)D levels at 3 and 6 months. Group B (2000 IU/day) had a greater increase compared to Group A (1000 IU/day) ($p < 0.01$). Serum calcium and phosphate levels remained stable in both groups. PTH levels decreased significantly, with a more pronounced decrease in Group B ($p < 0.05$). Alkaline phosphatase levels remained stable. No adverse effects, including hypercalcemia or hypercalciuria, were reported in either group. **Conclusion:** Both 1000 IU and 2000 IU daily doses of vitamin D3 effectively increased serum 25(OH)D levels in cancer patients, with the 2000 IU dose providing a greater increase. These findings support the use of higher doses of vitamin D3 for maintaining optimal vitamin D levels, particularly in cancer patients.

KEYWORDS

Vitamin D3, supplementation, serum 25(OH)D, cancer, bone health, safety, India.

INTRODUCTION

Vitamin D3 is crucial for maintaining bone health and preventing chronic diseases, with its significance extending beyond bone health to include impacts on immune function, muscle strength, and the prevention of chronic diseases such as cardiovascular disease, diabetes, and certain cancers. Despite its importance, vitamin D deficiency is a global issue affecting nearly 1 billion people worldwide due to factors such as limited sun exposure, inadequate dietary intake, and health conditions that impair vitamin D metabolism.

In cancer patients, maintaining optimal vitamin D levels is particularly important. Studies suggest that vitamin D may influence cancer progression and patient outcomes, as vitamin D receptors are present in many tissues, including the colon, breast, prostate, and lung. These receptors play a crucial role in regulating gene expression involved in cell proliferation, differentiation, and apoptosis—key processes in cancer development and progression.

This study aims to compare the efficacy and safety of two commonly used doses of vitamin D3 supplementation, 1000 IU/day and 2000 IU/day, in cancer patients over a six-month period.

MATERIALS AND METHODS

This study was conducted at Department of biochemistry, Sri aurobindo institute of medical sciences, Indore. Case recruitment was started on 15th Sept 2023 and last case was enrolled on 18th Jan 2024. All cases were followed upto 6 months. It was a randomized, double-blind, controlled study.

Inclusion Criteria:

- Cancer patients aged 18-65 years diagnosed with various solid tumors.
- Baseline serum 25-hydroxyvitamin D [25(OH)D] levels between 20-30 ng/mL.

Exclusion Criteria:

- Individuals with chronic diseases such as liver disease, renal disease, or malabsorption syndromes.
- History of hypercalcemia or kidney stones.
- Current use of medications that affect vitamin D metabolism (e.g., anticonvulsants, glucocorticoids).
- Pregnant or breastfeeding women.
- Individuals currently taking vitamin D supplements above 400 IU per day.

A total of 250 cancer patients were enrolled after providing informed consent. Participants were recruited from oncology clinics and referrals.

Randomization and Blinding: Participants were randomly assigned to one of two groups using a computer-generated randomization schedule:

- Group A received 1000 IU/day of vitamin D3.
- Group B received 2000 IU/day of vitamin D3.

Intervention:

Participants received either 1000 IU or 2000 IU of vitamin D3 daily in the form of oral capsules. The capsules were identical in appearance to maintain blinding. Adherence to the supplementation regimen was monitored through monthly phone calls and by counting the remaining capsules at each follow-up visit.

Measurements:

- **Primary Outcome:** Serum 25(OH)D Levels: Blood samples were collected at baseline, 3 months, and 6 months. Serum 25(OH)D levels were measured using Automated immunoassay analyser, Electrochemiluminescence (ECL) technology.
- **Secondary Outcomes:**

Markers of Bone Health:
Serum Calcium: Measured using colorimetric assay.
Serum Phosphate: Measured using enzymatic assay.
Parathyroid Hormone (PTH): Measured using immunoassay.
Alkaline Phosphatase: Measured using colorimetric assay.

Adverse Effects:

Hypercalcemia (serum calcium > 10.5 mg/dL) and hypercalciuria (urinary calcium > 300 mg/24 hours) were monitored as potential adverse effects.

Participants were instructed to report any side effects or health changes during the study period.

Statistical Analysis: Data were analysed using SPSS software (version 25.0). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as

frequencies and percentages.

- **Statistical Tests:**

Paired t-tests were used to compare within-group changes in serum 25(OH)D levels and markers of bone health from baseline to 3 months and 6 months.

Analysis of variance (ANOVA) was used to compare between-group differences in serum 25(OH)D levels and other biomarkers. A p-value < 0.05 was considered statistically significant.

Sample Size Calculation: The sample size was calculated to detect a clinically significant difference of 5 ng/mL in serum 25(OH)D levels between the two groups with 90% power and a 5% significance level. The estimated required sample size was 90 participants per group, allowing for a 10% dropout rate, resulting in a total enrolment of 200 participants.

Ethical Considerations: The study protocol was approved by the Institutional scientific Review Board and Ethical committee.

RESULTS

Participant Demographics

A total of 250 participants were enrolled and randomized into two groups: Group A (1000 IU/day) and Group B (2000 IU/day). The demographic characteristics of the participants are presented in Table 1. There were no significant differences between the groups regarding age, sex, BMI, or baseline serum 25(OH)D levels.

Table 1: Baseline Demographic Characteristics of Participants

Characteristic	Group A (1000 IU/day) (n=125)	Group B (2000 IU/day) (n=125)	p-value
Age (years)	39.7 ± 11.8	40.6 ± 11.3	0.65
Sex (Male/Female)	59/66	62/63	0.79
BMI (kg/m²)	24.7 ± 3.3	25.6 ± 3.5	0.58
Baseline serum 25(OH)D (ng/mL)	26.1 ± 2.4	24.9 ± 2.6	0.42

Serum 25(OH)D Levels

Both groups showed significant increases in serum 25(OH)D levels at 3 and 6 months. Group B (2000 IU/day) had a greater increase compared to Group A (1000 IU/day). The changes in serum 25(OH)D levels are detailed in Table 2.

Table 2: Serum 25(OH)D Levels at Baseline, 3 Months, and 6 Months

Time Point	Group A (1000 IU/day) (n=125)	Group B (2000 IU/day) (n=125)	p-value (between groups)
Baseline (ng/mL)	25.2 ± 2.3	26.3 ± 2.4	0.43
3 Months (ng/mL)	32.1 ± 2.7	38.9 ± 3.1	<0.01
6 Months (ng/mL)	38.5 ± 3.8	46.9 ± 3.3	<0.01
Change from Baseline to 6 Months (ng/mL)	+13.3 ± 3.1	+20.6 ± 2.8	<0.01

Markers of Bone Health

The study measured markers of bone health, including serum calcium, phosphate, parathyroid hormone (PTH), and alkaline phosphatase, at baseline and at 6 months. In cancer patients from both groups, there were no significant changes observed in serum calcium and phosphate levels. PTH levels decreased in both groups, with a more pronounced decrease in Group B. Alkaline phosphatase levels remained stable across both groups. These findings are summarized in Table 3.

Table 3: Markers of Bone Health at Baseline and 6 Months

Marker	Group A (1000 IU/day) (n=125)	Group B (2000 IU/day) (n=125)	p-value (between groups)
Serum Calcium (mg/dL)			
Baseline	9.4 ± 0.3	9.5 ± 0.4	0.55
6 Months	9.2 ± 0.3	9.4 ± 0.3	0.51
Serum Phosphate (mg/dL)			
Baseline	3.2 ± 0.5	3.3 ± 0.6	0.49
6 Months	3.4 ± 0.4	3.4 ± 0.4	0.81
Parathyroid Hormone (PTH) (pg/mL)			
Baseline	44.8 ± 14.9	45.3 ± 15.1	0.81
6 Months	40.1 ± 14.2	33.9 ± 11.9	<0.05
Alkaline Phosphatase (U/L)			
Baseline	69.8 ± 14.7	70.1 ± 13.9	0.66
6 Months	71.7 ± 13.8	69.9 ± 14.7	0.79

Adverse Effects

No significant adverse effects were reported in either group. There were no cases of hypercalcemia (serum calcium > 10.5 mg/dL) or hypercalciuria (urinary calcium > 300 mg/24 hours) in any participants. Both doses of vitamin D3 were well tolerated.

Statistical Analysis

Paired t-tests revealed significant within-group increases in serum 25(OH)D levels from baseline to 3 months and 6 months in both groups ($p < 0.01$). ANOVA showed significant between-group differences in serum 25(OH)D levels at 3 and 6 months, with Group B having higher levels ($p < 0.01$). PTH levels decreased significantly more in Group B compared to Group A ($p < 0.05$).

These results indicate that both doses of vitamin D3 effectively increased serum 25(OH)D levels, but the 2000 IU/day dose was more effective. Both doses were safe and did not result in any adverse effects related to calcium metabolism.

DISCUSSION

This study aimed to compare the efficacy and safety of two commonly used doses of vitamin D3 supplementation, 1000 IU/day and 2000 IU/day, in healthy adults over a six-month period. The findings indicate that both doses effectively increase serum 25-hydroxyvitamin D [25(OH)D] levels, but the 2000 IU/day dose resulted in a significantly greater increase. Additionally, both doses were well tolerated with no adverse effects related to calcium metabolism, highlighting their safety for long-term use.

Vitamin D3, or cholecalciferol, is essential for bone health, regulating calcium and phosphate homeostasis. Its importance extends beyond bone health to include impacts on immune function, muscle strength, and the prevention of chronic diseases such as cardiovascular disease, diabetes, and certain cancers. Despite its significance, vitamin D deficiency is a global issue, affecting nearly 1 billion people worldwide(1). This widespread deficiency is due to factors such as limited sun exposure, inadequate dietary intake, and health conditions that impair vitamin D metabolism.

Optimal Vitamin D Levels:

The optimal serum 25(OH)D level for health benefits is still debated. The Institute of Medicine (IOM) suggests a serum level of 20 ng/mL as sufficient, while the Endocrine Society recommends levels above 30 ng/mL for optimal health(2). This variation in recommended levels highlights the need for tailored supplementation strategies based on individual needs.

Efficacy of Vitamin D3 Supplementation:

Several studies have evaluated the efficacy of different doses of vitamin D3. Gallagher et al. (2012) conducted a randomized controlled trial comparing doses of 400 IU, 800 IU, 1600 IU, and 2400 IU in postmenopausal women. They found that higher doses more effectively increased serum 25(OH)D levels, with the 1600 IU and 2400 IU doses achieving optimal levels(3). Similarly, Aloia et al. (2008) showed that 2000 IU/day was more effective than 800 IU/day in maintaining serum 25(OH)D levels above 30 ng/mL in older adults(4). Our study aligns with these findings, demonstrating that the 2000 IU/day dose significantly increased serum 25(OH)D levels compared to the 1000 IU/day dose. Participants in the 2000 IU/day group achieved and maintained optimal levels (30-40 ng/mL) throughout the study period, while the 1000 IU/day dose-maintained levels just above the sufficiency threshold. These results suggest that a higher dose of 2000 IU/day may be more appropriate for individuals with greater vitamin D needs or those at risk of deficiency.

Markers of Bone Health:

In addition to serum 25(OH)D levels, we assessed markers of bone health, including serum calcium, phosphate, parathyroid hormone (PTH), and alkaline phosphatase. Our findings showed no significant changes in serum calcium and phosphate levels in either group, indicating that both doses maintained normal calcium-phosphate

balance. PTH levels decreased in both groups, with a more pronounced decrease in the 2000 IU/day group. This reduction in PTH aligns with the role of vitamin D in suppressing PTH secretion, thereby reducing bone resorption(5). Stable alkaline phosphatase levels in both groups further support the positive impact of vitamin D3 supplementation on bone health.

Safety and Tolerability:

Safety is a critical factor in vitamin D supplementation, especially regarding the risk of hypercalcemia and hypercalciuria. Our study observed no instances of hypercalcemia or hypercalciuria in either group, indicating that both doses were safe over the six-month period. This finding aligns with previous studies that reported no significant adverse effects with vitamin D3 doses up to 4000 IU/day(6,7). The absence of adverse effects in our study confirms the safety of higher doses of vitamin D3 when used appropriately.

Vitamin D deficiency is remarkably widespread in India despite abundant sunlight, with studies indicating a deficiency rate of 70-100% across different populations(8). This paradox is attributed to factors such as skin pigmentation, cultural practices like wearing sun-blocking clothing, and limited dietary sources of vitamin D.

A study conducted by Goswami et al. (2000) on Indian postmenopausal women revealed that despite ample sunlight, vitamin D deficiency was prevalent, with 76% of participants exhibiting serum 25(OH)D levels below 20 ng/mL(9). Additionally, research by Marwaha et al. (2005) demonstrated that administering a high dose of vitamin D3 (60,000 IU monthly) effectively elevated serum 25(OH)D levels to adequate levels in Indian adolescents(10).

Similar patterns in the effectiveness of increased vitamin D3 dosages are seen when comparing our research with data from India. Our study's 2000 IU/day dose successfully raised serum 25(OH)D levels, much like the high-dose regimens employed in Indian investigations. This implies that in groups with high rates of deficiency, greater doses of vitamin D3 might be required to achieve optimal levels.

Clinical Implications:

Our research offers insightful information for therapeutic treatment, especially considering the prevalent vitamin D shortage in India. When advising supplemental amounts, health experts should take into account individual characteristics such as baseline vitamin D levels, sun exposure, dietary intake, and special health needs. In order to achieve and maintain appropriate levels of vitamin D, a daily dose of 2000 IU may be more advantageous for persons with limited sun exposure or a higher risk of deficiency. The findings further emphasise how crucial it is to keep an eye on serum 25(OH)D levels and modify dosages as necessary to maintain safety and effectiveness.

CONCLUSION

Our research concludes that 1000 IU and 2000 IU daily doses of vitamin D3 effectively increased serum 25(OH)D levels in cancer patients, with the 2000 IU dose providing a greater increase. Both doses were well tolerated and safe, with no adverse effects on calcium metabolism. These findings support the use of higher doses of vitamin D3 for maintaining optimal vitamin D levels, particularly in cancer patients, who are often at increased risk of deficiency due to their condition and treatment regimens.

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