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ORAL VERSUS INTRAMUSCULAR VITAMIN D THERAPY FOR CHILDREN WITH VITAMIN D DEFICIENCY

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Abstract

Objective:
To compare oral vitamin D therapy and intramuscular vitamin D therapy in terms of mean increase in vitamin D levels in children with vitamin D deficiency.

Methods:
This trial included 200 patients with vitamin D deficiency from the Children's Hospital Lahore from June 2024 to January 2025. The patients were randomized into two groups: Group A received oral vitamin D, and Group B received intramuscular vitamin D. Baseline tests included serum calcium, phosphate, alkaline phosphatase, and 25-hydroxy vitamin D. Patients were followed at three, six, and twelve weeks, with the same tests repeated at these intervals.

Results:
The mean age of patients was 5.93±2.11 years. There were 114 (57.0%) male and 86 (43.0%) female patients. The mean increase in vitamin D levels at three weeks was 3.25±1.18 ng/mL in group A and 1.60±0.27 ng/mL in group B, with a p-value of <0.001. At six weeks, the increases were 10.97±2.08 ng/mL in group A and 7.93±1.38 ng/mL in group B, both with p-values <0.001. At twelve weeks, the increases were 16.09±2.99 ng/mL in group A and 11.52±3.58 ng/mL in group B, with a p-value of <0.001.

Conclusion:
Oral vitamin D is superior to intramuscular therapy in treating vitamin D deficiency in children.

INTRODUCTION

Vitamin D is a secosteroid that plays a crucial role in maintaining musculoskeletal health, and its deficiency is considered a pandemic.[1] The lack of this essential compound has been linked to the development of autoimmune diseases, cancer, and ischemic heart disease, among other conditions.[1] Insufficiency can manifest as hypocalcemia during rapid growth phases, such as infancy or adolescence. This suggests that the body's

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demands are not being fulfilled. In severe cases, it may lead to rickets or symptoms like seizures and tetany.[2] Furthermore, vitamin D deficiency is linked to various long-term health issues in children, including cystic fibrosis, childhood asthma, chronic obstructive pulmonary disease, interstitial lung disease, and the onset of hypertension and diabetes mellitus.[3, 4]

Considering the crucial role of vitamin D in the development and maintenance of a healthy human, treating vitamin D deficiency is essential. Various regimens are suggested for this purpose, with differences in dosage, frequency, and whether maintenance therapy is included.[5] Stoss therapy involves the use of a single large dose of vitamin D, and has been described in some detail in adults, however, data on the effectiveness of this method of administration is lacking in children. Moreover, it is unclear whether parenteral administration is required or whether an oral dose is sufficient.[6, 7] The aim of this study was to compare oral vitamin D therapy and intramuscular vitamin D therapy in terms of mean increase in vitamin D levels in children with vitamin D deficiency.

METHODS:

This randomized clinical trial involved 200 pediatric patients aged 3-10 years with vitamin D deficiency. Exclusion criteria included recent use of any vitamin D supplements within the past three months, malabsorption syndromes like Celiac or Whipple's disease, chronic pancreatitis, cystic fibrosis, or chronic liver or kidney disorders. Patients who had taken drugs affecting vitamin D absorption or metabolism—such as antituberculosis medications, antiepileptic drugs, or corticosteroids—within the last six months, or those with a history of allergic reactions to vitamin D therapy (oral or intramuscular), were also excluded.

Patients were then randomized to one of two groups via block randomization (allocation via manila envelopes): Group A received oral vitamin D therapy, while Group B received intramuscular vitamin D therapy. Patients in the oral group received a single oral dose of 300,000 IU vitamin D3, followed by daily oral calcium and vitamin D supplementation at 50 mg/kg and 400 IU, respectively, for 12 weeks. Patients in the intramuscular group received a single dose of vitamin D3 (600,000 IU) by intramuscular injection, followed by oral calcium and vitamin D supplementation at 50 mg/kg and 400 IU, respectively, daily for 12 weeks.

All patients were tested for serum calcium, phosphate, alkaline phosphatase, and 25-hydroxy vitamin D levels at baseline, i.e., before treatment. Patients were followed up at three-, six-, and twelve-week post-initiation of therapy and tested for serum calcium, phosphate, alkaline phosphatase, and 25-hydroxyvitamin D levels at these intervals. Patients were documented for age, baseline serum calcium, phosphate, alkaline phosphatase, and 25-hydroxy vitamin D levels at baseline and at three-, six-, and twelve-weeks, as well as whether vitamin D deficiency was corrected.

SPSS Version 26 was used for data analysis. The independent-samples t-test was applied to compare baseline and 3, 6, and 12-week serum calcium, phosphate, alkaline phosphatase, and 25-hydroxyvitamin D levels between the groups, with p-values ≤0.05 considered significant.

RESULTS:

The mean age of patients was 5.93±2.11 years. There were 114 (57.0%) male and 86 (43.0%) female patients.

There was no significant difference in baseline lab parameters between the groups. At 3 weeks, serum calcium, phosphate, and alkaline phosphatase remained similar, but vitamin D levels were higher in Group A (18.54 ± 2.94 ng/mL) than Group B (17.21 ± 2.62 ng/mL, $P < 0.001$). At 6 weeks, calcium, phosphate, and alkaline phosphatase still showed no difference, but vitamin D stayed higher in Group A (26.26 ± 3.70 ng/mL) versus Group B (23.54 ± 1.94 ng/mL, $P < 0.001$). At 12 weeks, calcium, phosphate, and alkaline phosphatase remained similar, but vitamin D continued to be higher in Group A (31.38 ± 1.44 ng/mL) than Group B (27.13 ± 2.40 ng/mL, $P < 0.001$) [Table 1].

The mean increase in vitamin D levels was significantly greater in Group A compared to Group B at all follow-up points. At 3 weeks, Group A showed a mean increase of 3.25 ± 1.18 ng/mL,

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while Group B had an increase of 1.60 ± 0.27 ng/mL (P < 0.001). At 6 weeks, the mean increase was 10.97 ± 2.08 ng/mL in Group A versus 7.93 ± 1.38 ng/mL in Group B (P < 0.001). By 12 weeks, Group A demonstrated a mean increase of 16.09 ± 2.99 ng/mL, compared to 11.52 ± 3.58 ng/mL in Group B (P < 0.001) [Table 2].

Table 1. Comparison of Laboratory Variables.

Study Outcome	Groups		P-value
	Group A (N=100)	Group B (N=100)	
Baseline			
Serum Calcium	9.91±0.60	9.97±0.61	0.407
Serum Phosphate	1.49±0.11	1.48±0.11	0.798
Alkaline Phosphatase	223.64±9.22	222.79±8.38	0.439
Serum Vitamin D Levels	15.29±2.59	15.61±2.45	0.303
At 3 Weeks Follow-up			
Serum Calcium	11.03±1.21	11.07±1.24	0.760
Serum Phosphate	1.55±0.14	1.57±0.14	0.204
Alkaline Phosphatase	239.06±4.78	238.21±4.43	0.136
Serum Vitamin D Levels	18.54±2.94	17.21±2.62	<0.001
At 6 weeks Follow-up			
Serum Calcium	11.11±1.16	11.15±1.26	0.835
Serum Phosphate	1.65±0.18	1.66±0.17	0.983
Alkaline Phosphatase	245.28±7.06	245.77±7.42	0.590
Serum Vitamin D Levels	26.26±3.70	23.54±1.94	<0.001
At 12 Weeks Follow-up			
Serum Calcium	11.21±1.19	11.12±1.23	0.562
Serum Phosphate	1.64±0.19	1.62±0.18	0.439
Alkaline Phosphatase	247.12±6.49	246.66±6.46	0.563
Serum Vitamin D Levels	31.38±1.44	27.13±2.40	<0.001

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Table 2. Mean Increase in Vitamin D Levels over time between the two Groups.

Mean Increase in Vitamin D Levels	Groups		P-value
	Group A (N=100)	Group B (N=100)	
At 3 Weeks Follow-up	3.25±1.18	1.60±0.27	<0.001
At 3 Weeks Follow-up	10.97±2.08	7.93±1.38	<0.001
At 3 Weeks Follow-up	16.09±2.99	11.52±3.58	<0.001

DISCUSSION:

Vitamin D plays a crucial role in regulating calcium and phosphorus homeostasis, especially in pathways related to bone mineralization and bone mass development. Besides these well-known skeletal functions, recent research shows that vitamin D also has other important extraskeletal effects, potentially contributing to the development of various health conditions, including infectious and autoimmune diseases diseases.[8]

Hypovitaminosis remains a widespread issue globally. Vitamin D deficiency affects roughly 30 to 50% of various populations, impacting over a billion children and adults. Adults may experience issues like musculoskeletal pain, fibromyalgia, osteopenia, osteoporosis, and rickets in children.[9] Rickets occurs in two forms: calcipenic and phosphopenic, with the former mainly caused by vitamin D deficiency. Treatment options include oral and injectable cholecalciferol, both of which are used for children under five and adults with deficiency.[10, 11] The choice of administration method often depends on the pediatrician's preference, as well as the patient's attitudes toward injections.

In present study we found that oral therapy of vitamin D is more effective than IM therapy in increasing vit. D levels. In our study mean vitamin D levels were significantly high in oral therapy group in comparison to IM group; 31.38±1.43 versus 27.13±0.21 respectively. Mean increase in vitamin D levels from baseline was also more in oral therapy group 16.09±2.99 versus 11.52±3.58 in IM group.

The current study's results support Zabihiyeganeh et al.'s findings, which indicated that after twelve weeks, the mean serum vitamin D level was higher with oral stoss therapy (90 ± 11.2 nmol/L) compared to intramuscular stoss therapy (58.8 ± 8.9 nmol/L).[12]

Contrary to our results, Gupta et al. reported that IM therapy is superior to oral therapy in vitamin D deficiency. They found that serum vitamin D levels were 20.20 ± 1.65 ng/mL at six weeks and 16.66 ± 1.36 ng/mL at twelve weeks with oral vitamin D stoss therapy, while levels with intramuscular (IM) stoss therapy were 20.74 ± 1.81 ng/mL and 25.46 ± 1.37 ng/mL at six and twelve weeks, respectively. IM therapy was associated with higher levels at twelve weeks but similar levels at six weeks as oral therapy. However, a major confounding factor was that baseline vitamin D levels in patients receiving IM stoss therapy were significantly higher than those taking oral therapy.[13]

Mondal et al. conducted a study comparing a single intramuscular dose of 600000 IU of vitamin D with an oral dose. The findings indicated no significant difference in efficacy between the two methods based on biochemical and radiological measures. The study concluded that both oral and single intramuscular injections of 600,000 IU of vitamin D are effective and safe for treating nutritional rickets.[14]

Wylon et al. studied the pharmacokinetics of a single intramuscular dose alongside long-term oral vitamin D supplementation. Their findings indicated no significant difference in serum 25 (OH) D levels after 28 days between the two administration methods.[15] Additionally, a different study indicated that both treatments were well tolerated, though the injectable form showed a statistically significant difference.[9]

The present study is limited by a small sample size. Studies with very large sample sizes across multiple

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institutions should be conducted to determine whether oral or IM vitamin D therapy is superior for treating vitamin D deficiency in children.

CONCLUSION:

Oral vitamin D is superior to intramuscular therapy in treating vitamin D deficiency in children.

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