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ORIGINAL ARTICLE

Efficacy of Daily Recommended Allowance of Vitamin D Given as Pulse Therapy (every 6 months) to Children at a Tertiary Care Hospital

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ABSTRACT

Objective: To determine the minimum effective maintenance dose of vitamin D supplements given as pulse therapy in children

Study Design: A Randomized Prospective Study

Place and Duration of Study: Pediatrics Department, Liaquat University Hospital, Hyderabad and Bachal Soomro Primary School, Hyderabad from March 2018 to February 2019

Material and Methods: Children between 6 months to 12 years having subclinical vitamin D deficiency were included in the study. A total of 110 Children who fulfilled the inclusion criteria i.e. result of a vitamin D level below ≤ 30 nmol/litre were enrolled for the study. There were 2 groups, group A (LUMHS OPD) children received 100,000 units of Vitamin D3 orally and group B children (Bachal Soomro Primary School) received 3 lac units orally. There were 37 children in group A, while 73 children in Group B. Serum vitamin D level was checked after 6 months of vitamin D supplement.

Results: Results showed, that in samples of 3-lac unit dose the mean vitamin D3 level was 15.7 (SD = ± 6.0) was raised significantly after six months of treatment with a mean value of 20.9 (SD ± 4.9), $p < 0.01$ obtained using paired sample t-test. More, in samples of 1-lac unit dose, the mean vitamin D3 level was 23.4 (SD = ± 15.5) did not give any significant effect of treatment, and after six months the mean value of vitamin D3 was 20.2 (SD ± 12.1). A Decrease in mean is considered statistically insignificant with a p-value of 0.268.

Conclusion: A bolus dose of Vitamin D3 three lac units can be given every six months as a maintenance dose, while one lac unit is not effective when given every six months.

Key Words: *Vitamin D deficiency, Maintenance dose, Bolus dose, Oral dose, Children*

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INTRODUCTION

Vitamin D deficiency is more common in children and women. Although it is a global problem but it

is very common in Asian countries. The reasons of vitamin D deficiency are dietary, cultural and poverty.¹ Vitamin D deficiency is common in healthy pregnant women that contribute to vitamin

D Deficiency in infants. In Pakistan, 79.7 % women of child bearing age and 62.7% of children are vitamin D Deficient.²

Vitamin D Deficiency causes rickets, birth defects, osteoporosis, osteomalacia, chronic muscle pain. It is also associated with heart cardiac disorder neurologic and autoimmune disease.³ Vitamin D deficiency can be prevented by giving daily vitamin D to infants (0 to 12 months) 200 IU to 400 IU and 200 IU to 600 IU to children (1 to 5 years).⁴

In our country, diet is not a good source of vitamin D that why its supplementation is required. There may be issues of Compliance with daily vitamin D Supplementation. Noncompliance with Routine Oral Vitamin D supplementation has been documented all over the world. In 1995 high dose of vitamin D given intermittently as prophylaxis was introduced.⁵ Although the problem of compliance is resolved with Pulse therapy but there can be an issue of toxicity with these regimens. A regimen of 6 lac IU vitamin D2 orally every three monthly, caused levels of 25-hydroxyvitamin D above normal along with hypercalcemia. High dose vitamin D is effective in preventing rickets, but there are concern about the hypervitaminosis D.⁶ The manifestations of Vitamin D toxicity are nephrocalcinosis, constipation, abdominal pain, polydipsia, excessive urination, headache, confusion and disorientation.⁷

keeping in mind the problem of compliance with routine Vitamin D administration and the problem of toxicity with Pulse Vitamin D therapy, we conducted a study to assess if maintenance therapy with reduced doses (1 Lac IU and 3 Lac IU every 6 monthly) of Vitamin D is effective in children. The rationale of this study is to assess the minimum effective dose of intermittent vitamin D supplements given as a maintenance dose in children because compliance with daily vitamin D supplements and toxicity with intermittent high doses is a concern.

MATERIAL AND METHODS

This randomized prospective study was done at Pediatrics Out Door Department, Liaquat University of Medical and Health Sciences Hyderabad and Bachal Soomro Primary School

Hyderabad, for total 12 months' duration from March 2018 to February 2019. Children between 6 months to 12 years having subclinical vitamin D Deficiency were included in the study. Children having signs of rickets or history of previous Vitamin D intake were excluded from the study. Approval was taken from Ethical committee of LUMHS Jamshoro. Consent was taken by the parents.

In Pakistan 66.7% children of <5 years of age suffers vitamin D deficiency. Total sample size calculated on open epi was 110 with 5% margin of error, 95% confidence interval and risk prevalence ratio of 1.6. History was taken for the prior vitamin D intake and children were examined to check for signs of rickets. After fulfilling the inclusion criteria, 2 ml venous blood sample was taken from the vein over dorsum of hand for vitamin D level; results of the vitamin D level below ≤ 30 nmol/liter were enrolled for study.⁸

The randomization list was computer generated prior to the start of the study and kept with third party who was not involved with the study at all. Further, to ensure concealment, the block sizes were also randomized.

There were 2 groups, group A (LUMHS OPD) children received 1 lac units of Vitamin orally and group B children (Bachal Soomro Primary School) received 3 lac units orally. The levels were known to the principal investigator but the researchers giving treatment were blinded to the results.

There were 37 children in group A, while 73 children in Group B. All children were reassessed after 6 months and their serum vitamin D level was rechecked. Those children whose serum vitamin D level at 6 months of follow-up was still low, then standard treatment was given. The data were analyzed by using SPSS version 22.0. Categorical variables like: gender and outcome were analyzed by applying Chi Sq. Test and numerical values were measured in mean and frequencies. Outcomes: 1) Improved: Vitamin D level >30 nmol/litre after 6 months of vitamin D therapy 2) Treatment Failure: Vitamin D level <30 after 6 months of vitamin D therapy 3) Defaulters: who left the follow-up

RESULTS

Result showed, in samples of 3-lac unit dose the mean vitamin D3 level was 15.7 (SD = ± 6.0) was

raised significantly after six month of treatment with a mean value of 20.9 (SD ±4.9), p<0.01 obtained using paired sample t-test (Table 1). More, in samples of 1-lac unit dose the mean vitamin D3 level was 23.4 (SD = ±15.5) did not give any significant effect of treatment , and after

six month the mean value of vitamin D3 was 20.2 (SD ±12.1). The Decrease in mean was considered statistically insignificant with p-value 0.268. Comparison of vitamin D3 levels in both group are given in fig 1. Demographic data of study participants is given in Table 2.

TABLE 1: Comparison of Vitamin D3 Levels using Paired Sample t-test

Parameters	Before		After 6-Months		p- value
	Mean	SD	Mean	SD	
Vitamin D3 (n=73) (3-Lack unit dose)	15.7	6.0	20.9	4.9	<0.01*
Vitamin D3 Before (n=37) (1-Lac Unit dose)	23.4	15.5	20.2	12.1	0.268

*p<0.05 was considered significant using paired sample t-test

TABLE 2: Demographic data of study participants

			Mean	Standard Deviation
Group	3 lack Units	Age (months)	88.11	31.19
		Height (cm)	120.96	15.17
		Weight (kg)	21.18	6.86
1 lack Units	Age (months)	33.65	15.15	
	Height (cm)	82.75	19.45	
	Weight (kg)	10.84	2.90	

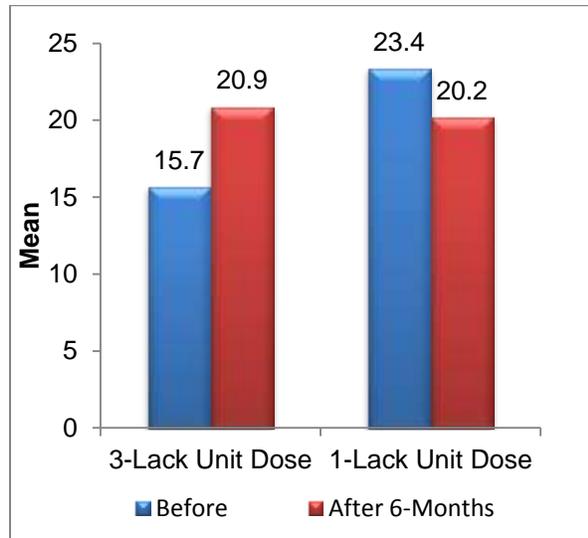


Fig 1: Bar Chart for Comparison

DISCUSSION

In this study we gave vitamin D to all children who did not have clinical signs of deficiency so it was given to normal children as a preventive strategy. The 300, 000 unit dose the of vitamin D3 level

raised serum vitamin D3 level significantly after six months of treatment with a mean value of 20.9 (SD ± 4.9), p<0.01. 1-lack unit dose of vitamin D3 level did not give any significant effect of treatment, and after six months the mean value of vitamin D3 was 20.2 (SD ± 12.1) p value 0.268. The logic for giving 100, 000 unit was to give a maintenance dose of 400 per day that will be around 100, 000 unit every six months but as other studies show that countries where vitamin D deficiency is common a stat dose of 50-100,000 units need to be given before putting them on daily, weekly or monthly dose.

Although the mean value significantly increased after the 3 lac units but still it is in the vitamin d insufficiency range, the reason may be that our study participants were already vitamin D deficient before the intervention.

Studies shows that low dose of vitamin D is safe and effective as compared to a high dose. Vitamin D-deficient children up to 1 year of age can be managed with 2000 IU/day of vitamin D₂ or D₃ for 6 weeks or 50,000 IU of vitamin D₂ or D₃ once a week for total 6 weeks. Once the vitamin D level reaches 30 ng/mL, then give 400-1000 IU/day.⁹

As compliance with daily maintenance dose is an issue in children that's why various studies were done to assess the response of bolus dose of vitamin D and serum concentration of vitamin D were checked at various intervals.

In our study we used the 1 lac and 3 lac units of vitamin D and serum vitamin D status was checked 6 monthly. In a randomized trial 50000 units of vitamin D were given to infants every 2 months, and their serum level of 25-hydroxy vitamin D reached significance.¹⁰ While in two other non-randomized clinical trials single oral bolus of 30,000 IU and 50000 IU of vitamin D was given to full-term infants among them over 90% of infants attained vitamin D sufficiency within one month.^{11,12} A study showed that when a group of children were treated with 50,000 IU every two months, their vitamin D levels reached ≥ 30 ng/mL (vitamin D sufficient) at 6 months.⁴

A study showed results similar to us, the children were given 150,000 IU every six months or 300,000 IU every six months. According to that study vitamin D, 300,000 IU every 6 months caused normal vitamin D levels in most of the children.¹³ In a study by Kuchay et al 60,000 IU of vitamin D were given per month for a year. After a year of monthly supplementation, average levels of 25(OH) D had risen from 12.0 ng/mL at the start to 32.6 ng/mL at the end of the study.¹⁴ In a pilot randomized control trial 1 lac units of oral vitamin D was given and serum vitamin D level was checked at 3.5 and 7 months. At 3.5 and 7 months, respectively, 63% and 56% of the children were vitamin D sufficient.¹⁵

To the best of our knowledge this is the first time that maintenance dose of one lac and three lac units of vitamin D were given as pulse therapy to children having subclinical vitamin D deficiency. Further large groups studies are needed to generate a consensus on this issue.

CONCLUSION

A bolus dose of Vitamin D3 three lac units can be given every six months as a stat dose, while one lac unit is not effective when given every six monthly

Conflict of interest: None

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