ORIGINAL ARTICLE

Comparison of Oral Versus Injectable Intramuscular Vitamin D in Treatment of Hypovitaminosis D in Children Under 5 Years of Age

ASIMA KHANAM[1], SAJID HUSSAIN SHERAZI[2], SADAF LIAQAT[3], NADIA BASHIR[4] AMNA RASHID BUTT[5]
[1]*Senior Registrar, Department of Paediatrics, Sargodha Medical College, Sargodha*
[2]*Assistant Professor,* [4]*Senior Registrar, Department of Paediatrics, Niazi Medical College Sargodha*
[3]*Assistant Professor, Department of Paediatrics, Rai Medical College Sargodha*
[5]*Senior Registrar, Department of Paediatrics, Shalamar Medical & Dental College, Lahore*
Correspondence to: Dr. Sadaf Liaqat, Email: sadafliaqat09@gmail.com Cell 0306-6006806

ABSTRACT

Objective: To compare difference in vitamin D level between two modes of therapy (intramuscular vs oral form) for hypovitaminosis D in children under five years of age.

Study Design: Randomized control trial

Place and Duration of Study: Pediatric Medicine, District Headquarter Hospital Sargodha from 15th November 2017 to 14th May 2018.

Subjects & Methods: Sixty children with hypovitaminosis D and age less than 5 years were included and randomly divided into two groups; A single intramuscular D3 injection (1-ml ampoule, 300 000 IU/ml in sesame oil) was given to Group I and a total dose of 300 000 IU D3 in the form of six pearls was given to Group II, each pearl containing 50000 IU. Hypovitaminosis D was determined by vitamin D levels less than 75nmol/l by standard laboratory procedure (Radioimmunoassay). Mean change in vitamin D level was measured at baseline and after three months of therapy.

Results: The mean age was 35.3±13.3 months. Baseline vitamin D level and vitamin D level after 3 months when compared with each other, using paired sampled test, results were highly significant (p value < 0.001). It implies that both oral and injectable forms of cholecalciferol are effective. Mean difference in intramuscular group from baseline was 51.0±16.1 nmol/l and in oral group, it came out 50.6±16.4 nmol/l. When independent sampled test was applied, results were non-significant (p=0.9). It implies that there is no difference in either modality.

Conclusion: No difference in vitamin D level was observed after three months between injectable and oral cholecalciferol therapy for treatment of low vitamin D level in children of age less than five years.

Keywords: Vitamin D, Cholecalciferol, Hypovitaminosis D

INTRODUCTION

Deficiency of Vitamin D is a worldwide health problem and now recognized as a pandemic, affecting more than one billion children and adults worldwide.[1-3] Prevalence of hypovitaminosis D is about 30 to 50% in normal population.[1] Causes of vitamin D deficiency include decreased dietary intake, inadequate sun exposure, exclusive breastfeeding and low maternal vitamin D level. It causes rickets in children.[4-6] Vitamin D is naturally found in small number of foods and they are not usually adequate to fulfill the Vitamin D requirement.[7,8]

Pakistan has increased sunlight exposure throughout the year but low level of Vitamin D is found in many children and adults.[2,9] Both oral and injectable forms of cholecalciferol are currently used in children and adults suffering from its deficiency.[6,10,11.]Single day vitamin D therapy avoids problems with compliance.[12] But mode of administration is pediatrician's personal choice along with patient's perception and behavior regarding injection.[13] There is no local evidence available which may compare the efficacy and safety of mode of drug administration in children.[8]

MATERIALS AND METHODS

The randomized control study was conducted at Department of Pediatrics, District Headquarter Hospital Sargodha from 15th November 2017 to 14th May 2018. Sixty children (30 in each group) of either sex, of age between 1-5 years having serum vitamin D levels less than 75 nmol/l were included. Those children with history of recent intake of Vitamin D supplements, primary hyperparathyroidism, thyrotoxicosis, active malignancy, liver disease, clinically apparent malabsorption syndrome, renal insufficiency and diabetes mellitus, patients on drugs as anticonvulsants and glucocorticoids (that affect vitamin D metabolism) were excluded. Children were advised baseline 25-hydroxyvitamin D level. The children were randomly divided into two groups; Group 1 was given injectable therapy (a single intramuscular D3 injection 1-ml ampoule, 300 000 IU/ml in sesame oil) and group II was given oral form of six pearls, each containing 50000 IU D3. The first oral dose was given at study entry, followed by next three doses one per weekly and then monthly for next two months. First doses were given by study personnel on site to both groups, resulting in 100% compliance. In Group II, compliance was assessed by pearl count and accepted if > 80%. The data was entered and analyzed through SPSS-20. Student t-test was applied to determine statistical difference in mean Vitamin D3 levels in both groups.

RESULTS

The mean age was 35.33±13.274 months ranged from 18 to 60 months. Mean baseline vitamin D level was 24.22±9.572, after 3 month it was 75.07±13.076 and mean difference was 50.8500±16.04847 (Table 1). Twenty nine (48.3%) children were males whereas 31 (51.7%) were females. When we cross tabulated gender with treatment group, results were non-significant on chi square test (p=0.796). Among 29 males, 15 were in intramuscular treatment group and rest of 14 in oral. Out of 31 females 15

were given intramuscular and 16 were given oral treatment. Mean age distribution in both groups, intramuscular and oral was same 32.50±13.838 and 38.17±12.262 months respectively. Results were significant. (Table 2) Baseline level of Vitamin D in both treatment groups was non-significant. Baseline level of Vitamin D in intramuscular was 23.63±9.065 and in oral it was 24.80±10.176. (Table 3) Baseline Vitamin D level and vitamin D level after 3 months when compared with each other, on paired sampled test results were non-significant (p=0.878) (Table 4).Mean difference in intramuscular group was 51.100±16.00937 and oral it was 50.600 ± 16.3572. On independent sampled test, results were non-significant (p=0.9) (Table 5). Mean difference among male was 53.8621±15.972 and among female it was 48.0323±15.8566 (Table 6). Mean difference below 36 months was 51.909±14.444 whereas 36 months and above was 49.555±18.0135 (Table 7).

Table 1: Vitamin D level distribution of sampled population (n=60)

Variable	Mean±SD
Baseline Vitamin D Level	24.22±9.572
Vitamin D Level after 3 months	75.07±13.076
Difference	50.85±16.04

Table 2: Comparison of age according to group

Group	Mean±SD	P value
Intramuscular	32.50±13.83	0.90
Oral	38.17±12.26	

Table 3: Comparison of vitamin D level in both groups

Group	Mean±SD	P value
Intramuscular	23.63±9.06	0.64
Oral	24.80±10.17	

Table 4: Comparison of Vitamin D Level before and after treatment

Variable	Mean±SD	P value
Baseline Vitamin D Level	24.22±9.6	<0.0001
Vitamin D Level after 3 months	75.07±13.1	

Table 5: Difference in Vitamin D Level after treatment

Treatment Group	Mean±SD	P value
Intramuscular	51.1±16.1	0.90
Oral	50.6±16.3	

Table 6: Comparison of vitamin D Level according to gender

Gender	Mean±SD	P value
Male	53.86±15.97	0.16
Female	48.03±15.85	

Table 7: Comparison of vitamin D Level according to age

Age	Mean±SD	P value
<36 months	51.90±14.44	0.58
36 months and above	49.55±18.01	

DISCUSSION

Hypovitaminosis is a global issue .[1,2] Prevalence of vitamin D deficiency is about 30 to 50% in different populations,[1] affecting more than one billion children and adults.[3] Adults are at risk of multiple complications like musculoskeletal pain, fibromyalgia, osteopenia, osteoporosis and it causes rickets in children.[9,14] Rickets has two types, calcipenic and phosphopenic. Calcipenic rickets is mainly caused by deficiency of vitamin D.[14] We have two modalities available for drug administration i.e. both oral and injectable forms of cholecalciferol are currently used in under five children and adults suffering from its deficiency.[6,10,11] Mode of administration is pediatrician's personal choice along with patient's perception and behavior regarding injection. In one study, parent's preferred intramuscular route.[13] There is no local evidence available which may compare the efficacy and safety of mode of drug administration.[8]

Baseline level of Vitamin D and vitamin D level after 3 months when compared with each other, using paired sampled test, results were highly significant (p value < 0.001). It implies that both oral and injectable forms of cholecalciferol are effective in treating Hypovitaminosis D in pediatric age group. Mean difference in intramuscular group from baseline was 51.0±16.1 nmol/L and in oral group, it came out 50.6±16.4 nmol/L. Results were non-significant (p=0.9). It implies that there is no difference in either modality of treatment.

Our results are different from previous study. In previous study, both oral and intramuscular treatment regimens significantly increased the serum vitamin D level, but change in vitamin D level from baseline at 3 months was significantly higher in group who received oral form than inectable one (90.0±11.2 and 58.8±8.9 nmol/L, respectively, P = 0.03) (calculated SD was 75.9 and 60.3 nmol/L respectively).[8] Whereas another study showed that at 12 weeks of treatment ,the mean level of vitamin D in intramuscular group was higher as compared to oral cholecalciferol group (25.46±1.37 vs 16.66±1.36 ng/ml; P<.001).[15] Another study showed that both treatment were well tolerated but injectable form of treatment was shown to be statistically significant.[13]

There was equal mean age distribution in either treatment groups, 32.5±13.8 and 38.17±12.2 months respectively in the present study and results were significant. Mean difference below 36 months was 51.909±14.4 nmol/l whereas children 36 months and above had Vitamin D Level 49.5±18.1nmol/L. This result implies that treatment is effective in all age groups. Twenty nine patients (48.3%) were males whereas 31 patients (51.7%) were females, when we cross tabulated gender with treatment group, results were non-significant on chi square test (p=0.796). When mean difference of Vitamin D Level was compared in either sex, among males it was 53.8±15.9 nmol/L and among female it was 48.03±15.9nmol/L, both male and female had responded to treatment.

CONCLUSION

No difference is observed in serum vitamin D level after 3 months, in two modalities of treatment (high-dose intramuscular versus oral cholecalciferol) for hypovitaminosis D in children under five years of age. Mean difference in intramuscular group from baseline was 51.0±16.1 nmol/l and in oral group, it came out 50.6±16.4 nmol/l. Further studies should be encouraged in this regard.

REFERENCES

1. Karaguzel G, Dilber B, Can G, Okten A, Deger O, Holick MF. Seasonal vitamin D status of healthy school children and predictors of low vitamin D status. J Pediatr Gastro Nutr 2014;58(5):654-60.

2. Karim SA, Nusrat U, Aziz S. Vitamin D deficiency in pregnant women and their newborns as seen at a tertiary-care center in Karachi, Pakistan. Int J Gyne Obstet 2011; 112(1):59-62.
3. Holick MF. The Vitamin D deficiency pandemic: approaches for diagnosis, treatment and prevention. Rev Endocr Metab Disord 2017;18(2):153-65
4. Khundmiri SJ, Murray RD, Lederer E. PTH and vitamin D. Compr Physiol 2016;6:561-601.
5. Taylor JA, Geyer LJ, Feldman KW. Use of supplemental vitamin D among infants breastfed for prolonged periods. Pediatrics 2010; 125:105-9.
6. Balasubramanian S, Dhanalashmi K, Amperyani S. Vitamin D deficiency in childhood- A review of current guidelines on diagnosis and management. Indian Pediatr 2013; 50:669-675.
7. Moffat T, Sellen D, Wilson W, Anderson L, Chadwick S, Amarra S. Comparison of infant vitamin D supplement use among Canadian-born, immigrant, and refugee mothers. J Transcultural Nurs 2015; 26(3): 261-9.
8. Zabihiyeganeh M, Jahed A, Nojomi M. Treatment of hypovitaminosis D with pharmacologic doses of cholecalciferol, oral vs intramuscular; an open labeled RCT. Clin Endocrinol 2013;78(2):210-6.
9. Shaheen S, Noor SS, Barakzai Q. Serum alkaline phosphatase screening for vitamin D deficiency states. J Coll Physicians Surg Pak 2012;22(7):424-7.
10. Holick MF, Binkley NC, Bischoff-Ferrari HA. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011; 96:1911-8.
11. Masood MQ, Khan A, Awan S, Dar F, Naz S, Naureen G, et al. Comparison of Vitamin D replacement stratigies with dose intramuscular or oral cholecalciferol: a prospective intervention study. Endocr Prac 2015; 21(10): 1125-33.
12. Schwarz SM, Bhatia J. Rickets treatment and management. Medscape 2017.
13. Billoo AG, Murtaza G, Memon A, Khashkheli SA. Comparison of oral versus injectable vitamin D for the treatment of nutritional vitamin D deficiency rickets. JCPSP 2019; 19(7):428-31.
14. Mazari R. Comparison of response of oral versus injectable Vitamin D in children having rickets. Vitam Miner 2017; 6(3):165-8.
15. 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):131-6.