VITAMIN D INTOXICATION IN INFANTS WITH VITAMIN D SUPPLEMENTS

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ABSTRACT

Background

Vitamin D supplementation can lead to a rare condition of vitamin D intoxication in infants develop. Thus, its supplementation had to raise concerns because the frequency of its intoxication is increasing.

Objectives

The aim was to look for frequencies of vitamin D intoxication among infants who had vitamin D supplements in Sulaimani City.

Patients and Methods

A cross-sectional study performed on 65 infants for a period of a month from February 1st to March 1st, 2019. Inclusion criteria were infants with vitamin D supplements for at least six consecutive months and aged between eight months to two years old. The ages and gender of the infants, as well as the level of vitamin D, and the daily amount and route of vitamin D supplements, were recorded. The "IBM SPSS Statistics version 25" was used for the analysis of the data, and a P-value of (≤0.05) was considered significant.

Results

The mean±SD of age was 1.26±0.52 years (range; 8 months to 2 years), and the genders were male (29.2%) and female (70.8%) with a female to male ratio of (2.4:1). Mean±SD vitamin of D3 level (ng/mL) was 37.97 ± 14.64 (range; 6.76 to 78). There were insignificant associations between the levels of vitamin D3 with age, gender of the infants, daily supplement and the route of vitamin supplementation. No infants were found to have vitamin D intoxication.

Conclusion

No infants had vitamin D intoxication, although they were provided with vitamin D supplements.

Keywords: *Infants Pediatrics, Vitamin D intoxication, Vitamin D supplement, Sulaimani.*

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INTRODUCTION

Vitamin D is a fat-soluble vitamin which is naturally present in few foods in addition to dietary supplements [1-2]. It can be produced endogenously when ultraviolet light from the sun strikes skins [1]. The vitamin D which is obtained from diet or sun exposure is inert; therefore, it should be hydroxylated in liver and kidneys for its activation [1, 2]. In the liver, vitamin D undergoes the first hydroxylation and then converted to 25-hydroxy vitamin D [25(OH)D] which is also known as calcidiol. [1, 2] While in the kidneys, it undergoes the second hydroxylation and forms the physiologically active 1, 25-dihydroxy vitamin D [1, 25$(OH)_2$ D] which is also known as calcitriol [1, 2].

Vitamin D is essential for the homeostasis of calcium and phosphorus, mineralization of bone and tooth, in addition to the regulation of cell proliferation, differentiation and apoptosis, regulation of the immune system, hormonogenesis, and other physiological processes of body organs [2-5].

In the past and because of high prevalence of vitamin D deficiency and insufficiency, its action on bone, and its high threshold of safety when it was taken, had led to increased use of its supplementation—both as medical prescription and over-the-counter—in order to decrease the prevalence of its deficiency and to prevent chronic diseases [2, 6]. Therefore, the extensive use of its supplementation had led to increased concentration of 25-hydroxycholecalciferol in serum above normal ranges in those people [2, 6].

Vitamin D intoxication is rare from natural dietary or sun exposure [2, 6]. In this regard, intoxication from vitamin D supplementation had raised concern because its frequency is increased [6]. Vitamin D intoxication is defined when the serum level of 25-hydroxyvitamin D is above 100-150 ng/mL (250-375 nmol/L) [3].

The recommended daily dose of vitamin D intake—either as a supplement or as an addition to food—that can satisfy the body needs is 400 IU for the ages of 18 years old or below [2]. Although vitamin D has a high safety threshold, as other bioactive substances of the body, it is accomplished within strictly defined limits [2]. Therefore, its excess can endanger health [3]. Although vitamin D deficiency and insufficiency are common in the world nowadays, in rare cases, the opposite can also be observed [2, 7].

Vitamin D intoxication usually develops due to a high dose of vitamin D given by healthcare providers before the precise diagnosis of vitamin D insufficiency or rickets is established or inappropriate administration of it by the families for complaints like delayed teething or walking and knock-knees gait [7]. Moreover, vitamin D intoxication due to its supplementation was mentioned in adults as well as in infants in the literature [2, 7].

In this regard, we wanted to know the frequencies of vitamin D intoxication among infants who had vitamin D supplementation. We also wanted to clarify the future choices and methods of administration for vitamin D supplements in infants.

PATIENTS AND METHODS

A cross-sectional study was done on 65 infants who have received vitamin D supplements for more than six consecutive months for a period of a month from February 1st to March 1st of 2019. The infants were randomly selected from Sulaimani Pediatric Teaching Hospital by using a simple random sampling method.

Research Ethical Committee of the Kurdistan Board of Medical Specialties (KBMS) approved the study proposal, and a formal acceptance letter was obtained from Sulaimani Pediatric Teaching Hospital before starting the study. Besides, informed consent had also been taken from the parents of the infants for their inclusion in this study.

The inclusion criteria were infants with vitamin D supplementation for at least six consecutive months who were aged between eight months to two years old. Furthermore, the exclusion criteria were the age of less than eight months or more than two years old, and those whom took only a single high dose of vitamin D.

The age and gender of the infants were recorded. The daily vitamin D supplements and the route of its administration —through oral drops, oral or intramuscular injections, and gum—were also documented. Besides, the level of vitamin D in infants was measured by immunofluorescence assay in a laboratory in Sulaimani city using Conas e411 machine.

The "IBM SPSS Statistics version 25" was used for the analysis of the data, and both descriptive and inferential statistics were used. Moreover, P-values of ($\leq$0.05, and <0.001) were considered as statistically significant, and highly significant associations, respectively. Besides, Pearson Chi-Square was used to find out the significance of the association between independent and dependent variable pairs, and Pearson's R Correlation was used to

calculate the direction of the correlation between the two variables.

RESULTS

The mean age was 1.26±0.52 years (ranged from eight months to two years) (Table 1). Also, 19 (29.2%) of the infants were male, and 46 (70.8%) of them were females with a female to male ratio of (2.4:1) (Table 2). Moreover, mean level of vitamin D3 (ng/mL) in the infants was 37.97 ± 14.64 (ranged from 6.76 to 78).

There was a statistically insignificant association between the levels of vitamin D3 with age groups of the infants, i.e. no association was found between these two independent (i.e. age) and dependent (i.e. vitamin D3 level) variable pairs,Table 1.

There was a statistically insignificant association between vitamin D3 level, and gender of the infants, i.e. no association was found between these two independent (i.e. gender) and dependent (i.e. vitamin D3 level) variable pairs,Table 2.

There was a statistically insignificant association between vitamin D3 level and the route of vitamin D supplement administration to the infants, i.e. no association was found between these two independent (i.e. route of vitamin D supplement administration) and dependent (i.e. vitamin D3 level) variable pairs, Table 3.

There was also a statistically insignificant association between vitamin D3 level and the daily supplement amount of vitamin D given to the infants, i.e. no association was found between these two independent (i.e. daily supplement amount of vitamin D) and dependent (i.e. vitamin D3 level) variable pairs, Table 4.

Table 1. Association of the age of the infants with vitamin D3 level.

Vitamin D3 level groups (ng/mL)	Age groups			Total (%)	P-value* (Pearson R Correlation)
	<1 year (%)	1 year (%)	1 to 2 years (%)		
Deficient (<20)	1 (1.5)	4 (6.2)	2 (3.1)	7 (10.8)	
Insufficient (20-29)	1 (1.5)	4 (6.2)	8 (12.3)	13 (20)	
Adequate (30-39)	2 (3.1)	10 (15.4)	4 (6.2)	16 (24.6)	
Optimal (40-59)	6 (9.2)	15 (23.1)	5 (7.7)	26 (40)	0.34 (-0.185)
Therapeutic (60-100)	0 (0)	2 (3.1)	1 (1.5)	3 (4.6)	
Toxic level (>100)	0 (0)	0 (0)	0 (0)	0 (0)	
Total	10 (15.4)	35 (53.9)	20 (30.8)	65 (100)	

* Measured by Pearson Chi-Squared test

Table 2. Association of the gender of the infants with vitamin D3 level.

Vitamin D3 level group (ng/mL)	Gender		Total	P-value* (Pearson R Correlation)
	Male	Female		
Deficient (<20)	1 (1.5)	6 (9.2)	7 (10.8)	0.59 (0.014)
Insufficient (20-29)	6 (9.2)	7 (10.8)	13 (20)	
Adequate (30-39)	4 (6.2)	12 (18.5)	16 (24.6)	
Optimal (40-59)	7 (10.8)	19 (29.2)	26 (40)	
Therapeutic (60-100)	1 (1.5)	2 (3.1)	3 (4.6)	
Toxic level (>100)	0 (0)	0 (0)	0 (0)	
Total	19 (29.2)	46 (70.8)	65 (100)	

* Measured by Pearson Chi-Squared test

Table 3. Association of vitamin D3 level with the route of vitamin D supplement administration.

Vitamin D3 level group (ng/mL)	Route of vitamin D administration			Total (%)	P-value* (Pearson R Correlation)
	Oral drop (%)	Injection (either orally or intramuscularly) (%)	Gum (200 IU/day) (%)		
Deficient (<20)	5 (7.7)	1 (1.5)	1 (1.5)	7 (10.8)	
Insufficient (20-29)	11 (16.9)	1 (1.5)	1 (1.5)	13 (20)	
Adequate (30-39)	12 (18.5)	2 (3.1)	2 (3.1)	16 (24.6)	
Optimal (40-59)	19 (29.2)	2 (3.1)	5 (7.7)	26 (40)	0.904 (0.06)
Therapeutic (60-100)	2 (3.1)	1 (1.5)	0 (0)	3 (4.6)	
Toxic level (>100)	0 (0)	0 (0)	0 (0)	0 (0)	
Total	49 (75.4)	7 (10.8)	9 (13.8)	65 (100)	

* Measured by Pearson Chi-Squared test

Table 4. Association of vitamin D3 level with the daily supplement amount of vitamin D given to the infants.

Vitamin D3 level group (ng/mL)	Daily supplement amount (IU/day)				Total (%)	P-value* (Pearson R Correlation)
	Adequate (400) (%)	200-300 (%)	100-150 (%)	500-800 (%)		
Deficient (<20)	6 (9.2)	1 (1.5)	0 (0)	0 (0)	7 (10.8)	
Insufficient (20-29)	6 (9.2)	4 (6.2)	0 (0)	3 (4.6)	13 (20)	
Adequate (30-39)	11 (16.9)	2 (3.1)	2 (3.1)	1 (1.5)	16 (24.6)	
Optimal (40-59)	14 (21.5)	5 (7.7)	4 (6.2)	3 (4.6)	26 (40)	0.54 (0.048)
Therapeutic (60-100)	3 (4.6)	0 (0)	0 (0)	0 (0)	3 (4.6)	
Toxic level (>100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Total	40 (61.5)	12 (18.5)	6 (9.2)	7 (10.8)	65 (100)	

* Measured by Pearson Chi-Squared test

DISCUSSION

Vitamin D intoxication is due to its high dose prescriptions by healthcare providers before a precise diagnosis of rickets or vitamin D insufficiency is made, or patients may ingest high maintenance dose of it prescribed by a medical doctor [8] .Another cause of intoxication of vitamin D is the inappropriate administration of high doses of vitamin D to infants by their families due to complaints like late walking or knock-knees gait [8]. Moreover, excessive-high oral intake of this vitamin is not followed by limited intestinal absorption and transport or limiting the high activation.[3] These facts, with the high deficient capacity of calcidiol and calcitriol inactivation and elimination, are the basics of the pathogenesis for intoxication of this vitamin [3]. In our study, although all the infants were provided with vitamin D supplementation, no one of them was suffering from vitamin D intoxication as shown in the Tables 1-4.

The half-life of 25-hydroxyvitamin is about 15 days [3]. Since we used a cross-sectional design for our study and the samples were collected during one month, we could not know the exact date of ingesting vitamin D by the infants. Therefore, this may explain the fact that no one of the infants in our study had vitamin D intoxication, as shown in the (Tables 1-4). Another explanation may be because vitamin intoxication is not common but serious disease [3, 8-9].

Vitamin D deficiency has been reported in all age groups from infants through adults [10]. Conversely, vitamin D intoxication has been mentioned less

frequently in infants and adults [3, 8-10]. Therefore, it was not possible for us to compare the frequency of age and gender in other studies with our results. But, the frequency of deficiency and insufficiency among the ages were as follows: less than a year (3%), one year (12.4%), and one to two years (15.4%) as shown in (Table 1), and among the genders were as follows: female (20%) and male (10.7%) as shown in (Table 2). Besides, no infants have had vitamin D intoxication as shown in the (Tables 1-4). Although, the association of the level of vitamin D with the route of administration and daily supplement amount of vitamin D was insignificant, most of those who took a daily 400 IU/day through oral drops of vitamin D supplement was either adequate or optimal—16.9% and 21.5% for those who took 400 IU/day and 18.5% and 29.2% for the oral route of administration, respectively (Tables 3 and 4). These results may allow considering a 400 IU/day dose of vitamin D supplement through oral use as a better choice.

In conclusions, the study age groups and gender had a statistically insignificant association with the level of vitamin D. Moreover, no infant was found to have vitamin D intoxication, although they had been provided with vitamin D supplements. There was also no statistically significant association between vitamin D level with the route of administration and daily amount of vitamin D supplementation. Therefore, we can conclude that vitamin D supplementation in the doses and durations mentioned in this study are generally safe.

The limitation of our study may be the study design with the shortage of its sample size. We do recommend collecting a larger sample size for future studies about this topic in our population.

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Conflicts of interests

The authors declare no conflict of interests

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