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Growing Pains in Children and Vitamin D Deficiency, The Impact of Vit D Treatment for Resolution of Symptoms

Ahmed I. Insaf MD
Department of Pediatrics, Faculty of Medicine, Wasit University, Al-Kut Maternity and Child Hospital, Iraq

Abstract
Objectives:
The point of the review was to assess vitamin D levels in kids having growing pains and to evaluate the reaction to vitamin D supplement on the diminishing of pain manifestations.
Subjects and Methods:
Thirty six child had features of growing pains were considered. Serum levels of vitamin D was measured at the time of initial presentation. Patients with low level of vitamin D are incorporated into a prospective cohort study. The pain intensity was measured utilizing a pain "visual analogue scale" (VAS). After a solitary oral or intramuscular dosage of vitamin D given to kids with low vit D Levels, the pain intensity was re measured by methods for the (VAS) at 1 month. The vit D levels and (VAS) scores prior and then afterward vitamin D treatment were looked at by methods for a matched Student's t test.
Results: 36 child with features of growing pains are evaluated.
One child had normal Vit D level and not given Vit D treatment, the majority {97.2%} 35 had low vit D level and included in the study. During period of pretreatment of Vitamin D, most of the children (62%) were suffered from moderate pain according to {VAS} pain score, while in post treatment period 88.6% of them became with no pain symptoms. the mean level of Vitamin D in pre-treatment phase was 16.3 ng/ml while in post treatment phase is 35 ng/ml with highly significant P value 0.0001.
Conclusion: large number of children with growing pain had low vitamin D level. Treatment with vitamin D resulted in a critical diminishment in pain severity among these kids with growing pains who had low vitamin D.

Introduction:
Growing pain (GP) is considered to be a normal phenomenon in about 25% to 40% of children with no organic pathology. (1, 2)

The evaluated prevalence of (GP) overall reaches from 3 to 37% (2). It is fundamentally situated in the muscles and ordinarily include anterior thighs, shins, calves or backs of the knees (1, 3)

The Physical examination should be normal, no signs of inflammation, and laboratory test are negative (4)

The (GP) more often happens at night or evening, but never happen at morning. It might be severe that can make the kid cry (3)

(GP) can runs in families and the major influenced kids aged 4-12 years, and are most basic in those matured 4-6 years (5).

Vitamin D is a critical and fundamental segment of bone and mineral metabolism. It accelerate calcium absorption in the digestive tract and it is of fundamental importance for ordinary bone plate calcification and bone mineralization. It assumes an essential part in the homeostasis of calcium and phosphorus and keeping up development of bone and skeleton (6)

The relations between the vitamin D inadequacy and chronic bone pain conditions has been discussed in adults (7, 8)

In this review, we surveyed the serum vitamin D level in kids with (GP) and assessed whether pain intensity declined with vitamin D treatment.

Subjects and Methods :
Aprospective cohort study was carried out at the Zahraa University Hospital and AL-Kut Maternity and child hospital in Kut –Iraq. The kids who attended the daily child clinics from September 2016 to May 2017.

Data about the goals of study was disclosed to the children's parents at the time of first meetings, and their composed educated assent was gotten. .
The study included 36 kids aged 3-12 years with GP features were distinguished.
36 children (18 males and 18 females) with growing pain (GP) presented
as recurrent limb pain that lasted >6 months according to the criteria of Evans (9)
The inclusion criteria for a diagnosis of (GP) were:
1. If the children experienced intermittent (non articular) pains in both legs, generally occurring at night and not associated with limping or limited movement.

2. The kids needed to have typical psychological and physical capacity for understanding the agony (VAS) Visual Analog Scale

Exclusion criteria:

1. If the children had persistent pain, severe pain at night that continue to the following morning and 2. If had joint pain 3. If they had organic causes of pain or signs of inflammation such as local tenderness, redness or swelling, or underlying diseases such as rickets, malnutrition, rheumatologic problems , gluten sensitivity or were taking vitamin or mineral supplements.

The study group represented pediatric population living in an sunny area from beginning of winter (September) till the begin of summer (May)

All subjects experienced an entire physical examination. At starting introductions, stature and weight were measured utilizing a standard stadiometer and an advanced scale, separately.

Demographic data were taken involving the date of examination, gender, and residency. The site, the time and frequency of pain were obtained, family history of same pain and the pain relieving methods used.

Venous blood tests were taken in the morning taking after a 12-hour overnight fast.The serum vit D level was measured using an electro-chemiluminescence enzyme immunoassay method(ADVIA Centaur; USADPC Co., USA ,procedure done according to manufacture instructions)

As indicated by Vit D Council Baseline vitamin D levels were measured and the kids were separated into the following groups:

Vitamin D sufficiency: at or more prominent than 30 ng/mL

Vitamin D insufficiency: under 30 ng/mL yet more prominent than 20 ng/mL

Vitamin D deficiency: under 20 ng/mL

Kids with Vit D at or more than30 ng/mL were not given any vitamin D supplementation and excluded in the associate review. Those with vitamin D insufficiency were given a solitary oral supplement of vitamin D [150,000 IU (≤6 years old) or 300,000 IU (>6 years of age)] and oral calcium supplementation (1,000 mg/day) for 1 month.

Those recognized as having vitamin D insufficiency were assessed for pain seriousness using a pain Visual Analog Scale (VAS) at the start. The pain (VAS) estimation was rechecked at 1 month after vitamin D treatment,

With estimation of serum vitamin D to check if the vitamin D measurement had been effective and to monitor side effects such as hypercalcemia.

Pain severity was evaluated using a {VAS} consisting of a linear scale (a horizontal line 100 mm long). The number of centimeters marked was recorded as a score from 0 to 10: (no pain = 0, moderate pain = 5 and very severe pain that was so intense to make the child cry = 10). Children and their parents were taught in detail how to use the {VAS}. Were asked to mark the severity of pain they experienced during the most recent attack.

Adaptation 20 of the Statistical Package for the Social Sciences (SPSS) factual program for Windows (SPSS Inc., Chicago, Ill., USA) was utilized for the measurable investigation. Numerical parameters are introduced as means and standard deviations, and the dispersions of straight out estimations are exhibited as frequencies and rates. The vitD levels and pain (VAS) scores prior and then afterward oral vitamin D organization were contrasted and a matched Student's t test. Straight out information were looked at by methods for the $\chi 2$ test. A p estimation of <0.05 was acknowledged as demonstrative of measurable importance.

Results :

36 children with growing pains are evaluated. One child had normal Vit D (30ng/ml) level and 35 had low vit D level (97.2%) and this is highly significant result.

According to the demographic data of the children with bone pain, the gender of the children is equally same for both male and female, (50 %)

About more than three quarter of the children were from the urban area (77.1%), more than half of them were presented with pain in night

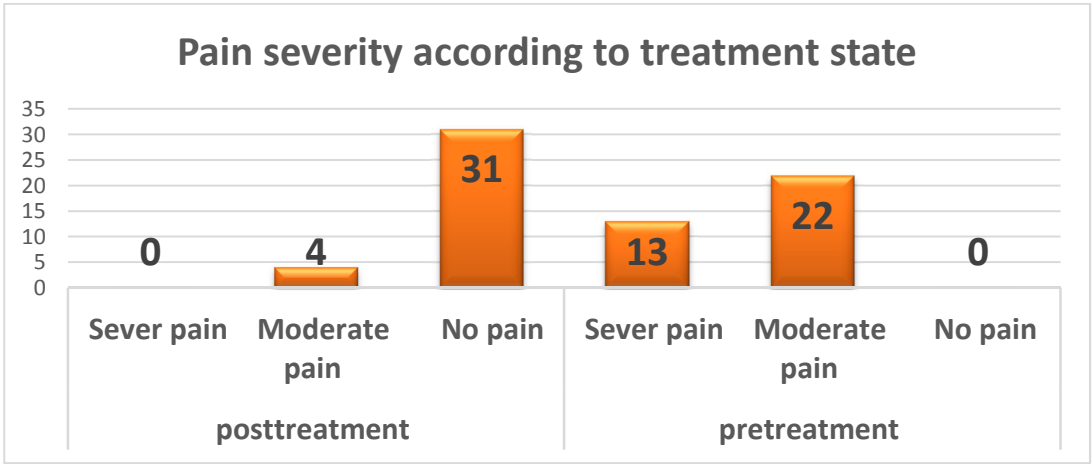
period (60%). 35 five child with low vit D level included in the cohort prospective study.

Sixty five percent of the children were with family history of same condition. Parents were used analgesia and message to relieve pain in 54% of the children when pain occur. Calf and chin were the main site of pain were reported in 51.4% of the children, while 37.1% of them complained from knee and thigh pain. During period of pretreatment of Vitamin D, most of the children (62%) were suffered from moderate pain according to pain score, while in post treatment period 88.6% of them became with no pain state. Table No.1 and figure No.1 show these finding.

Table No. (1): demographic data of the children with bone pain.

Item	Frequency	(%)
Gender		
Male	**18**	50
Female	**18**	50
Address		
Urban	**27**	77.1
Rural	**8**	22.9
Time of pain		
Afternoon	3	8.6
Evening	11	31.4
Night	21	60
Family history		
Yes	23	65.7
No	12	34.3
Pain relieve		
Message	13	37.1
Analgesia	3	8.6
Both	19	54.3
Site of pain		
Knee and thigh	13	37.2
Calf and shin	18	51.4
Popliteal and shin	4	11.4
Pain severity pre treatment		
No pain	0	0
Moderate pain	22	62.9
Sever pain	13	37.1
Pain severity post-treatment		
No pain	31	88.6
Moderate pain	4	11.4
Sever pain	0	0

Figure No (1): pain status of the children



mean age of the children with bone pain was 7 year (3-11 year range), weight mean was 22 kg (13-33 kg), height mean was 119 cm (85-147 cm).

the mean level of Vitamin D in pre-treatment phase was 16.3 ng/ml while in post treatment phase is 35 mg/ml with highly significant P value 0.0001 as showed in table No. 2, table No. 4 and figure No.2.

Table No.(2): mean and SD non parametric data of the children with bone pain

Item	Age/years	Weight/kg	Height/cm	Vit D level pre-treatment/ng/ml	vit D level post treatment /ng/ml
N	35	35	35	35	35
Mean	7	22	119.4	16.3	35
Std. Deviation	2.4	5.9	14.6	7.2	7.3
Minimum	3	13	85	3	20
Maximum	11	33	147	29	52

Table No (3) shows the correlation of many variable to mean level of Vit, D in pretreatment phase. Vit. D mean level was lower in male than female with no statistical significant, P value 0.1. the same Vit. D level were reported in urban and rural area, 16 ng/ml. the lower level of Vit D was reported in children with severe pain (13.6 ng/ml) and level in children with moderate pain was 17.9 ng/ml.

Table No. (3): variable correlated to Vit. D level.

Item	Type	N	Vit D mean Ng/ml	Std. Deviation	P value
family history	no	12	18.4	5.9	0.2
	yes	23	15.2	7.7	
Gender	male	17	14.6	7.0	0.1
	female	18	17.9	7.3	
Address	urban	27	16.3	7.1	0.9
	rural	8	16.1	8.0	
Pain severity	moderate pain	22	17.9	6.1	0.09
	sever pain	13	13.6	8.4	
Time of pain	afternoon	3	5.3	4.0	0.01
	evening	11	16.9	6.5	
	night	21	17.6	6.8	
Sit of pain	knee and thigh	13	17.9	7.5	0.4
	calf and shin	18	16.0	7.2	
	popliteal and knee	4	12.4	6.6	

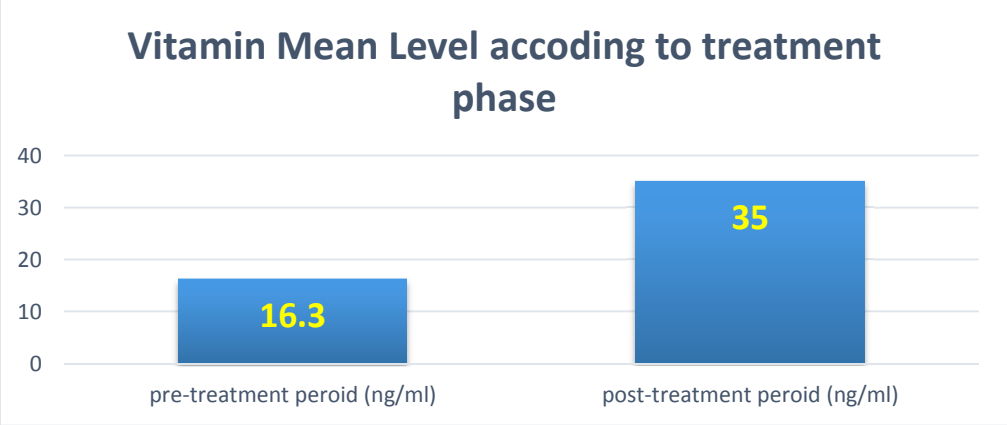
Children with afternoon pain were reported with Vit D level 5.3 ng/ml which is lower than what reported in children with evening and night pain, with significant P value (0.01).

Children with popliteal and knee pain were had Vit D level lower than children with others site of pain.

Table No. 4 shows the difference in Vit D level according to treatment phase, there was high increment in Vit D level with highly significant P value, 0.0001. this increment reflect on pain status of the children as there was no sever pain status in post treatment children.

Table No.(4): Vitamin D mean level according to treatment state

Item	N	Mean ng/ml	Std. Deviation	P value
Vit D level pre-treatment	35	16.3	7.2	0.0001
vit D level post-treatment	35	35.0	7.3	



Discussion

Our previous believe of the normality of growing pain and explaining it as a normal growth of bone and muscle make us give no treatment for such children.

That make the families took their children to many pediatricians, rheumatologist ….etc seeking for other opinion and hope .

It was really surprising to see who much children with growing pain are vit D deficient and more surprising the response to vit D supplement.

The child was crying, distressed at night sometimes daily seeking for help and the parents didn't know what to do.

After taking treatment the sleep return normal, magic response making the child and parent happy and forget the previous pain nights.

We found that vitamin D inadequacy and insufficiency is an extremely common medical issue among kids in Kut inspite that it is a sunny city. (97.2 %) of children with growing pains had low vitD level this may be explained that the time of study was mainly in winter. And this nearly similar to Aysel et al. (6) done in Istanbul in 2015 about the vit D deficiency and growing pain(GP) in children showed that 86.6% of children with growing pains had low vitamin D.

Studies surveying the predominance of vitamin D level in kids with leg pains are constrained (1,10). In 2011,Qamar et al. (1) exhibited a connection between developing agonies and low vit D , yet they didn't expect to evaluate the impact of vitamin D treatment on agony determination.They demonstrated that 94% of youngsters with developing torments had low vit D and this near our outcomes.

Low vit D is accounted for to be inside the scope of 70– 90% among sound kids and teenagers in Korea and Italy (11, 12). In China, in winter and spring, more than 50% of school-matured children and youths supposedly have a D hypovitaminosis; in winter, 100% of teenagers and 93.7% of school-matured kids were found to have diminished vitamin D in another review (13).

In our long summer days in Kut city in Iraq , the number of children with growing pain are much less than what we see in winter may be due sun exposure.

Pretreatment mean vit D level was 16.3 ng/ml and post treatment 35ng/ml. Morandi et al. (10) assessed 33 kids with (GP). They found a mean vit D level of 15.0 ± 6.9 ng/ml. They found that vitamin D treatment prompted a huge increment in vit D level that was related with a huge reduction in pain seriousness. These outcomes are near our discoveries.

Aysel et al.(6)The level of vit D in the kids with (GP) and vitamin D inadequacy expanded following 1 month of vitamin D treatment from 13.4 ± 7.2 to 44.5 ± 16.4 ng/ml, and the distinction was measurably critical ($p < 0.001$) and this likewise near our outcomes .The mean age in our study 7 years and this similar to Aysel et al.(6) was 7.8 years

We trust that the term Growing pains (GP) is a misnomer in light of the fact that most influenced kids are at a time of generally slower development period

We concur with the proposed thought of Morandi G et al. (10), in that kids with GP are frequently vitamin D inadequate and insufficient, the agony is might be because of less thick bones subsequently of having a low vitamin D level. That may leads anomalous weight on tactile nerves of the bone, bringing on agony.

After vitamin D supplementation, we watched a huge diminishment in pain seriousness in kids with GP; this could be due to a greater amount of mineralized cortical bone.

We found that weight and height parameters were inside the ordinary percentile ranges. What's more, this similar to the review in Istanbul Aysel et al.(6)

Many hypothesis have been proposed to explain the causes of growing pains, including muscular fatigue in the affected extremity, emotional or psychological distress, and a theory of lower pain threshold (14) , changes in vascular perfusion and joint hypermobility (15)

We trust that low vit D may have a part in the pathogenesis of GP, and that vitamin D supplementation may influence the bone and muscle status and reduction seriousness of agony in youngsters encountering these torments

Pain Visual Analog Scale{VAS} is a substantial and dependable technique for surveying pain seriousness in the kids as Aysel et al.(6) utilize it for kids with GP and Wehby et al. (16) utilized a pain {VAS} to quantify wellbeing related personal satisfaction in kids with oral clefts. Dhanani et al. (17) utilized a {VAS} to decide the seriousness in agony related with changes in personal satisfaction in youngsters with rheumatic diseases. They inferred that the {VAS} can be a substantial and dependable technique for evaluating pain in the pediatric populace, particularly when kids are enough taught to utilize it legitimately.

Concerning meaning of the vitamin D status in pediatrics. We characterized vitamin D effective level from 30 to90 ng/ml as per the Vitamin D Council in USA.We trust this esteem is adequate to identify the hypovitaminosis of vitD. Vitamin D substitution treatment is fundamental for kids with low vitamin D levels. An assortment of dosing plans are utilized: in kids more than12 months old, 2,000 IU/day for a 6 weeks or

50,000 IU every week for 6 two months taken after by maintenance dosing of 600-1,000 IU/day. Another proposal is {stoss therapy} 2.5-15.0 mg or 100,000-600,000 IU of vitamin D as a solitary oral or intramuscular measurement. We favored stoss treatment, keeping in mind the end goal to guarantee the taking of a full dosage and to avoid poor compliance to treatment.

After the vitamin D supplementation, we watched a critical increment in Vit D levels and a huge diminishment in pain severity in kids with GP.

We couldn't play out a randomized controlled study in light of the fact that a large portion of the kids had low vitamin D, and it would have been unethical to withhold the vitamin D treatment. However , future randomized controlled reviews will supply more information about the viability of vitamin D treatment in kids with GP.

After a huge diminishment in pain severity among the kids with GP who treated by vit D. we recommends that vitamin D may improve the symptoms of this condition.

However, alternative reasons for improvement cannot be ruled out. To resolve this, a well-designed randomized controlled trial is required.

Conclusion

In the present review, there was a high prevalence of low vit D in kids with GP. Vitamin D supplementation altogether expanded the vit D levels and cause a huge decrease in pain severity in kids with GP. This finding could propose that vitamin D treatment may diminish the intensity of pain among kids with GP.

Monitoring vit D levels and, when indicated, supplementing nutritional calcium and vitamin D could resolve growing pains. A reduction in pain can lead to an improved personal satisfaction. Additional studies ought to address this important topic.

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