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Vitamin D Levels in Growth-Paining Children

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Abstract

The most common cause of non-inflammatory recurrent musculoskeletal pain in children is growing pains. History and physical examination are often sufficient to diagnose these patients. Since the exact etiology is not known, different treatments can be applied. The effect of vitamin D levels on children with growing pains was investigated. Clinical and laboratory findings of 138 pediatric patients with growing pain and 30 healthy control subjects were examined and then the changes in pain scores of children and their families with follow-up and treatment were evaluated. The pain was most commonly seen in the form of lower extremity pain at night and in girls. Although growing pains can be treated with nonpharmacological methods, there were also patients who required pharmacological treatment. Vitamin D deficiency was observed in children with growing pain. Vitamin D treatment was given to 46 patients with vitamin D deficiency. Pain scores made by both themselves and their families decreased in 91.4% of the patients who came for control. After the use of vitamin D in children with growing pains, the mean pain score reported by the children decreased from 7.26±1.757 to 2.46±2.38. The mean pain score reported by families about their children decreased from 7.56±1.97 to 2.51±2.53 after vitamin D supplementation. Although most of the time growing pain is a self-limiting clinical picture, vitamin D supplementation may be necessary after a differential diagnosis was made because of the high level of anxiety in the families of children who do not respond to non-pharmacological approaches.

Keywords: Growing pain, vitamin D, children

Introduction

Growing pain is the most common cause of intermittent musculoskeletal pain in children.[1] Although there is no definite consensus on the definition of growing pains, they are defined as pains of unknown cause that usually occur in the evening and night in children in the developmental age without any musculoskeletal disease, sometimes awakening them from sleep at night and lasting from a few minutes to several hours.[2,3] Anatomical/mechanical factors, fatigue, psychological, pain threshold, and vitamin D deficiency theories have been proposed to explain the etiology of growing pains. Vitamin D levels are normal in very few children with growing pains.[4,5] The relationship

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between growing pain, vitamin D level and perception of pain was evaluated in this study.

Material and Method

A total of 138 children who presented to the pediatric rheumatology outpatient clinic with the complaint of limb pain and were diagnosed with growing pain and 30 healthy age-matched children who were referred to the general pediatric outpatient clinic without any joint-muscle complaint and included in the follow-up protocol of healthy children were enrolled in the study after Fırat University Non-Interventional Research Ethics Committee approval (date: 23/02/2017, decision no: 04/04). The families of the patients were asked to sign an informed consent form. Diagnosis of growing pain was made with detailed medical history and physical examination according to the specified criteria.[6,7]

Highlights

- The effect of vitamin D supplementation in children with growing pains was demonstrated in a case-controlled prospective study.
- Pain scores were reduced by administering vitamin D to children with growing pains and vitamin D deficiency.
- Our study is important because it is a case-controlled prospective study.

Information on personal and family medical history was obtained from all patients included in the study. Age at the time of presentation, gender, postal and e-mail addresses, kinship between parents (if any), number and ages of siblings, indication for previous hospitalization, previous surgery and presence of other individuals with growing pain in the family were questioned. Detailed physical examination, body weight, and height measurements were performed in all patients.

Complete blood count, creatine kinase, calcium, alkaline phosphatase (ALP), phosphorus, magnesium, parathormone (PTH), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and 25(OH)-VitD3 were assessed.

Pain scoring was performed in patients aged 6 years who were evaluated as having growing pains using the Wong-Baker FACES Pain Rating scale.[8] According to this scoring system, patients aged below 6 years selected the intensity of pain they felt from their faces on the pain scale chart.

Pain was scored using the Visual Analog scale (VAS) in patients aged 6 years who were assessed as having growing pain. For the parents, the VAS was used to measure pain intensity as described by their children.[8]Among the patients who were evaluated as having growing pain, those with 25(OH)-VitD3 levels below 12ng/mL (vitamin D deficiency)[9] were prescribed single oral doses of 150,000 IU cholecalciferol (DEVIT-3 oral drops DEVA Holding Co, İstanbul, Türkiye) if the child was under 6 years of age and 300,000 IU if the child was 6 years of age or older. These children were called for follow-up appointments two months later. At the follow-up visit, 25(OH)-VitD3, PTH, calcium and phosphorus levels were measured and pain scoring was performed.

A data evaluation form was prepared for each patient to record demographic data, clinical conditions, laboratory values, and treatment regimen information.

Statistical Analysis

For data analysis in this study, computerized version 22.0 of the statistical program Statistical Package for Social Science for Windows was used. Normally distributed data were expressed as mean ± standard deviation and non-normally distributed continuous variables were expressed as median (minimum-maximum). The Wilcoxon test was used to compare dependent groups, Mann-Whitney U test was used to compare different groups and the chi-square test was used to compare percentage values. Results were considered statistically significant at $p<0.05$.

Results

The patients in the growing pain group comprised 138 patients, including 62 (44.9%) men and 76 (55.1%) women. In the control group, 11 (36.7%) of 30 patients were male, and 19 (63.3%) were female. The median ages of patients in the growing pain group and healthy controls were 7.8 (3.8-14.8) and 9.4 years (4.3-14.8) respectively. No statistically significant differences were found between the study and control groups in terms of age and gender ($p>0.05$).

Six (4.3%) patients in the growing pain group and four (13.3%) control subjects had a family history of growing pain.

Patients in the growing pain group were evaluated according to the time of presentation to the hospital, location and frequency of pain, whether the pain woke them up from sleep or was relieved by massage, the need for a painkiller, and any other symptoms accompanying the pain. The clinical characteristics of the group with increasing pain are presented in **Table 1**.

Table 1. *Clinical characteristics of growing pain in patients*

Time of pain onset	**N**	**%**
At night	87	63
In the afternoon	19	13.8
In the afternoon and at night	32	23.2
Pain location	**N**	**%**
Calf	45	32.4
Thigh	16	11.6
Thigh/calf	61	44.2
Other	16	11.6
Frequency of pain	**N**	**%**
Every day	33	23.9
2-4 days a week	63	45.6
Once a week	29	21
Less than once a week	13	9.4
Pain waking up children from sleep	**N**	**%**
Yes	89	64.5
Pain relieved by massage	**N**	**%**
Yes	110	79.7
Not massaged	11	7.9
Need for a painkiller	**N**	**%**
Yes	81	58.7

The patients in the growing pain group (total n=138) experienced only abdominal pain (n=23, 16.6%), headache (n=17, 12.3%), both abdominal pain and headache (n=8, 5.8%), or any other accompanying pain (n=4, 2.9%), whereas 86 (62.3%) patients had not any accompanying pain.

The median body weights of the patients in the growing pain group and the healthy controls were 25 kg (13.8-73.5) and 29 kg (16-70) respectively. The median heights of the patients in the growing pain group and the healthy controls were 128 cm (98.5-185) and 134.5 cm (105-178). When the anthropometric measurements were evaluated, no statistically significant difference was found between the study and control groups in terms of height or body weight (p>0.05).

Laboratory parameters of the growing pain and control groups were evaluated. The hemoglobin and hematocrit values were lower in the growing pain group than in the control group, with a statistically significant intergroup difference (p<0.05). In patients with anemia, the lowest hemoglobin value was 10.2, and microcytic anemia was detected. Nutritional anemia was also considered. Malignancy was not considered based on laboratory and physical examination findings. The 25(OH)-VitD3 levels were lower in the growing pain group than in the control group, with a statistically significant intergroup difference (p<0.05). When acute-phase reactants (ESR, CRP) of patients in the growing pain and control groups were evaluated, no statistically significant difference was not found between the groups (p>0.05) (**Table 2**).

Among patients in the growing pain group, pre-treatment pain scoring was applied to 46 children with deficient 25(OH)-VitD3 levels, and in addition, the families of these children were requested to score the growing pains of their children before treatment.

Forty-six children with 25(OH)-VitD3 level below 12ng/mL were prescribed single oral doses of cholecalciferol (DEVIT-3 ampoule, DEVA Holding, İstanbul, Türkiye) and were called for control visits 2 months later. There were seven children under the age of six and 39 children over the age of six.

Mean pain scores of children in the growing pain group were evaluated after vitamin D supplementation. The mean self-reported pain score was 7.26±1.757 points. After the use of vitamin D, the mean pain score reported by the children themselves was 2.46±2.38 points. The mean pain score reported by the families for their children was 7.56±1.97 points at baseline. After vitamin D supplementation, the mean pain score recorded by the families for their children was 2.51±2.53 points (**Figure 1**). The change in pain scores of 35 children who used vitamin D due to growing pains and came for control was evaluated. There was a statistically significant difference between vitamin D use and the pain scores reported by both the children themselves and their families regarding their children (p<0.001) (**Table 3**). We also evaluated whether there were differences in PTH, calcium, and phosphorus levels among children with growing pain and vitamin D deficiency after vitamin D supplementation.

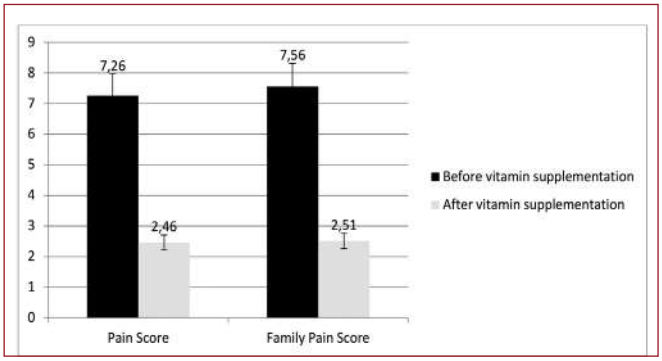

Figure 1. Changes in pain scores with vitamin D supplementation among children with growing pains

Table 2. *Laboratory values of the patients in each group*

	Growing pain group	Control group	P value
25(OH)-VitD3 (ng/mL)*	14.1 (1.5-70.0)	22.50 (5.80-56.60)	**p<0.05**
Hematocrit (%)*	39.6 (32.3-50.6)	42.00 (35.10-47.90)	**p<0.05**
Hemoglobin (g/dL)*	13.2 (10.2-16.5)	13.45 (11.40-15.40)	**p<0.05**
Parathormone (pg/mL)*	46.4 (17.9-449.0)	31.20 (23.20-111.30)	**p<0.05**
Platelets (10e3/µL)*	322500 (139000-764000)	318000 (212000-538000)	p>0.05
Phosphorus (mg/dL)*	5.0 (3.6-15.0)	4.80 (3.50-6.10)	p>0.05
WBC (10e3/µL)*	6900 (2790-16520)	7065 (4120-11910)	p>0.05
Alkaline phosphatase (u/L)*	195.0 (19.4-506.0)	191.50 (2.64-320.00)	p>0.05
Calcium (mg/dL)*	9.7 (8.7-10.6)	9.48 (8.80-10.25)	p >0.05
Sedimentation (mL/sa)*	11.0 (1.0-71.0)	9.00 (1.00-41.00)	p>0.05
Magnesium (mg/dL)*	2.2 (1.3-3.7)	2.11 (1.83-3.10)	p>0.05
Creatine kinase (u/L)*	95.0 (8.0-505.0)	87.00 (18.00-268.00)	p>0.05
C-reactive protein level (mg/L)*	3.1 (3.0-67.9)	3.23 (3.13-38.30)	p>0.05

(*) Results are presented as median (minimum-maximum) values, WBC; White blood cell

Table 3. *Changes in pain scores with vitamin D supplementation in children with growing pains*

	Decreased	Increased	No change	P value
Pain score	32	1	2	**<0.001**
Family pain score	32	0	3	**<0.001**

Table 4. *Changes in PTH, calcium, and phosphorus levels with vitamin D supplementation*

	Pre-treatment	Post-treatment	P value
25(OH)-VitD3 (ng/mL)*	8.3 (6.1-10.4)	23.9 (17.2-38.5)	**<0.001**
Parathormone (pg/mL)*	66.95 (45.25-92.32)	39.4 (33.33-60.9)	**<0.001**
Calcium (mg/dL)*	9.74 (9.24-9.97)	9.72 (9.48-10)	>0.05
Phosphorus (mg/dL)*	4.8 (4.58-5.2)	4.95 (4.65-5.4)	>0.05

(*) Results are presented as median (minimum-maximum) values, PTH; Parathormone

The PTH level was significantly lower after vitamin D supplementation than after pre-treatment values ($p<0.001$). There was no statistically significant difference in calcium and phosphorus levels with vitamin D use relative to pre-treatment values ($p>0.05$) (**Table 4**).

Discussion

In our study, hemoglobin and hematocrit values were found to be significantly lower in children in the growing pain group than in the control group. In a case-control study conducted by Evans et al.[10] with 77 children, vitamin D hypovitaminosis and anemia were found in 85.7% and 10.7% of the children with growing pains, respectively. The mean vitamin D level in children with growing pain was found to be low, consistent with other studies.[5,11-13] In a study conducted by Park et al.[4], the mean vitamin D level was found to be higher in children with pain compared with that in our study. However, none of these studies included a control group. Although vitamin D levels have been reported at different rates, vitamin D deficiency is generally observed in children with pain, as observed in our study. Acute phase reactants (ESR, CRP) were evaluated in children in the growing pain and control groups, and parameters indicating inflammation were found to be at normal levels in our study, similar to other studies.[11]

In a recent study on diagnosing growing pains in children using machine learning, it was observed that more than half of the patients woke up at night due to pain, similar to our study.[14] In another recent study, ALP levels were considered a biomarker of pain. In our study, no significant difference was found in ALP levels between the growing pain and control groups.[15] Mean pain scores were evaluated in children with increasing pain after vitamin D supplementation. We observed that the pain scores of the children themselves and the families of their children decreased after vitamin D supplementation. It was found that there was regression in pain in children after vitamin D supplementation.[11-13] However, none of these studies have employed a different pain scoring system to inform families about the growing pains of their children has not been performed so far.

In addition, the relationship between pain and vitamin D levels has been investigated in adult studies in recent years, and it was found that vitamin D levels were deficient or severely deficient in 89.3% of patients with non-specific muscle pain.[16] In adult studies, a significant decrease in the back pain score was found with vitamin D supplementation in patients with back pain whose 25(OH)-VitD3 level was below 30 nmol/L, and vitamin D replacement in women with chronic diffuse pain relieved pain and improved the quality of their lives, while it did not seem to affect spinal inhibitory pathways.[17,18]

Conclusion

In conclusion, although growing pain is a self-limiting clinical feature, the benefits of supportive treatment should be explained to families after a differential diagnosis is made because families have a high level of anxiety. In addition, as understood, vitamin D levels should be evaluated in patients with persistent complaints despite supportive treatment. In children with increasing pain and vitamin D deficiency, the clinical picture may improve earlier with vitamin D supplementation.

Ethical Approval: The study after Fırat University Non-Interventional Research Ethics Committee approval (date: 23/02/2017, decision no: 04/04).

Informed Consent: The families of the patients were asked to sign an informed consent form.

Author Contributions: Günbey Ö: Surgical and Medical Practices, Design, Data Collection or Processing, Analysis or Interpretation, Literature Search, Writing.; Gürgöze MK: Surgical and Medical Practices, Concept, Design, Analysis or Interpretation.; Günbey FB: Surgical and Medical Practices, Data Collection or Processing, Literature Search.

Conflict of Interest: Metin Kaya Gürgöze is Editorial Board Member in the Journal of Pediatric Academy. He had no involvement in the peer-review of this article and had no access to information regarding its peer-review.

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