Serum Levels of Vitamin D in Children with or without Isolated Distal Radius Fractures: A Prospective Clinical Study*

Níveis séricos de vitamina D de crianças com ou sum fraturas isoladas da extremidade distal do rádio: Um estudo clínico prospectivo

Mehmet Ali Talmac[1] Mehmer Akif Gorgel[1] Ali Varol[2] Semih Ak[3] Bekir Eray Kilinc[3] Hacı Mustafa Ozdemir[1]

[1] Department of Orthopedic Surgery and Traumatology, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey
[2] Health Ministry, Department of Orthopedic Surgery and Traumatology, Silopi State Hospital, Sirnak, Turkey
[3] Department of Orthopedic Surgery and Traumatology, Fatih Sultan Mehmet Education and Research Hospital, Istanbul, Turkey

Address for correspondence Bekir Eray Kilinc, MD, İçerenköy Mahallesi Zübeyde Hanım Sok., Şekerevler Sitesi No:1 D:B43, Ataşehir/Istanbul (e-mail: dreraykilinc@gmail.com).

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Abstract

Objective To compare the serum levels of vitamin D and minerals in children with or without isolated distal radius fractures.

Methods The present prospective clinical study included 50 children (aged between 5 and 15 years) with isolated distal radius fractures who were admitted to our emergency unit between February and May 2018 as the study group (group A), and 50 healthy children with no history of fracture as the control group (group B). Peripheral venous blood samples were obtained and analyzed for measurements of 25-hydroxyvitamin D (25(OH)D), calcium (Ca), magnesium (Mg), phosphorus (P), alkaline phosphatase (ALP), and parathyroid hormone (PTH) in both groups. Patient characteristics and peripheral venous blood samples were compared between the groups.

Results The mean age, height, weight, body mass index (BMI) and gender distribution were similar in both groups. There were no statistical differences in the blood analyses, including Ca, Mg, P, ALP, and PTH. However, the serum levels of 25(OH)D were statistically lower in group A when compared to group B ($p < 0.001$), and the number of

Keywords
- alkaline phosphatase
- children
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patients with 25(OH)D insufficiency was statistically higher in group A than in group B ($p = 0.012$).

Conclusion Children with isolated distal radius fracture should be informed about vitamin D deficiency, and, in children with low levels of vitamin D, supplementation may be considered.

Resumo

Objetivo Comparar os níveis séricos de vitamina D e minerais de crianças com ou sem fraturas isoladas da extremidade distal do rádio.

Métodos Este estudo clínico prospectivo incluiu 50 crianças (com idade entre 5 e 15 anos) com fratura isolada distal do rádio que deram entrada em nossa unidade de emergência entre fevereiro e maio de 2018 como grupo de estudo (grupo A), e 50 crianças saudáveis sem histórico de fratura como grupo controle (grupo B). Foram obtidas e analisadas amostras de sangue venoso periférico para medições de 25-hidroxivitamina D (25(OH)D), Cálcio (Ca), Magnésio (Mg), Fósforo (P), fosfatase alcalina (FA) e hormônio da paratireoide (HPT) em ambos os grupos. As características dos pacientes e as amostras de sangue venoso periférico foram comparadas entre os grupos.

Resultados A média de idade, altura, peso, índice de massa corporal (IMC) e distribuição de gênero foram semelhantes em ambos os grupos. Não houve diferenças estatísticas nas análises sanguíneas, incluindo Ca, Mg, P, FA e HPT. No entanto, os níveis séricos de 25(OH)D foram estatisticamente menores no grupo A do que no grupo B ($p < 0{,}001$), e o número de pacientes com insuficiência de 25(OH)D foi estatisticamente maior no grupo A do que no grupo B ($p = 0{,}012$).

Conclusão Crianças com fratura isolada distal do rádio devem ser informadas sobre deficiência de vitamina D, e, em crianças com baixos níveis de vitamina D, a suplementação pode ser considerada.

Palavras-chave
- fosfatase alcalina
- crianças
- hormônio da paratireoide
- fraturas do rádio
- vitamina D

Introduction

Distal radius fractures are one of the most common types of fractures, with an incidence of 25% in the pediatric population.[1] With puberty, the incidence of these fractures rises, with a peak in the age group between 8 and 11 years in girls, and between 11 and 14 years in boys.[2] Although the exact cause has not yet been discovered, the incidence has demonstrated a steady increase over the past 40 years.[2,3] Several studies have been conducted to find out the source of the increased rates, trying to carefully elucidate the potential factors. A general increase in the participation in sports-related activities, gender, ethnic and racial differences, and nutritional status are some of the factors which have been investigated in the literature related with the occurrence of distal radius fractures in the pediatric population.[4,5]

The positive effects of vitamin D on bone density and the association between vitamin D deficiency and low bone density have been established with several studies.[4–6] Low dietary intake of minerals, such as calcium, magnesium, and phosphate, also causes decreased bone mineral density and increased risk of osteoporotic fracture.[7–9] Primary or secondary osteoporosis caused by various underlying chronic illnesses may lead to low serum levels of minerals and vitamin D in the pediatric population, as well as to an increase in the risk of pediatric fracture.[10,11] Although there is a consensus in the literature about the direct correlation between low dietary mineral intake or low levels of vitamin D and osteoporotic fractures in adults, there is no adequate data to find any correlation between the serum levels of vitamin D and minerals and isolated distal radius fractures in children. Therefore, we aimed to compare the serum levels of vitamin D and minerals in children with and without isolated distal radius fractures.

Materials and Methods

The present prospective clinical study was performed with the approval of the Insitutional Review Board (approval number: 19/12/2017-2427) and in line with the ethical principles of the Declaration of Helsinki. After the approval, informed consent was obtained from the guardians of all participants.

The inclusion criteria were: children aged between 5 and 15 years, with similar socioeconomic background, no history of malnutrition or undernutrition, those needing to examine the bone mineral density, with adequate sunlight exposure, otherwise healthy apart from the distal radius fracture after mild trauma, with no history of upper-extremity surgery, and no neurological diseases. The exclusion criteria were: children with concurrent ulnar fractures, history of major trauma, with mineralization disorders (osteopenia, osteogenesis imperfecta, etc.), undergoing steroid treatment, and with chronic diseases or cerebral palsy.

Fig. 1 Anteroposterior and lateral radiograps of an isolated distal radius fracture.

In total, 50 children who were admitted to our emergency unit between February and May 2018 with isolated distal radius fractures (►**Fig. 1**) were included in the study group (group A), and 50 healthy children with no history of fracture were included as the control group (group B). The patients in group B were randomly recruited from pediatric outpatient units; they had upper respiratory tract infection or were being submitted to routine examinations.

The following characteristics of the study sample were included: age (years), gender distribution, height (cm), weight (kg), and body mass index (BMI; kg/m^2). Peripheral venous blood samples were obtained and analyzed for measurements of 25-hydroxyvitamin D (25(OH)D), calcium (Ca), magnesium (Mg), phosphorus (P), alkaline phosphatase (ALP), and parathyroid hormone (PTH).

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS, IBM Corp., Armonk, NY, US) software, version 22.0 for Windows 7, was used for all statistical analyses. The data was presented as means and standard deviations, medians, minimum and maximum ranges, frequencies and rates. The distributions of the parametric data were analyzed with the aid of the Student *t*-test, and the Mann-Whitney U test was used for the non-parametric data. The Chi-squared test was employed to compare the rates between the two groups. Values of $p < 0.05$ were considered statistically significant.

Results

The sample was composed of 100 patients, with 50 patients in the control group and 50 in the study group. All patients in the study group had isolated distal radius fractures, and those in the control group had no history of fracture.

The mean age, height, weight, BMI and gender distribution were similar in both groups (►**Table 1**). In addition, there were no obese patients (BMI > 30) in the sample. There were no statistical differences in the blood analyses, including Ca, Mg, P, ALP, and PTH (►**Table 2**). However, the serum levels of 25(OH)D were statistically lower in the group A when compared to group B ($p < 0.001$), and the number of patients with 25(OH)D insufficiency was statistically higher in group A than in group B ($p = 0.012$).

Discussion

Fractures compose around 10% to 25% of all pediatric injuries, and one of the most common in the pediatric population is distal radius fracture.[12,13] Approximately 1 in 100 children are hospitalized for orthopedic surgery after distal radius fractures yearly. The wide spectrum of fracture presentation, the variety of surgical and non-surgical techniques, the growth potential of the skeletal structure of the children, and family expectations are some of the challenging factors in the treatment of distal radius fractures, especially in the pediatric population.[14] Due to accelerated skeletal maturation, children and adolescents are at a high risk for these fractures. Ryan et al.[15] revealed a significant higher rate of fractures caused by minor trauma in the age group between 10 and 14 years in comparison with the age group between 5 and 9 years. This finding implies that rapid skeletal development may jeopardize bone mineralization, which is disproportional to the growth rate, and may lead to a distal radius fracture even after a minor trauma.

Solar ultraviolet B (UV-B) radiation is the primary source of vitamin D (other than dietary intake). Vitamin D3, which is produced by the skin with the action of sunlight, and dietary vitamin D undergo two consecutive hydroxylations: in the liver,

Table 1 Comparison of the patient characteristics

	Group A (n = 50)	Group B (n = 50)	*p*-value
Age (years)	8.3 ± 2.8 (5–15)	7.9 ± 3.4 (5–15)	0.352
Gender (female); n (%)	18 (36.0)	16 (32.0)	0.765
Height (cm)	118.8 ± 22.3 (90–165)	116.4 ± 24.9 (76–160)	0.716
Weight (kg)	29.8 ± 9.8 (15–56)	27.8 ± 11.9 (13–55)	0.268
Body mass index (kg/m^2)	21.4 ± 4.9 (13.6–29.6)	20.5 ± 3.2 (12.2–28.1)	0.412

Note: The values are expressed as means ± standard deviations, minimum–maximum ranges, or as numbers of patients and percentages.

Table 2 Comparison of the peripheral venous blood analyses of the patients

	Group A (n = 50)	Group B (n = 50)	*p*-value
Calcium (mg/dL)	10.0 ± 0.4 (9.4–10.7)	10.1 ± 0.6 (9.1–11.4)	0.542
Magnesium (mg/dL)	2.11 ± 0.14 (1.8–2.4)	2.10 ± 0.15 (1.9–2.4)	0.830
Phosphorus (mg/dL)	5.0 ± 0.40 (4.3–5.8)	5.12 ± 0.48 (4–6.3)	0.350
Alkaline phosphatase (IU/L)	276.4 ± 69.4 (200–482)	286.6 ± 72.6 (167–447)	0.478
Parathyroid hormone (pg/mL)	41.7 ± 22.3 (10.9–97.1)	40.1 ± 19.1 (18.6–77.2)	0.676
25-hydroxyvitamin D (ng/mL)	19.4 ± 4.2 (10.7–28.3)	29.4 ± 11.1 (13–48.7)	< 0.001
25-hydroxyvitamin D insufficiency; n (%)	22 (44.0)	6 (12.0)	0.012

Note: The values are expressed as means ± standard deviations, minimum–maximum ranges, or as numbers of patients and percentages.

the former becomes 25(OH)D, and, in the kidneys, the latter takes on its biologically-active form, 1,25-dihydroxyvitamin D (1,25(OH)2D); 1,25(OH)2D enhances the serum levels of calcium and phosphorus by increasing the intestinal absorption of these minerals, which are involved in the processes of bone formation, mineralization, and resorption.[16] Serum 25(OH)D is a major circulating metabolite of vitamin D, and it clinically reflects the status of this vitamin, which may be used as an indicator of the lifestyle and dietary habits of the patients. The serum concentrations of 25(OH)D that indicate deficiency or insufficiency of vitamin D are controversial, and the cut-off values are not well–established. The American Academy of Pediatrics (AAP) and the Institute of Medicine (IOM) both define vitamin D insufficiency as concentrations of 25(OH) D < 20 ng/mL in the pediatric population.[10] We used the Endocrine Society guideline, which defines the deficiency of 25(OH)D as levels < 20 ng/mL, and the insufficiency as levels < 30 ng/mL.[17]

Vitamin D deficiency affects the intestinal absorption of calcium and phosphorus, which results in decreased serum levels of those minerals. The parathyroid gland releases hormone to increase the serum calcium back into the adequate range. The PTH increases the calcium reabsorption in the kidneys and the excretion of phosphorus. Meanwhile, it has also negative effects on bone mineralization, with the aim of increasing the serum levels of calcium.

Over time, chronic severe vitamin D deficiency in infants and children causes stunted growth, osteomalacia, and rickets.[10] Moore et al.[18] reported that vitamin D deficiency has a higher incidence among obese children and those with darker skin. Similarly, vitamin D deficiency was found to be more frequent in girls than in boys.

Vitamin D, PTH and calcium levels have been correlated with bone mineral density.[19] The association between 25(OH) D and bone mineral density has been examined in several studies.[20–23] Most of these studies showed a connection between the adequate intake of vitamin D and high bone mineral density. Low bone mineral density may increase the rate of fracture both in the adult and pediatric populations.[23–25] A study[21] that assessed the status of vitamin D in adolescent girls during winter found that low levels of vitamin D have a negative effect on bone mineral density. Another study,[24] which analyzed calcium supplementation and bone mineral density, showed a positive effect of vitamin D supplementation on high bone mineral density, which may reduce the rate of pediatric fracture. In the present study, we found that children with distal radius fracture have statistically lower levels of vitamin D than the healthy group. On the other hand, between the two groups there were no statistically significant differences regarding the levels of Ca, Mg, P, ALP, and PTH.

Adolescents are prone to vitamin D insufficiency due to the mineral demands of their growing skeleton. A study[25] conducted in northern India found a high prevalence of clinical and biochemical hypovitaminosis D in healthy schoolchildren. Vitamin D deficiency in healthy children has been subjected to several studies,[26–29] which showed that sunlight exposure alone is not enough to prevent hypovitaminosis D, and that nutritional habits (high dietary phytate intake) or genetic tendency (Asian) may lead to vitamin D deficiency. In the present study, we observed that 12% of the healthy children had vitamin D levels < 20 ng/mL, which are considered deficient.

One of the limitations of the present study is that the blood samples were collected from the children regardless of the season; thus, some children may not have had enough time to produce vitamin D, especially at the end of winter. Another limitation of the study is the lack of information about the dietary habits of the children in the sample. More detailed studies with larger samples are needed in order to find more convincing data about the correlation of vitamin D and pediatric fractures.

Conclusion

Although optimal vitamin D levels have not been well-established in the literature, they have been used to determine bone health.[29] Besides vitamin D levels, minerals such as Ca, Mg and P or endocrine hormones (PTH) have also been used as determinants of bone turnover. In adults, an association between hypovitaminosis D and osteoporotic fractures has been examined in several studies.[26,28] However, in the pediatric population, there is no adequate study to determine any correlation between pediatric fractures and vitamin D deficiency. With the present study, we have shown that the status of vitamin D may be used as a predictor of pediatric fractures. Especially in spring and summer, families with children with

isolated distal radius fractures should be informed about vitamin D deficiency, and, in children with low levels of vitamin D, supplementation may be considered.

Conflict of Interests

The authors have no conflict of interests to declare.

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