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Evaluation of Patients Diagnosed with Nutritional Rickets: A Single Center Study

Nutrisyonel Rikets Tanısı Alan Hastaların Değerlendirmesi: Tek Merkez Çalışması

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ABSTRACT

Objective: Nutritional rickets continues to be an important health care problem. Its incidence has decreased in our country following the free vitamin D distribution that started in 2005 but it continues to stay on the agenda as a preventable disorder. Our aim was to evaluate patients diagnosed with nutritional rickets following the vitamin D supplementation program.

Material and Methods: A total of 93 cases diagnosed with nutritional rickets were included in the study. The data were retrospectively collected from patient records and laboratory analyses.

Results: The 93 nutritional rickets patients we evaluated consisted of 39 (41%) girls and 54 (59%) boys. The mean age was 19.1±35.1 months. The physical examination usually revealed widening of the wrists and rachitic beads. The most common sign at presentation was hypocalcemic seizure (28%, n= 26). Hypocalcemia was present in 46% (n= 43) and single large doses of vitamin D (stoss) therapy had been administered to 53% (n= 49). A concurrent disorder was present in 46%. The patients had presented mostly in February and May and only 20% had been receiving vitamin D supplementation.

Conclusion: The 400 IU vitamin D supplementation dose needs to be revised and the program made more widely available.

Key Words: Child, Nutritional rickets, Vitamin D

ÖZET

Amaç: Nutrisyonel rikets önemli bir halk sağlığı problemi olmaya devam etmektedir. Ülkemizde 2005 yılında başlanan ücretsiz D vitamini desteğinden sonra nutrisyonel rikets insidansı azalmış olsa da hâlâ daha önlenebilir hastalıklar arasında yer almaya devam etmektedir. D vitamini suplementasyonu sonrası nutrisyonel rikets tanısı alan hastaları değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Çalışmaya nutrisyonel rikets tanısı konulan toplam 93 olgu dahil edildi. Hastaların dosya bilgileri ve laboratuvar tetkikleri retrospektif olarak incelenerek veriler elde edildi.

Bulgular: 39'u (41%) kız, 54'ü (%59) erkek olan 93 nutrisyonel riketsli hasta değerlendirildi. Hastaların ortalama yaşı 19±35,1 ay'dı. Fizik muayenede en sık el bilek kemiklerinde genişleme ve raşitik rozari saptandı. En sık bulgu olarak hipokalsemik nöbet (28%, n= 26) saptandı. Hipokalsemi olguların 46%'sında (n= 43) görüldü ve sitos tedavisi olguların 53%'üne uygulandı. Olguların 46%'sında eşlik eden başka bir hastalık vardı. Olgular sıklıkla Şubat ve Mayıs arasında başvurdu ve olguların yalnızca 20%'si D vitamini desteği almaktaydı.

Sonuç: 400 IU D vitamini desteği gözden geçirilmeli ve daha yaygın kullanımı sağlanmalıdır.

Anahtar Sözcükler: Çocuk, Nutrisyonel rikets, D vitamini

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INTRODUCTION

Normal bone growth and mineralization require adequate calcium and phosphate. Inadequate mineralization can cause rickets and/or osteomalacia. Low serum phosphorus and calcium cause disturb bone mineralization and growth in children. Excessive osteoid tissue accumulates in the epiphyseal plates of growing bones due to inadequate mineralization in rickets. Rickets and osteomalacia are generally seen together when the growth plates are open while osteomalacia is seen by itself when the growth plates are closed (1).

The most common cause of rickets worldwide is vitamin D deficiency (2). The most important sources of vitamin D in early infancy are sunlight, placental transmission of vitamin D, and maternal milk. Vitamin D deficiency has been an important problem in our country for many years and studies have reported the disorder at a rate of 46-80% in women of childbearing age and/or pregnant women (3). A program to distribute 400 IU vitamin D per day from the first days of life to all infants free of charge from healthcare centers has been started in 2005. The positive effects of this program are reflected in the decrease of the rickets incidence from 6% to 0.1% according to the preliminary regional data (3). However, nutritional rickets continues to be stay on the agenda as a preventable health problem.

The aim of our study was to evaluate cases diagnosed as nutritional rickets following our country's program to distribute vitamin D free of cost and to contribute to determining new strategies for the prevention and treatment of this disorder.

MATERIAL and METHOD

A total of 93 cases diagnosed with nutritional rickets at Dr. Sami Ulus Obstetrics and Gynecology and Pediatrics Training and Research Hospital's Endocrinology Clinic between 01 January 2006 and 31 December 2011 were included in the study. We obtained the date of birth, date of presentation, age at presentation, gender, nutritional status, vitamin D intake status, presentation symptoms, anthropometric evaluations, physical examination findings, initial and follow-up laboratory findings, radiological findings, treatment methods, follow-up duration and the physical examination and laboratory findings at last follow-up through the patient charts.

Statistical Analysis

Descriptive statistics were presented as mean±standard deviation for the continuous variable while count and percent for the categorical variables. Two-proportion Z test was performed to compare proportions for the categorical variables. Statistical significance level was considered as 5% for all statistical comparisons and the SPSS (ver. 15.0) for Windows software was used for statistical data analysis.

RESULTS

A total of 93 cases consisting of 39 (41%) females and 54 (59%) males aged 1.5 months to 15 years were diagnosed with nutritional rickets. The mean age was 19.1±35.1 months. The cases were distributed into 3 age groups as 0-3 months, 3 months - 3 years and >3 years with percentages of 17% (n= 16), 74% (n= 69) and 9% (n= 8) respectively (Table I).

The most common physical examination findings were widening of the wrist (n=16), rachitic beads (n=14) and the O-bain deformity of the lower extremities (n=13). Our cases had presented with hypocalcemic seizure, walking disorder, bowing of the legs, delayed closure of the anterior fontanelle or wide anterior fontanelle, short stature or sweating while 26 cases had been brought for other reasons but had been diagnosed with nutritional rickets when rickets findings such as widening of the wrist, caput quadratum, rachitic beads, craniotabes, Harrison's sulcus, or O-bain deformity had been found during physical examination. Table II presents the symptoms on presentation and the physical examination findings that enabled the diagnosis. However, there is no significant relationship between the age of the patients and the hypocalcemic seizure (p= 0.233). The first presentation was with a hypocalcemic seizure in 28% (n= 26) of the cases while the rate of initial hypocalcemic seizure was found 44% (n= 7) in the 0-3 months age group.

Hypocalcemia was present in 46% (n=43) and hypophosphatemia (p<3.5 mg/dl) in 26% (n= 25) of the cases at the time of presentation. The 25-hydroxyvitamin D (25-OHD) level was 0-10 ng ml in 58% of our cases, 10-20 ng/ml in 30% and 20-30 ng/ml in 12%. The laboratory values at presentation have been provided in Table III. Radiologically active rickets findings were present in 78% (n= 73) of the cases. The most common radiological finding was cupping of the radius and ulna distal end (49%, n= 36). A subchondral cyst was found in two cases with markedly high parathormone levels.

Pneumonia, malnutrition, anemia, epilepsy, or motor-mental retardation were also present in 43 (46%) cases and 18 patients (19%) had received the nutritional rickets diagnosis while being evaluated for pneumonia. A history of anti-epileptic drug use that could affect the calcium metabolism was present in 9% (n= 8) cases.

Patients were divided into 4 groups according to their vitamin D usage. The findings ratio observed was 63% for non-users of vitamin D, 12% for those who said they used vitamin D but not regularly 12%, and 20% for regular vitamin D users 20%. Table IV presents the vitamin D intake status of 73 cases whose history was known.

Most of the nutritional rickets cases had been born in August (n= 17, 18%), followed by July and December. For the 0-3 month age group, 31% (n= 5) had been born in December and were winter babies.

Table I: Age distribution of the nutritional rickets patients at the time of presentation.

Age	Mean age (months)±SD	n (%)
0-3 months	2.3±0.7	16 (17)
3 months-3 years	11.5±8.2	69 (74)
>3 years	117±57	8 (9)
Total	19.1±35.1	93 (100)

Table II: The symptoms and physical examination findings of the nutritional rickets cases.

Presentation symptom and physical examination findings	n
Hypocalcemic seizure	26
Widened wrist	16
Rachitic beads	14
O-bain deformity of the lower extremities	13
Walking disorder	8
Developmental delay	7
Late anterior fontanelle closure / wide anterior fontanelle	7
Craniotabes	7
Caput quadratum	6
Frontal bossing	5
Harrison's sulcus	4
Bone deformities	4
Short stature	3
Sweating	3
Fracture	2
Genu valgum	1

Table III: Laboratory findings at presentation in nutritional rickets cases.

Laboratory values	Mean±SD (Range)
Calcium (mg/dl)	7.9±1.7 (4.6-10.2)
Phosphorus (mg/dl)	4.3±1.3 (1.2-8.1)
Alkaline phosphatase (IU)	1425±1381 (461-7954)
25-hydroxyvitamin D (25-OHD) (ng/ml)	10.6±9.3 (1-29)
PTH (pg/ml)	280±229 (83-1084)

Table IV: Vitamin D intake status of the nutritional rickets cases.

Vitamin D intake status	n (%)
No intake	46 (63)
Irregular intake	12 (17)
Regular intake	15 (20)
Total	73 (100)

DISCUSSION

Nutritional rickets is most commonly seen in Africa, India, Asia, Latin America and the Middle East (4). The incidence of nutritional rickets also varies between different regions in the same country. The rates reported for our country vary between 1.67 and 19% (3). A study has reported socioeconomic and maternal factors and inadequate vitamin D intake as the risk factors for rickets in our country and Middle East countries (4).

A program to administer 400 IU vitamin D to all infants has been started in 2005 in our country (5). Our study includes the period between 2006 and 2011 and we were only able to find 93 cases in our endocrinology departments where 25000 patients are seen on average per year, an indirect indicator of the success of the program. However, nutritional rickets is still on the agenda as a preventable health problem. The increase in rickets cases in developed countries in the last 10 years, the need to review vitamin D supplementation doses, the increased interest on the extraskeletal effects of vitamin D, the increased awareness of the importance of vitamin D among the mothers and the new "subclinical vitamin D deficiency" concept have made the issue current once again (6-10).

We found that the age of 74% (n= 69) of the nutritional rickets cases was 3-36 (19.1±35.1) months and 59% (n= 54) were male. A previous study from Nigeria reported a male percentage of 75% while a study from Tehran reported 63% (11,12). The more common nutritional rickets in males could be because of the parents being more sensitive regarding male children due to sociocultural characteristics and bringing them to the physician sooner and also because the different vitamin D sensitivity in male and female children as a result of vitamin D receptor polymorphism (13).

Najada et al. (13) reported from their study on rickets patients with a mean age of 8 months that the most common physical finding was rachitic beads (93%) followed by widening of the wrist (55%) and craniotabes (42%). Cesur et al. (14) studied 946 nutritional rickets patients and reported the most common physical finding as rachitic beads (54.5%) followed by widening of the wrists (61.8%). The most common physical finding among our patients was rachitic beads, widening of the wrist and O-bain deformity of the lower extremities, in order of frequency.

A definite diagnosis of rickets always requires biochemical data. There may be hypo/normocalcemia, hypo/normophosphatemia, increased ALP, increased PTH and decreased 25-OHD in the period before the clinical and radiological findings appear. The biochemical findings of rickets generally change according to the rickets stage. Hypocalcemia was present at the time of presentation in 46% (n= 43) of our cases. The study by Salama from Egypt reported a 56% rate of hypocalcemia in rickets patients (15). Clinical findings due to hypocalcemia

usually appear in the early infancy period (16). However, it is not statistically significant that we found 27% of our patients had presented with a hypocalcemic seizure and that this rate was 44% in the 0-3 months age group. A previous study has evaluated 42 early-period rickets cases aged 60±19 (32-112) days and found that 78% of these babies had presented with hypocalcemic convulsions (17). The phosphorus level was normal in 35% and high in 45% of these cases. This was thought to be due to the limited evolution of rickets cases from stage I to stage II during infancy resulting in their presentation with a hypocalcemic seizure but without the appearance of radiological/clinical findings and a significant change in the serum phosphorus level (3).

Radiological findings can support the rickets diagnosis. Early radiological changes appear in the distal ulnar region in infants and in the knee region in older children (18). We found active rickets findings in the left wrist x-ray of 78% (n= 73) of our cases. A 2007 study from Canada has reported the presence of radiological findings in 93% of rickets cases and most cases with normal x-rays were young infants (19).

Hypocalcemia was present at presentation in 46% (n= 43) of our patients. We started calcium first for our patients with hypocalcemic symptoms. We first used parenteral treatment followed by elemental calcium in patients who could take the drug orally and whose general condition was good. The serum calcium level of our hypocalcemic patients returned to normal in 4.8 ±3.4 days on average. Single large doses of vitamin D treatment (stoss) was started in 53% (n= 49) of our patients. The others received high-dose daily oral vitamin D treatment according to their 25-OHD levels. There is a significant risk of hypercalcemia following stoss therapy and this treatment should therefore only be used in children where the usual treatment regimes are unsuccessful due to incompliance (20).

Upper and lower respiratory tract infections are especially common in rickets (21). There may be recurrent gastroenteritis attacks and constipation (20). Pneumonia was present in 18 of our cases at presentation. A study from Pakistan has reported rickets in 101 of 137 cases with severe pneumonia (22). Another study has found a lower 25-OHD level in bronchiolitis and pneumonia patients at the pediatric intensive care unit (ICU) than a healthy control group and pneumonia patients followed-up in the non-ICU unit (23). The number and activity of 'natural killer' cells is lower in rickets patients. Vitamin D also has an immunomodulatory effect on B and T cells (24). Vitamin D deficiency is currently thought to be possibly involved in the etiopathogenesis of cancer, heart disease, hypertension, type 1 diabetes, immune deficiency, chronic fatigue syndrome, obesity, infections, and autoimmune disorders such as multiple sclerosis, Sjogren syndrome, Crohn disease, thyroiditis and rheumatoid arthritis (25).

Evaluation of the vitamin D intake history of our patients revealed that only 20% were taking vitamin D regularly, meaning that 80% of our rickets patients were not taking vitamin D at all or taking it very irregularly. Mutlu and Kusdal (26) reported from their study on 85 healthy babies that 59 took vitamin D regularly and that none showed clinical or laboratory rickets findings although the 25-OHD level was below 20 ng/ml in 10 of the cases (four of these cases were taking vitamin D regularly). In contrast, we found rickets in 15 (16%) of our patients although they had received regular vitamin D. This indicates that the 400 IU administered as a supplementation dose could be inadequate and needs to be reviewed. However, an important limitation of our study is the determination of vitamin D administration status according to the family's declaration.

Evaluation of our cases according to month of birth revealed that August was the most frequent month of birth. This may be because babies are usually kept at home after birth and the August birth is followed by winter in three months. Evaluation of cases in the 0-3 month age group shows that 31% of the patients were born in December. The angled entry of sunlight into the atmosphere during winter months, the generally cloudy weather and the air pollution decreases the percentage and effect of UV rays reaching the earth (27). The 25-OHD level is therefore high in the summer and autumn and low in the winter and spring.

Our results indicate that vitamin D is an important factor for rickets prevention and that the vitamin D distribution strategy used across our country is successful. However, family physicians and pediatricians need to work harder for the vitamin D support program to be used by families more commonly. The fact that rickets cases can develop despite vitamin D supplementation also indicates that the 400 IU vitamin D dose currently used needs to be reviewed. The continued existence of rickets in the 0-3 months age group despite a decrease in numbers emphasizes the importance of providing vitamin D supplementation to pregnant and nursing women. Rickets is seen commonly under the age of 3 years and mostly in the winter and spring seasons so cases that present in these seasons should be especially queried regarding vitamin D prophylaxis and evaluated for rickets. The most common physical examination findings of rickets are widening wrists and rachitic beads, requiring the examination of every case under three years old for these signs.

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