

Loss of Appetite May Be The First Sign of the Vitamin D Deficiency in Healthy Children; May The Clinician's Perception Be Wrong?

Sağlıklı Çocuklarda Vitamin D Eksikliğinin İlk Bulgusu İştahsızlık Olabilir: Klinisyenin Yanlış Algısı Olabilir mi?

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ABSTRACT

Background: Loss of appetite in children is a cause of complaint or concern for many parents. In this study, we aimed to investigate the status of vitamin D in children admitted with a complaint of loss of appetite.

Methods: The study included 40 children aged between 1 and 5 years with loss of appetite between January and September 2016. Control group included 96 healthy children.

Results: There was no significant difference in the sex, age and laboratory results, except vitamin D level, of the both groups. Vitamin D levels were significantly lower in the poor appetite group

Conclusion: In conclusion, it should be kept in mind that seemingly healthy children with family concern of poor appetite may have vitamin D deficiency. Loss of appetite may be the first sign of the vitamin D deficiency. Yet, high costs can be prevented only by regular use of vitamin D prophylaxis.

Anahtar Kelimeler: Vitamin D, Loss of appetite, Healthy children

Introduction

Loss of appetite in children is a cause of complaint or concern for many parents. Although loss of appetite can be physiological in some patients, poor appetite can be a symptom of malnutrition and other diseases (1). Appetite is a conscious desire to eat that is felt as hunger and it regulates energy intake necessary for the supply of metabolic requirements. The development of eating behavior is regulated by the child's development, mother-child interaction, social factors, and neural mechanisms (2). Approximately 20 to 35% of healthy children present to the physicians due to eating problems and loss of appetite, while this rate is even up to 33 to 90% in children with developmental delay

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ÖZ

Giriş: İştahsızlık, birçok ebeveyn için şikayet ve kaygı sebebidir. Bu çalışmada, iştahsızlık şikayeti ile başvuran çocuklarda D vitamini durumunu araştırmayı amaçladık.

Metod: Çalışmaya Ocak-Eylül 2016 tarihleri arasında iştahsızlığı olan 1-5 yaş arası 40 çocuk dahil edildi. Kontrol grubu olarak 96 sağlıklı çocuk alındı.

Bulgular: Her iki grup arasında cinsiyet, yaş ve D vitamini harici diğer testlerde istatistiksel anlamlı fark bulunmadı. İştahsız grupta, d vitamini düzeyi anlamlı olarak düşüktü.

Sonuç: Sonuç olarak, iştahsızlık kaygısı olan ailelerin sağlıklı görülen çocuklarında vitamin D eksikliği akılda tutulmalıdır. İştahsızlık vitamin d eksikliğinin ilk bulgularından biri olabilir. Fakat, yüksek maliyetler sadece düzenli olarak D vitamini profilaksisi kullanılmasıyla da önenebilir.

Keywords: Vitamin D; İştahsızlık; Sağlıklı Çocuk

(3). There are many organ systems and endocrine-paracrine systems affecting appetite. Short-term control of food intake is regulated mainly by gastrointestinal system as well as central nervous system, adrenal glands, and pancreas, while long-term control of food intake is regulated by fat tissue through release of paracrine and endocrine factors such as leptin, adiponectin, resistin, and tumor necrosis factor alpha (4).

Vitamin deficiencies and anemia are more common among other causes of poor appetite in children (5). The studies recommend vitamin supplementation upon diagnosis of vitamin deficiency. However, no studies, to date, have demonstrated increased appetite with multivitamin supplementation (6). Iron deficiency anemia has been reported to be associated with loss of appetite, in patients with reduced ghrelin levels (7). On the other hand, previous studies have not shown a strong relationship between the loss of appetite and vitamin deficiency.

Vitamin D plays an important role for the health of neuromuscular and skeletal systems due to its role in calcium and phosphorus homeostasis. Recent studies have shown a relationship of vitamin D deficiency with diabetes mellitus, cancer, frequent infections, and urticaria (8-10). In the practice of pediatrics, patients presenting with loss of appetite are common, although they are deemed healthy and to have normal weight for height. During well child examinations, patients with poor appetite are often overlooked due to normal height and weight measurements.

In this study, we aimed to investigate the effect of vitamin D in children admitted to the general pediatrics outpatient clinics with a complaint of loss of appetite.

Materials and Methods

This study was planned retrospectively. The study included 40 children aged between 1 and 5 years with loss of appetite who were admitted to General Pediatrics and Well Child Outpatient Clinics complaining of poor appetite between January 2016 and September 2016 and who did not have neurological, metabolic, cardiac, psychological or chronic disease. The children with malnutrition, malabsorption, and obese children were excluded. The children with concomitant infections or any other disease were also excluded.

Patient's files were examined in the hospital data system. The study population was divided into two groups: study group who was healthy and had loss of appetite (n=40) and control group (n=96). Hemoglobin, leukocyte count, C-reactive protein (CRP), ferritin, calcium, phosphorus, magnesium, alkaline phosphatase (ALP), vitamin B12, vitamin D, free T4, and thyroid-stimulating hormone (TSH) levels were obtained in the two groups. The children with deficiency and administered necessary treatment and for whom information was provided to the parents were re-assessed at three and six months for their complaints. The control group was composed of 96 healthy children who were admitted to General Outpatient clinics with non-specific complaints. Patients who were found to be healthy according to the examination and laboratory results were

included. The visits at three and six months in the poor appetite group were performed by a same pediatrician who was kept blind to the group information of the patients.

The chronological age, weight, height and percent of ideal weight for height were evaluated in all patients. All blood samples were withdrawn in the morning at the same time.

In the present study, we accepted the vitamin D levels defined by Misra et al, for healthy children and adolescents. Levels of vitamin D at or below 15 ng/mL were defined as vitamin D deficiency and a level of 15-20 ng/mL (37.5-50 nmol/L) as insufficiency, and a level of 20-100 ng/mL (50-250 nmol/L) as normal (sufficient). Vitamin D replacement therapy: Children followed by maintenance dosing of 600 to 1000 int. U/day (11).

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 20.0. (Armonk, NY: IBM Corp). During data analysis, independent groups were compared using the t test (Student's t test) or Mann-Whitney U test, two dependent groups were compared with the t test (paired sample t test) or Wilcoxon test statistics. The relationship between two continuous variables was tested with Pearson's Correlation Coefficient, and Spearman's Correlation Coefficient. The categorical variables were tested using the Fisher's exact test and chi-square test.

Results

There was no significant difference in the sex of the both groups. No statistically significant difference in age, ferritin, hemoglobin, leukocyte count, platelets, vitamin B12, fT4, and TSH levels between the children with poor appetite and healthy children. Vitamin D levels were significantly lower in the poor appetite group (Table 1).

In the poor appetite group, vitamin D levels were found to be significantly higher at three months after oral vitamin D supplementation, compared to baseline values. The difference with the

control group at three months was not statistically significant (mean vitamin D: 32.25 versus 33.001 $p > 0.05$).

Also, there was a weight gain at three- and six-month visits and the complaints decreased. There was no report of poor appetite during interview with the parents.

The history of colic, duration of breastfeeding and age at onset of supplementary food did not significantly differ.

In the present study, weight gain stopped before the study in children complaining of poor appetite who received vitamin D supplementation and these children put on weight at three- and six-month visits.

Discussion

In this-study, it was aimed to evaluate the anxiety concerns about the children of the families who applied to the outpatient clinic. While there was no statistical difference in these children in terms of sociodemographic and laboratory, there was a statistically significant difference only at vitamin D level.

The patients presented with poor appetite and eating problems represent 25 to 30% of all admissions to the pediatric outpatient clinics (3). The studies have reported that children that were reported to have eating problems by their parents were shorter and thinner and below 5 percentile until two years of age (12). Francis et al. reported that children in the 3 to 5 years age group have not yet developed sufficient autonomy to eat simultaneously while watching television, and they explained loss of eating control by environmental factors due to forcing the child to eat by the caregiver (13). Wright et al. reported that reduced appetite was a risk factor for growth and forcing the child to eat by the mother was reported as a familial risk factor negatively affecting weight gain (14). Kutluk et al. also discussed other causes of poor appetite in their manuscript and suggested that defecation problems, psychological problems, lack of family training, chronic diseases, hypothyroidism, and

anemia should be also taken into consideration (5). The present study found no statistically significant difference between the two groups in TSH, free T4, ferritin, and hemoglobin levels. These factors were discussed during interview with the parents and the families were informed in this regard. The parents in the two groups had sufficient level of knowledge. Children with chronic disease were already excluded and the effect of hypothyroidism was also evaluated; there was no significant difference in the thyroid function tests between the two groups.

Furthermore, vitamin deficiency and anemia are defined as the causes of poor appetite (5). Although the relationship between iron deficiency anemia and poor appetite has been well-established, the studies to date have not clearly described a relationship between poor appetite and vitamin deficiency (6,7). The present study evaluated children who presented to the well child outpatient clinics with a single complaint of poor appetite and who did not have chronic disease or a known vitamin deficiency or supplementation therapy in the medical history and who had normal height for weight and normal height and weight for age. There was no significant difference in the age, ferritin, hemoglobin, and serum vitamin B12 levels between the two groups. Serum vitamin D level was significantly lower in the poor appetite group ($p < 0.05$).

Vitamin D deficiency results in systemic complications such as bone deformity, osteoporosis and fractures, and it was also associated with cardiovascular diseases, diabetes mellitus, cancer, infections, autoimmune diseases, and schizophrenia (8-9,15-16). Gordon et al. reported a prevalence rate for vitamin D deficiency ranging between 12% and 24% (17). Only 39% of the subjects were found to have sufficient vitamin D levels, while the rest had poor vitamin D status in Amasya, Turkey (18). In particular, vitamin D deficiency is thought to be more frequent in breastfed infants (19). Thus, dietary vitamin D supplementation is recommended for infants. The history of colic, duration of breastfeeding and age at onset of supplementary food did not significantly differ

between the two groups in the present study. There was also no statistically significant difference in the frequency of infections sustained during the follow-up period between the two groups. Unlike to the present study, Ozdemir et al. reported a relationship between frequent infections and vitamin D deficiency (9). Yıldız et al showed a relationship between recurrent tonsillopharyngitis and vitamin D deficiency (20). In addition, there was a relationship between urticaria and vitamin D deficiency in another study by Ozdemir et al., while there was no urticaria or history of atopy in vitamin D-deficient group (8). Uysalol et al showed that children who had asthma, had hypovitaminosis D (21). Park et al. also reported a relationship between vitamin D deficiency and growing pain, although there was no growing pain in children with vitamin D deficiency in the poor appetite group (16). In addition, Moore et al. reported a relationship between increased adipose tissue and vitamin D insufficiency (22). In this study, there was no obese children, and children with poor appetite and vitamin D deficiency had normal weight gain at three- and six-month visits and their appetite improved as reported by their parents.

Moreover, the mothers perceived their child slim, although 26% of the children were at 90 to 110% evaluated according to the weight for height (23). In the study by Laraway et al., 24% of mothers of 6-27 month-old children perceived their child as low-weight, and 29% of the mothers considered 90 percentile as healthy (24). The parents perceive children with normal weight for height and normal weight and height for age as slim and having poor appetite and use inadvertent vitamin supplements and appetite enhancers, while health care professionals sometimes overlook medical problems considering these children as healthy. The parents in the present study did not have a perception of slimness for their children. Vierucci et al. showed hypovitaminosis D in healthy adolescent in Italy (25). Our study was about younger children and we didn't show Vitamin D deficiency in healthy group. Our loss of appetite group had hypovitaminosis D. Vitamin D supplement is important among childhood.

This study's limitations were number of study group. Although we corrected statistically significant between two groups, large population study may be required to show association.

Conclusion

It should be kept in mind that seemingly healthy children with family concern of poor appetite may have vitamin D deficiency. However, further large-scale studies are required to confirm these findings. Loss of appetite may be the first sign of the vitamin D deficiency. However, in children who do not have any problem in physical examination, if close monitoring can be performed, they can be monitored without any laboratory test. Families' loss of appetite concerns should be taken into consideration, but high costs can be prevented only by regular use of vitamin D prophylaxis.

Table 1: Poor Appetite and the Control group (Ankara-2016)

	<i>Poor Appetite Group</i>	<i>Control Group</i>	<i>P value</i>
<i>Age (year)</i>	3.87 n=41	3.61 n=96	p>0.05
<i>Hemoglobin g/dl</i>	12.72 n=41	12.61 n=96	p>0.05
<i>Leukocyte</i>	8582 n=41	9630 n=96	p>0.05
<i>MCV fl</i>	76.8 n=41	77.7 n=96	p>0.05
<i>Ferritin ng/ml</i>	39.41 n=41	41.77 n=96	p>0.05
<i>Vitamin B12 pg/ml</i>	596.43 n=21	584.55 n=67	p>0.05
<i>TSH µIU/ml</i>	1.82 n=11	1.65 n=68	p>0.05
<i>fT4 ng/dl</i>	1.13 n=10	1.1 n=48	p>0.05
<i>Vitamin D ng/ml</i>	17.08 n=41	33.001 n=96	p<0.05

**p<0.01

REFERENCES

- 1- Behrman RE, Kliegman RM, Jenson HB. *Nelson's Textbook of Pediatrics*, 20 th ed. Saunders, Philadelphia, 2004
- 2- Gahagan S. *J Dev Behav Pediatr* 2012; 33:261-71
- 3- Wright C, Birks E. Risk factors for failure to thrive: a population-based survey. *Child Care Health Dev* 2000;26:5-16.
- 4- Ünal F. İştahsız çocuklara klinik yaklaşım, *The Journal of Current Pediatrics* 2011; 9: 79-84
- 5- Kutluk G, Ertem D, Pehlivanoğlu E. Bebek ve cocuklarda onemli bir beslenme sorunu: İştahsızlık. *Clinic Pediatric* 2008; 4:32-6.
- 6- Briefel R, Hanson C, Fox MK, Novak T, Ziegler P. *Feeding Infants and Toddlers Study: Do vitamin and mineral supplements contribute to nutrient adequacy or excess among US infants and toddlers?* *J Am Diet Assoc* 2006; 106:52-65
- 7- Isguven P, Arslanoğlu I, Erol M, Yıldız M, Adal E, Erguven M. Serum levels of ghrelin, IGF-I, IGFBP-3, insulin thyroid hormones and cortisol in prepubertal children with iron deficiency. *Endocr J* 2007; 54:985-90.
- 8- Özdemir B, Köksal BT, Karakaş NM, Özbek OY. Serum vitamin D levels decrease in children with acute urticaria. *Allergol Immunopathol (Madr)*. 2016 Nov - Dec;44(6):512-516. doi: 10.1016/j.aller.2016.04.007. Epub 2016 Jul 28.
- 9- Özdemir B, Köksal BT, Karakaş NM, Tekindal MA, Özbek ÖY. Serum Vitamin D Levels in Children with Recurrent Respiratory Infections and Chronic Cough. *Indian J Pediatr*. 2016 Jan 29.
- 10- Bischoff-Ferrari HA, Giovannucci E, Willett WC, et al. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. *Am J Clin Nutr*. 2006;84:18–28.
- 11- Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. *Pediatrics* 2008; 122: 398
- 12- Wright CM, Parkinson KN, Shipton D, Drewett RF. How to toddler eating problems relate to their eating behavior , food preferences, and growth? *Pediatrics* 2007;120:1069-75.
- 13- Francis LA, Birch LL. Does eating during television viewing affect preschool children's intake. *J Am Diet Assoc* 2006;106:598-600.
- 14- Wright CM, Parkinson KN, Drewett RF. How does maternal and child feeding behavior relate to weight gain and failure to thrive? Data from a prospective birth cohort. *Pediatrics* 2006;117:1262-9.
- 15- Holick MF. Vitamin D deficiency. *N Engl J Med* 2007; 357:266-81.
- 16- Park MJ, Lee J, Lee JK, Joo SY. Prevalence of Vitamin D Deficiency in Korean Children Presenting with Nonspecific Lower-Extremity Pain. *Yonsei Med J* 2015 Sep;56(5):1384-1388
- 17- Gordon CM, Feldman HA, Sinclair L, et al. Prevalence of vitamin D deficiency among healthy infants and toddlers. *Arch Pediatr Adolesc Med*. 2008;162(6):505-512.
- 18- Celep G, Durmaz ZH, Çamurdan AD. Vitamin D status in a population of well children: Amasya Sample. *P R Health Sci J* 2019; 38: 255-261.
- 19- Casey FC, Slawson DC, Neal LR. Vitamin D Supplementation in Infants, Children, and Adolescents. *Am Fam Physician* 81,6, March 2010
- 20- Yıldız I, Umuvar E, Zeybek U, Topbas B, Cacina C, Toprak S, Kilic A, Aydin S. The role of vitamin D in children with recurrent tonsillopharyngitis. *Italian Journal of Pediatrics* 2012, 38:25
- 21- Uysalol M, Mutlu LC, Saraçoğlu GV, Karasu E, Güzel S, Kayaoğlu S, Uzel N. Childhood asthma and vitamin D deficiency in Turkey: is there cause and effect relationship between them? *Italian Journal of Pediatrics* 2013, 39:78
- 22- Moore CE, Liu Y. Low serum 25-hydroxyvitamin D concentrations are associated with total adiposity of children in the United States: National Health and Examination Survey 2005 to 2006. *Nutrition Research* 36 (2016) 72 – 79
- 23- Özmert E, 1997, *Epidemiyoloji Ders Uygulama Raporu*
- 24- Laraway K. *Clinical Pediatrics* 2010; 49: 343-349
- 25- Vierucci F, Del Pistoia M, Fanos M, Erba P, Saggese G. Prevalence of hypovitaminosis D and predictors of vitamin D status in Italian healthy adolescents. *Italian Journal of Pediatrics* 2014, 40:54