

Investigation of vitamin D and thyroid hormone levels in children with enuresis nocturna

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ABSTRACT

Objective: The present study aims to investigate the levels of 25 (OH)₂ D vitamins, thyroxine (T4), and thyroid-stimulating hormone (TSH) levels in children diagnosed with monosymptomatic Enuresis Nocturna (MEN), and any potential relationship between these levels and the disorder.

Material and Methods: 49 children with Primary Monosymptomatic Enuresis Nocturna (PMEN) who applied to our pediatric departments were included in the study. Patients with secondary enuresis associated with chronic diseases were excluded. The study took place between February 2012–July 2013. 99 healthy children with age and gender distribution similar to the enuresis group were included in the study as well, as the control group. Complete urine analysis and complete blood cell count were performed on all the children, and their urea, creatinine, glucose, serum electrolyte levels, 25 (OH)₂ vitamin D, and thyroid hormone levels were measured.

Results: Compared to children who don't wet themselves, children with MEN were found to have statistically higher 25 (OH)₂ Vitamin D levels ($p<0.001$), while the two groups were found to have similar glucose, urea, creatinine, sodium, potassium, hemoglobin, TSH and fT4 values.

Conclusion: In the present study where the patient count was relatively low, no relationship could be established between enuresis thyroid hormone levels. Vitamin D levels were significantly higher in Enuresis group. Yet we still humbly believe that our study will provide valuable reference data for future studies which will inspect 25 (OH) Vitamin D levels and urine calcium levels together.

Keywords: Nocturnal enuresis; vitamin D; thyroid hormones.

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Enürezis nokturnalı çocuklarda tiroid hormonları ve D vitamini düzeylerinin araştırılması

ÖZET

Amaç: Bu çalışmada monosemptomatik nokturnal enürezis tanıılı çocuklarda 25 (OH)₂ D vitamini, tiroksin (T4) ve tiroid stimulan hormon (TSH) düzeylerinin çalıřılması ve hastalıkla iliřkisinin saptanması amaçlanmıřtır.

Gereç ve Yöntemler: Çalışmamıza çocuk polikliniğimize başvuran 5–15 yaş arasındaki 49 primer monosemptomatik nokturnal enürezisli çocuk alındı. Kronik hastalıklara bağılı sekonder enürezisli hastalar çalışmadan çıkarıldı. Arařtırmamız Şubat 2012, Temmuz 2013 tarihinde bir buçuk yıl süre ile yapıldı. Çalışmaya kontrol grubu olarak, çalışma grubu ile benzer yaş ve cinsiyetteki 99 sağlıklı çocuk alındı. Laboratuvar ölçümlerinde hastaların tam kan sayımları, böbrek fonksiyon testleri, kan elektrolitleri, kan glukoz deęerleri, tam idrar tetkikleri, 25 (OH) vitamin D ve tiroid hormon düzeylerinin ölçümü yapıldı.

Bulgular: Altını ıslatmayan çocuklarla karşılařtırıldıđında MNE’li çocukların 25(OH) D vitamini düzeylerinin anlamlı düzeyde yüksek olduđu; glukoz, üre, kreatinin, sodyum, potasyum, hemoglobin, TSH ve fT4 düzeylerinin iki grupta benzer olduđu belirlendi.

Tartıřma: Göreceli olarak vaka sayısının az olduđu çalışmamızda, enürezis tiroid hormonları arasında bir iliřki saptayamadık. Çalışmamızda D vitamini düzeyleri Enürezis grubunda anlamlı olarak yüksekti. Fakat bunun hangi mekanizmayla Enürezise sebep olduđu belirlenemedi. Çalışmamızın D vitamini ve hiperkalsiüri düzeylerinin birlikte deęerlendirileceđi çalışmalara dayanak sađlayacađını düşünüyüz.

Anahtar Kelimeler: Nokturnal enürezis; D vitamini; tiroid hormonları.

INTRODUCTION

Primary monosymptomatic enuresis nocturna (PMEN) is defined as frequent urination into clothes or bed at least two times per week for three successive months in children ≥ 5 years old who have not acquired urinary continence (1).

The physiology of enuresis nocturna has not been fully revealed. Low bladder capacity, sleep disorders, deficiencies in anti-diuretic hormone secretion during the night, and consequently increased urinary production have been suggested as primary mechanisms. Such incontinence has been associated with genetic disposition, male gender, low socioeconomic status, crowded families, and difficulty in waking up (2–5).

Thyroid hormones are known to influence numerous mechanisms of the body. It is possible to surmise that changes in thyroid hormone levels might have a connection with enuresis, considering their influence on the sleep cycle (2).

Meanwhile, changes in vitamin D levels can influence calcium levels in urine besides the well-established neuromuscular effects. As such, this study aimed to investigate the levels of 25 (OH)₂ vitamin D, thyroxine (T4), and thyroid-stimulating hormone (TSH) levels in children diagnosed with monosymptomatic enuresis nocturna (MEN) and any potential relationship between these levels and the disorder.

MATERIAL AND METHODS

Forty-nine children with PMEN who applied to our pediatric departments were included in the study. Patients with secondary enuresis associated with chronic diseases were excluded. The study took place between February 2012 and July 2013. Ninety-nine healthy children with age and gender distribution similar to the enuresis group were included in the study as well,

as the control group. Complete urine analysis and complete blood cell count were performed on all the children, and their urea, creatinine, glucose, serum electrolyte levels, 25 (OH)₂ vitamin D, and thyroid hormone levels were measured.

Vitamin D level measurements were seasonally similar in the enuresis and control groups. It is worth mentioning here that none of the patients in any of the groups were medicated with vitamin D or any form of multivitamin supplements. Similarly, patients in the enuresis group were under no medication that would affect levels of thyroid hormones and electrolytes.

Biochemical analyses were performed using an Abbott C-16000 chemical analyzer. Glucose levels were measured using the photometric hexokinase method, urea levels were determined using the photometry method, and creatinine level was determined using a photometrical modified Jaffe method. Sodium and potassium levels were determined using the ion-selective electrode method. The high-pressure liquid chromatography method was used to determine 25 (OH)₂ vitamin D levels, while free T3, free T4, and TSH levels were determined using the chemiluminescent microparticle immunological assay (CMIA, Architect system, Abbot Diagnostics) method. The hemograms were obtained using a Bayer diagnostic ADVIA 120 device.

Statistical analyses were performed using the SPSS (Statistical Package for Social Sciences, Inc., Chicago, IL, USA) for Windows version 16.0 package software. Frequency analysis was performed for all the data obtained as part of the study, and median and standard deviation values were calculated. To determine the presence of any significance between the groups, the Mann–Whitney U test was used when the data did not show a homogenous distribution, and Student’s t-test when they did. Our study was conducted in accordance with the Declaration of Helsinki. The ethics committee approval was obtained from the local hospital.

RESULTS

Of the 148 children included in the study, 76 were males and 72 were female. The demographic properties of the enuresis and control groups are provided in Table 1.

In children with enuresis nocturna, the parameters of being male and history of enuresis in the family were found to be higher compared with the children of the control group, and the difference was statistically significant ($p < 0.05$ and $p < 0.001$, respectively, Table 1).

Biochemical survey and full blood cell count results for enuresis and control group children are provided in Table 2.

Compared with children who do not wet themselves, children with MEN were found to have statistically higher 25 (OH)₂ vitamin D levels ($p < 0.001$, Fig. 1), while the two groups were found to have similar glucose, urea, creatinine, sodium, potassium, hemoglobin, TSH, and fT4 values.

DISCUSSION

Numerous studies were performed on enuresis nocturna. In the present study, the aim was to compare the serum TSH, free T4, and 25 (OH)₂ vitamin D levels of children with enuresis with that of healthy children and to determine if there were any meaningful differences between the values.

Thyroid hormones cause an increase in the efficiency and concentration of enzymes, structural/transporter proteins, and other similar agents within almost every type of cell, and increase the number and activity of the mitochondria. They also stimulate Na⁺-K⁺-ATPase enzyme activity and increase the pace at which ions are transported through the cell wall. Thyroids further increase most endocrine gland secretion and net basal metabolism rates. These hormones have general and specific influences on the growth and development of the organism. In fetal life and the first years after birth, they play a significant role in the growth and development of the nervous system. They are also required for optimal growth and development during puberty (to ensure normal sexual development and fertility). Our study was based on the idea that hormones with such effects could have a potential influence over urinary system development, which in turn might affect whether a child wets him/herself during the night or not.

In addition to urinary system development, thyroid hormones can also have effects on the central nervous system and sleep physiology especially when bedwetting is a problem during sleep (2). This fact formed an additional basis for our study.

In this study, no meaningful difference was determined between the TSH and free T4 levels of the patient and control groups. No study was encountered in the literature that surveyed TSH and/or thyroid hormones in children with enuresis nocturna. One study stands apart regarding the subject, which belongs to Meir et al. (6) presenting a case of a 9-year-old enuresis nocturna patient with hyperthyroidism. The study claimed for this case was that the central control mechanisms of enuresis were temporarily disabled, leading to incontinency during sleep. This situation requires more inquiry through wide-scope studies.

Table 1. Comparison of the demographic properties of the children with primary monosymptomatic enuresis nocturna and the control group

	Enuresis group (n=49)	Control group (n=99)	p
Gender (M/F)	33/16	43/56	0.006
Age (years)	9.3±2.4	9.7±3.4	0.393
Height (cm)	140.2±12.7	135.8±13.0	0.165
Weight (kg)	37.6±10.8	36.6±10.9	0.703
Parental consanguinity (yes/no)	13/27	11/18	0.728
History of enuresis in family (yes/no)	35/5	16/13	<0.001

Table 2. Comparison of blood parameters between groups

	Enuresis group (n=49)	Control group (n=99)	p
Glucose (mg/dL)	89.4±9.7	86.0±8.3	0.324
Urea (mg/dL)	24.1±5.3	22.2±5.4	0.065
Creatinine (mg/dL)	0.4±0.1	0.5±0.5	0.078
Sodium (mEq/L)	139.0±3.0	139.5±2.5	0.293
Potassium (mEq/L)	4.4±0.4	4.4±0.5	0.622
Hemoglobin (g/dL)	12.3±1.1	12.6±1.1	0.122
25 (OH) ₂ vitamin D	41.8±20.0	28.7±13.6	<0.001
TSH	2.8±2.2	2.4±1.6	0.265
Free T4	0.9±0.1	0.9±0.8	0.373

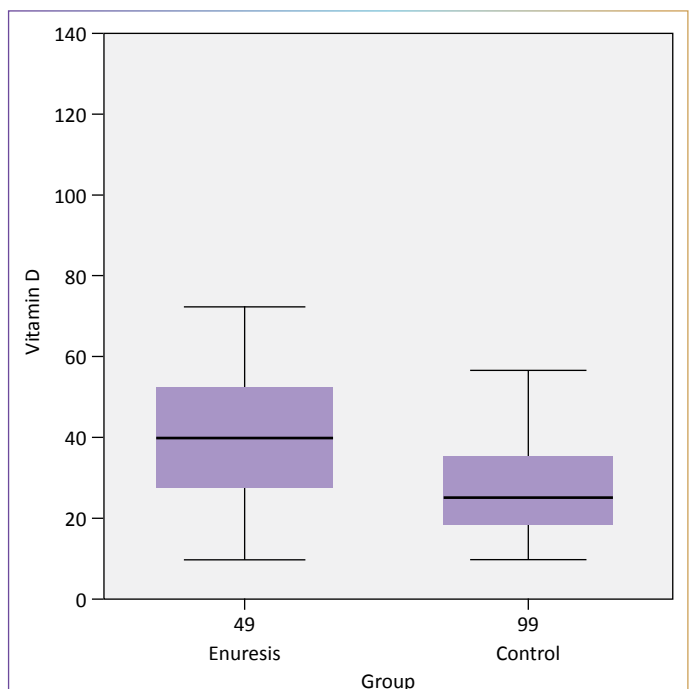


Figure 1. Comparison of serum 25(OH) vitamin D levels.

The effects of vitamin D are reported not only for regulating calcium homeostasis to maintain bone health but also for pro-apoptotic, anti-inflammatory, and immune-modulating properties. Epidemiological studies performed in recent years have shown that low vitamin D levels increase cancer incidences and cardiovascular mortality and accompanied autoimmune diseases such as diabetes and multiple sclerosis. Furthermore, the fact that vitamin D has significant effects on encephalic functions and the muscular system has led to the idea might also be influential over enuresis.

The only study that investigated a potential relationship between enuresis and vitamin D was performed by Li et al. (7) in China. The study included a total of 240 enuretic children (ages varying between 5 and 7 years) and, contrary to our study, determined that 25 (OH)₂ vitamin D levels were significantly lower in enuretic children compared with the control group. Our study was performed in children with ages varying between 5 and 14 years, and the 25 (OH)₂ vitamin D levels of enuretic children were higher compared with their healthy counterparts. We believe that the difference between the two studies can be attributed to the differences in age, race, and geographical conditions of the children involved.

Many studies showed that hypercalcinuria can cause enuresis. In their study, Vachvanichsanong et al. (8) determined that 23% of children with hypercalcinuria had incontinence. The reason for this is described as the irritation of the bladder with calcium crystals, and the bladder contractions and relaxation of the bladder outlet are associated with such irritations. The study also reports that treatment of hypercalcinuria significantly reduces urinary incontinence.

In another study by Civilibal et al., (9) the calcium excretion through the urine of 120 children (between 7 and 14 years of age) with MPEN was measured. The aim of this study was to determine if any connection existed between hypercalcinuria and enuresis. The study revealed that a significant portion of the children had hypercalcinuria, and the researchers suggested that such children should be monitored in terms of urine calcium levels.

Despite numerous studies focusing on the relationship between hypercalcinuria and enuresis, no study regarding the potential correlation between high 25 (OH)₂ vitamin D levels and enuresis. It is unfortunate that our previous study did not inspect the vitamin D levels, while the present study did not measure urine calcium levels. Yet we still humbly believe that the results obtained in our study will provide valuable reference data for future studies which will inspect 25 (OH)₂ vitamin D levels and urine calcium levels together.

Ethics Committee Approval: The Haseki Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 16.01.2012, number: 33).

Informed Consent: Written informed consent was obtained from the families of the patients who participated in this study.

Conflict of Interest: No conflict of interest was declared by the authors.

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Authorship Contributions: Concept – MÇ, MHHT; Design – GT, MHHT; Supervision – MÇ, ME; Fundings – GT, ME; Materials – MHHT, GT; Data collection and/or processing – MHHT, GT; Analysis and/or interpretation – MHHT, GT, MÇ, ME; Literature review – MHHT, GT, MÇ, ME; Writing – MHHT, MÇ; Critical review – MHHT, GT, MÇ, ME.

Etik Kurul Onayı: Haseki Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu'ndan bu çalışma için onay alınmıştır (tarih: 16.01.2012, sayı: 33).

Hasta Onamı: Yazılı hasta onamı bu çalışmaya katılan hastaların ailelerinden alınmıştır.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

Yazarlık Katkıları: Fikir – MÇ, MHHT; Tasarım – GT, MHHT; Denetleme – MÇ, ME; Kaynaklar – GT, ME; Malzemeler – MHHT, GT; Veri Toplanması ve/veya İşlenmesi – MHHT, GT; Analiz ve/veya Yorum – MHHT, GT, MÇ, ME; Literatür Taraması – MHHT, GT, MÇ, ME; Yazıyı Yazan – MHHT, MÇ; Eleştirel İnceleme – MHHT, GT, MÇ, ME.

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