Evaluation of Etiological Risk Factors of Primary Monosymptomatic Enuresis

Primer Monosemptomatik Enürezisin Etiyolojik Risk Faktörlerinin Değerlendirilmesi

Fatih Yanaral[1], Ali Eroğlu[2], Nusret Can Çilesiz[2], Cem Tuğrul Gezmiş[2], Zafer Tandoğdu[3], Mustafa Bahadır Can Balcı[2], Barış Nuhoğlu[4]

[1]Department of Urology, Haseki Training and Research Hospital, İstanbul, Turkey
[2]Department of Urology, University of Health Sciences Gaziosmanpaşa Taksim Training and Research Hospital, İstanbul, Turkey
[3]Northern Institute for Cancer Research, Newcastle University, Newcastle Upon Tyne, UK
[4]Department of Urology, Yeni Yüzyıl University School of Medicine, Istanbul, Turkey

Cite this article as: Yanaral F, Eroğlu A, Çilesiz NC, Gezmiş CT, Tandoğdu Z, Balcı MBC, et al. Evaluation of Etiological Risk Factors of Primary Monosymptomatic Enuresis. JAREM 2019; 9(3): 102-6.

ABSTRACT

Objective: A child who has not been dry previously, i.e., wets the bed, for more than 6 months without any lower urinary tract symptoms is considered to have primary monosymptomatic nocturnal enuresis (MNE). The aim of this study was to investigate the etiological risk factors in primary MNE.

Methods: We retrospectively evaluated the medical records of children with enuresis. Children with known anatomic malformations, non-monosymptomatic enuresis, and secondary enuresis were excluded. Only children with primary MNE were included in the study. The control group included healthy children with no history of bedwetting. The etiological risk factors were compared between the groups.

Results: Eighty-nine children with primary MNE (mean age: 9.7 years) and 70 healthy children (mean age: 9 years) were included in the study. Both groups were similar for age, gender, birth type, birth weight, gestational duration, and sleep duration. The mean body mass index (BMI), mean duration of only breastfeeding, and mean duration of breastfeeding with infant formula were 19.1 and 16.8 kg/m2, 5.4 and 7.3 months, and 13.2 and 17.9 months in the enuresis group and control group, respectively, (p=0.012, p=0.005, p=0.034). The family history for enuresis was positive in 58 (65.2%) and 12 (17.1%) patients in the enuresis group and control group, respectively, (p=0.001). The multivariate regression analysis identified family history and breastfeeding as independent risk factors for enuresis (p=0.001, p=0.012).

Conclusion: We have documented that high BMI, positive family history, and low duration of breastfeeding are risk factors for enuresis. The present study has shown that longer breastfeeding is protective for bedwetting.

Keywords: Breast feeding, enuresis, etiology, risk factors, urinary incontinence

ÖZ

Amaç: Primer monosemptomatik enurezis nokturna (PMEN) gündüz alt üriner sistem semptomları olmayan ve 6 aydan daha uzun süre kuru kalmamış enürezisi olan hastaları tanımlamaktadır. Bu çalışmada PMEN tanılı hastalarda etiyolojik risk faktörlerini araştırmayı amaçladık.

Yöntemler: Enürezisi olan hastaların dosyaları geriye dönük incelendi. Anatomik malformasyonu, nonmonosemptomatik ve sekonder enürezisi olanlar çalışma dışı bırakıldı, sadece PMEN tanılı çocuklar çalışmaya dahil edildi. Kontrol grubu olarak yatak ıslatma öyküsü olmayan sağlıklı çocuklar belirlendi. Her iki grup etiyolojik risk faktörleri açısından karşılaştırıldı.

Bulgular: Ortalama yaşları sırasıyla 9,7 ve 9 olan, PMEN tanılı 89 çocuk ve kontrol grubunda 70 sağlıklı çocuk çalışmaya dahil edildi. Her iki grup yaş, cinsiyet, doğum tipi, doğum kilosu, gebelik süresi ve uyku süresi açısından benzerdi. Ortalama vücut kitle indeksi (VKİ), ortalama sadece anne sütü süresi, ortalama anne sütü ve ek gıda süreleri enürezis ve kontrol grupları için sırasıyla 19,1 ve 16,8 kg/m2, 5,4 ve 7,3 ay, 13,2 ve 17,9 aydı (p=0,012, p=0,005, p=0,034). Ailede enürezis öyküsü, enuresis ve kontrol gruplarında sırasıyla, 58 (%65,2) ve 12 (%17,1) çocukta pozitifti (p=0,001). Multivariate regresyon analizinde aile öyküsü ve anne sütü süresi enurezis için bağımsız risk faktörleridir (p=0,001, p=0,012).

Sonuç: VKİ, pozitif aile öyküsü ve kısa anne sütü alım süresi enürezis için risk faktörleridir. Bu çalışma, bebekken uzun süre anne sütü ile beslenmenin çocukluk çağında enürezis gelişimine karşı koruyucu olduğunu göstermiştir.

Anahtar kelimeler: Emzirme, etiyoloji, gece idrar kaçırma, risk faktörleri, üriner inkontinan

ORCID IDs of the authors: F.Y. 0000-0002-7395-541X; A.E. 0000-0002-5545-5892; N.C.Ç. 0000-0003-2115-698X; C.T.G. 0000-0002-1634-4516; Z.T. 0000-0002-5309-3656; M.B.C.B. 0000-0003-0395-1154; B.N. 0000-0002-8737-4050.

"This study was presented as an oral presentation at the 23rd National Urology Congress and published in the abstract book, 16 October 2014, Antalya, Turkey.
Bu çalışma 23. Ulusal Üroloji Kongresi'nde sözlü bildiri olarak sunulmuş ve özet kitabında yayınlanmıştır, 16 Ekim 2014, Antalya Türkiye."

Corresponding Author / Sorumlu Yazar: Fatih Yanaral,
E-mail / E-posta: fatihyanaral@gmail.com

Received Date / Geliş Tarihi: 23.02.2018 **Accepted Date / Kabul Tarihi:** 13.06.2018

DOI: 10.5152/jarem.2019.1997

INTRODUCTION

The International Children's Continence Society defines enuresis as incontinence of urine in discrete episodes while sleeping in a child aged ≥5 years (1). Enuresis is the term used irrespective of whether other lower urinary tract symptoms exist. When only enuresis exists in children in the absence of a history of lower urinary tract dysfunction, the disorder is termed monosymptomatic enuresis. Enuresis in a child with bladder dysfunctions is termed as non-monosymptomatic enuresis (2).

Monosymptomatic enuresis can also be classified as primary and secondary. A child who has never achieved at least 6 months of nighttime dryness is known to have primary enuresis, whereas secondary enuresis is defined as enuresis that starts after a dry period of more than 6 months (3). Thus, a child who has not been dry for more than 6 months previously without any bladder dysfunction is considered to have primary monosymptomatic nocturnal enuresis (MNE).

Enuresis is an important psychosocial problem for both parents and children. Although it is one of the most prevalent conditions in childhood, there is still debate regarding the etiology. It is generally accepted that multiple pathologic factors are probably involved. The aim of the present study was to investigate the etiological risk factors in primary MNE.

METHODS

We retrospectively evaluated the medical records of children with enuresis. Data were recorded prospectively by direct interview with the families and the children through history, physical examination, urinalysis, and a voiding diary by a single observer. Verbal informed consent was obtained from the parents of the children participating in this study. The research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects". Only children (older than 5 years of age) with primary MNE (at least 2 times per week) were included in the study. Controls were selected from a general pediatric practice during well-child visits. Healthy children who had normal developmental history and those who did not have enuresis after 4 years of age were included in the control group.

A history of the frequency of bedwetting, primary or secondary enuresis, associated daytime symptoms, any period of dryness, constipation, and encopresis were noted. Additionally, birth type, birth weight, gestational week, duration of breastfeeding, duration of infant formula, number of siblings, body mass index (BMI), family history, and duration of sleep were recorded. The external genitalia and lumbosacral spine were examined. A voiding diary in the form of a frequency volume chart was recorded including voided volume along with the time of each micturition for at least 24 hours for identifying any underlying bladder dysfunction. Urinalysis was performed to exclude urinary tract infections. Children with known anatomic malformations, non-monosymptomatic enuresis, secondary enuresis, and recurrent urinary tract infection were excluded.

Statistical Analysis

The Statistical Package of the Social Sciences version 20 (IBM Corp; Armonk, NY, USA) was used for statistical analysis. For the analysis of quantitative data, the normal distribution suitability was examined using the Kolmogorov–Smirnov test; parametric methods were used for the analysis of normal distribution variables, and nonparametric methods were used for the analysis of variables that did not show normal distribution. An independent t test was used to compare independent groups; the Pearson correlation test was used to examine the relationship between variables, and the Pearson Chi-square, Chi-square, and Fisher Exact tests were used to compare categorical data. Multivariate analysis was performed using logistic regression analysis from the parameters that were significant in the univariate analysis. Quantitative data were expressed as mean±standard deviation values on tables. Categorical data were expressed as n (frequency) and percentages (%). Data were analyzed at 95% confidence level, and statistical significance was considered when the $p<0.05$.

RESULTS

Eighty-nine children with primary MNE aged 5–16 years (mean: 9.7 years) and 70 healthy children aged 6-15 years (mean: 9 years) were included in the study. The enuresis group and control group were similar for age, gender, birth type, and birth weight, gestational duration, and duration of sleep. However, there were significant differences between the groups for BMI, family history, duration of only breastfeeding, and duration of breastfeeding with infant formula (Table 1).

The mean BMI, mean duration of only breastfeeding, and mean duration of breastfeeding with infant formula were 19.1 kg/m2 and 16.8 kg/m2, 5.4 and 7.3 months, and 13.2 and 17.9 months in the enuresis group and control group, respectively, ($p=0.012$, $p=0.005$, $p=0.034$). The family history for enuresis was positive in 58 (65.2%) and 12 (17.1%) patients in the enuresis group and control group, respectively, ($p=0.001$; Table 1).

Sixty-five (73%) children wet every night and 72 (80%) children had severe enuresis. In the enuresis group, 56 (63%) children exclusively breastfed for the first 6 months as a World health Organization (WHO) suggestion. In control group, this rate was 91% (64/70). Multivariate regression analysis identified family history and breastfeeding as independent risk factors for enuresis ($p=0.001$ and $p=0.012$, respectively; Table 2).

DISCUSSION

The overall prevalence of MNE was found to be 3.8%–18.9% in different countries (4, 5). In Turkey, Gumus et al. (6) reported the prevalence of enuresis as 15% and Serel et al. (7) reported as 11%. The prevalence decreases with age; about 10% of 7-year-old children, 5% of all 10-year-old children, and 0.5%–1% of adults are effected. The spontaneous cure rate is around 15% annually, and 1% of cases are resistant to all treatment methods (1, 8). In the present study, the groups were similar for age and sex ($p=0.265$ and $p=0.138$, respectively). This equivalence is very important because bedwetting is more common in younger children and boys. Similar to literature, enuresis was more common in boys (68%) in our study (9).

This is a common health problem; however, the causes of this problem have not yet been fully defined. Enuresis pathophysiology is complicated and involves the central nervous system (CNS), circadian rhythm, and bladder function disorders (10).

Table 1. Demographic data

	Groups		
	Enuresis (n=89)	Control (n=70)	p
Gender (Girls/Boys)	28/61	32/38	0.138
Age (year)*	9.69±2.91	9.06±2.53	0.265
Body Mass Index (kg/m^2)*	19.15±4.89	16.86±3.18	0.012
Family History	58 (65.2%)	12 (17.1%)	0.001
Gestational Duration (Weeks)*	38.91±2.00	39.54±0.92	0.078
Gestational Duration (Preterm/Term/Postterm)	7/82/0	2/66/2	0.836
Birth Weight (Grams)*	3247.67±534.54	3270.14±643.83	0.849
Birth Weight (Low/Normal/Large for Gestational Age)	5/79/5	10/52/8	0.079
Birth Type (Vaginal delivery/Cesarean Delivery)	66/23	44/26	0.212
Duration of Only Breastfeeding (Months)*	5.42±2.85	7.31±4.29	0.005
Duration of Breastfeeding with Infant Formula (Months)*	13.24±10.84	17.97±11.34	0.034
Duration of Sleep (Hours)*	9.20±1.52	9.53±1.34	0.265

*: Mean±standard deviation

Table 2. Multivariate analyses

	Odds ratio*	p
Gender	0.42 (0.13-1.35)	0.144
Family History	12.29 (3.65-41.35)	0.001
Birth Weight	0.22 (0.03-1.61)	0.070
Body Mass Index	0.85 (0.14-5.33)	0.759
Breastfeeding	8.87 (1.63-48.34)	0.012
Birth Type	1.33 (0.47-3.79)	0.588

Logistic regression analysis, 95% confidence interval

Enuresis is most likely a disorder caused by the combination of these etiologies in a multi-factor manner. In general, enuresis occurs when nighttime urine volume surpasses functional bladder capacity, and the child cannot inhibit bladder emptying due to lack of awakening. These etiologies are associated with delayed maturation of a normal developmental process as they are seen as normal in younger age (10).

Enuresis is known to be strongly associated with family history. Bakwin showed that the incidence of enuresis was 15% in children from non-enuretic parents, while 44% and 77% of children were enuretic when enuresis was present in one and both parents, respectively (11). In the present study, a family history of enuresis was more likely among the enuretic children (65.2%) compared with controls (17.1%; p=0.001). Moreover, we found family history as an independent risk factor for enuresis in the multivariate analysis (p=0.001). Several candidate enuresis genes have been found, but it also became clear that there was no one gene to explain all cases of enuresis and that genotype and phenotype showed a poor correlation (12, 13).

Children with nocturnal enuresis are reported to have lower bladder capacity (functional), even though they have no daytime complaints (11). Whether sleep disorders are a consequence of enuresis or they conduce to the pathophysiology of enuresis remains controversial. A study has shown that children with enuresis were slightly sleeping in reality, but they did not wake before voiding. Authors have suggested that the arousal center might be suppressed by signals from the bladder (14). It is unclear whether enuresis is caused by sleep disturbances or problems with the bladder-brain communication. Yeung et al. (15) have demonstrated that children with enuresis have detrusor instability while asleep but not while awake. Although the relationship between sleep parameters and MNE is interesting; we did not find a relationship between sleep duration and MNE (p=0.265).

The extended family structure, low socioeconomic status, low birth weight, prematurity vote, neuromotor retardation, male gender, and low school achievement have been reported as risk factors for MNE (16). In our study, there was no significant difference in the mean of birth type, gestational duration, and birth weight between the groups (p=0.212, p=0.836 and p=0.849, respectively). We found that the mean BMI was significantly high in the enuresis group than the controls (p=0.012).

This result was similar to the study reported by Weintraub et al. (17) in 2013. They showed that enuresis is more common in obese children than in normal weight control subjects. The probable explanations for this are common comorbidities in these patients, such as obstructive sleep apnea and type 2 diabetes mellitus (18). Obese children may have a slightly underestimated enuresis, and it warrants close attention to prevent unnecessary psychological distress in these children.

In enuretic children, psychiatric disorders are higher compared to healthy children. This relationship may be due to the etiological association, enuresis symptoms, or may be coincidental (19).

It has been suggested that both enuresis and attention deficit hyperactivity disorder may be due to delays in CNS maturation. The hypothesis that there is a difference in the CNS maturation in children with primary enuresis compared with controls is supported by neurophysiological data (20, 21). Progressive maturation of bladder stability occurs in conjunction with electroencephalogram findings. It suggests that the CNS may suppress the onset of detrusor contraction. In some studies, among children with enuresis, it was found that the incidence of delayed language and slowed motor performances were increased (22). Most of the MNE cases resolve spontaneously, which is considered the result of delayed maturation of the normal developmental period (10).

Over time, bladder stability and striated urinary sphincter control are achieved through neurological development and neurological maturation. Breastfeeding may provide visual, cognitive, and neurologic developmental advantages to children compared with infant formula (23). In addition, studies have shown that preterm infants fed with formula have lower scores in visual and developmental tests than breastfed preterm infants (24, 25). Gumus et al. (6) analyzed clinical factors related with enuresis and showed no difference between enuretics and non-enuretics by breastfeeding. However, Barone et al. (26) evaluated the relationship between breastfeeding and enuresis in 55 children and they showed a significant difference in the incidence of enuresis when breastfed for longer than 3 months. Singh et al. (27) examined the relationship between enuresis and several clinical factors in 100 children. The authors concluded that the rate of enuresis was higher in babies fed with infant formula compared to babies fed with mother's milk (27). Similar to the previous studies, we found the duration of only breastfeeding and breastfeeding with infant formula were statistically low in the enuresis group (p=0.005 and p=0.034, respectively). Based on multivariate analysis, breastfeeding was an independent risk factor for enuresis (p=0.012). This finding showed the importance of breastfeeding in the prevention of the enuresis in children probably by providing neurodevelopment advantages. This may be due to the fact that high n-3 and n-6 long chain polyunsaturated fatty acids in the breast milk have a significant effect on neural development (23). It is also known that breastfeeding establishes a link between the mother and baby and has a positive psychological effect.

Sancak et al. (28) investigated the effect of breastfeeding on spontaneous resolution of monosymptomatic enuresis on 181 children. The authors found that at least 5 months of breastfeeding may contribute to the age of spontaneous recovery of enuresis in children (28). WHO recommends mothers to exclusively breastfeed infants for the child's first 6 months to achieve optimal growth, development, and health. Thereafter, they should be given nutritious complementary foods and continue breastfeeding up to the age of 2 years or beyond (29). In our study, the mean duration of only breastfeeding was 5.4 and 7.3 months in the enuresis and control groups, respectively, (p=0.005). The duration of breastfeeding in the enuresis group was below the WHO recommendation. However, it was appropriate in the control group. The mean duration of breastfeeding with infant formula was significantly lower in the enuresis group. Yet, this period was below the WHO recommendation in both groups.

The study has some limitations including its retrospective nature and absence of population-based data. However, the single-observer nature of the procedure and the prospective collection of data were the strengths of the study.

CONCLUSION

Enuresis is a self-healing disorder in most of the cases, which support the delayed maturation in children with enuresis. We have documented that high BMI, positive family history, and low duration of breastfeeding are risk factors for enuresis. The present study has shown that longer breastfeeding is protective for bedwetting. This effect is both in exclusively breastfeeding and breast milk supplemented with formula, and it may be another good reason to encourage breastfeeding. Prospective, population-based trials should be performed to support this finding.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013).

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - F.Y.; Design - Z.T.; Supervision - B.N., M.B.C.B.; Resources - A.E., C.T.G.; Materials - N.C.Ç.; Data Collection and/or Processing - A.E.; Analysis and/or Interpretation - N.C.Ç., Z.T.; Literature Search - C.T.G.; Writing Manuscript - F.Y.; Critical Review - B.N., M.B.C.B.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Etik Komite Onayı: Yazarlar çalışmanın World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013) prensiplerine uygun olarak yapıldığını beyan etmişlerdir.

Hasta Onamı: Bu çalışmaya katılan hastaların ailelerinden sözlü onam alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - F.Y.; Tasarım - Z.T.; Denetleme - B.N., M.B.C.B.; Kaynaklar - A.E., C.T.G.; Malzemeler - N.C.Ç.; Veri Toplanması ve/veya İşlemesi - A.E.; Analiz ve/veya Yorum - N.C.Ç., Z.T.; Literatür Taraması - C.T.G.; Yazıyı Yazan - F.Y.; Eleştirel İnceleme - B.N., M.B.C.B.

Çıkar Çatışması: Yazarların beyan edecek çıkar çatışması yoktur.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

REFERENCES

1. Franco I, von Gontard A, De Gennaro M. International Children's Continence Society. Evaluation and treatment of nonmonosymptomatic nocturnal enuresis: a standardization document from the international children's continence society. J Pediatr Urol 2013; 9: 234-43. [CrossRef]
2. Austin PF, Bauer SB, Bower W, Chase J, Franco I, Hoebeke P, et al. The standardization of terminology of lower urinary tract function in children and adolescents: Update report from the standardization committee of the International Children's Continence Society. J Urol 2014; 191: 1863-5. [CrossRef]

3. Nevéus T, von Gontard A, Hoebeke P, Hjälmås K, Bauer S, Bower W, et al. The standardization of terminology of lower urinary tract function in children and adoles-cents: report from the Standardisation Committee of the International Children's Continence Society. J Urol 2006; 176: 314-24. [CrossRef]
4. Ouedraogo A, Kere M, Ouedraogo TL, Jesu F. Epidemiology of enuresis in children and adolescents aged 5–16 years in Ouagadougou (Burkina Faso). Arch Pediatr 1997; 4: 947-51. [CrossRef]
5. Kalo BB, Bella H. Enuresis: Prevalence and associated factors among primary school children in Saudi Arabia. Acta Paediatr 1996; 85: 1217-22. [CrossRef]
6. Gumus B, Vurgun N, Lekili M, Iscan A, Muezzinoglu T, Buyuksu C. Prevalence of nocturnal enuresis and accompanying factors in children aged 7-11 years in Turkey. Acta Paediatr 1999; 88: 1369-72. [CrossRef]
7. Serel TA, Akhan G, Koyuncuoğlu HR, Oztürk A, Doğruer K, Unal S, et al. Epidomiology of enuresis in Turkish children. Scand J Urol Nephrol 1997; 31: 537-9. [CrossRef]
8. Kajiwara M, Inoue K, Usui A, Kurihara M, Usui T. The micturition habits and prevalence of daytime urinary incontinence in Japanese primary school children. J Urol 2004; 171: 403-7. [CrossRef]
9. Wen JG, Wang QW, Chen Y, Wen JJ, Liu K. An epidemiological study of primary nocturnal enuresis in Chinese children and adolescents. Eur Urol 2006; 49: 1107-13. [CrossRef]
10. Von Gontard A, Schmelzer D, Seifen S, Pukrop R. Central nervous system involve-ment in nocturnal enuresis: evidence of general neuromotor delay and specific brain-stem dysfunction. J Urol 2001; 166: 2448-51. [CrossRef]
11. Haid B, Tekgül S. Primary and secondary enuresis: pathophysiology, diagnosis, and treatment. Eur Urol Focus 2017; 3: 198-206. [CrossRef]
12. Eiberg H. Total genome scan analysis in a single extended family for primary nocturnal enuresis: evidence for a new locus (ENUR3) for primary nocturnal enuresis on chro-mosome 22q11. Eur Urol 1998; 33: 34-6. [CrossRef]
13. Von Gontard A, Eiberg H, Hollmann E, Rittig S, Lehmkuhl G. Molecular genetics of nocturnal enuresis: clinical and genetic heterogeneity. Acta Paediatr 1998; 87: 571-8. [CrossRef]
14. Yeung CK, Diao M, Sreedhar B. Cortical arousal in children with severe enuresis. N Engl J Med 2008; 358: 2414-5. [CrossRef]
15. Yeung CK, Chiu HN, Sit FK. Bladder dysfunction in children with refractory mono-symptomatic primary nocturnal enuresis. J Urol 1999; 162: 1049-55. [CrossRef]
16. Norgaard JP, Djurhuus JC, Watanabe H, Stenberg A, Lettgen B. Experience and cur-rent status of research into the pathophysiology of nocturnal enuresis. Br J Urol 1997; 79: 825-35. [CrossRef]
17. Weintraub Y, Singer S, Alexander D, Hacham S, Menuchin G, Lubetzky R, et al. Enuresis--an unattended comorbidity of childhood obesity. Int J Obes (Lond) 2013; 37: 75-8. [CrossRef]
18. Erol M, Yiğit Ö, Zengi O, Çömçe M, Bostan Gayret Ö, Fuçucuoğlu D, et al. Factors affecting the risk of childhood obesity in the bağcılar region of istanbul. JAREM 2017; 7: 45-50. [CrossRef]
19. Sureshkumar P, Jones M, Caldwell PH, Craig JC. Risk factors for nocturnal enuresis in school-age children. J Urol 2009; 182: 2893-9. [CrossRef]
20. Iscan A, Ozkul Y, Unal D, Soran M, Kati M, Bozlar S, et al. Abnormalities in event-related potential and brainstem auditory evoked response in children with nocturnal enuresis. Brain Dev 2002; 24: 681-7. [CrossRef]
21. Freitag CM, Röhling D, Seifen S, Pukrop R, von Gontard A. Neurophysiology of noc-turnal enure-sis: evoked potentials and prepulse inhibition of the startle reflex. Dev Med Child Neurol 2006; 48: 278-84. [CrossRef]
22. Von Gontard A, Freitag CM, Seifen S, Pukrop R, Röhling D. Neuromotor development in nocturnal enuresis. Dev Med Child Neurol 2006; 48: 744-50. [CrossRef]
23. Vestergaard M, Obel C, Henriksen TB, Sorensen HT, Skajaa E, Ostergaard J. Duration of breast-feeding and developmental milestones during the latter half of infancy. Acta Paediatr 1999; 88: 1327-32. [CrossRef]
24. Fleith M, Clandinin MT. Dietary PUFA for preterm and term infants: review of clinical studies. Crit Rev Food Sci Nutr 2005; 45: 205-29. [CrossRef]
25. Gibson RA, Makrides M. Long-chain polyunsaturated fatty acids in breast milk: are they essential? Adv Exp Med Biol 2001; 501: 375-83. [CrossRef]
26. Barone JG, Ramasamy R, Farkas A, Lerner E, Creenan E, Salmon D, et al. Breastfeeding during infancy may protect against bed-wetting during childhood. Pediatrics 2006; 118: 254-9. [CrossRef]
27. Singh H, Kaur L, Kataria SP. Enuresis: analysis of 100 cases. Indian Pediatr 1991; 28: 375-80.
28. Sancak EB, Oguz U, Aykac A, Demirelli E, Bozkurt OF, Cimen S. The effect of breastfeeding on spontan resolution of monosymptomatic enuresis. Int Braz J Urol 2016; 42: 550-7. [CrossRef]
29. Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding. Cochrane Data-base Syst Rev 2012; 8: CD00351. [CrossRef]