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The Relation between Dietary Components and Body Mass Index with Urinary Prostaglandin E2 Level in 5-15 Years Children with Nocturnal Enuresis

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ABSTRACT

Background: Nocturnal enuresis is known as a common urinary bladder complication in children. Recent studies associated some dietary components with nocturnal enuresis. To our knowledge, no study has designed to evaluate the relation between dietary components with urinary prostaglandin E2 in enuretic children.

Methods: In this cross-sectional study, we enrolled 135 children with nocturnal enuresis from children who referred to pediatric ward of Imam Reza Clinic in Shiraz, Iran. The samples were selected by the multistage cluster random sampling. Participant`s information (age, sex, number of wet-nights/week) were gathered through interview and body mass index (BMI) and waist-to-hip ratio (WHR) were assessed through anthropometric measures also dietary fat, calcium, calorie, vitamin B12, folic acid, iron and some foods usually limited for enuretic children (e.g. milk and dairy products, eggs, citrus fruits and juices, tomatoes, chocolate) and carbonated beverages were measured through validated food frequency questionnaire (FFQ). Fasting urine was also collected for measuring prostaglandin E2 level.

Results: Our study showed that food components and energy intake were not correlated with urinary PGE2. Participants' BMI and WHR were moderately correlated with PGE2 which were not significant. Of allergic foods, only cheese had significant correlation with urinary PGE2.

Conclusion: There were no significant correlations between dietary components and BMI and urinary prostaglandin E2. Cheese consumption caused lower PGE2 level probably by decreasing omega6 especially arachidonic acid level.

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Introduction

Nocturnal enuresis, the most common behavior disorder studied in children, results from multifactorial processes, including both genetic and environmental factors. It was shown that nocturnal urine production in children is generally higher

when there is an enuretic episode (1) and dietary components and body mass index (BMI) play important roles in regulation of night-time urine production through prostaglandin changes. Altered prostaglandin production have been observed in children with enuresis, and prostaglandin inhibitors are known to be of therapeutic value (2).

One of the pro-inflammatory eicosanoids derived from the omega6 fatty acid, arachidonic acid, is prostaglandin E2 (PGE2) which is known to decrease the reabsorption of sodium and magnesium in the first part of the distal tubule in enuretic children. Indeed, they have an increase in nocturnal sodium and magnesium excretion in comparison with healthy controls and changes in urine production in nocturnal enuresis seems to be due to a decrease in the water and ion reabsorption in the thick ascending limb of Henle's loop because of a changed regulation of ion transport in this part of the kidney (3).

On the other hand, *in vitro* studies showed that bladder contraction is produced by the direct action of prostaglandins on urinary smooth muscle and also, it was demonstrated that E series-prostaglandins stimulate voiding through vesical contraction and urethral relaxation (4). Researches on lipidomic profiles revealed that high omega6 polyunsaturated fatty acid content of the diet caused high cellular concentration of PGE2 (5), and the elevated PGE2 level cause an increase in nocturnal diuresis. So some of dietary fatty acids may prevent instability and overcontractility of bladder muscles through reduction of prostaglandin E2 synthesis. Also, it was demonstrated that children with nocturnal enuresis have mean serum and urine PGE2 levels that are twice that of healthy controls (6).

BMI and waist-to-hip ratio (WHR), reliable indicators of obesity, which are defined as excessive fat accumulation cause low-grade chronic inflammation of adipose tissue (7, 8). It was noted that hypoxia in obese adipose tissue causes inflammation and secretion of pro-inflammatory cytokines (9). So higher body mass index and WHR could increase the risk of nocturnal enuresis through increasing prostaglandin production. Many studies showed that some foods (milk and dairy products, eggs, citrus fruits and juices, tomatoes, chocolate) and carbonated beverages can promote diuresis or detrusor over-activity, which in some people can exacerbate overactive bladder symptoms and nocturnal enuresis (10-12).

On the other hand, it was found that average vitamin B12 and folate levels of patients with nocturnal enuresis were significantly lower compared to those of a control group (13). Therefore, one of the aim of present study was to find the possible role of foods and micronutrients on urinary PGE2 in children with incontinence. In this study, we aimed to examine the association between diet factors and PGE2 production. Findings can help in developing food strategies for preventing and possibly treating urinary incontinence.

Materials and Methods

This cross-sectional study was performed between July and February 2015 on 135 enuretic children who were referred to Pediatric Ward of Imam Reza Clinic in Shiraz, Iran. The sample size was calculated according to the prevalence of nocturnal enuresis in children (15%) (14). The confidence interval of 99%, and the margin of error of 2% were defined. Participants were selected using multistage cluster random sampling method. Children were included, if they were aged 7 to 15 years old and they were suffering from nocturnal enuresis for at least three months and desired to participate in the study.

Information on age, sex, number of wet-nights/week was obtained through the interview. Height was measured to the nearest 0.5 cm using a non-stretchable tape fixed on the wall, while the child was standing without shoes, and the buttocks and shoulders touched the wall. Weight was measured by a digital scale (Glamor BS-801, Hitachi, China) without any shoes. BMI was calculated by dividing weight in kilograms by the square of height in meters. Waist circumference was measured at mid-distance between the last floating rib and the iliac crest at the end of normal expiration with a standard tape measuring to the nearest 0.5 cm and hip circumference was measured at maximal protrusion of the buttocks, by a non-elastic flexible tape to the nearest 0.5 cm. The waist circumference was divided by the hip to determine WHR.

Consumption of milk and dairy products, eggs, citrus fruits and juices, tomatoes, chocolate and carbonated beverages (11, 12) was measured for the past 12 months through 161-item validated food frequency questionnaire (FFQ) (15, 16). These reports were converted to weekly intakes. The Nutritionist 4 software was used for analyzing nutrient intakes of each food and beverages. A Written informed consent was obtained from all parents before interview. The study protocol was approved by the Ethics Committee and Research Council of the Research Institute of School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran (Project number: 9988).

Fasting urine samples were collected and kept at -80ºC for further analysis. Prostaglandin E2 levels were measured by enzyme-linked immunosorbent assay (ELISA) method using commercially available

kit (Crystal day, China). Data collected in this study were analyzed using SPSS software (version 16, Chicago, IL, USA). Normality of data was checked by Kolmogorov-Smirnov test, and non-parametric (i.e. Mann-Whitney's) test was used where required. Correlation between two scale variables was measured by Pearson correlation coefficient. The level of significance (P value) was set to less than 0.05.

Results

The number of participants entered the study was 135 enuretic children with the mean age of 8.64 years. Anthropometric characteristics and dietary components were presented in Table 1. As shown in Table 2, food components and energy intake were correlated with urinary PGE2. Children BMI and WHR were not also correlated with PGE2. Interestingly, omega6 consumption did not show any relationship with PGE2 production. Also, energy intake and dietary fat were not associated with PGE2 secretion. Except for cheese, the rest of allergenic foods (milk and dairy products, eggs, citrus fruits and juices, tomatoes, and chocolate) did not show any significant correlation with PGE2, but cheese consumption had significant correlation with urinary PGE2 (r=-0.22, P=0.008) (Table 3).

Discussion

Although nocturnal enuresis is benign, it is clear that it can be extremely distressing, with a negative psychological impact on children and their families (17). A previous study showed that one of the causes of nocturnal enuresis was a higher nightly diuresis due to an elevated solute excretion (18). Also, another study demonstrated that in children with nocturnal enuresis, the increase in diuresis and solute excretion might be due to either a reduction of the effect of vasopressin on cells of the thick ascending limb of Henle's loop, an increase in production of prostaglandins, or both (3).

In this study, the association of children food consumption and anthropometric characteristics with urinary PGE2 was studied. The data revealed that children with nocturnal enuresis had average BMI of 17 which was not associated with their urine PGE2. We found a negative relationship between dietary fat and urinary PGE2, but it was not significant and omega6 fatty acid had no correlation with urinary PGE2; which is not in agreement with previous studies showing an increase in pro-inflammatory cytokine production in response to higher omega6 consumption (19).

Table 1: Descriptive statistics of some study factors

Variable	Max	Min	Mean	SD
Age (year)	15	5	8.64	2.28
BMI (kg/m^2)	25.04	11.19	17	3.02
WHR	1	0.7	0.84	0.06
Fat (gr/week)	1283	11.19	487.44	201.67
Calcium (mg/week)	10478	849	4509.95	2438.03
Vitamin B12 (ng/week)	74.2	3.8	23.96	13.8
Folic acid (ng/week)	5364	13	1465.78	863.99
Fe (mg/week)	119	13.8	51	23.78
Energy (Kcal/week)	16786	1078	7713.87	2898.58
PGE2 (pg/ml)	899	403	637.14	129.34

Body mass index (BMI), Waist-to-hip ratio (WHR), Prostaglandin E2 (PGE2)

Table 2: Pearson correlation coefficient between some study variables and urinary PGE2

Variable	N	r	P value
Age (year)	135	0.027	0.76
BMI (kg/m^2)	129	0.15	0.08
WHR	135	0.12	0.15
Fat (mg/week)	135	-0.05	0.54
Omega6 (mg/week)	135	-0.04	0.64
Calcium (mg/week)	135	-0.007	0.93
Vitamin B12 (ng/week)	135	0.00	0.99
Folic acid (ng/week)	135	0.01	0.89
Fe (mg/week)	135	0.04	0.57
Energy (kcal/week)	135	0.00	0.91

r: Pearson correlation coefficient, n: number of children, *P value<0.005, **P value<0.001, BMI: Body mass index, WHR: Waist-to-hip ratio , PGE2: Prostaglandin E2

Table 3: Pearson correlation coefficient between some allergenic food and urinary PGE2

Variable (unit/week)	N	r	P value
Milk	135	-0.12	0.15
Yogurt	130	0.05	0.49
Cheese	135	-0.22	0.008**
Dough	135	-0.13	0.12
Cream	135	-0.04	0.6
Curd	135	-0.06	0.47
Ice cream	135	-0.03	0.71
Tomato	135	0.03	0.67
Egg	135	-0.01	0.85
Citrus fruits	135		
Carbonated beverages	135	-0.1	0.25
Chocolate	135	-0.12	0.13

r: Pearson correlation coefficient, n: number of children, *P value<0.005, **P value<0.001

There were no significant correlations between other food components (e.g. calcium, vitamin B12, folic acid, iron) and urinary prostaglandin E2. So they probably cause incontinence through another mechanism. Foods such as dairy products, citrus fruits, tomato, carbonated beverage and chocolate which are restricted as behavioral therapy for enuretic children (20) showed no association with urinary PGE2 except cheese. Our study showed that children who consume more cheese in their diet, they produce less PGE2. Dairy products containing milk fat are major food sources of saturated fatty acids. Cheese consumption is the leading contributor of saturated fatty acid in the US diet (21). A recent study reported that the frequency of consumption of cheese was negatively associated with serum lipids (22). So children who consume more cheese probably have lower omega6, especially arachidonic acid level and they produce lower PGE2. Further studies are needed to determine lipidomic profile of enuretic children and to find the exact mechanism of cheese in reducing urinary PGE2.

Conclusion

Dietary components and BMI have shown no correlation with urinary PGE2 in enuretic children. Cheese consumption caused lower PGE2 level probably by decreasing omega6, especially arachidonic acid level.

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Conflict of Interest

None declared.

References

1 Rittig S, Schamburg H, Schmidt F, et al. Long-term home studies of water balance in patients with nocturnal enuresis. *Scand J Urol Nephrol*. 1997;183:25-6; discussion 26-7. PMID:9165600.

2 Logan AC, Lesperance F. Primary nocturnal enuresis: omega-3 fatty acids may be of therapeutic value. *Med Hypotheses*. 2005;64:1188-91. DOI:10.1016/j.mehy.2004.11.030. PMID:15823714.

3 Natochin Y, Kuznetsova A. Nocturnal enuresis: correction of renal function by desmopressin and diclofenac. *Pediatr Nephrol*. 2000;14:42-47. DOI:10.1007/s004670050011. PMID:10654330.

4 Abrams P, Feneley R. The Actions of Prostaglandins on the smooth muscle of the Human Urinary Tract in vitro. *Br J Urol*. 1975;47:909-15. DOI:10.1111/j.1464-410x.1975.tb04075.x. PMID: 1222358.

5 James MJ, Gibson R, Cleland L. Dietary polyunsaturated fatty acids and inflammatory mediator production. *Am J Clin Nutr*. 2000;71:343S-8S. DOI:10.1093/ajcn/71.1.343s. PMID:10617994.

6 Sener F, Hasanoglu E, Soylemezoglu O. Desmopressin versus indomethacin treatment in primary nocturnal enuresis and the role of prostaglandins. *Urology*. 1998;4295:878-81. DOI:10.1016/s0090-4295(98)00327-6. PMID:9801119.

7 Xu H, Barnes G, Yang Q, et al. Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. *J Clin Invest*. 2003;112:1821-30. DOI:10.1172/jci19451. PMID:14679177.

8 Weisberg S, McCann D, Desai M, et al. Obesity is associated with macrophage accumulation in adipose tissue. *J Clin Invest*. 2003;112:1796-1808. DOI:10.1172/JCI19246. PMID:14679176.

9 Trayhurn P. Hypoxia and adipose tissue function and dysfunction in obesity. *Physiol Rev*. 2013;93:1-21. DOI:10.1152/physrev.00017.2012. PMID:23303904.
10 Dallosso H, McGrother C, Matthews R, et al. The association of diet and other lifestyle factors with overactive bladder and stress incontinence: a longitudinal study in women. *BJU Int*. 2003;92:69-77. DOI:10.1046/j.1464-410x.2003.04271.x. PMID:12823386.
11 Esperanca M, Gerrard J. Nocturnal enuresis: comparison of the effect of imipramine and dietaryrestriction on bladdercapacity. *Can Med Assoc J*. 1969;101:65-8. PMID:5362303.
12 Ferrara P, Del Volgo V, Romano V, et al. Combined dietary recommendations, desmopressin, and behavioral interventions may be effective first-line treatment in resolution of enuresis. *Urol J*. 2015;12:2228-32. PMID:26341763.
13 Albayrak S, Zengin K, Tanik S, et al. Vitamin B12, folate and iron levels in primary nocturnal enuresis. *Pak J Med Sci*. 2015;31:87-90. DOI:10.12669/pjms.311.6424. PMID:25878620.
14 Lawless MR, McElderry D. Nocturnal enuresis: current concepts. *Pediatr Rev*. 2001;22:399-407. DOI:10.1542/pir.22-12-399. PMID:11731679.
15 Mirmiran P, Esfahani F, Mehrabi Y, et al. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. *Public Heal Nutr*. 2010;13:654-62. DOI:10.1017/S1368980009991698. PMID:19807937.
16 Esfahani F, Asghari G, Mirmiran P, et al. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran lipid and glucose study. *J Epidemiol*. 2010;20:150-8. DOI:10.2188/jea.je20090083. PMID:20154450.
17 Jalkut M, Lerman S, Churchill B. Enuresis. *Pediatr Clin North*. 2001;48:1461-88. DOI:10.1016/s0031-3955(05)70386-2. PMID:11732125.
18 Kuznetzova A, Natochin Y, Papajan A. Physiological analysis of the ionregulatory renal function in children with nocturnal enuresis. *Physiol J*. 1996;82:78-86.
19 Maes M, Smith R. Fatty acids, cytokines, and major depression. *Biol Psychiatry*. 1998;43:313-4. PMID:9513744.
20 Wyman J, Burgio K, Newman D. Practical aspects of lifestyle modifications and behavioral interventions in the treatment of overactive bladder and urgency urinary incontinence. *Int J Clin Pr*. 2009;63:1177-91. DOI:10.1111/j.1742-1241.2009.02078.x. PMID:19575724.
21 US department of health and human services dietary guidelines for Americans. the report of the dietary guidelines advisory committee on dietary guidelines for Americans. 2011.
22 Høstmark A, Haug A, Tomten S, et al. Serum hdl cholesterol was positively associated with cheese intake in the Oslo Health Study. *J Food Lipids*. 2009;16:89-102. DOI:10.1111/j.1745-4522.2009.01134.x.