

Original Article

Functional constipation and bladder capacity and severity of enuresis in children: a correlation study

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Received June 2, 2017; Accepted November 26, 2017; Epub February 15, 2018; Published February 28, 2018

Abstract: Background: Primary nocturnal enuresis (PNE) is the most common voiding problem among pediatric patients. Enuresis has a complex etiology involving bladder function derangements, circadian rhythm, genetics, psychological factors, and the central nervous system. In this study, we studied the correlations among constipation, bladder capacity, and severity of PNE in children. Methods: The study was conducted in children and adolescents aged 5-15 years and diagnosed with PNE in Beijing Children's Hospital, Capital Medical University. Severity of nocturnal enuresis was classified as mild-moderate and severe according to the frequency of enuresis. In particular, more than six wet nights weekly was classified as severe and six or less as mild-moderate. Rome III questionnaire was used to determine whether a patient has constipation. Urinalysis and urinary ultrasound were performed for all participants. A logistic regression model was used to investigate the relationship between the severity of enuresis and possible predictive variables. Results: The mean age of the patients was 7.13 ± 2.45 years. A total of 92 patients were male, and 72 were female. Sixty percent of the patients had constipation for more than 6 months, and a negative association was found between constipation and bladder capacity ($P = 0.000$, $r = -0.656$). Rome III score was an independent predictor of severity of enuresis ($P < 0.05$). Constipated children were 1.47 times more likely to have severe enuresis than those not constipated ($P = 0.002$, 95% CI: 1.147-1.877). However, no significant relationship was observed between constipation and bladder residual urine volume ($P = 0.725$). Conclusion: Constipation was correlated with the severity of enuresis and bladder capacity. We strongly recommend careful inspection of constipation in each patient with enuresis.

Keywords: Constipation, enuresis, bladder capacity, correlation, Rome III score

Introduction

Functional constipation is characterized by infrequent stool evacuation, passing of hard stools, or painful defecation without fundamental organic causes [1]. No structural, endocrine, or metabolic etiology is identified in childhood constipation, which is often categorized as "functional" [2, 3]. The worldwide prevalence of childhood constipation ranges from 0.3% to 28% [4]. Functional constipation is the second most common reason that a child is referred to a pediatric gastroenterologist, and such children account for up to 25% of all visits [3, 5].

Nocturnal enuresis (NE) refers to urinary incontinence during sleep in children aged 5 years

and above [6] and is the most common voiding problem in children. NE can be classified as primary or secondary. Primary nocturnal enuresis (PNE) is defined as enuresis since childhood without at least 6 months of dryness. The pathophysiology of enuresis is complex and involves bladder function derangements, circadian rhythm (e.g., sleep and diuresis), genetics, psychological factors, and the central nervous system (e.g., several neurotransmitters and receptors).

Recently, Veiga et al. [7] demonstrated that constipation is associated not only with dysfunctional urination but also with overactive bladder. Rectal distention is stimulatory in humans, decreasing bladder capacity and increasing contractility [8, 9]. Meanwhile, night-

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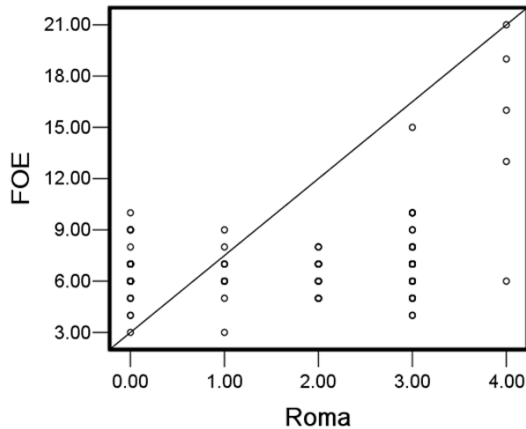


Figure 1. Spearman correlation between frequency of enuresis (FOE) and Rome III criteria ($R^2 = 0.097$ Linear).

time detrusor overactivity, which is associated with constipation, plays an important role in enuresis.

The association between enuresis and constipation is also well established and known. Hogdes [10] showed that 80% of enuretic patients are also constipated and laxative therapy obtained significant resolution of their enuretic problem. However, this association remains unclear. To the best of our knowledge, there is a lack of studies that extensively assessed the association of constipation systems with bladder capacity and severity of enuresis in enuretic children. Thus, this study aims to discuss these issues.

Materials and methods

The study was conducted in children and adolescents aged 5-15 years and diagnosed with PNE between September 2016 and February 2017 in Beijing Children's Hospital, Capital Medical University. The inclusion criteria were as follows: (1) age of 5-15 years, PNE (i.e. two or more wet nights per week and not dry for more than 6 months); (2) no medication for PNE received during the last 6 months; (3) lack of clinical or laboratory signs suggestive of some underlying diseases other than NE (e.g., kidney diseases, endocrine diseases, and nervous system diseases that may contribute to enuresis); (4) voluntarily agreed to participate in this study and signed the informed consent. The exclusion criteria were as follows: (1) a presence or a history of organic urological, hepatic,

pulmonary, cardiovascular, endocrinological, or neurological disease that would interfere with evaluation; (2) received treatment for NE within the past 6 months; (3) unwillingness to sign informed consent.

To evaluate the presence of constipation, we used the Rome III child questionnaire for patients aged 4-18 years. All patients were encouraged to complete the questionnaire by themselves. When the patients experienced any difficulty, they sought help from their parents. The questionnaires can be completed by parents if necessary (e.g., for those with reading difficulty, 5-8 years old). Participants who responded positively to two of the six questions were considered constipated [11]. The severity of NE was classified as mild-moderate and severe according to the frequency of enuresis. More than six wet nights weekly was classified as severe, whereas six or less as mild-moderate. Urinalysis and urinary ultrasound were performed in all the participants. The study was submitted to the ethics committee of our institution and obtained approval for its implementation. Written consent was obtained from the parents.

Statistical analysis

The collected data were analyzed using SPSS 20.0 (Statistical Package for the Social Sciences, version 20.0, SPSS Inc., Chicago, Illinois, USA). Numerical variables, such as age, were expressed as mean and SD. Categorical variables, such as the incidence of severe or mild-moderate enuresis, were compared using the chi-square test, where a P value of < 0.05 was considered significant. Nonparametric variables of bladder capacity and Rome III scores and frequency of enuresis were compared using the Spearman correlation, where $P < 0.05$ was considered significant. A logistic regression model was used to investigate the relationship between the severity of enuresis and possible predictive variables.

Results

Patient characteristics

A total of 164 PNE patients aged between 5 and 15 years fulfilled the inclusion criteria. Of them, 92 patients (56.1%) were male and 72 (43.9%) were female. The mean age of the

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Table 1. Incidence of severe and mild-moderate enuresis in constipated and not constipated patients with enuresis

	mild-moderate enuresis	Severe enuresis	P value
Not constipated	36 (55.4%)	29 (44.6%)	0.003
Constipated	31 (31.3%)	68 (68.7%)	
Total	67	97	

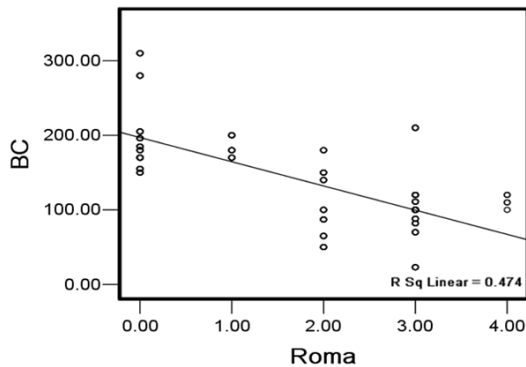


Figure 2. Spearman correlation between bladder capacity and Rome III criteria ($R^2 = 0.474$ Linear).

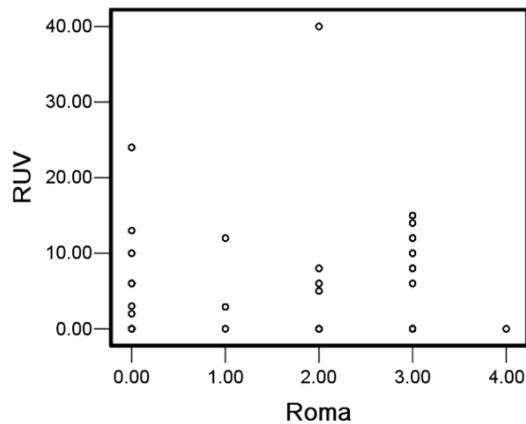


Figure 3. Spearman correlation between residual urine volume (RUV) and Rome III criteria ($P = 0.725$).

patients was 7.13 ± 2.45 years. A total of 99 patients (60.0%) had constipation for more than 6 months, and 60.9% of them were male and 59.7% were female.

Correlation between constipation and symptoms of enuresis

A positive correlation was found between constipation (Rome III scores) and frequency of enuresis (**Figure 1**, $P = 0.001$, coefficient and correlation of 0.267).

We also found that constipated children, according to the Rome III criteria, had a higher incidence of severe enuresis and lower incidence of mild-moderate enuresis than those without constipation (68.7% versus 44.6%, 31.3% versus 55.4%, $P = 0.003$, **Table 1**).

Correlation between constipation and bladder capacity

A negative association was found between constipation (Rome III scores) and bladder capacity (**Figure 2**, $P = 0.000$, coefficient and correlation of -0.656).

Correlation between constipation and bladder residual urine volume

No significant relationship was observed between constipation and bladder residual urine volume (**Figure 3**, $P = 0.725$, coefficient and correlation of 0.028).

Multivariate analysis of predictive risk factors of severe enuresis

A logistic regression model was used to investigate the relationship between severity of enuresis and possible predictive variables, including age, gender, family history of NE, residual urine volume, and Roman III score, which was the only independent predictor of severe enuresis (**Table 2**). Constipated children were 1.47 times more likely to have severe enuresis than those not constipated.

Discussion

Constipation is a common pediatric problem that remains underdiagnosed and poorly treated and thus often lead to severe functional impairment [12]. It is a commonly unrecognized etiologic factor in enuresis, and its treatment contributes to the resolution of enuresis [13]. The reported prevalence of constipation among enuretic children ranged from 7.06% in a Turkish population study [14] to 69.8% at a tertiary US pediatric voiding dysfunction clinic [15]. The prevalence of constipation among enuretic children in this study (60.0%) was consistent with findings of Robson [15]. Hodges [10] determined that 80% of enuretic children are constipated, and their conditions can be improved through laxative therapy. Given the high incidence of constipation in children with enuresis, thoroughly assessing constipation in

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Table 2. Multivariate analysis of severity of enuresis

Factors	Standard error	Wald value	P	OR	95% confidence interval	
					Lower limit	Upper limit
Rome III scores	0.126	9.313	0.002	1.47	1.147	1.877

each enuretic patient is necessary. In the present study, a positive correlation between constipation (Rome III scores) and frequency of enuresis was observed, although the correlation coefficient was low, suggesting a weak relationship between them. From another perspective, constipated children, according to the Rome III criteria, had a higher incidence of severe enuresis and lower incidence of mild-moderate enuresis than those without constipation, and the differences had statistical significance. Furthermore, Rome III score was the only independent predictor of severe enuresis. Constipated children were 1.47 times more likely to have severe enuresis than those not constipated. Previous research also supports this view. McGrath et al. [16] conducted a prospective cross-sectional study and found that the prevalence of constipation is high among children with NE. The severity of bedwetting was higher in their cohort (95.3% wetted the bed at least once per week) compared with 5.1% in a large Australian population study of school-aged children [17], supporting that the severity of wetting may be associated with the presence of constipation. Thus, severe enuresis often occurs concomitantly with constipation, and constipation should be identified and treated before managing enuresis if necessary.

Nevertheless, the relationship between constipation and enuresis remains controversial. Our results are in contrast to those in previous studies, indicating no association between nocturnal enuresis and constipation. Sampaio [18] reported that 12.6% of children and adolescents had constipation in association with NE, although this association was nonsignificant ($P = 0.483$). Sureshkumar et al. [19] evaluated potential risk factors for the presence and severity of nocturnal enuresis and found no significant association between constipation and severe nocturnal enuresis. These differences might be related to different definitions and severity of NE used in different studies, different scales for evaluating constipation [19], different age groups, different race, and sociocultural differences.

As previously stated, urinary and bowel dysfunction are associated because the bladder, urethra, and rectum are close in anatomical structure [20]. Rectal distension due to

fecal retention in chronic functional constipation causes bladder distortion and stimulation of detrusor stretch receptors, resulting in detrusor proneal dyssynergism [21]. Bladder function derangements play an important role in the pathogenesis of enuresis [22]. One important finding in our study was that children with more severe constipation symptoms had more reduced bladder capacity ($r = -0.656$). According to a study by Burgers [23], rectal distention significantly and at times markedly affects bladder capacity, contractility, and sensation. Franco [24] also suggested that when the rectum is distended, it compresses the adjacent bladder and decreases functional bladder capacity. Kim et al. [25] reported that overactive bladder symptoms that contribute to enuresis can be improved by treating constipation. Constipation induces bladder dysfunction when the rectum is filled with stool and stretch receptors are stimulated and transmitted to the brain, inducing temporary involuntary contraction of the external anal sphincter and the puborectalis muscles [25]. In our study, we analyzed the relationship between constipation and residual urine volume, but the difference was not statistically significant ($P = 0.725$), suggesting no correlation between the two.

Our study has several limitations. Restricted by objective reality condition, we did not evaluate constipation by digital rectal examination or by rectal diameter on ultrasound. As this is a cross-sectional study, we cannot establish any causal relationship because of the small sample size, and no participant responded positively to five or six of the six questions based on Rome III criteria. Therefore, future research in this direction is necessary.

Conclusions

Constipation was negatively associated with bladder capacity. Children with more severe constipation exhibited more reduced bladder capacity. Constipation was also correlated with the severity of enuresis. For enuretic patients with constipation, constipation should be evaluated and treated to increase bladder capacity and therefore relieve enuresis.

Acknowledgements

The authors gratefully acknowledge the patients and clinical investigators who participated in this trial and thank the support from the research special project of capital health development. This study was funded by research special project of capital health development (grant number 2016-1-2095).

Disclosure of conflict of interest

None.

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