

Research Article

The Correlation Between Hypercalciuria and Nocturnal Enuresis

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Abstract

Introduction: The word enuresis is derived from a Greek word (*enourein*) that means “to void urine.” Enuresis can be divided into primary enuresis (PE) and secondary enuresis (SE). **Aim of the Work:** To detect incidence of nocturnal enuresis and hypercalciuria in patients who has primary nocturnal enuresis for better evaluation and management. **Patients And Methods:** This study included 200 children, 100 with primary nocturnal enuresis and 100 apparently healthy children serving as controls matched in age and sex. Enuretic children were selected from the pediatrics nephrology Clinic and the urology clinic at El Minia University Hospital, El Minia. In the period from May to November 2017.

Results: This study was done over the period from May to November 2017 from the pediatrics nephrology Clinic and the urology clinic at El Minia University Hospital, El-Minia. **Conclusions:** (1) Ur. Ca/Cr ratio was elevated in nocturnal enuretic patients. (2) Ur. Ca/Cr ratio correlated with nocturnal enuresis

Keywords: Enuresis, Hypercalciuria, nocturnal, nephrology

Introduction

The word enuresis is derived from a Greek word (*enourein*) that means “to void urine.” Enuresis can be divided into primary enuresis (PE) and secondary enuresis (SE). A child who has been continent for at least 6 months before the onset of the bedwetting is considered to have SE. ⁽¹⁾

The International Children's Continence Society (ICCS) has developed standardized terminology for lower urinary tract function and malfunction in children. **Enuresis** (synonymous with intermittent nocturnal incontinence) is discrete episodes of urinary incontinence during sleep in children ≥ 5 years of age. **Monosymptomatic enuresis** means enuresis in children without any other lower urinary tract symptoms and without a history of bladder dysfunction. **Non-monosymptomatic enuresis** means enuresis in children with other lower urinary tract symptoms e.g., increased frequency, daytime incontinence, urgency, genital or lower urinary tract pain. ⁽²⁾

Monosymptomatic enuresis is the focus of this topic review.

Primary nocturnal enuresis is caused by a disparity between bladder capacity and

nocturnal urine production and the child's failure to awaken in response to a full bladder. Small subgroup of children with primary nocturnal enuresis has little or no arousal to bladder distention and exhibit uninhibited bladder contractions before voiding (i.e., detrusor-dependent enuresis). ⁽³⁾

In general, the goal of NE treatment will include Reducing the total number of enuretic nights, avoiding enuresis on specific nights in specific locations, stress reduction for the child and family and the avoidance of NE recurrence. ⁽⁴⁾

Combining enuresis alarms with other behavioral modalities enhances treatment success. Adding overlearning (i.e., encouraging children to drink extra fluids before bedtime to improve bladder capacity) and combining an enuresis alarm with arousal training (i.e., rewarding children for awakening in response to the alarm) is effective in more than 90% of children. ⁽⁵⁾

Pharmacologic therapies are not curative, but they decrease the frequency of enuresis or temporarily resolve symptoms over time until spontaneous resolution occurs. In addition to

alarm therapy, Desmopressin therapy is recommended as first line treatment for patients with primary monosymptomatic NE.

Anticholinergic medications such as oxybutynin (Ditropan) have been used to treat urinary urgency, frequency and incontinence. For children with NE refractory to behavioral therapy, desmopressin and anticholinergic therapy imipramine (tricyclic antidepressant) is indicated. ⁽⁶⁾

Hypercalciuria, or excessive urinary calcium excretion, is the most common identifiable cause of calcium kidney stone disease. In children, hypercalciuria is often associated with some degree of hematuria and back or abdominal pain and is also sometimes associated with voiding symptoms

Medical therapy as Diuretics, Orthophosphates, Bisphosphonates, Calcium-binding agents are rarely used to treat hypercalciuria whenever dietary treatment as limiting daily calcium, oxalate, purines and animal protein, reducing sodium (salt) and sugar to as minimum as possible, increasing dietary fiber, limiting alcohol and caffeine intake, increasing fluid intake, especially water alone is inadequate, ineffective or intolerable for the patient. ⁽⁷⁾

Aim of the Work

To detect incidence of nocturnal enuresis and hypercalciuria in patients who has primary nocturnal enuresis for better evaluation and management.

Patients and Methods

This study included 200 children, 100 with primary nocturnal enuresis and 100 apparently healthy children serving as controls matched in age and sex. Enuretic children were selected from the pediatrics nephrology Clinic and the urology clinic at El Minia University Hospital, El Minia. In the period from May to November 2017.

They were classified into:

- Group (I) Cases: Included 100 children with primary nocturnal enuresis.
- Group (II): Included 100 healthy control children with matched age and sex with the previous group.

Inclusion Criteria:

- Children with primary nocturnal enuresis aged from 5 to 18 years old

Exclusion Criteria:

- The presence of vesico-ureteral reflux
- History of urinary tract infection during the last month,
- Nutrition with ketogenic diet
- Any treatment with corticosteroids, or diuretics in the last month, or high-dose vitamin D in the last 6 months (medications like drops, syrup, or ampule)
- major fracture in lower extremities or bed rest for a long time
- Symptoms (including urgency, frequency, dysuria) or abdominal pain, untreated constipation (to avoid coincidence of above-mentioned urinary symptoms)

All children were subjected to the following:

- 1) Careful history taking
- 2) Thorough Clinical examination
- 3) Laboratory investigations including:
 1. Determining the urine calcium/ creatinine ratio for subjects in both case and control groups.
 2. subjects with hypercalciuria were investigated for the etiology of their hypercalciuria via blood samples including measuring;
 - alkaline phosphatase
 - phosphorus
 - calcium
 - potassium
 - sodium
 - blood urea nitrogen
 - serum creatinine
 - Urine analysis and culture if needed.
 - Lumber x-ray.

Results

This study was done over the period from May to November 2017 from the pediatrics nephrology Clinic and the urology clinic at El Minia University Hospital, El Minia.

This study included:

- 1- Group (I): 100 children suffering from primary nocturnal enuresis.
- 2- Group (II): 100 healthy children were taken as a control group, they were age and sex matched.

(Table I): Comparison between patients and control group regarding demographic data:

| Variable | | Group (I) Patients (n=100) | Group (II) Control (n=100) | P. value (Sig.) |
|------------|--------|-------------------------------|-------------------------------|--------------------|
| Age (year) | | 9.9 ± 1.7 | 10.2 ± 1.5 | 0.41 ^{NS} |
| Gender | Male | 48 (48.0%) | 42 (42.0%) | 0.54 ^{NS} |
| | Female | 52 (52.0%) | 58 (58.0%) | |

NS Not significant ** Significant ($P \leq 0.01$).

The previous table showed that the mean age of enuretic children was 9.9 ± 1.7 and that of the control group was 10.2 ± 1.5 years.

Also the previous table showed that 48.0% of the enuretic children were males and 52.0% were females. In the control group 42% were males and 58% were females with no significant difference between both groups regarding sex.

Discussion

Nocturnal enuresis (NE) is a multifactorial disease and is a common problem in children⁽⁸⁾. It is a distressing condition that has been defined as 'involuntary wetting during sleep without any inherent suggestion of frequency of bedwetting or pathophysiology'⁽⁹⁾ or can be defined as an involuntary passage of urine during sleep beyond the age of 5 years Abu Salem et al., (2016). Diurnal enuresis is involuntary leaking of urine during waking hours. Nocturnal enuresis refers to involuntary passage of urine during sleep and is classified as primary (no prior period of sustained dryness) or secondary (recurrence of nighttime wetting after 6 months or longer of dryness). Recent urology literature describes another classification of nocturnal enuresis based on the presence or absence of other bladder symptoms. Abu Salem et al., (2016).

Monosymptomatic nocturnal enuresis is defined as a normal void occurring at night in bed in the absence of any other symptoms referable to the urogenital tract, and it precludes any daytime symptomatology. Polysymptomatic nocturnal enuresis is bed-wetting associated with other bladder symptoms such as

urgency, frequency, instability, or voiding dysfunction. Children develop stable bladder control in the 3rd to 6th year of life—initially during the day and later also during the night. At age 7, 10% still have nocturnal enuresis, 2% to 9% are affected during the day. The spontaneous remission rate is about 15% per year.⁽¹⁰⁾

The etiology of NE has been widely debated but is still not completely understood but the most commonly established causes of nocturnal enuresis are small bladder size, abnormal sleep patterns, lack of increment in plasma vasopressin at night, uninhibited nocturnal detrusor muscle contractions and lack of arousal mechanisms, the high amount of urine produced during sleep at night and delayed functional maturation of the central nervous system⁽¹¹⁾. Nocturnal enuresis had high prevalence and has remained a focus of extensive scientific research over the past few decades. The prevalence of NE is reported as follows, 8-20% of 5-year-olds, 1.5-10% of 10-year-olds and 0.5-2% of adults and 2.6% of children aged 7.5 years wet their bed on two or more nights a week⁽¹²⁾

Conclusions

- (1) Ur. Ca/Cr ratio was elevated in nocturnal enuretic patients.
- (2) Ur. Ca/Cr ratio correlated with nocturnal enuresis.

Recommendation

From our study we recommend that:

- 1) Adding the measurement of urine calcium level in patients with nocturnal enuresis in the process of looking for the etiologies.

- 2) Based on accompanying enuresis and hypercalciuria, its therapeutic approach may need to be changed.
- 3) More studies should be done considering the controversy which exists about the role of hypercalciuria in the pathogenesis of nocturnal enuresis.

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