Prevalence of Enuresis and Daytime Urinary Incontinence in Children and Adolescents With Sickle Cell Disease

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Purpose: There is a known association between sickle cell disease and enuresis. However, the cause of this association is unclear. We tested the hypothesis that children with sickle cell disease would have more symptoms of overactive bladder than a control group.

Materials and Methods: Questionnaires were distributed to 155 legal guardians of children and adolescents 5 to 17 years old with sickle cell disease and to 100 legal guardians of a control group of children.

Results: Individuals with and without sickle cell disease were distributed uniformly regarding gender and age. A total of 50 patients (32.3%) in the sickle cell disease group had enuresis vs 5 (5%) in the control group ($p = 0.000$). Daytime urinary incontinence was observed in 36 individuals with (23.2%) and 11 (11.0%) without sickle cell disease ($p = 0.014$). A total of 52 patients with sickle cell disease (33.5%) complained of urgency, compared to 10 controls (10%, $p = 0.000$). A total of 49 patients with sickle cell disease (31.6%) had frequency, compared to 6 controls (6%, $p = 0.000$). Of all patients who reported enuresis or daytime incontinence only 1 with enuresis had received specific treatment.

Conclusions: There is a significant association between sickle cell disease and enuresis and overactive bladder symptoms such as daytime incontinence, urgency and frequency. Thus, all children and adolescents with sickle cell disease should be questioned regarding the presence of these symptoms to facilitate treatment for these conditions.

Key Words: anemia, sickle cell; child; enuresis; urinary incontinence; urination disorders

Abbreviations and Acronyms

OAB = overactive bladder

SCD = sickle cell disease

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ENURESIS is a frequent problem in children and is associated with emotional issues such as anxiety, guilt and low self-esteem.[1] These conditions can be resolved with treatment. Approximately 250,000 cases of sickle cell disease are diagnosed in the world yearly.[2] There is a known association between sickle cell disease and enuresis.[3–8]

OAB is clinically manifested by urgency, and is usually associated with daytime incontinence and frequent urination. OAB is associated with psychological problems such as low self-esteem and behavioral alterations, as well as urinary tract infection and vesicoureteral reflux.[9–11] Daytime incontinence is present in around 4% of boys and 8% of girls at age 7 years.[12]

The etiopathology of enuresis in patients with SCD is not well understood. Some theories include the inability of the kidneys to concentrate urine, social and genetic factors, and

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delays in neurophysiological development.[1,6] Some of these factors could also lead to daytime urinary symptoms. We tested the hypothesis that children with SCD have more symptoms of OAB than children without SCD.

MATERIALS AND METHODS

We distributed confidential questionnaires to the legal guardians of children and adolescents with SCD who had been attended to at hematology clinics as well as a control group from a public school in the same city. All questionnaires were filled out by the legal guardians in the waiting room of the hematology (outpatient) office. Older children and adolescents helped their parents and legal guardians with the answers. Professionals were present to clarify any questions. Everyone who was approached by a researcher agreed to complete the questionnaire. The study included 155 children with and 100 without sickle cell disease, and was performed between April 2009 and May 2010.

The project was evaluated and approved by the hospital ethics committee. The individuals with SCD included in the study were outpatients from a referral hematological disease center. Controls consisted of individuals from a public school whose legal guardians denied the presence of sickle cell disease. Patients with sickle cell trait, other sickle cell syndromes or thalassemias were excluded. Questions addressed the present frequency of nocturnal enuresis, primary or secondary, and the presence of OAB symptoms. Statistical analysis was done using SPSS®, version 15.0 and $p < 0.05$ was considered significant. Pearson, Fisher and chi-square tests were performed to analyze categorical variables and the Student t test to analyze continuous variables.

RESULTS

Individuals with and without SCD were distributed uniformly regarding gender and age. Mean ± SD patient age was 11.12 ± 3.88 years (range 5 to 17) and mean age of controls was 10.84 years ($p = 0.705$). Gender distribution was almost identical, with the percentage of males at 65% and 64.5%, respectively. Age distribution was the same between the groups (table 1).

Enuresis was significantly more frequent in patients with SCD than controls (table 2). Seven of 50 patients (14%) with SCD and enuresis had secondary enuresis, while the remaining patients had primary enuresis. All bedwetting patients in the control group had primary enuresis. Of patients with SCD 21 (42%) had monosymptomatic enuresis, and in 29 the enuresis was associated with urgency or daytime incontinence. There was a significant difference regarding the prevalence of enuresis by gender, with 39 of 100 males (39%) being affected, compared to 11 of 55 females (20%, $p = 0.019$).

Daytime incontinence was observed in more children with than without SCD (table 2). There was no significant gender difference in the prevalence of daytime incontinence ($p = 0.165$). The highest prevalence of enuresis was in patients 5 to 7 years old, and the highest prevalence of daytime incontinence was in patients 11 to 14 years old (fig. 1). The highest prevalence of enuresis and daytime incontinence in controls was seen in those 5 to 7 years old (fig. 2).

Urgency was another symptom found more commonly in patients with SCD vs controls (table 2).

Table 1. *Age distribution of children with and without SCD*

Age (yrs)	No. Pts (%)	No. Controls (%)	Totals (%)
5–7	30 (19.4)	20 (20)	50 (19.6)
8–10	47 (30.3)	30 (30)	77 (30.2)
11–14	41 (26.5)	26 (26)	67 (26.3)
15–18	37 (23.9)	24 (24)	61 (23.9)
Totals	155 (100)	100 (100)	255 (100)

$p < 0.999$ for patients with vs without SCD.

Table 2. *Prevalence of enuresis, daytime incontinence, urgency and frequency in children with and without SCD*

	No. Present (%)	No. Absent (%)	Totals	p Value
		Enuresis		
Pts	50 (32.3)	105 (67.7)	155	
Controls	5 (5)	95 (95)	100	
Totals	55 (21.6)	200 (30.2)	255	0.000
		Daytime incontinence		
Pts	36 (23.2)	119 (76.8)	155	
Controls	11 (11.0)	89 (89.0)	100	
Totals	47 (18.4)	208 (81.6)	255	0.014
		Urgency		
Pts	52 (33.5)	103 (66.5)	155	
Controls	10 (10.0)	90 (90.0)	100	
Totals	62 (24.3)	193 (75.7)	255	0.000
		Increased voiding frequency		
Pts	49 (31.6)	106 (68.4)	155	
Controls	6 (6.0)	94 (94.0)	100	
Totals	62 (24.3)	193 (75.7)	255	0.000

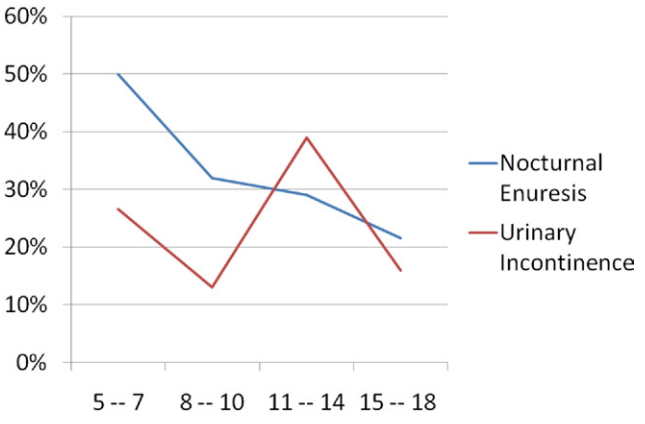

Figure 1. Prevalence of enuresis and urinary incontinence in participants with SCD, distributed by age.

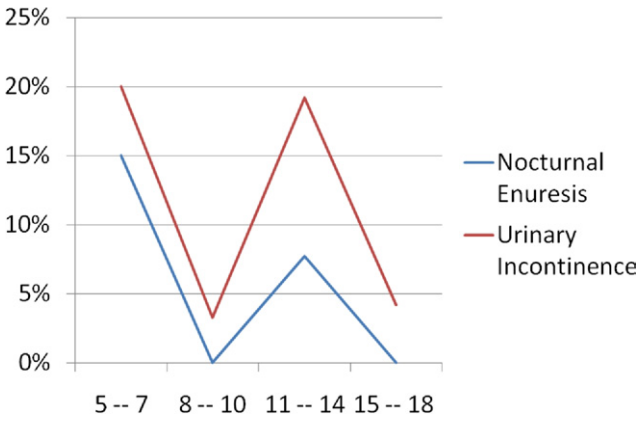

Figure 2. Prevalence of enuresis and urinary incontinence in participants without SCD, distributed by age.

Among patients with SCD there was no significant difference between genders regarding the prevalence of urgency ($p = 0.598$). There was a significant difference between individuals with and without SCD concerning frequency. However, there were no significant gender differences regarding frequency ($p = 0.071$).

Of patients with enuresis 70% had the nonmonosymptomatic form. Because the control group contained only 5 children with enuresis, no statistical analysis was performed between the groups. Of all patients who reported enuresis or daytime incontinence only 1 with enuresis reported having undergone specific treatment.

DISCUSSION

Enuresis is significantly increased in individuals with sickle cell disease, as evidenced by 32.3% of patients in this study 5 to 17 years old. This result supports other studies that highlight the association between SCD and enuresis.[3–8] Figueroa et al reported that 29.9% of 91 patients with SCD manifested primary enuresis, of whom 17 had SCD, 5 sickle cell trait and 4 β-thalassemia.[3] In another study of patients 6 to 20 years old Field et al recorded 33% of patients with SCD as having enuresis.[4] Nevertheless, these series lack a control group without SCD. Since studies have revealed a higher prevalence of nocturnal enuresis among patients with SCD, further investigation is required, using more objective data such as monitoring urinary volume.

Considering that Brazilian individuals who study in public schools and access the public health system share socioeconomic and ethnic backgrounds, we understand that the control group is also of similar background to the group of patients with SCD. Barroso et al reported that there is a higher prevalence of nocturnal enuresis and urinary incontinence in institutionalized orphans 4 to 11 years old compared to noninstitutionalized children of the same age, demonstrating that the conjunction of social and emotional factors has an important effect on these symptoms.[13] These findings may also be observed in patients with SCD. Readett et al reported that children with SCD had a significantly higher prevalence of enuresis if they were from a large family.[8] The use of a control group with the same socioeconomic characteristics minimizes bias in our results.

Among patients with SCD there is a persistence of enuresis with age. Despite the inverse relationship between enuresis and maturation, around 21% of the patients between 15 and 18 years old still exhibited symptoms of enuresis. This result corroborates the findings of Field et al, who identified enuresis in 11% of individuals with SCD between 16 and 18 years old.[4] They also found that 9% of the subjects 18 to 29 years old had nocturnal enuresis. We found that among patients with SCD enuresis was more prevalent in boys than in girls. This finding is in agreement with Barakat et al, who reported that enuresis was present in 22% of boys and 11% of girls in their study.[14] Readett et al found enuresis in 52% of boys and 38% of girls with SCD (difference not significant).[8]

We also found that 14% of the patients with SCD had secondary enuresis and only 42% had monosymptomatic enuresis. To our knowledge these data have not been reported before. Stressful events related to SCD could provoke this incidence of secondary enuresis. Considering that SCD is the most common monogenic pathological condition in Brazil, its association with the development of OAB symptoms is relevant because these patients could benefit from specific treatment at specialized centers.

In our study only 1 individual (1.8%) with nocturnal enuresis received specific treatment for this condition. Figueroa et al offered treatment with intranasal desmopressin in 27 patients with SCD and enuresis, and 15 abstained from treatment, not considering enuresis to be a significant enough problem to treat.[3] This attitude was attributed to the fact that children with SCD already experience frequent hospitalizations because of the disease, so their legal guardians tend to minimize or ignore less severe conditions such as nocturnal enuresis. Hence, there is a need for propagation of the therapeutic measures available for urinary tract dysfunction in patients with and without SCD. These individuals should be referred for specialized treatment, which will help improve their self-esteem and quality of life.

There are no previous known studies evaluating the prevalence of OAB in patients with SCD. In this series we observed a higher prevalence of daytime incontinence, urgency and frequency in patients with SCD compared to controls. Daytime incontinence was present in 23% of the patients. This

symptom was still present in 16% of the patients 15 to 18 years old, showing that it lingers as individuals mature. It is important to consider the impact of urinary incontinence on the quality of life of these patients, especially the older ones. Urgency was found in around 33% of the SCD group and 10% of controls. These symptoms, as well as urinary incontinence, were similarly prevalent in males and females.

Enuresis in patients with sickle cell disease may be a result of genetic factors, clinical characteristics of the disease, intrinsic neurophysiological immaturity or associated social factors. Studies have been designed to elucidate the mechanism through which enuresis develops in patients with SCD and the cause has been thought to be an inability of the kidneys to concentrate urine. This condition has been attributed to renal medulla infarctions due to vascular occlusion leading to a loss of the counterflow system and, consequently, to diabetes insipidus and hyposthenuria.[6,7] However, Readett et al compared 16 patients with SCD and enuresis to patients with SCD and no enuresis, and found no difference in urine osmolarity or total urinary volume, suggesting that the lower urine concentration status may not be a central factor in the genesis of nocturnal enuresis in the presence of SCD.[8] Figueroa et al studied 10 patients treated with intranasal desmopressin and observed complete resolution of enuresis in 60% and significant improvement in 20%.[3] Desmopressin exerts an antidiuretic effect in the kidney and would be inefficient in patients with nephrogenic diabetes insipidus, suggesting that the mechanism of enuresis is multifactorial.[14]

Thus far, there is no scientific evidence to ascertain the underlying cause of enuresis in patients with SCD. The higher rates of enuresis and daytime urinary symptoms could be related to an immaturity of the central nervous system. This condition could be genetically predetermined or could have to do with the presence of a chronic disease. Special attention given to children who require it may be a factor in the delay of neurophysiological development. However, because we did not have a control group of patients with chronic diseases aside from SCD, we could not prove this hypothesis.

A limitation of our study is that we did not evaluate the rate of constipation or urinary tract infection. It is well known that there is a strong relationship between constipation and lower urinary tract symptoms. Also, patients with SCD are often treated with narcotics for their pain crises. This treatment can lead to constipation, one of the major causes of nocturnal enuresis and lower urinary tract symptoms. Additionally a voiding diary was not kept, nor was urinary output measured in the evaluation of symptoms. Although these could be valuable data, they are difficult to apply in asymptomatic children. Furthermore, lower urinary tract dysfunction diagnosis is based on patient symptoms and not on the voiding diary.[15]

CONCLUSIONS

This study demonstrates a significant association between SCD and enuresis and OAB symptoms such as daytime incontinence, urgency and frequency. Thus, all children and adolescents with SCD should be questioned regarding the presence of these symptoms to facilitate treatment for these conditions. Considering the importance of lower urinary tract dysfunction, which may be associated with emotional disorders, urinary tract infection, vesicoureteral reflux and renal injury, patients with SCD would benefit from a multidisciplinary approach, including the opinion of a urologist.

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