

The Effects of Oxybutynin on Urinary Symptoms in Children with Williams-Beuren Syndrome

Zein M. Sammour, Cristiano M. Gomes,* Jose de Bessa, Jr., Marcello S. Pinheiro, Chong A. Kim, Rachel S. Honjo, Flavio E. Trigo-Rocha, Homero Bruschini and Miguel Srougi

From the Division of Urology and Genetics Unit of the Children's Institute, University of São Paulo School of Medicine, São Paulo, Brazil

Purpose: Williams-Beuren syndrome is a genomic disorder caused by a hemizygous contiguous gene deletion on chromosome 7q11.23. Lower urinary tract symptoms are common in children with Williams-Beuren syndrome. However, there are few data on the management of voiding symptoms in this population. We report our experience using oxybutynin to treat urinary symptoms in children with Williams-Beuren syndrome.

Materials and Methods: We prospectively analyzed 42 patients with Williams-Beuren syndrome and significant lower urinary tract symptoms due to detrusor overactivity diagnosed on urodynamics in a 12-week, open-label study. Urological assessment included symptomatic evaluation, the impact of lower urinary tract symptoms on quality of life, frequency-volume chart, urodynamics and urinary tract sonography. After 12 weeks of treatment with 0.6 mg/kg oxybutynin per day given in 3 daily doses, patients were assessed for treatment efficacy and side effects.

Results: A total of 17 girls and 19 boys completed medical therapy and were assessed at 12 weeks. Mean \pm SD patient age was 9.2 ± 4.3 years (range 3 to 18). The most common urinary complaint was urgency, which occurred in 31 patients (86.1%), followed by urge incontinence, which was seen in 29 (80.5%). Compared to baseline, urinary symptoms were substantially improved. The negative impact of storage symptoms on quality of life was significantly decreased from a mean \pm SD of 3.3 ± 1.7 to 0.5 ± 0.9 ($p < 0.001$). Mean \pm SD maximum urinary flow improved from 14.2 ± 15.0 to 20.5 ± 6.4 ml per second ($p < 0.001$).

Conclusions: A total of 12 weeks of therapy with 0.6 mg/kg oxybutynin daily resulted in improvement of lower urinary tract symptoms, quality of life and maximum flow rate in most patients with Williams-Beuren syndrome.

Abbreviations and Acronyms

WBS = Williams-Beuren syndrome

Submitted for publication October 26, 2011.

* Correspondence: Hospital das Clínicas da Universidade de São Paulo, Divisão de Clínica Urológica, Caixa Postal 11273-9, CEP 05422-970 São Paulo, SP, Brazil (telephone: 55-11-3069-8080; FAX: 55-11-3069-8081; e-mail: crismgomes@uol.com.br).

Key Words: lower urinary tract symptoms, oxybutynin, urination disorders, urodynamics, Williams syndrome

WILLIAMS-BEUREN syndrome is a rare genomic disorder caused by a hemizygous contiguous gene deletion on chromosome 7q11.23. Clinical findings of the syndrome consist predominantly of typical dysmorphic faces, supravalvular aortic stenosis, hypertension, mental retardation and atypical hypersocial behavior.¹⁻⁴

Voiding symptoms including urinary incontinence are frequent in patients with WBS. It is estimated that 32% to 78% of patients present with lower urinary tract symptoms. The most common urinary complaints are increased urinary frequency, nocturnal enuresis, urgency and urge incontinence, which have a significant neg-

ative effect on patient quality of life.^{5,6} Several factors account for the high prevalence of voiding symptoms among patients with WBS, including bladder and sphincteric abnormalities. Urodynamic evaluation is abnormal in up to 82% of patients, with detrusor overactivity and dysfunctional voiding being the main findings.⁵ The causes of vesico-sphincteric dysfunction are not completely understood and may include neurological abnormalities, which are common in patients with WBS, and structural changes of the urinary tract such as bladder diverticula.

Antimuscarinic treatment has been successfully used in children with neurogenic voiding dysfunction and idiopathic detrusor overactivity.⁷ However, the population with WBS has never been evaluated for medical treatment of voiding dysfunction. Additionally most of these patients have cognitive impairment. Finally, little is known regarding pharmacological treatment of voiding dysfunction in patients with cognitive limitations in terms of efficacy and the impact on cognitive impairment.

MATERIALS AND METHODS

A total of 20 girls and 22 boys with a diagnosis of WBS who had overt urinary storage symptoms and urodynamic proved detrusor overactivity and post-void residual volume less than 20 ml were enrolled in this prospective 12-week, open-label study between January 2004 and December 2009. The diagnosis of WBS was confirmed by fluorescence in situ hybridization, polymorphic markers or multiplex ligation dependent probe amplification.

After written informed consent was obtained, a history of storage symptoms including frequency, urgency, urge incontinence and nocturnal enuresis was jointly obtained from the parents and child, and a structured questionnaire of urinary symptoms was completed.⁸ A 3-day frequency-volume chart was obtained. Additionally we used the quality of life question of the International Prostate Symptom Score concerning urinary symptoms, which was answered on a scale of 0 ("delighted") to 6 ("terrible") by the parents.⁹

Patients completed a urological evaluation consisting of urinalysis, urine culture, serum creatinine, renal/bladder ultrasound and urodynamics consisting of free uroflowmetry and measurement of post-void residual urine, filling cystometry and pressure flow voiding studies. Each patient received 0.6 mg/kg immediate release oxybutynin daily divided into 3 doses (maximum daily dose 15 mg) and instructions for timed voiding. Patients were reevaluated at 12 weeks, and treatment efficacy was assessed by analyzing treatment related changes from baseline to week 12 in terms of urinary symptoms, quality of life, frequency-volume chart data and maximum urinary flow. Parents were counseled regarding potential side effects of oxybutynin. They were specifically alerted about dry mouth, obstipation, drowsiness and changes in behavior. Any adverse events spontaneously reported by patients or observed by parents or investigator during the study du-

ration were recorded. Terms and definitions are in accordance with the International Children's Continence Society standards.¹⁰

Data were expressed as mean \pm SD or absolute values and fractions. The Student t test or paired t test was used to compare continuous variables, while categorical variables were compared using the Fisher exact test. All tests were 2-sided with $p < 0.05$ considered statistically significant. Data were processed using commercially available statistical software (GraphPad Prism®, version 5.00 for Windows).

RESULTS

Of the 42 patients 6 (14.3%) were excluded from the study due to inadequate followup. The remaining 17 girls and 19 boys completed medical therapy and were reevaluated at 12 weeks. Mean \pm SD patient age was 9.2 ± 4.3 years (range 3.0 to 18). The most common urinary complaint was urgency, occurring in 31 patients (86.1%). Increased urinary frequency was seen in 30 patients (83.3%), urge incontinence in 29 (80.5%) and nocturnal enuresis in 26 (72.2%). Six patients (16.6%) were using diapers. Parents of 29 patients (80.5%) acknowledged that the voiding symptoms had a significant negative impact on patient quality of life. No differences were noted between boys and girls in terms of storage symptoms.

A total of 10 patients (27.7%) had a history of urinary tract infections but no patient had a positive urine culture at evaluation. Serum creatinine was normal in all patients. Urinary tract sonography was normal in 28 patients (77.7%), while 3 (8.3%) had bladder wall thickening and 2 (5.5%) had unilateral hydronephrosis. Other abnormalities were renal cysts, urachal cyst and small kidney stones, each affecting 1 patient (2.7%).

Urodynamic Findings

Mean \pm SD maximum urinary flow was 14.2 ± 15.0 ml per second. Mean \pm SD voided volume was 86.6 ± 51.3 ml. Mean \pm SD post-void residual volume after initial uroflowmetry was 2.6 ± 15.4 ml. Only 1 patient had residual volume greater than 20 ml.

Detrusor overactivity was diagnosed in all patients. This finding was associated with dysfunctional voiding in 14 children (38.9%), while detrusor underactivity was present in 2 (5.5%). Mean \pm SD cystometric capacity was 157.8 ± 81.8 ml, which represents 64.2% of expected bladder capacity. Only 3 patients (8.3%) had a cystometric capacity that matched that expected for age. Mean \pm SD bladder compliance was 17.1 ± 13.4 ml/cm H₂O. Analysis of pressure flow studies revealed a mean \pm SD detrusor pressure at maximum flow of 70.9 ± 103.3 cm H₂O and maximum flow of 14.3 ± 7.6 ml per second. Mean \pm SD residual volume after the pressure-flow study was 3.5 ± 9.5 ml.

Download English Version:

<https://daneshyari.com/en/article/3866735>

Download Persian Version:

<https://daneshyari.com/article/3866735>

[Daneshyari.com](https://daneshyari.com)