UIJ UroToday International Journal®

www.urotodayinternationaljournal.com
Volume 3 - December 2010

Nonpharmacological Treatment Using Transcutaneous Electrical Nerve Stimulation for Children With Benign Joint Hypermobility Syndrome and Overactive Bladder

Tarek Salem,[1] Hashim Hafez,[1] Manal Ali[2]

[1]Urology Department, Faculty of Medicine, Suez Canal University, Egypt; [2]Rheumatology and Rehabilitation Department, Faculty of Medicine, Ain Shams University, Egypt

Submitted September 30, 2010 - Accepted for Publication October 23, 2010

ABSTRACT

INTRODUCTION: Joint hypermobility is a condition in which there is extreme mobility of the joints, often leading to manifest symptoms. Overactive bladder (OAB) is a commonly associated problem. The purpose of the present study was to evaluate the use of transcutaneous electrical nerve stimulation (TENS) as a sole treatment for children with OAB associated with benign joint hypermobility syndrome (BJMS).

METHODS: A total of 26 children with OAB and without voiding dysfunction or constipation participated in the study. Their ages ranged from 5-14 years. All patients were evaluated by uroflowmetry to exclude patients with high flow rate, ultrasound of the urinary tract to exclude organic causes and high postvoid residual urine, and urine analysis and culture to exclude infection. None of the patients were taking anticholinergics during the investigation. All patients were treated by TENS, using 2 superficial 4 cm electrodes that were placed on each side of sacral segment 3. Sessions lasted for 20 minutes and were conducted every other day, to a maximum of 20 sessions. Sessions were terminated if the physician and parent agreed that the child had attained complete success. All parents (or patients) completed a voiding diary before treatment and for 1 month after the last session. Improvement was assessed on an analog scale. Chi-square was used to test the hypotheses that response rates were the same in each category with regard to patient age and sex.

RESULTS: The total number of sessions ranged from 12-20. Out of 26 patients, 19 (73%) complained of urge incontinence following treatment (13 girls; 6 boys). Of these 19 patients, 15 had associated nocturnal enuresis (11 girls; 4 boys). None of the 7 patients without urge incontinence had enuresis. Eleven patients (42.36%) had complete clinical improvement, 6 (23%) had excellent improvement, 3 (11.54%) had mild improvement, and 6 (23%) had no change. There were no significant differences in the degree of improvement regarding the patient's sex or age ($P > .05$).

CONCLUSION: Transcutaneous electrical nerve stimulation shows promise as an alternative to pharmacological treatment for OAB symptoms in children with BJHS.

KEYWORDS: Benign joint hypermobility syndrome; Transcutaneous electrical nerve stimulation; Overactive bladder

CORRESPONDENCE: Dr. Tarek Salem, Department of Urology, Suez Canal University, Faculty of Medicine, Ismailia 31911, Egypt (tareksalem100@hotmail.com).**CITATION**: *UroToday Int J*. 2010 Dec;3(6). doi:10.3834/uij.1944-5784.2010.12.10

Abbreviations and Acronyms

BJHS = benign joint hypermobility syndrome
GJH = general joint hypermobility
LUTD = lower urinary tract dysfunction
OAB = overactive bladder
PVR = postvoid residual
S3 = sacral segment 3
TENS = transcutaneous electrical nerve stimulation
UI = urge incontinence
UTI = urinary tract infection

INTRODUCTION

Joint hypermobility is a condition in which there is extreme mobility of the joints, often leading to manifest symptoms [1,2]. Benign joint hypermobility syndrome (BJHS) should be distinguished from connective tissue diseases such as Marfan syndrome, Ehlers-Danlos syndrome, osteogenesis imperfecta, and systemic rheumatic diseases [3,4]. Numerous extraarticular manifestations of BJHS have been similarly reported in children including, but not limited to, chronic constipation, encopresis, enuresis, and lower urinary tract dysfunction (dysfunctional voiding). Urinary urgency and/or incontinence (overactive bladder) is the other form of lower urinary tract dysfunction that could be present in these patients. Other characteristics of BJHS include urinary tract infection (UTI), low systemic blood pressure, low bone quantitative ultrasound measurements, chronic fatigue syndrome, temporomandibular joint disease, fibromyalgia, and gross motor developmental delay [5-8].

Lower urinary tract dysfunction (LUTD) is classified as *irritative* (ie, disturbance in the filling phase) and *obstructive* (ie, disturbance in the voiding phase). Overactive bladder (OAB) is considered only a disturbance in the bladder filling phase, but it is classified as *dysfunctional voiding* when there is vesicoperineal dyscoordination in the voiding phase.

Classically, LUTD is managed with anticholinergic drugs, regardless of whether it is related to bladder filling or voiding disturbance. However, according to Reinberg et al [9] the symptoms of urgency and daily urinary incontinence were resolved in less than 30% of children treated with oxybutynin or tolterodine (although most of the patients had improved symptoms). In addition, the rate of side effects is not low [10]. Finally, adherence to prolonged usage of the drugs may be difficult for children because treatment requires daily oral ingestion.

Patients with OAB are usually treated with electrical stimulation; patients with dysfunctional voiding are often treated with biofeedback training of the pelvic floor muscles. Authors of most research series have used invasive means to administer electrical stimulation that are unsuitable for children with no neurological abnormalities.

Hoebeke et al [11] reported the first study using transcutaneous electrical nerve stimulation (TENS) over sacral segment 3 (S3) in children with detrusor hyperactivity. They reported resolution of symptoms in 51% of the children 1 year after treatment. Electrical stimulation was delivered at low frequency (2 Hz) with long session (2 hours) and over a long period (6 months). Unfortunately, their results are difficult to interpret because some of the children took anticholinergics during the treatment.

Additional research is needed to separate the effects of electrical stimulation from the effects of drug therapy for children with OAB. The purpose of the present study was to evaluate the use of TENS as a sole treatment for children with OAB associated with BJHS.

METHODS

This was a prospective study that was conducted from March 2009 through February 2010. The protocol was approved by the hospital ethics committee. The parents of the patients provided informed consent.

Participants

The study included children with joint hypermobility syndrome and typical symptoms of OAB, with or without enuresis. BJHS was diagnosed according to the revised (Brighton, 1988) diagnostic criteria [12]. OAB was defined as the presence of frequency or urgency associated with or without urge incontinence, with no interrupted urinary flow and no postvoid residual (PVR) urine [13].

The patients were selected from children attending the rheumatology and urology clinics. The diagnoses of BJHS and OAB were confirmed by a rheumatologist and urologist, respectively. Detailed voiding history and local genitourinary examination of the patients was carried out by the urologist; the musculoskeletal and neurological history and examination were done by the rheumatologist.

Exclusion criteria included the presence of: (1) any connective tissue disease other than BJHS (eg, juvenile idiopathic arthritis); (2) any neurological problems, as confirmed by a neurologist; (3) OAB secondary to anatomic abnormalities (eg, ureterocele, ectopic ureter, megaureter); (4) vesicoureteral reflux, as confirmed by a voiding cystourethrogram; (5) constipation or dysfunctional voiding; (6) high PVR urine or high flow fate, as confirmed by uroflowmetry and ultrasound urinary tract studies.

There were 42 patients with BJHS and OAB, but 11 patients were excluded based on the defined criteria. A total of 31 patients participated in the investigation. There were 21 girls and 10 boys. Their ages ranged from 5-14 years.

Pretreatment Evaluation and Instructions

All children were evaluated by an ultrasound of the urinary tract. A postvoiding film was used to estimate the PVR urine. The PVR was considered high when it was > 10% of the bladder capacity seen in an ultrasound [14]. Flow rate was determined by using the weight transducer uroflowmeter device Urocap-11 Flow Analyzer, version V5.02 (Laborie Medical Tech, Quebec, Canada). All children had a urine analysis before treatment. Those with UTI were treated until they had negative urine culture and sensitivity before starting the electrical stimulation treatment. We defined UTI as the growth of > 100,000 colonies of bacteria/mL, obtained from a midstream urine sample [15]. All children

doi:10.3834/uij.1944-5784.2010.12.10
http://www.urotodayinternationaljournal.com
ISSN 1944-5792 (print), ISSN 1944-5784 (online)

with a history of recurrent UTI were given prophylactic antibiotic during the treatment period using sulphamethoxazole and trimethoprim (5 mg/kg for sulphamethoxazole; 20 mg/kg for trimethroprim). Patients were instructed to break their follow-up schedule if they developed symptoms of UTI.

Prior to treatment, all patients completed a voiding diary for 1 month. The voiding diary included a record of the quantity of liquid ingested, the number of voids/day, the quantity of urine eliminated, leakage of urine during the voiding intervals, and the episodes of nocturnal enuresis. Nocturnal enuresis was included because most of the patients were older than the age when it would be expected to occur. Additionally, some patients had secondary enuresis characterized by recurrence after a period without it. Therefore, we considered this characteristic a symptom of pathology and not delayed toilet training.

Children and their families were given information about behavioral training, such as voiding every 3 hours or at the onset of the desire to void, avoiding fluid intake 2 hours before sleep (especially tea, coffee, soda, and chocolate), and passing urine just before going to sleep.

Electrical Stimulation Treatment

All participants were treated as outpatients with superficial parasacral electrical stimulation, according to the method of Barroso et al [16]. We used 2 superficial 4 cm electrodes that were placed on each side of S3. Electrical energy was produced by a Sonopuls 992 generator (Enraf-Nonius, Netherlands). A biphasic symmetrical waveform was used. The current frequency was 10 Hz. The current intensity was increased to the maximum level tolerated by the child (8-45 mA).

Sessions lasted for 20 minutes and were conducted every other day. There was a maximum of 20 sessions. Fewer sessions were used if the physician and parent agreed that the child had attained complete success.

Measurement of Outcomes

All patients were asked to complete a voiding diary for 1 month after the last session. The diary was submitted to the urologist for assessment during the final follow-up visit.

Assessment of improvement was determined by the patient's parents or the patient (if the patient was old enough to understand) and by the urologist. The patient's self assessment used an analogue scale with a range from 0 (no improvement) to 10 (no more symptoms present); this value was multiplied by 10 to give a percentage. The physician compared the responses on the pretreatment and posttreatment voiding diaries. *Complete clinical improvement* was defined as disappearance of symptoms listed on the voiding diary and 100% response to treatment as assessed by the patient or parents; *excellent improvement* was defined as 70-80% disappearance of symptoms and 70-80% self-reported or parent-reported response to treatment; *mild improvement* was defined as 30-60% disappearance of symptoms and 30-60% self-reported or parent-reported response to treatment; *no change* was defined as < 30% improvement of the symptoms as judged by the urologist and by the patient or parents.

Chi-square was used to test the hypotheses that response rates were the same in each category with regard to age and sex. A probability < .05 was used to indicate statistical significance.

RESULTS

Patient Characteristics

During the course of treatment, 3 of the 31 children were lost to follow-up, and 2 additional children did not attend the urology clinic for the final assessment; the data of these 5 patients were not included in the final analysis. Therefore, a total of 26 children completed the treatment and their data are illustrated here.

Table 1. Number of Patients With Frequency of Urge Incontinence and Nocturnal Eneuresis Before and After Treatment (N = 26).
doi: 10.3834/uij.1944-5784.2010.12.10t1

Outcome Measure	Before Treatment		After Treatment	
	n	% n	n	% n
Urge incontinence per month				
> 10 episodes	11	57.89	2	10.53
3-10 episodes	6	31.57	5	26.31
< 3 episodes	2	10.52	12	63.15
Nocturnal enuresis per month				
> 10 episodes	10	66.6	6	40
3-10 episodes	4	26.6	6	40
< 3 episodes	1	6.6	3	20

Table 2. Clinical Outcomes Following Treatment; Probability of Significant Differences (N = 26).

doi: 10.3834/uij.1944-5784.2010.12.10t2

Outcome Measure	Complete Improvement	Excellent Improvement	Mild Improvement	No Improvement	*P*
Total patients, n	11	6	3	6	
Sex, n					
Female	8	3	2	4	.826
Male	3	3	1	2	
Age, n					
5-6 years	1	2	0	3	.247
6-10 years	9	4	3	3	
> 10 years	1	0	0	0	

The age of the patients ranged from 5 years to 14 years and were distributed as: 5-6 years (n = 6), 6-10 years (n = 19), and > 10 years (n = 1). There were 17 females and 9 males. A total of 12 of the 26 patients had a past history of using anticholinergics for treatment of OAB, but none of the patients were taking any anticholinergics during the investigation. All 26 patients showed a normal, bell-shaped uroflowmetry curve and none demonstrated PVR urine on ultrasound examination. None of our patients developed UTI during the treatment period.

Treatment Outcomes

The total number of sessions ranged from 12 to 20. Table 1 contains the distributions of the frequency of urge incontinence (UI) and nocturnal enuresis before and after treatment. After treatment, 19 out of 26 patients (73%) complained of UI (13 girls; 6 boys). Of these 19 patients, 15 had associated nocturnal enuresis (11 girls; 4 boys). None of the 7 patients without UI had enuresis.

Results of the physician's comparison of the voiding diaries before and after treatment are shown in Table 2. The parent (or patient) assessments were almost always in complete agreement with those of the urologist, so they are not presented. Of the 26 patients, 11 (42.36%) had complete clinical improvement, 6 (23%) had excellent clinical improvement, 3 (11.54%) had mild improvement, and 6 (23%) had no change. Results of the chi-square test revealed there were no significant differences in the degree of improvement with regard to the patient's sex (χ^2 = 0.896, *P* = .826) or age group (χ^2 = 7.879, *P* = .247).

DISCUSSION

OAB is a term that is applied to patients with nonneurogenic irritative voiding symptoms (previously called *urge syndrome*). The symptoms include frequency, urgency, and urge incontinence. In the present study, we used the nonpharmacologic treatment of parasacral electrical stimulation for children with OAB that was associated with BJHS.

The relationship between joint hypermobility and urinary symptoms has been discussed by many authors. de Kort et al [17] assessed the relationship between general joint hypermobility (GJH) in children and lower urinary tract symptoms presenting as nonneurogenic bladder sphincter dysfunction (ie, daytime urinary incontinence, nighttime urinary incontinence, urinary tract infection). Other symptoms included constipation and fecal soiling. Constipation was reported in 19% of boys with GJH and 4% of male controls (*P* = .02). Fecal soiling occurred more often in the group with GJH than in the control group (34% versus 18%; *P* = .07). In girls, daytime and nighttime urinary incontinence was more prevalent in the group with GJH (38% and 14%, respectively) than in the control group (13% and 2%, respectively; *P* = .004 and *P* = .02, respectively). Of the girls with GJH, 24% had a history of urinary tract infections compared with 11% of the control group (*P* = .08). The authors concluded that symptoms of nonneurogenic bladder sphincter dysfunction are more prevalent in children with GHJ than in the healthy population. In boys, this condition more commonly manifests as constipation and possibly fecal soiling, whereas in girls it manifests as urinary incontinence and possibly UTI.

The dynamics of electrical stimulation are not well known, but there are many theories. One reasonable theory is that the reflexogenic activation of hypogastric inhibitor neurons (sympathetic) and the central inhibitor of the excitatory neurons of the bladder (parasympathetic) seem to be playing the main role in the dynamics of electrical stimulation [13,18]. Various sites of electrical stimulation have been used, including the anal sphincter and intravaginal, intravesical, and the transcutaneous locations. In 2001, Gladh et al [19] conducted a study about anogenital electrical stimulation as treatment of urge incontinence in children. They reported successful treatment in their group of patients using genital and anal electrodes. Although these authors reported that the anal and genital electrodes were well tolerated by the children, they admitted that there was discomfort especially with the anal electrodes.

Hoebeke et al [11] described the first series of superficial electrical stimulation over S3, evaluated in 15 girls and 26 boys. The frequency was 2 Hz daily for 2 hours and the treatment was prolonged for 6 months in those who had satisfactory initial response on daily UI. In all, 13 patients (31%) had no response. In our study, 11 patients (42%) had complete cure, 6 (23%) had excellent improvement, 3 (12%) had mild improvement, and 6 (23%) had no change of symptoms following treatment. The advantage of our study over the previous study may be that we used a simpler method to apply the electrical stimulation, shorter sessions, and more frequent sessions (up to a maximum of 20). Hobeke et al also continued anticholinergics in some cases, which makes it difficult to the evaluate the results. In their series, there were also more boys more than girls, which is opposite of the sex distribution in our study. It is known that UI is more common in girls [20], which could have resulted in the sample difference between the 2 studies. Barroso et al [16] used methods that are similar to ours with 19 children and found that 12 patients (63.5%) had a complete clinical improvement, 6 patients (31.5%) had significant improvement, and 1 patient (5%) had mild improvement. The higher percentage of improvement in their study could be explained by the difference in patient selection; all of our patients had associated BJHS.

In our study, 12 patients had previously tried anticholinergic medications and behavioral training. However, treatment was stopped due to side effects, noncompliance with the medicine, or lack of improvement. All of these patients improved with TENS: 7 patients had complete resolution, 1 patient had excellent improvement, and 4 patients had mild improvement.

None of our children developed UTI during the treatment, including those with a previous history of UTI. These results are in contrast to those found by Snodgrass [21], who showed a 40% incidence of UTI in children with daily UI who were treated with anticholinergics and prophylactic antibiotics.

Limitations of the present study include the small sample size and lack of a control group. In addition, we did not conduct regular follow-up evaluations after stopping treatment to check for any recurrence of symptoms. This was a preliminary study and we will address these issues in future research.

CONCLUSIONS

Using transcutaneous electrical nerve stimulation as a nonpharmacological treatment for OAB in children with BJHS appears to be a viable alternative therapy. Over a short-term period, it was a safe and effective treatment. There was a significant reduction in urgency, UI, and nocturnal enuresis. If available, this procedure could be tried before pharmacological treatment.

Conflict of Interest: none declared.

REFERENCES

1. Grahame R. Joint hypermobility and genetic collagen disorders: are they related? *Arch Dis Child*. 1999;80(2):188-191.
2. Jessee EF, Owen DS Jr, Sagar KB. The benign hypermobile joint syndrome. *Arthritis Rheum*. 1980;23(9):1053-1056.
3. Grahame, R. 'The hypermobility syndrome'. *Ann Rheum Dis*. 1990;49(3):199-200.
4. Grahame R. Heritable disorders of connective tissue. *Baillieres Best Pract Res Clin Rheumatol*. 2000;14(2):345-361.
5. Arroyo IL, Brewer EJ, Giannini EH. Arthritis/arthralgia and hypermobility of the joints in schoolchildren. *J Rheumatol.* 1988;15(6):978-980.
6. Gedalia A, Person DA, Brewer EJ Jr, Giannini EH. Hypermobility of the joints in juvenile episodic arthritis/arthralgia. *J Pediatr*. 1985;107(6):873-876.
7. Gedalia A, Press J, Klein M, Buskila D. Joint hypermobility and fibromyalgia in schoolchildren. *Ann Rheum Dis.* 1993;52(7):494-496.
8. Kirk JA, Ansell BM, Bywaters EG. The hypermobility syndrome. Musckloskeletal complaints associated with generalized joint hypermobilty. *Ann Rheum Dis.* 1967;26(5):419-425.
9. Reinberg Y, Crocker J, Wolpert J, Vandersteen D. Therapeutic efficacy of extended release oxybutynin chloride, and immediate release and long acting tolterodine tartrate in children with diurnal urinary incontinence. *J Urol*. 2003;169(1):317-319.
10. Youdim K, Kogan BA. Preliminary study of the safety and efficacy of extended-release oxybutynin in children. *Urology*. 2002;59(3):428-432.
11. Hoebeke P, Van Laecke E, Everaert K, et al. Transcutaneous neuromodulation for the urge syndrome in children: a pilot study. *J Urol*. 2001;166(6):2416-2419.
12. Coulthard MG, Kalra M, Lambert HJ, Nelson A, Perry JD. Redefining urinary tract infections by bacterial colony counts. *Pediatrics*. 2010;125(2):335-341.
13. Woodhouse JB, Patki P, Patil K, Shah J. Botulinum toxin and the overactive bladder. *Br J Hosp Med (Lond).* 2006;67(9):460-464.
14. Roehrborn CG, Peters PC. Can transabdominal ultrasound estimation of postvoiding residual (PVR) replace catheterization? *Urology*. 1988;31(5):445-449.

15. Grahame R, Bird HA, Child A. The revised (Brighton 1998) criteria for the diagnosis of benign joint hypermobility syndrome (BJHS). *J Rheumatol*. 2000;27(7):1777-1779.

16. Barroso U Jr, Lordelo P, Lopes AA, Andrade J, Macedo A Jr, Ortiz V. Nonpharmacological treatment of lower urinary tract dysfunction using biofeedback and transcutaneous electrical stimulation: a pilot study. *BJU Int*. 2006;98(1):166-171.

17. de Kort LM, Verhulst JA, Engelbert RH, Uiterwaal CS, de Jong TP. Lower urinary tract dysfunction in children with generalized hypermobility of joints. *J Urol.* 2003;170(5):1971-1974.

18. Fall M, Erlandson BE, Carlsson CA, Lindström S. The effect of intravanginal electrical stimulation on the feline urethra and urinary bladder. Neuronal mechanisms. *Scand J Urol Nephrol Suppl*. 1977;44:19-30.

19. Gladh G, Mattsson S, Lindström S. Anogenital electrical stimulation as treatment of urge incontinence in children. *BJU Int*. 2001;87(4):366-371.

20. Koff SA, Murtagh DS. The uninhibited bladder in children: effect of treatment on recurrence of urinary infection and on vesicoureteral reflux resolution. *J Urol.* 1983;130(6):1138-1141.

21. Snodgrass W. The impact of treated dysfunctional voiding on the nonsurgical management of vesicoureteral reflux. *J Urol*. 1998;160(5):1823-1825.