At-home transcutaneous electrical nerve stimulation: a therapeutic alternative in the management of pediatric overactive bladder syndrome

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ABSTRACT

Introduction. In recent years, bladder electroneurostimulation or TENS (Transcutaneous Electrical Nerve Stimulation) has emerged as a new alternative in the management of lower urinary tract dysfunctions. Our objective was to evaluate the efficacy and safety of this therapy in children with overactive bladder.

Materials and methods. Prospective study of patients diagnosed with overactive bladder and treated with electroneurostimulation. The system was maintained for 6 months. The severity of urinary symptoms was assessed using the PLUTSS (Pediatric Lower Urinary Tract Scoring System) questionnaire.

Results. A total of 21 patients were included in the study, with an average age of 10 years (range: 6-16). The most frequent symptoms were incontinence (89%) and urgency (100%). Statistically significant differences ($p<0.05$) in mean PLUTSS scores between treatment initiation and treatment completion were found: PLUTSS was 17.8 (range: 10-29) at baseline, 7.21 (range: 2-16) at month 3, and 5.6 (range: 3-12) at month 6. The maximum voiding volume of all patients increased after 6 months of treatment. All patients had their quality of life improved at the end of the study.

Conclusions. Home TENS therapy is a safe and effective option in the management of overactive bladder in the pediatric population. However, further randomized studies should be carried out to protocolize and clarify the effectiveness of this therapeutic approach.

KEY WORDS: Overactive bladder; Urgency; Incontinence; Transcutaneous electrical nerve stimulation.

ELECTROESTIMULACIÓN TRANSCUTÁNEA DOMICILIARIA: UNA ALTERNATIVA TERAPÉUTICA EN EL MANEJO DE LA VEJIGA HIPERACTIVA PEDIÁTRICA

RESUMEN

Introducción. La electroneuroestimulación vesical o TENS (*transcutaneous electrical nerve stimulation*) ha surgido como nueva alternativa en el manejo de las disfunciones del tracto urinario inferior. Nuestro objetivo fue evaluar la eficacia y seguridad de esta terapia en niños con diagnóstico de vejiga hiperactiva.

Material y métodos. Estudio prospectivo de pacientes con diagnóstico de vejiga hiperactiva tratados con electroneuroestimulación. La terapia con TENS domiciliario se mantuvo durante 6 meses. Evaluamos la severidad de la sintomatología urinaria utilizando el cuestionario PLUTSS (*Pediatric Lower Urinary Tract Symptoms Score*).

Resultados. Un total de 21 pacientes (13 niñas) fueron incluidos en el estudio, con una edad media de 10 años (Rango: 6-16). Los síntomas más frecuentes fueron: incontinencia (89%) y urgencia (100%). Encontramos diferencias estadísticamente significativas ($p< 0,05$) en los valores medios del PLUTSS antes de iniciar tratamiento y al finalizar el mismo: PLUTSS inicial 17,8 (Rango: 10-29), a los 3 meses: 7,21 (Rango: 2-16), a los 6 meses: 5,6 (Rango: 3-12). El volumen miccional máximo de todos los pacientes aumentó a los 6 meses de tratamiento. Todos los pacientes sintieron una mejora en su calidad de vida al finalizar el estudio.

Conclusiones. La terapia con TENS domiciliario parece una opción segura y eficaz en el manejo de la vejiga hiperactiva, sin embargo, deben ser realizados más estudios randomizados para demostrar su efectividad y protocolizar su aplicación en los pacientes en edad pediátrica.

PALABRAS CLAVE: Vejiga Hiperactiva; Urgencia; Incontinencia; Estimulación eléctrica transcutánea.

INTRODUCTION

Lower urinary tract dysfunction (LUTD) is one of the most frequent pathologies in pediatric patients and the most frequent reason for consultation with pediatric urologists[1-3].

Traditionally, LUTD has not been properly considered by healthcare professionals and the patients' families them-

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selves[2,3]. However, this pathology has a great influence on the children's lives. On the one hand, the great variety of signs and symptoms it causes, often incapacitating (day incontinence, enuresis, dysuria, voiding urgency, and voiding frequency alteration, among others), cause stress and anxiety in the children, thus deteriorating their quality of life and impacting their social integration capacity[3-5]. And on the other hand – even though not that frequently –, free evolution without adequate management and specific treatments may cause progressive upper renal tract deterioration and chronic renal insufficiency, which would have a great impact on patients and their families[2,3].

LUTD presents in various clinical forms, with overactive bladder (OAB) being the most frequent pattern[1]. The International Children's Continence Society (ICCS) defines OAB as the presence of voiding urgency, with or without day incontinence, and usually with an increase in voiding frequency and enuresis[6]. Complications frequently associated with OAB include vesicoureteral reflux and recurrent urinary tract infections (UTI).

In spite of its high frequency and pathogenic potential, there is still no optimal therapeutic alternative for OAB management. Standard urotherapy and constipation management measures are little aggressive, but only effective in 25-45% of patients[1,7,8]. Today, anticholinergics are the main drug of choice, but with low treatment adherence owing to the many adverse effects they cause[1,9].

Bladder electroneurostimulation (ENS) has become a new alternative in the management of patients with various voiding disorders[10]. However, the scientific literature currently available in this field is scarce.

The objective of our work is to assess transcutaneous ENS (TENS)'s safety and effectiveness at the sacral level in pediatric patients diagnosed with OAB in our reference healthcare area.

MATERIALS AND METHODS

Prospective and observational study including patients diagnosed with OAB and treated with TENS at the sacral level. Follow-up took place from January 2018 to December 2018.

Patients aged 5-16 and assessed in our pediatric urodynamics unit owing to LUTD with final diagnosis of OAB were included. Parent consent was requested to participate in the study.

Patients with associated urological pathology, increased post-void residual volume following ultrasound examination, neurogenic dysfunction, mixed LUTD, or UTI at assessment were excluded from the study, as well as those patients undergoing specific drug treatment for OAB management up to two months prior to study assessment.

At baseline, all patients with suspicion of LUTD underwent control ultrasound examination (to rule out associated urological pathology), urinary sediment test, urine culture, and flowmetry; a 48-hour voiding calendar was also recorded. OAB diagnosis was established according to the ICCS's definition[6], with the presence of voiding urgency – with or without incontinence –, and tower-shaped or bell-shaped on uroflow curve, and abcense of postvoidiing residue; all these symptoms in absence of urinary tract infection. Constipation diagnosis was carried out according to Rome IV criteria[11].

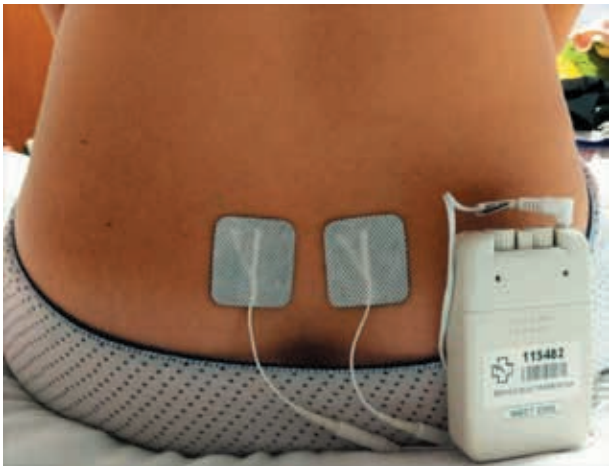

Figure 1. Cutaneous electrode placement in the sacral region, at the level of S2-S3.

Once OAB diagnosis had been established, all patients received standard urotherapy and constipation management measures – if needed – for 3 months. Following this initial period, all patients with persistent symptoms – in spite of these measures – were eligible for TENS treatment versus drug therapy (oxybutynin or solifenacin).

Once TENS therapy at the sacral level had been selected, both patients and their families directly in charge of them were educated in the use of the electrical nerve stimulation system. Then, the therapy was carried out at home[12].

Technique

Two surface electrodes are placed at the cutaneous level, in the sacral region (S2-S3), through which electricity is directed towards the sacral plexus (voiding's parasympathetic center) (Fig. 1). Electricity parameters used in TENS therapy include frequency (in hertz, Hz), pulse width – which determines the duration of each impulse – (in microseconds, μs), and pulse wave's intensity or height (in milliamps, mA). In our unit, the parameters used were 10 Hz and 200 μseg. Regarding mA, they were individually regulated and established according to the patient' maximum tolerated intensity without pain. The instrument used during therapy was UroSTIM 2.0, specifically designed for LUTD management and widely used in the adult population. Sessions took place daily, and they lasted for 20 minutes. Therapy was maintained for 6 months at home.

Table 1. Pediatric lower urinary tract malfunction scale (PLUTSS- Pediatric Lower Urinary Tract Scoring System)

1. Does your child have daytime wetting?	No 0	Sometimes 1	1-2 times a day 3	Always 5
2. To what extent?	Humid underwear 1	Underwear and trousers 3	Soaked clothes 5	
3. Does your child have night wetting?	No 0	1-2 nights a week 1	3-5 nights a week 3	6-7 nights a week 5
4. To what extent?	Humid sheets 1	Soaked sheets 4		
5. How many times does your child urinate?	< 7 a day 0	≥ 7 a day 1		
6. Does your child strain while urinating?	No 0	Yes 4		
7. Does your child have pain while urinating?	No 0	Yes 1		
8. Does your child urinate with pauses?	No 0	Yes 2		
9. Does your child go to urinate again after finishing urinating?	No 0	Yes 2		
10. Does your child say a sudden need of urinating?	No 0	Yes 1		
11. Does your child try to hold urinating with abnormal maneuvers? (for example, by crossing his/her legs)	No 0	Yes 2		
12. Does your child get wet after sudden need of urinating?	No 0	Yes 2		
13.Does your child have constipation?	No 0	Yes 1		
Quality of life				
If your child has the symptoms previously described, does this impact his/her family, social, or school life?	No 0	Sometimes 1	Yes, indeed 2	He/she is seriously impacted 3

Patient follow-up was carried out in external pediatric urology consultations, in series. Voiding symptom severity was established in each consultation using the PLUTSS[13] (Pediatric Lower Urinary Tract Scoring System) questionnaire (Table 1), previously validated by our working group. Scores of 8.5 points or higher in this questionnaire correspond to LUTD diagnosis (maximum score: 35 points), and the higher the score, the more severe the dysfunction. A voiding calendar was recorded prior to each visit in order to assess patients' bladder capacity and voiding frequency. In addition, patient satisfaction regarding LUTD was assessed in each visit. All adverse effects reported during treatment were recorded.

The analytical study was developed with the SPSS 22® statistical software. A descriptive analysis of all variables included in the study was carried out. Quantitative variables were expressed as mean ± standard deviation. Qualitative variables were expressed as absolute value and percentage. Mean comparison was performed using the Wilcoxon test for coupled data. In all tests conducted, $p<0.05$ values were considered as significant.

RESULTS

A total of 148 patients with LUTD were assessed in our pediatric urodynamics unit during the study period, where OAB presented a prevalence of 71% (103 patients). Of the 103, up to 27 (26%) responded to standard urotherapy and constipation management measures. The remaining patients (76) were eligible for treatment initiation with drug therapy or sacral TENS.

TENS treatment was postponed – randomly based on system availability in the unit – in 21 of the 76 patients with persistent clinical signs in spite of the initial basic measures, with a 100% acceptance rate. A total of 21 patients diagnosed with OAB were included in the study, 13 girls (62%) and 8 boys (38%). Mean age at sacral TENS treat-

Table 2. Comparison before and after sacral TENS therapy.

	Baseline	*6 months after treatment initiation*	*p-value (Wilcoxon)*
PLUTSS score	17.8 (range: 10-29)	5.6 (range: 3-12)	p< 0.001
No. of voidings	8.9 (range: 6-22)	5.5 (range: 4-7)	p< 0.05
MVL (ml)	121.25 (range: 50-350)	186.8 (range: 300-80)	p> 0.05

PLUTSS: Pediatric Lower Urinary Tract Scoring System; MVL: Maximum voiding level in ml (leaving the first voiding of the day aside).

ment initiation was 10 years (range: 6-16 years). One of the female patients had a XXX genotype, another one had a heart pathology operated on at birth, and the remaining patients had no previous medical history.

The ultrasound examination carried out before the procedure was normal in all patients. Flowmetry had a tower pattern, with no sphincter activity in any case. None of the patients had an altered urine sediment before treatment initiation.

Up to 11 patients (52%) had previously received anticholinergic treatment. In 5 patients, the reason for discontinuation was the lack of response, and in the remaining 6, the presence of adverse effects (face blush mainly). 100% of patients in this group had their symptoms totally or partially improved with the introduction of TENS therapy.

The most frequent symptoms at diagnosis were urgency, present in 100% of patients, and incontinence, present in 89% of the series (19 patients). Enuresis was noted in 38% of patients (8).

PLUTSS questionnaire scores during follow-up decreased progressively. Baseline PLUTSS score was **17.8** (range: 10-29), PLUTSS score at 3 months was **7.21** (range: 2-16), and PLUTSS score at 6 months was **5.6** (range: 3-12). Statistically significant differences were found between mean scores at treatment initiation and mean scores following treatment completion (Table 2).

Mean voiding number before TENS treatment initiation (8.9) was significantly higher than after TENS treatment completion (5.5) (Table 1). Patient bladder capacity improved after TENS treatment completion, with a 65 ml increase in mean maximum voiding level (MVL) (Table 1). Even though such difference was not statistically significant, it was clinically relevant for patients. All patients had their quality of life improved after the study.

No complication during TENS application was recorded. All patients had their quality of life improved after the study.

DISCUSSION

OAB is a highly prevalent dysfunction in the pediatric population, with potentially severe consequences in the long term unless adequate treatment is implemented. However, alternatives available up until now are limited.

OAB patient management is progressively changing. Formerly, this pathology, as well as most dysfunctions, was underestimated. This caused an absence of treatment and patient follow-up, with adverse effects on the upper urinary tract in the long term[2]. Various resolution-focused treatments were subsequently developed, but none of them has demonstrated to be totally effective and free from adverse effects[1,9].

Of all therapeutic possibilities, standard urotherapy and basic constipation management measures represent the most widely considered option. This therapeutic alternative is little aggressive and accessible to all patients. However, good result rates range between 25 and 40%[1,7,8], with most patients requiring additional therapies. In this respect, anticholinergics (with oxybutynin standing out as the only antimuscarinic drug currently approved by the Food and Drug Administration for pediatric use), improve symptoms in approximately 70% of patients. However, total symptom resolution is only achieved in 30% of cases[14-16]. In addition, despite causing a positive response in most OAB patients, treatment adherence is limited in these cases, with high treatment withdrawal levels, since the adverse effect rate with these drugs (with facial blush and constipation standing out) is above 50%, so therapy needs to be discontinued[15,16].

Currently, in an attempt to fight these limitations, ENS has become a new alternative in pediatric OAB patient management[10]. Although the exact mechanism through which this therapy acts on bladder nervous control has not been demonstrated since it was first described in 2001 by Bower et al.[17], multiple authors have subsequently reported good results with this technique[18-24]. Furthermore, the adverse effects described up until now are scarce and mild (dermatitis following electrode placement)[18-24]. In our study, the results regarding effectiveness and complications are consistent with those from other studies.

In 2014, Tugtepe et al.[25] demonstrated TENS effectiveness over anticholinergics, in a study where TENS was applied in 11 patients resistant to previous drug treatment, with a response rate over 90%. In our study, 52% of patients had previously received anticholinergics, and all of them improved as a result of TENS initiation.

Up until now, multiple studies have described improvement in constipation in OAB patients as a result of TENS treatment initiation[10,22,26]. Veiga et al.[22] (2016) conclude that ENS has an impact both on OAB and on constipation, with favorable results in both cases, but independently – the responses of both conditions are not related to one another. In our study, as in most publications up until now, ENS's direct effect on OAB-related constipation could not be assessed, since none of our patients had received TENS treatment before basic urotherapy and baseline constipation control measures.

CONCLUSIONS

At-home ENS at the sacral level seems a safe and effective option in the management of OAB in the pediatric population. Most patients and their parents are satisfied with the results after treatment application. In addition, it has an easy and quick learning process for at-home daily application. However, further randomized studies are required to demonstrate effectiveness and protocolize application in pediatric patients.

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