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ORIGINAL ARTICLE

Posterior tibial nerve stimulation as treatment for the overactive bladder

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KEYWORDS

Neuromodulation;
Overactive bladder;
Posterior tibial nerve
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ABBREVIATIONS

DO, detrusor overac-
tivity;
OAB, overactive blad-
der;
PTN(S), posterior
tibial nerve (stimula-
tion);
RCT, randomised

Abstract Objective: To evaluate the efficacy of posterior tibial nerve stimulation (PTNS) as a treatment for the overactive bladder (OAB) resistant to medical treatment.

Patients and methods: The study included 60 patients, comprising 55 women (92%) and five men (8%) with a mean (SD) age of 41.4 (10.8) years, who presented to the Urology Department of Benha University Hospital from June 2010 to October 2012. All patients were assessed initially by taking a history, a physical examination, urine analysis, routine laboratory investigations, and a urodynamic evaluation in the form of flowmetry, cystometry, and a pressure-flow study in some cases. A voiding diary (daytime and night-time frequency, voiding volume, and leakage episodes) was completed by all patients, and all underwent 12 sessions of PTNS using a personal computer-based system, and were reassessed after the sixth session, at the end of the course, and at 3 and 6 months after the last session, using the same methods as in the baseline visit.

Results: There was a statistically significant improvement in all the variables assessed. No infection or failure of the PTNS mechanism was detected while using

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controlled trial;
TENS, transcutaneous
neuromodulation
stimulation

the technique, but there were rare instances of minor bleeding and a temporary painful feeling at the insertion site.

Conclusion: PTNS is safe, and gives statistically significant improvements in the patient's assessment of OAB symptoms.

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Introduction

An overactive bladder (OAB) includes urgency, frequent voiding, nocturia and urge incontinence [1]. The symptoms of an OAB often remain a therapeutic problem, despite the optimal use of conservative treatment methods, including drug therapy, behavioural therapy, pelvic floor exercises and biofeedback [2]. Anticholinergic therapy is the first therapeutic line for the OAB, but it is limited by its side-effects or if the therapeutic goal is not attained. In that situation neuromodulation is an effective alternative treatment and its efficacy has been well established [3].

For thousands of years acupuncture has played a key role in the traditional Chinese medicine. This technique has been used in the treatment of lower urinary tract dysfunctions such as enuresis, incontinence, frequency, urgency, dysuria and retention of urine, by acting on the so-called S6 region located in the posterior border of the tibia, 5 cm above the tibial malleolus [4].

Knowledge of the afferent nerves going from the posterior tibial nerve (PTN) to the sacral centre of micturition facilitated the invention of percutaneous PTN stimulation (PTNS) for managing the symptoms of an OAB [5]. Inhibition of detrusor activity (DO) by peripheral neuromodulation of the PTN was first described by McGuire et al. [6] and recent authors [7–9] confirmed a 60–80% positive response rate after 10–12 weekly treatments with PTNS.

The precise mode of action of neuromodulation is unknown. Its effects can be explained by the modulation of reflex pathways at the spinal cord level [10]. Paradoxically, neuromodulation also works in patients with urinary retention even if there is no anatomical obstruction. It was postulated that neuromodulation interferes with the increased afferent activity arising from the urethral sphincter, restoring the sensation of bladder fullness and reducing the inhibition of the detrusor muscle contraction [11]. Thus, the aim of the present study was to evaluate the efficacy of PTNS as a treatment for OAB that was resistant to medical treatment.

Patients and methods

This study was a case series evaluating the efficacy of PTNS in management of OAB, and included 60 patients (55 women and five men, mean age 41.4 years, SD 10.8) who presented to the Urology Department of Benha

University Hospital from June 2010 to October 2012. Informed written consent was obtained from all patients after the study protocol was approved by the Research Ethics Committee, Faculty of Medicine, Benha University. The inclusion criteria for patients with symptoms of OAB were; age ≥ 18 years, with no previous history of continence surgery, or history of current bladder malignancy, and who had failed medical therapy for ≥ 3 months with different types of anticholinergic agents, either as a single drug or a combination. The exclusion criteria included; pregnant women, or planning to become pregnant during the course of treatment, patients with pacemakers or implantable defibrillators, uncorrectable coagulopathies, patients with nerve damage that might affect either the PTN or pelvic floor function, or a current UTI. All patients were assessed initially by taking a history, a physical examination, urine analysis, routine laboratory investigations, and a urodynamic evaluation in the form of flowmetry, cystometry, and a pressure-flow study in some cases. A 1-day voiding diary (daytime frequency, daytime voiding volume, daytime leakage episodes, night-time frequency, night-time voiding volume, night-time leakage episodes) was completed by all patients. A frequency/volume chart, recording symptoms of leakage episodes per day and night, was used to evaluate the patients before and after PTNS.

PTNS

The technique used consisted of inserting a 0.22-mm needle ≈ 5 cm above the medial tibial malleolus, approximated as three finger breadths. The needle was connected to an electric generator producing external pulses of 0–10 mA, which increased progressively until the response was achieved in the form of flexor muscle contraction of the first toe, fanning of all toes, or tingling sensation in the sole. The voltage remained at one point below the stimulus that generated the muscular contraction.

Patients had to experience a tolerable but not painful sensation. If there was no response or there was pain at the insertion site, the stimulation device was switched off and the needle was repositioned. The treatment was repeated weekly for a 30-min period for 12 weeks.

All the patients had 12 sessions of PTNS using the Urgent™ system (Uroplasty, Inc., Minnetonka, MN,

USA), and were re-evaluated after the sixth session, at the end of the course, and at 3 and 6 months after the last session, using the same methods as used for the baseline visit.

Categorical data are presented as the number and percentage, while quantitative data were expressed as the mean (SD). A paired *t*-test, McNemar's test and Friedman's test were used to assess significant differences, with $P < 0.05$ taken to indicate statistical significance.

Results

There was a statistically significant difference ($P < 0.001$) when analysing both the daytime and night-time voiding frequency between before and after six and 12 sessions of PTNS, the changes in voiding volume before and after PTNS, and in leakage episodes (day and night time, ($P < 0.001$).

Comparing the results at baseline, the last session of PTNS, and 3 and 6 months after the last session showed that the mean frequency per day and night at 3 and 6 months slightly increased from that at the last session of treatment, but remained lower than at baseline. The mean voiding volume per day and night also decreased slightly from the value after the last treatment, but remained higher than at the baseline. Although the mean number of leakage episodes per day and night increased slightly from that after the last treatment, it remained lower than at baseline. All these differences were statistically significant ($P < 0.001$; Table 1).

The study group included 48 patients with DO (80%) and 12 without DO (20%). After 6 weeks of treatment, 12 (25%) patients who had DO became normal, while those with no DO remained unchanged. Moreover, after 12 weeks of treatment, half of the patients with DO became normal but all patients with no DO remained unchanged. At 3 months later there was no change in these values from those measured after the last session. Final-

ly, at 6 months after the intervention, 12 (25%) of the patients with DO became normal, while those patients with no DO remained the same.

There was no infection or failure of the PTNS mechanism detected when using the technique, but there was minor bleeding (five cases) and a temporary painful feeling at the insertion site (10 cases), classified as grade I according to the modified Clavien system [12].

Discussion

OAB is a common condition in adults, with an effect on their physical, psychological and social well-being. Moreover, it is an important economic burden to the health services [13]. The PTN is a mixed nerve containing sensory and motor fibres. The correct placement of the needle electrode induces a motor and sensory response. Centrally the PTN projects to the sacral spinal cord in the same area where the bladder projection is located. The sacral micturition centre and the nucleus of Onuf are most probably the areas where the therapeutic effect of neuromodulation of the bladder, by PTNS, takes place [9].

From our results, the current study showed clinically significant improvements in all measured values. Vandoninck et al. [9] reported a subjective response in 64% and an objective response in 57% of their patients (defined as $\geq 50\%$ reduction in urinary leakage episodes per 24 h). Ruiz et al. [4] reported statistically significant improvements in daytime frequency, daytime voiding volume, and night-time frequency in patients using PTNS. Of 26 women with frequency or urgency, 12% rated the results as excellent, 65% as favourable, 15% as fair and 8% considered there was no difference. In another study, PTNS produced a statistically significant improvement in LUTS, especially daytime and night-time voiding frequency, volume and leakage episodes [8]. Govier et al. [7] showed a 25% reduction in mean daytime voids, a 21% reduction in mean night-time

Table 1 The changes from the baseline values after 12 sessions, and at 3 and 6 months after the last session.

Variable	Mean (SD)			
	Before	After 12 sessions	3 months	6 months
Frequency/day	10.8 (0.99)	5.0 (3.60)*	6.2 (3.01)*,†	6.8 (2.90)*,†,‡
Voiding volume/day (mL)	124 (22.6)	220 (60.5)*	194 (50.8)*,†	196 (55.8)*,†
Leaking episode/day	3.7 (2.3)	1.6 (1.2)*	1.8 (1.4)*,†	1.8 (1.6)*,†
Frequency/night	7.0 (1.3)	2.8 (2.1)*	3.6 (2.2)*,†	3.6 (2.2)*,†
Voiding volume/night (mL)	144 (41.1)	220 (60.5)*	190 (49.4)*,†	196 (55.8)*,†
Leaking episode/night	2.7 (1.7)	1.0 (0.92)*	1.2 (0.95)*,†	1.4 (0.97)*,†,‡
<i>Urodynamic</i>				
Maximum urinary flow rate (mL/s)	20.52 (2.6)	18.84 (4.1)*	18.49 (1.8)*	20.23 (2.6)
Residual urine volume (mL)	17.85 (4.2)	39.54 (36.3)*	25.35 (3.4)	20.11 (3.2)
Voided urine volume (mL)	152.7 (39.7)	260.3 (26.1)*	255.2 (22.2)*	250.1 (22.4)*
Cystometric capacity (mL)	282.2 (20.11)	380.6 (13.97)*	375.5 (18.12)*	320.3 (19.60)

* Significant vs. before intervention.

† Significant vs. after 12 sessions.

‡ Significant vs. after 3 months, by a paired *t*-test.

voids, and a 35% improvement in urge incontinence. Van der Pal et al. [14] reported a subjective response of 55% (defined as a patient requesting continuous chronic treatment to maintain the response) and an objective response of 37% (defined as a decrease in symptoms of > 50%). Also, PTNS had a subjective efficacy of 64% and an objective efficacy of 46–54% in a non-neurogenic population with complaints of OAB [15]. MacDiarmid et al. [3] reported on 33 patients who responded to an initial 12 sessions of PTNS and who were offered additional treatment sessions at varying intervals for a further 9 months; 94% of patients considered themselves to be cured or improved at 6 months, and 96% at 12 months.

Arrabal-Polo et al. [16] reported a statistically significant improvement in diurnal frequency, urgency and urge incontinence. Furthermore, Peters et al. [17], in a randomised controlled trial (RCT) of 100 patients, compared PTNS with medication; 55% of patients in the medication group and 80% in the PTNS group considered themselves to be cured or improved. In another RCT including 220 patients, comparing PTNS with a sham treatment, 21% of those in the sham group and 55% in the PTNS group had a moderate or marked improvement in overall bladder symptoms at 13 weeks [18]. Also, Klinger et al. [19] used this technique in 15 patients who had a urodynamic evaluation, and reported an improvement in bladder instability. Urodynamic evidence of bladder instability was eliminated in 11 of them after the treatment. Recently, Peters et al. [20], using PTNS, reported that the improvements in urge incontinence, frequency, moderate-to-severe urgency episodes and night-time voids, from voiding diaries at 6, 12, 18 and 24 months, were statistically significant compared to baseline (before the initial 12 weekly treatments).

Janssen et al. [21] used the Urgent-SQ™ system, an implant that is surgically placed near the PTN and activated by an external pulse generator, allowing for ‘on-demand’ PTNS, with no need for needle insertion. After 9 years of clinical experience they reported that implant-driven PTNS with the Urgent-SQ is a safe therapy for OAB. Recently, Barroso et al. [22] reported a study on 22 consecutive patients treated by PTNS and 37 by transcutaneous neuromodulation stimulation; there was no significant difference between these treatments in the variables assessed.

Durability of PTNS

Levin et al. [23] reviewed reports on PTNS for treating idiopathic OAB in women, published in English from January 2000 to August 2010, and identified using the Medline/PubMed, Cochrane and Embase databases. They found success rates of 54–93% and limited high-quality data on PTNS for OAB in women. Furthermore,

it was reported that continuous therapy is necessary in patients with OAB that is treated successfully by PTNS, and the efficacy of PTNS can be reproduced successfully in formerly treated patients [14].

Stoller afferent nerve stimulation has a short-term positive effect in patients with resistant OAB, but it was also established that the efficacy was maintained at 1 year in only 23% of subjects [24]. However, Geirsson et al. [25] reported that PTNS or traditional acupuncture produced no difference in voiding frequency, or mean and maximum voided volume. Also, Fjorback et al. [26] noted that PTNS had no effect or failed to suppress detrusor contractions in patients with neurological DO.

Safety of PTNS

No infections or failures of the PTNS mechanism were detected in the present study, although there were rare cases of minor bleeding and a temporary painful feeling at the insertion site. Most studies reported that there were no serious adverse events associated with PTNS for OAB. In the RCT [17] comparing PTNS with anticholinergic medication, in the PTNS group there was one report of a worsening of incontinence, and reports of haematuria, headache, inability to tolerate stimulation, generalised swelling, intermittent foot/toe pain, leg cramps, and a vasovagal response to needle placement. Constipation and dry mouth were reported less frequently in the PTNS group than in the medication group. Also, in the other RCT [18] of 220 patients comparing PTNS with sham treatment, there were some adverse symptoms, i.e. bleeding at the needle site (3%), ankle bruising (1%), discomfort at the needle site (2%) and tingling in the leg (1%), but no adverse events reported in the sham group. Throbbing pain at the needle site, stomach discomfort and foot pain were also reported previously [7].

Finally, from the previous discussion and according to the other reports, we suggest that PTNS, which is minimally invasive and easily applied, is associated with an improvement in OAB symptoms and with negligible side-effects. However, maintenance therapy should be considered as the next step in future research [27–29].

In conclusion, PTNS is safe, and is associated with statistically significant improvements in patient-assessed OAB symptoms. Although initial studies showed promise, a more comprehensive evaluation of PTNS is needed to support its universal use for treating the OAB.

Conflict of interest

None.

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