Maintenance Percutaneous Posterior Nerve Stimulation for Refractory Lower Urinary Tract Symptoms in Patients with Multiple Sclerosis: An Open Label, Multicenter, Prospective Study

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Purpose: Percutaneous tibial nerve stimulation is an effective second line therapy for lower urinary tract symptoms. Data on percutaneous tibial nerve stimulation maintenance treatment are scarce. In this study we evaluate its effectiveness and propose an algorithm of percutaneous tibial nerve stimulation maintenance treatment in patients with multiple sclerosis.

Materials and Methods: In this prospective, multicenter, open label trial consecutive patients with multiple sclerosis and lower urinary tract symptoms unresponsive to medical therapy were treated with 12 weekly sessions of percutaneous tibial nerve stimulation. Responder patients (50% or greater improvement of lower urinary tract symptoms as measured by the patient perception of bladder condition questionnaire) entered a maintenance phase with individualized treatment frequency based on patient response. Lower urinary tract symptoms were assessed using a 3-day frequency volume chart, urodynamics and patient perception of bladder condition questionnaire. Treatment satisfaction was evaluated using a global response assessment scale and a treatment satisfaction visual analog scale.

Results: A total of 83 patients were included in the study and 74 (89%) responded to initial treatment. Persistent efficacy occurred in all initial responders after a mean treatment of 24 months. The greatest frequency of maintenance percutaneous tibial nerve stimulation was every 2 weeks. Lower urinary tract symptoms and patient treatment satisfaction improved with time compared to initial treatment ($p < 0.05$). Bladder diary parameters and voiding parameters improved compared to baseline ($p < 0.05$).

Conclusions: Prolonged percutaneous tibial nerve stimulation treatment leads to a persistent improvement of lower urinary tract symptoms in patients with multiple sclerosis.

Abbreviations and Acronyms

BCI = bladder contractility index
BVE = bladder voiding efficiency
DO = detrusor overactivity
DSD = detrusor sphincter dyssynergia
EDSS = expanded disability status scale
GRA = global response assessment
INFB = interferon-beta
LUTS = lower urinary tract symptoms
MS = multiple sclerosis
OAB = overactive bladder
$PdetQ_{max}$ = detrusor pressure at maximum flow rate
PPBC = patient perception of bladder condition
PTNS = percutaneous tibial nerve stimulation
Q_{max} = maximum flow rate
QoL = quality of life
SNM = sacral neuromodulation
TS = treatment satisfaction
VAS = visual analogue scale

Accepted for publication September 17, 2013.

* Nothing to disclose.

† Financial interest and/or other relationship with Medtronic, Allergan and Astellas.

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Editor's Note: This article is the second of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 878 and 879.

0022-5347/14/1913-0697/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2013.09.036
Vol. 191, 697-702, March 2014
Printed in U.S.A.

Key Words: transcutaneous electric nerve stimulation, multiple sclerosis, urinary incontinence, urination disorders

LOWER urinary tract symptoms such as increased daytime frequency, nocturia, urgency, urinary incontinence and voiding difficulties are common in multiple sclerosis, being reported by 50% to 90% of patients with MS.[1–4] LUTS tend to become more severe with time, possibly leading to urinary retention and upper urinary tract complications.[5] Anticholinergic or antispasmodic medication, behavioral therapy and/or clean intermittent self-catheterization are current first line treatment options.[6,7] However, patients with MS experience a wide range of neurological dysfunctions such as cognitive impairment that can be precipitated by the use of anticholinergics, and limited manual dexterity may limit the use of clean intermittent self-catheterization. Detrusor injection of botulinum toxin is a second line therapy whose efficacy and safety in the long term have been poorly investigated in patients with MS to date.[6,7] Further treatment options include SNM, which has been shown to be effective for LUTS in neurological patients with a particularly high success rate in MS populations.[8] However, these patients need regular magnetic resonance imaging, thus limiting the use of SNM in this population. If those treatments fail, more invasive approaches may be offered to patients such as suprapubic catheters and/or surgery.[9–11] However, patients are often reluctant to undergo such invasive treatments. In this setting PTNS has been demonstrated to be a safe and effective second line treatment for patients with MS with a reported subjective and objective cure rate between 60% and 80%.[12–16] Initial PTNS treatment is usually delivered during a period of 10 to 12 weeks and generally followed in responders by a poorly defined maintenance therapy.[17] In this study we evaluate its effectiveness and propose an algorithm of PTNS maintenance treatment in patients with MS who responded to initial treatment in a prospective, multicenter, open label trial.

MATERIALS AND METHODS

Consecutive males and females with MS with LUTS unresponsive to medical treatment were recruited in 3 tertiary referral centers and prospectively treated with 12 weekly sessions of PTNS followed by an individualized maintenance protocol. All patients were evaluated with saline urodynamics before entry into the study using a standard protocol following International Continence Society guidelines.[18] All recruited patients were counseled and gave their consent to participate.

Inclusion and Exclusion Criteria

Inclusion criteria were age 18 years or older; being affected with relapsing remitting, secondary progressive or primary progressive MS; being affected with LUTS (OAB symptoms and/or voiding difficulties, namely hesitancy, poor or slow flow, prolonged and interrupted flow, incomplete bladder emptying and straining to void); unresponsiveness to at least 2 anticholinergics and/or 2 or more α-blockers; urodynamic diagnosis of DO and/or detrusor underactivity and/or DSD. The selection of these urodynamic inclusion criteria reflects the evidence reported in the literature on the efficacy of PTNS in patients with MS, and urodynamic diagnosis of DO and/or detrusor underactivity and/or DSD.[12–16]

The main exclusion criteria were urinary tract infections, EDSS greater than 8, pregnancy and cardiac pacemakers. Patients who were unable to attend/complete the weekly treatment sessions were also excluded from study.

Assessments

LUTS were assessed using a 3-day frequency volume chart and patient perception of bladder condition questionnaire,[19] before and after 12 weeks of treatment. Patients were defined as responders if they reported an improvement in LUTS of greater than 50% as measured by the PPBC questionnaire.[13,17,20] Patient perception of treatment satisfaction was also assessed using a visual analog scale (TS-VAS) and a 7-level GRA scale at the end of the 12 PTNS sessions.[21–23] For the TS-VAS, patients were asked to mark their level of satisfaction on the 100 mm horizontal scale. The VAS score was recorded as the distance in millimeters from the start of the horizontal bar to the patient's mark, with 0 indicating no satisfaction and 100 indicating very satisfied.

Urodynamics

Urodynamics were performed before the start and 24 months after PTNS. $PdetQ_{max}$, Q_{max}, BCI and BVE were also calculated. BCI was derived from the formula, $BCI = PdetQ_{max} + 5\ Q_{max}$. BVE (a measure of bladder emptying that reflects bladder contractility against urethral resistance) was derived from the formula, [voided volume/total bladder capacity] $\times$ 100. The postmicturition residual was measured by transabdominal ultrasonography before and after treatment.

PTNS Procedure and Treatment Schedule

Initial treatment involved weekly 30-minute sessions for 12 weeks. Electrical stimulation was applied by the unilateral insertion of a 34 gauge needle electrode at a 60-degree angle, approximately 5 cm cephalad to the medial malleolus and slightly posterior to the tibia. A PTNS surface electrode was placed on the ipsilateral calcaneus. The PTNS lead set was connected to the Urgent® PC stimulator and a current level between 0.5 and 9 mA was selected using charge compensated 200