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TREATMENT INTERVAL FREQUENCY OF PERCUTANEOUS TIBIAL NERVE STIMULATION: 18-MONTH RESULTS FROM THE STEP STUDY

Hypothesis / aims of study

Overactive bladder syndrome (OAB) affects the lives of millions of people. Neuromodulation therapy uses electrical stimulation to target specific nerves in the sacral plexus that control bladder function. The Urgent® PC Neuromodulation System delivers percutaneous tibial nerve stimulation (PTNS) that targets the sacral plexus from an accessible, minimally invasive entry point into the nervous system, the posterior tibial nerve. The aim of the Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation (STEP) Study is to evaluate long-term therapy with PTNS therapy for OAB with an initial prescribed tapering protocol followed by a Personal Treatment Plan. The objective of this review is to evaluate the treatment interval frequency through 18 months of sustained therapy.

Study design, materials and methods

Subjects participating in the multi-center, randomized, double-blind SUmiT Trial who met the primary endpoint of success after 12 weekly PTNS treatments were invited to participate in the long term STEP Study. Subjects were prescribed a tapering protocol of PTNS for 3 months (2x2 weeks, 2x3 weeks, 1x4 weeks) and then received ongoing therapy according to a Personal Treatment Plan. The frequency of treatment was determined by the investigator and subject to maintain sustained improvement in the subject's OAB symptoms. The mean ± SD and median PTNS treatments per month were calculated at 3-month intervals through 18 months. Follow-up OAB-q questionnaires were completed every 3 months, and 3-day voiding diaries were completed every 6 months from initial treatment baseline. Voiding diaries were analyzed at 6-month intervals with recorded parameter mean ± SD at each time point and changes from baseline. Adverse events were recorded throughout the trial.

Results

Of the 60 PTNS subjects eligible to continue into the STEP Study, 87% (52/60) were enrolled. Of the 52 subjects, all 52 completed the tapering protocol and followed-up at 6 months, 49 received the ongoing treatment at individualized frequencies through 9 months, 46 through 12 months, 45 through 15 months, and 42 continued through 18 months. The 42 subjects who returned for their 18-month follow-up received a mean and median of 1.1 PTNS treatments per month. A total of 22 adverse events in 9 subjects were reported; no treatment-related adverse events, 4 of unknown origin-all resolved (UTI, puffing of feet, slow stream, pinched nerve pain), and 18 not treatment-related. Voiding diary parameters at 6, 12, and 18 months were significant for improvement compared to baseline for frequency, urge incontinence episodes, nighttime voids and moderate to severe urgency episodes ($p < 0.0001$ for all parameters and time intervals). The OAB-q Symptom Severity Score and Health Related Quality of Life scores remained significantly improved from baseline at 6, 9, 12, 15, and 18 months ($p<0.001$ for all domains).

Table 1: Summary of PTNS Treatments Per Month in the STEP Study

Follow-up interval from baseline	n	Mean ± SD	Median
3-6 months	52	1.9 ± 0.5	1.8
6-9 months	49	1.3 ± 0.8	1.1
9-12 months	46	1.2 ± 0.6	1.1
12-15 months	45	1.2 ± 0.7	1.1
15-18 months	42	1.1 ± 0.6	1.1

Table 2: Voiding Diary Results (Mean ± SD)

Visit	n	Frequency	Nighttime voids	Urge incontinence episodes	Moderate to severe urgency
Baseline	48	12.4 ± 2.6	2.8 ± 1.6	3.8 ± 3.3	8.6 ± 3.8
13 weeks (after 12 treatments)	48	9.2 ± 2.2	1.8 ± 1.2	0.8 ± 1.5	3.4 ± 2.9
6 months	48	9.5 ± 2.9	2.1 ± 1.5	0.8 ± 1.5	3.9 ± 3.4
12 months	42	8.9 ± 2.0	1.8 ± 1.3	0.6 ± 1.2	3.2 ± 3.3
18 months	36	8.8 ± 2.4	1.8 ± 1.6	0.6 ± 1.0	2.8 ± 3.3

Table 3: Change in Voiding Diary Parameter from Baseline (Mean ± SD)
(Pr > |t|= <0.0001 for all parameters and time intervals)

Visit	n	Frequency	Nighttime voids	Urge incontinence episodes	Moderate to severe urgency
13 weeks (after 12 treatments)	48	-3.2 ± 1.9	-1.0 ± 1.2	-3.0 ± 3.0	-5.2 ± 3.6
6 months	48	-2.9 ± 2.2	-0.7 ± 1.1	-3.0 ± 3.3	-4.7 ± 3.4

12 months	42	-3.3 ± 2.1	-0.9 ± 1.3	-2.7 ± 3.0	-5.1 ± 4.0
18 months	36	-3.3 ± 2.1	-0.9 ± 1.1	-2.4 ± 3.1	-5.0 ± 3.6

Interpretation of results

Subjects who clinically respond to initial 12 weekly 30-minute PTNS sessions can successfully sustain safe, clinically meaningful improvement of their OAB symptoms with continued PTNS therapy according to a Personal Treatment Plan determined jointly with their clinician. This plan may best be determined by a tapering schedule with increased time between treatments to identify the optimal interval required to maintain control of symptoms. There is also no evidence of safety concerns with continued PTNS therapy through 18 months.

Concluding message

Sustained significant efficacy and safety of PTNS therapy for OAB was demonstrated over 18 months with a mean and median of 1.1 treatments per month following initial success after twelve 30-minute weekly treatments. Treatment interval frequency results in this study closely mimic those of 12 month outcomes reported in similar trials.

Specify source of funding or grant	**Uroplasty, Inc**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**ClinicalTrials.gov NCT 00928395**
Is this a Randomised Controlled Trial (RCT)?	**Yes**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**HIC-Beaumont Hospital**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**