

A Randomized Multicenter Study Comparing Percutaneous Tibial Nerve Stimulation with Pharmaceutical Therapy for the Treatment of Overactive Bladder

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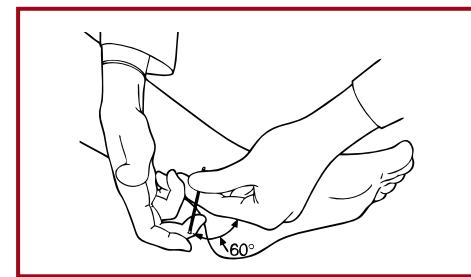
Introduction and Objectives

Overactive bladder (OAB) affects millions of American men and women. The mainstay of treatment is pharmacologic therapy using antimuscarinics. In subjects refractory to pharmacologic therapy, sacral nerve stimulation has been approved since 1997 and until 2005 was the only neuro-modulation procedure actively marketed in the United States. Percutaneous Tibial Nerve Stimulation (PTNS) using the Urgent[®] PC (Uroplasty Inc.) (*figure 1*) is an office based neuromodulation procedure that was approved by the FDA in 2005 for the treatment of urinary urgency, frequency and urge incontinence. This procedure involves advancing a 34 gauge needle to the tibial nerve cephalad to the medial malleolus (*figure 2*). Electrical current is delivered from 1 to 9 mA at 20 Hz and a pulse width of 200 micro seconds for 30 minutes. Subjects are treated once per week for 12 weeks. This multicenter study compared the effectiveness of Percutaneous Tibial Nerve Stimulation (PTNS) versus pharmacological therapy for the treatment of Overactive Bladder (OAB).

Figure 1: Urgent PC device (Uroplasty, Inc)



Figure 2: Placement of needle cephalad to medial malleolus



Materials and Methods

100 patients with OAB (94 female) across 11 U.S. centers were randomized 1:1 to either PTNS treatment (Urgent PC, Uroplasty, Inc) weekly for 12 weeks or tolterodine tartrate (Detrol LA[®], Pfizer, Inc) 4 mg/day for 12 weeks (few patients reduced to 2mg/day based on tolerability)

Results

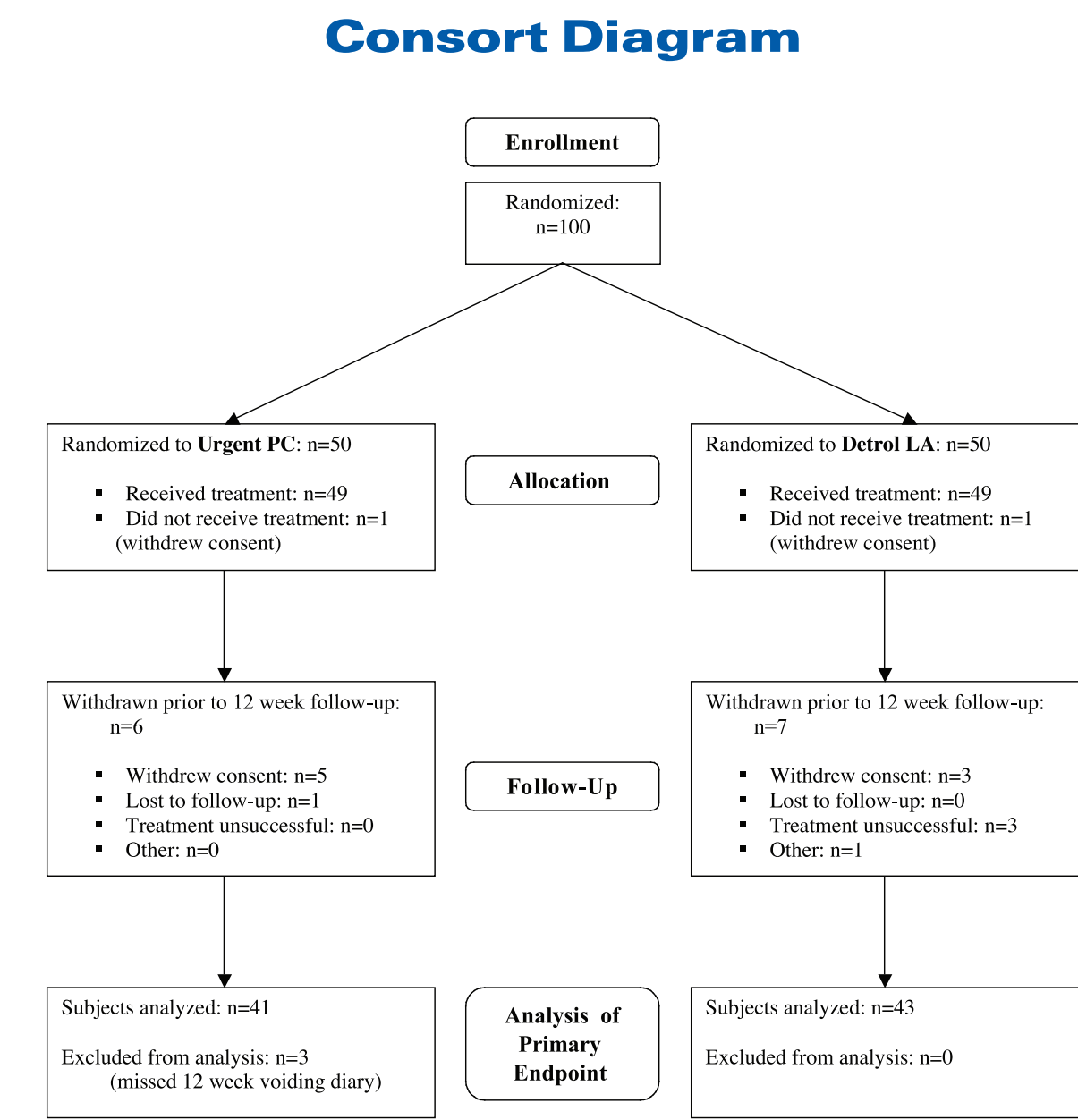


Table 1: Baseline Characteristics

Baseline Characteristics	PTNS Mean ± SD	Tolterodine LA Mean ± SD
Age (Min, Max)	57.5 ± 15.2 (24, 85)	58.2 ± 11.3 (34, 84)
Percent 65 years and older	17/50 (34.0%)	15/50 (30.0%)
Gender (% Female)	48/50 (96.0%)	46/50 (92.0%)
Race (% Caucasian)	42/50 (84.0%)	44/50 (88.0%)
Weight (kg) (Min, Max)	82.9 ± 21.7 (43.2, 143.2)	79.9 ± 19.0 (32.3, 122.7)
OAB years (Min, Max)	9.8 ± 12.3 (0.4, 66.2)	9.4 ± 12.1 (0.3, 61.1)
Average number of voids per day (Min, Max)	12.1 ± 3.1 (7.5, 22.5)	12.5 ± 3.5 (7.0, 21.5)

Table 2: Baseline OAB symptoms

Baseline OAB Symptoms	PTNS	Tolterodine LA
≥ 10 voids per day	41/50 (82.0%)	37/50 (74.0%)
≥ 1 leak per day	38/50 (76.0%)	40/50 (80.0%)
≥ 1 moderate to severe urgency episode per day	48/50 (96.0%)	48/50 (96.0%)
≥ 1 waking episode per night	46/50 (92.0%)	48/50 (96.0%)
≥ 1 urge incontinence episode per day	35/50 (70.0%)	39/50 (78.0%)

*No significant difference at baseline between PTNS and tolterodine groups

Table 3: Voiding Diary Data (Among subjects with 12 week data)

	PTNS				Tolterodine LA			
	N	baseline	12 weeks	% change	N	Baseline	12 Weeks	% Change
voids/day	41	12.1±3.1	9.8±3.0	15.8%	43	12.5±3.7	9.9±3.8	17.7%
Nocturia	41	2.5±1.2	1.7±1.1	23.2%	43	2.5±1.4	1.9±1.6	10.2%*
Urge Incont	41	2.2±2.3	1.2±1.6	52.6%	43	3.5±3.5	1.8±2.5	37.4 %*
Voided volume (cc)	41	152.7±79.3	185.5±81	35.2%	43	141.2±76.2	158.7±99.8	23.6%

*% change calculated for patients with greater than "0" at baseline
 No statistical difference between PTNS and Tolterodine LA

Table 4: Global Response Assessment

Patient Assessment of Improvement in OAB Symptoms at 12 Weeks	PTNS	Tolterodine LA
	Cured	1/44 (2.3%)
Improved	34/44 (77.3%)	21/42 (50.0%)
No improvement/worsening	9/44 (20.5%)	19/42 (45.2%)
Cured or Improved*	35/44 (79.5%)	23/42 (54.8%)

*p-value: 0.01

Physician Assessment of Improvement in OAB Symptoms at 12 Weeks	PTNS	Tolterodine LA
	Cured	2/44 (4.5%)
Improved	33/44 (75.0%)	24/43 (55.8%)
No improvement/worsening	9/44 (20.5%)	17/43 (39.5%)
Cured or Improved*	35/44 (79.5%)	26/43 (60.5%)

*p-value: 0.053

Quality of Life

- The OAB-Q questionnaire showed similar values between arms at baseline and a non-significant trend of improvement of PTNS over Tolterodine LA groups.
- QOL scores (overall and subscales) showed statistically significant improvement from baseline for both treatment groups (p<0.001 for all comparisons).

Adverse events

- Both treatments were well tolerated
- Subjects with at least one adverse event related to treatment is 9/49 (18.4%) for PTNS and 12/49 (24.5%) for Tolterodine LA (NS)
- No serious adverse events related to treatment

Symptom Assessment:

- Constipation reported less often in PTNS arm compared to Tolterodine LA (p=0.04)
- Dry mouth reported less often in PTNS arm compared to Tolterodine LA (p=0.0004)
- PTNS group reported pain, discomfort or redness at ankle (assessed for PTNS group only)

Discussion

- 12 weekly Percutaneous Tibial Nerve Stimulation treatments result in similar objective improvements compared to Tolterodine LA for the treatment of OAB
- Patient's perception of improvement was greater in the PTNS arm than the Tolterodine LA treatment arm
- Both treatments were found to be safe with dry mouth and constipation reported more commonly in the tolterodine treated group and pain at the needle site and bruising/erythema in the PTNS group
- Subjects in the PTNS group were placed on a maintenance program and 1 year data is pending analysis
- Limitations include:
 1. No placebo in the tolterodine arm and no sham in the PTNS arm
 2. Subjects not blinded to treatment assignment

Conclusions

This multicenter, randomized, trial demonstrated that PTNS provides comparable effectiveness to pharmaceuticals for the treatment of OAB. Percutaneous tibial nerve stimulation may be considered a first line therapy for the treatment of OAB.

Supported by: Uroplasty, INC.