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TRIGONAL DENERVATION BY SELECTIVE RADIOFREQUENCY ABLATION FOR THE TREATMENT OF OAB

Hypothesis / aims of study

Overactive bladder is a chronic syndrome characterized by urinary urgency, increased day or night-time voids, with or without urinary incontinence. Currently available treatment options, while providing benefit for many patients, have challenges that can affect adoption [1,2,3]. Some of these therapies act on the detrusor muscle (such as antimuscarinics or B3 agonist), others target peripheral nerves (SNS or PTNS), while others target synaptic transmission (OnabotulinumtoxinA).
A novel treatment using RF energy aiming to fulgurate the nerve rich layers of the deep detrusor beneath the trigone including the adventitial space while sparing the bladder mucosa is currently being studied. Effacement of these nerves, including the C-Fiber (afferent) nerves, followed by collagen remodeling is intended to cause interruption of the signals causing the OAB symptoms.

Study design, materials and methods

34 female subjects with OAB were enrolled in the single arm, initial study cohort at 4 sites in Belgium and Canada. Primary inclusion criteria (via bladder diary) included ≥8 voids/day and ≥3 episodes of urgency with or without incontinence. Additionally, subjects had to have failed or were not candidates for drug therapy. Subjects received trigone RF ablation via a transurethrally placed proprietary device using cystoscopic guidance in a single procedure then were assessed for the primary endpoint at 12 weeks and followed out to 12 months. Assessments at baseline and follow-up included completion of a bladder diary, PVR and pad weight test along with subject completed questionnaires (OAB-q, PISQ-IR and King's Health Questionnaire). An independent clinical events committee (CEC) adjudicated applicable adverse events.

Results

Overall, the mean subject baseline demographics and OAB characteristics include an age of 67.4 yrs range [38.7-81.5], a PVR of 29.7ml range [0-121], 12.9 voids/day, 7.3 urgency episodes/day and 2.8 urgency urinary incontinence (UUI) episode per day. 73.5% (25/34) reported at least 1 UUI/day while 4/34 (11.8%) reported no incontinence via the baseline bladder diary. The remaining 5/34 patients (14.7%) reported minimal incontinence at baseline but did not have at least 1 UUI/day. With regard to the procedure, 73.5% (25/34) of subjects were treated under IV sedation. The median number of ablations was 4 [range 3 – 6] and subjects reported a mean post-op pain score of 1.9 out of 10 at 4 hours post-op.
At 12 weeks, 59.4% of subjects reported improvement via the Treatment Benefit Scale (TBS) with a mean decrease of -1.7 voids/day, -2.3 urgency episodes/day and 0.6 UUI/day. Improvement continued to 12 months with subjects reporting a 65.5% improvement in the TBS and mean decrease of -2.4 voids/day, -4.2 urgency episodes/day and -1.3 UUI/day each with a significant p-value of <0.001 by paired t-test. The mean PVR of 29.7ml, range [0-121ml] had decreased by 47.1% at 12 weeks, 40.4% at 6mo and 36.0% at 12 months. The 25 subjects with urgency urinary incontinence (≥1 UUI) at baseline also improved by similar margins in voids/day of -1.8 and urgency episodes/day of -3.0 at 12 weeks along with a decrease in UUI daily episodes of –0.9. Improvement via TBS of 52.2% was also reported and maintained out to 12 months at 59.1%.
Four subjects (11.8%) developed a UTI within 12 weeks of procedure and one retention was reported (2.9%) that resolved within 2 days without sequela. Three subjects (8.8%) had an increase in LUTS and two (5.9%) reported dysuria all of which resolved within seven days of procedure. Two serious adverse events were reported, both were musculoskeletal in nature and unrelated to OAB or the urinary system.

Interpretation of results

Fulguration of the trigone via RF ablation shows significant improvement in OAB symptoms. In particular, the reductions of voids/day and urgency episodes/day appear consistent with outcomes of other OAB therapies and have maintenance of improvement through 12 months. This can be seen in both analysis groups; all subjects and urgency urinary incontinent subjects. Additionally, the treatment benefit scale data supports improvement of symptoms as well. While modest improvement in urgency urinary incontinence was seen, the magnitude of efficacy was less than anticipated as compared to other OAB therapies. While the rationale for this is not completely understood, it is theorized that the ablation size and/or depth was not substantial enough to fully efface the nerves necessary for disruption of incontinence signals. Safety events were as expected for this population and treatment modality considering the transurethral delivery.

Concluding message

This early data documents minimal adverse effects and suggests safety of this innovative treatment. RF fulguration beneath the bladder mucosa, via ablation of the trigone, provides significant improvement in OAB symptoms. Additionally, the possibility of longer term durability of treatment effect, especially in patients with urgency urinary incontinence is encouraging. Additional studies are needed to confirm these early results.

Table 1: Summary of Bladder Diary Outcomes

Parameter	All Subjects N=34		Urgency Urinary Incontinent Subjects N=25 (≥1 UUI at Baseline)			
	Baseline (N) Mean Change from Baseline (N)	Mean Change from Baseline p-value	Mean % Change from Baseline	*Baseline (N)* Mean Change from Baseline (N)	Mean Change from Baseline p-value	Mean % Change from Baseline
Voids/Day						
Baseline	*12.9 (34)*	*NA*	*NA*	*12.6 (25)*	*NA*	*NA*
12 week	-1.7 (32)	<.0001	-12.8%	-1.8 (23)	0.0004	-13.7%
6 month	-1.9 (30)	<.0001	-13.4%	-1.7 (21)	0.0017	-12.1%
12 month	-2.4 (27)	<.0001	-18.2%	-2.4 (20)	0.0004	-18.5%
Urgency Episodes/Day						
Baseline	*7.3 (34)*	*NA*	*NA*	*8.7 (25)*	*NA*	*NA*
12 week	-2.3 (32)	0.0009	-28.6%	-3.0 (23)	0.0005	-35.1%
6 month	-2.5 (30)	0.0017	-35.1%	-3.3 (21)	0.0008	-41.1%
12 month	-4.2 (27)	<.0001	-58.1%	-5.4 (20)	<.0001	-64.1%
Urge Urinary Incontinence/Day						
Baseline	*2.8 (34)*	*NA*	*NA*	*3.7 (25)*	*NA*	*NA*
12 week	-0.6 (32)	0.0711	-5.5%	-0.9 (23)	0.0375	-26.3%
6 month	-0.6 (30)	0.0873	-48.2%	-0.8 (21)	0.1126	-38.3%
12 month	-1.3 (27)	<.0001	-67.4%	-1.7 (20)	<.0001	-60.9%

Table 2: Treatment Benefit Scale

Parameter	All Subjects N=34	UUI Subjects N=25 (≥1 UUI at Baseline)
	Percent Reporting Improvement	Percent Reporting Improvement
Treatment Benefit Scale (TBS) 12 week	59.4%	52.2%
6 month	67.7%	61.9%
12 month	65.5%	59.1%

References

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