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# EVALUATION OF A NOVEL, NON-INVASIVE, PATIENT-MANAGED NEUROMODULATION SYSTEM (PMNS) ON URGENCY URINARY INCONTINENCE AND PATIENT-REPORTED OUTCOMES IN SUBJECTS WITH OVERACTIVE BLADDER (OAB) SYNDROME WHO HAD PREVIOUSLY FAILED THERAPY: A FOUR-WEEK, MULTICENTER, PROSPECTIVE RANDOMIZED TRIAL

Hypothesis / aims of study

A novel, non-invasive PMNS has been developed for the treatment of OAB syndrome. The PMNS transmits a transdermal amplitude-modulated signal (TAMS) wirelessly, through a patch applied to the skin. The primary objective of this study was to evaluate the efficacy of the PMNS treatment in reducing urgency urinary incontinence and on patient-reported symptoms, life impact, and satisfaction using validated, disease-specific Patient Reported Outcome (PRO) measures. Differences in efficacy, depending on whether the non-invasive patch was positioned by the investigator (Investigator Placement Group, IPG) or the subject (Subject Placement Group, SPG), were also determined. Safety of PMNS treatment was assessed throughout the study.

Study design, materials and methods

Male and female subjects at least 18 years of age with documented symptoms of OAB syndrome were recruited. All subjects had failed primary OAB treatment in addition to treatment with at least one anti-cholinergic drug. Subjects underwent a 7 day washout from anti-cholinergic medications, if applicable. A 3-day voiding diary was completed immediately prior to the study to establish a baseline and confirm eligibility. A mean of eight or more voids and one urgency urinary incontinence episode per 24-hour day was required for enrollment. A minimum of 72 subjects were targeted for enrolment. Subjects were randomized on a 1:1 basis into either the SPG or the IPG. The study was self-controlled, thus blinding of participants was not possible. The protocol and adjunctive materials were approved by an Institutional Review Board/Ethics Committee, and all subjects provided written informed consent. All subjects underwent PMNS treatment for a total of 4 weeks. The investigator placed the disposable adhesive patch in a precise location of the sacral region; thereafter, subjects in the SPG replaced their own patches with the aid of a placement tool. Patches were replaced every 7 days on the contra-lateral side. A second, 3-day voiding diary was completed during the last 3 days of Week 4. Five PRO instruments, validated for assessment of OAB patients, were evaluated. OAB symptom composite score (OAB-SCS), Overactive Bladder Questionnaire (OAB-q), and Patient Perception of Bladder Condition (PPBC) were evaluated at baseline and Week 4. Treatment Benefit Scale (TBS) and OAB Satisfaction with Treatment Questionnaire (OAB-SAT-q) were assessed at the Week 4 endpoint. Safety was evaluated as reported and observed adverse events. Statistical comparison of the IPG and SPG was performed using a Pearson Chi-Square or Fisher's exact test for frequencies and the Wilcoxon rank-sum test for mean values.

Results

A total of 74 eligible subjects were enrolled, with final numbers of n = 30 in the IPG and n = 34 in the SPG. Baseline levels of urgency incontinence were comparable between the IPG and SPG. After 4 weeks of PMNS treatment, the number of urgency incontinence episodes was significantly reduced by an average of 47.8%. Symptoms improved by at least 50% in 62.5% of all subjects (95% CI (50.6%, 74.4%). Statistical comparison of the IPG vs. SPG for all PROs also revealed that these groups did not differ at the Week 4 endpoint. The only statistically significant difference between the IPG and SPG was the baseline score for PPBC, which was marginally significant (P = .0425). Hence, data from the two groups were combined for the final outcomes analysis. All four OAB-q scores showed significant improvement at Week 4 (Table 1). This was also reflected by the total HRQL score, which represents a summary of the four scores. A similar trend was observed in PPBC, where scores decreased in severity by Week 4 (Fig. 2). Improvement occurred in 43 (67.2%) patients with 23 (35.9%) considered as a major improvement. No change or deterioration occurred in 18 (28.1%) or 3 (4.7%) cases, respectively. TBS indicated that 42 subjects (65.6%) experienced improvement while none worsened (Table 2). OAB-SAT-q scores were a sign of subjects' satisfaction with various aspects of PMNS and showed a positive preference compared with their prior treatment. There were no serious or unanticipated adverse events. The majority of adverse events were mild (90.6%), and 76.6% involved skin reactions, all of which resolved.

Table 1. Change in OAB symptom composite score and OAB-q scores after 4 weeks of PMNS treatment

| PRO | Baseline | Week 4 | Change | % Change | *P* value[a] |
|---|---|---|---|---|---|
| **OAB-SCS** | | | | | |
| Symptom composite score | 38.6 (18.2) | 26.3 (11.3) | -12.4 (15.7) | -26.6 (29.7) | <.0001 |
| **OAB-q** | | | | | |
| Total severity score | 65.4 (16.3) | 39.7 (22.2) | -25.7 (23.0) | -39.0 (31.6) | <.0001 |
| Coping scale | 48.2 (28.3) | 71.2 (29.1) | 23.0 (24.6) | 90.5 (158.2) | <.0001 |
| Concern scale | 45.6 (42.9) | 69.6 (27.1) | 24.1 (24.4) | 99.7 (226.9) | <.0001 |
| Sleep scale | 49.1 (26.9) | 68.1 (27.9) | 19.0 (21.3) | 85.7 (225.2) | <.0001 |
| Social scale | 76.9 (21.7) | 87.7 (19.1) | 10.8 (19.2) | 22.4 (47.2) | <.0001 |
| Total HRQL | 53.4 (21.6) | 73.5 (23.0) | 20.1 (20.0) | 68.4 (151.5) | <.0001 |

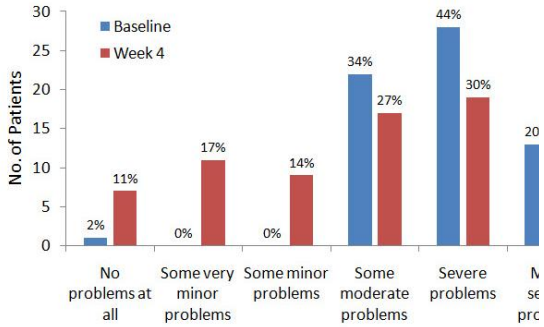
[a] Statistical analysis of change between baseline and Week 4 (Wilcoxon signed-rank test).

Table 2. Effect of PMNS treatment on TBS and OAB-SAT-q

| PRO | Week 4 |
|---|---|
| **TBS** | |
| Greatly improved | 18 (28.1%)[a] |
| Improved | 24 (37.5%)[a] |
| Not changed | 22 (34.4%)[a] |
| Worsened | 0 |
| **OAB-SAT-q** | |
| Satisfaction | 44.2 (27.8)[b] |
| Side effects | 66.1 (39.5)[b] |
| Convenience | 35.7 (29.2)[b] |
| Endorsement | 41.6 (24.5)[b] |
| Preference | 68.9%[a] |

[a] No. of subjects (% of total),

Figure 1. PPBC scores at baseline and after 4 weeks of PMNS treatment.



[b] Mean score (SD)

Interpretation of results

A 4-week course of treatment with PMNS significantly reduced the frequency of urgency urinary incontinence episodes in OAB syndrome subjects. PMNS shifted OAB-q scores from severe to mild/moderate for coping, moderate/severe to mild/moderate for concern and social, moderate/severe to below minor for sleep, and moderate/severe to mild/minor for HRQL total. PPBC, as with OAB-q, demonstrated that subject groups had moderate-to-severe symptoms that improved with PMNS treatment. TBS indicated that subjects' personal evaluation of their symptoms was positive. For OAB-SAT-q, a positive preference for PMNS treatment was demonstrated compared with the treatment received immediately prior to this study.

Concluding message

The PMNS patch appears to be an effective, noninvasive treatment for the symptoms of OAB syndrome, causing significant reductions in urgency urinary incontinence after 4 weeks of treatment. Additionally, five PRO measures commonly used to evaluate efficacy of OAB treatment consistently indicate that this novel PMNS improves symptoms and quality of life for OAB patients after 4 weeks of therapy, regardless of whether the patch is placed by an investigator or subject, and despite failure of previous treatments. Short-term PMNS treatment appears to be safe, with only minor adverse events that resolved spontaneously.


| | |
|---|---|
| ***Specify source of funding or grant*** | **Study was funded by Ethicon Endo-Surgery** |
| ***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: NCT01125722** |
| ***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*** | **Wheaton Franciscan Healthcare**<br>**Compass IRB**<br>**Beaumont Hospitals Research Institute**<br>**IRB for Human Research Medical University of South Carolina**<br>**Vanderbilt University IRB**<br>**Carolinas Healthcare System IRB**<br>**National Research Ethics Service**<br>**Stockholm Regional Ethical Review Board** |
| ***Was the Declaration of Helsinki followed?*** | **Yes** |
| ***Was informed consent obtained from the patients?*** | **Yes** |