Pelvic PT Distance Journal Club: December 9, 2020 (Moderator: MJ Strauhal PT, DPT, BCB-PMD)

Topic: Patient reported outcomes (PROs)

Articles:


   This is a follow up article to one that was reported on by Meghan Swenck, PT during Journal Club on March 13, 2019:


Background:

Article #2- Percutaneous tibial nerve stimulation (PTNS) is recommended after initial therapies fail for idiopathic OAB (iOAB), including behavioral changes and pharmacologic regimens. PTNS has been proven effective via several previous studies, but transcutaneous delivery of stimulation may be more comfortable and feasible. This research demonstrated non-inferiority in decreasing daytime frequency. Reductions in urinary urge incontinence and in improvements in QoL were also demonstrated.

   • By definition, a non-inferiority trial aims to demonstrate that the test product is not worse than the comparator by more than a small pre-specified amount. This amount is known as the non-inferiority margin, or delta.

Article #1- Idiopathic overactive bladder syndrome (OAB) causes a great impact on the quality of life (QoL). The impact of OAB on health-related QoL (HRQL) causes:

   • dependence
   • feelings of shame
   • home confinement
   • sexual psychological dysfunction
   • sleep disturbances
   • impairment of social life
   • frequent use of the bathroom impairing work performance
It has been observed that the disturbance caused in QOL does not always correlate with the amount of urine loss. There is a universal agreement that supports the assessment of the impact that OAB produces not only in terms of symptoms but also in relation to the subjective evaluation of patients QoL. The International Consultation on Incontinence Research Society recommends that a comprehensive evaluation of OAB should include measures of satisfaction, symptoms, HRQL and adverse events in the outcome measurement.

**Aim:** To compare the efficacy of transcutaneous tibial nerve stimulation (TTNS) with percutaneous tibial nerve stimulation (PTNS) regarding patient reported outcomes measures, specifically quality-of-life (QoL) improvement and patient's treatment benefit, on symptoms associated with overactive bladder (OAB).

**Study Design:** prospective randomized clinical trial

**Methods:** previously reported on (see outline from March 13, 2019). Patients were randomized in a 1:1 ratio to receive either TTNS (surface electrode 5 cm above the medial malleolus) or PTNS (percutaneous insertion of a needle 5 cm above the medial malleolus) 1 day/week at 20Hz x 30 minutes x 12 weeks (total of 12 sessions).

- Pretreatment data included a 3-day voiding diary, PROs: OAB-q-SF and I-QoL
- F/U data collected at week 6 and week 12
  - Included the patient’s treatment benefit on symptoms questionnaire (TBS)

**Description of PROs:**

- OAB-q-SF
  - Symptom-based condition-specific questionnaire (validated in Spanish)
  - 2 scales:
    - Symptom bother scale- 6 items rated on a 6 point Likert scale (score range 6-36, with higher score indicating greater bother)
      - MID (minimally important difference) = 10.7
    - HRQL scale- 13 items rated on a 6 point Likert scale (score range 13-78, with higher score indicating lower interference in QoL)
      - MID = 9.6 (set according to ref #13 Spanish version OAB-q-SF)
      - Per Blanker 2019 (see below) MID is 11.2
  - Valid and reliable for use in clinical practice
  - Takes 5 minutes to complete
- I-QOL
Condition specific for incontinence (validated in Spanish)

- 22 items each using a 5 point ordinal scale (1 = extremely, 2 = quite a bit, 3 = moderately, 4 = a little, 5 = not at all)
  - 3 subscales included: Avoidance and limiting behavior (8 items), psychosocial impact (9 items), social embarrassment (5 items)
- Mean score for each subscale is calculated
- Total score is calculated by summing the subscale scores and transforming them to a 100 point scale where 0 = most severe and 100 = no problem
  - MID = 10 points (4 for small effect or 11 for medium effect)
- Takes 30 minutes to complete (cost $500)

TBS (not mentioned in the original study, article #2)

- Treatment Benefit Scale
- Allows for rapid response of overall patient self-perception of treatment benefit
- Self-administered
- Single question, easily adapted into Spanish
  - Patients are asked to compare their current state regarding OAB with their pre-treatment state by the sentence: “My condition (urinary problems, UI) has... 1- greatly improved, 2- improved, 3- not changed, 4- worsened during treatment.”
    - 1-2 indicate response to treatment
    - 3-4 indicate no response to treatment

Statistics (SPSS 21.0 software):

- Descriptive date are reported as mean values and standard deviations when qualitative
  - Within group comparisons conducted using Student’s t test and $\chi^2$ test
  - Correlation measured with Pearson’s coefficient
- Non-inferiority assessed by estimating the difference (95% confidence interval) between the initial and final mean values (CONSORT recommendation)
- Analysis performed per protocol (PP) and by intention to treat (ITT)
- Level of significance set at $p < .05$

Results:

- 68 patients (46 females, 22 males with mean age of 59.6 years and mean BMI 27.4 kg/m²) were enrolled and considered for the ITT analysis
• A total of 61 OAB-q-SF, I-QoL, and TBS were completed correctly and used for analysis
• Table 1
  o Baseline scores

*A note about the Tables:

Intention-to-treat analysis is a comparison of the treatment groups that includes all patients as originally allocated after randomization (N= 34 in each group). This is the recommended method in superiority trials to avoid any bias. For missing observations, “last value carried forward” is the recommended method.

Per-protocol analysis is a comparison of treatment groups that includes only those patients who completed the treatment originally allocated (N=32 in TTNS, 29 in PTNS). If done alone, this analysis leads to bias.

In non-inferiority trials, both intention to treat and per-protocol analysis are recommended; both approaches should support non-inferiority.

• Table 2 (N = 34 in each group)
  o Statistically significant improvement between baseline scores and week 12 scores in both groups and in both PROs
  o No PRO scores support a difference between the groups
  o I-QoL scores between pre and post-treatment were comparable and beyond the 10 point MID (TTNS -20.2, PTNS -18.8)
• Table 3 (N =32 in TTNS and 29 in PTNS)
  o Significant correlation found between the OAB-q-SF HRQL scale and the I-QoL questionnaire from baseline, at week 6, and at week 12
    ▪ Positive correlation between I-QoL (condition specific for ANY type of UI) and OAB-q-SF HRQL scale (condition specific for OAB)
• Figure 1 (N =32 in TTNS and 29 in PTNS)
  o Decrease in OAB-q-SF bother scale for both groups (lower score = milder symptoms)
    ▪ TTNS group 56.3-31.4 = 24.9
    ▪ PTNS group 54.7-36.7 = 18
    ▪ MID = 10.7 (*7.07?)
  o Increase in OAB-q-SF HRQL scale (higher score = better HRQoL)
- TTNS group 78.5 (final score) - 58.7 (initial score) = 19.8
- PTNS group 77.3 (final score) - 55.8 (initial score) = 21.5
- MID 9.6 (*11.2 per Blanker 2019)

- Table 4 (N = 32 in TTNS and 29 in PTNS)
  - No differences in scores observed between groups on TBS
    - TTNS group: 87.5% experienced clinical response, 12.5% no response
    - PTNS group: 86.2% experienced clinical response, 13.8% no response
  - No differences on TBS regarding sex, age, BMI

- Similar by sex
  - TTNS group: 90.0% of women and 83.3% of men
  - PTNS group: 86.4% women and 85.7% men

- Better in patients aged 19-50 (younger) compared to those aged 51-90 (older) in both groups
  - TTNS group younger: 100% vs 84.0% older
  - PTNS group younger: 100% vs 78.9% older

- No difference by BMI

**Article #2** showed that the objective results from a 3 day voiding diary were similar in both groups (adjusted analysis Table 3 page 263)

- Primary outcome = at least 2 fewer daytime micturition frequency
  - TTNS from 8.9 to 7.6
  - PTNS from 8.4 to 8.0

- Upper limits of the confidence interval (95% CI) was below 2, the value that was established as the non-inferiority margin

- Secondary outcomes = reductions in nocturia, urgency, UI episodes

**Article #1** demonstrated that PRO measure improvement after TTNS is non-inferior to PTNS

**Study Limitations:**
- Study was powered only to identify a difference in urinary frequency, as measured by the voiding diary, between the 2 groups
  - However, they did explore secondary outcomes and comparisons of PROs
• Study wasn’t blinded (no needle or sticker placebo), so there is possible bias
• Cost-effectiveness analysis was not considered

Study conclusion
• Both TTNS and PTNS similarly enhance QoL and perception of improvement in OAB
• Because of these results, the ease of application, and less invasiveness of TTNS, PT’s might want to consider this as an acceptable approach to OAB

Discussion and clinical application:
1. What PROs are you using in the clinic for UI of any kind or for OAB specifically?
   ○ Condition-specific, general, you cannot choose due to the EMR software you are using
2. What do you look for when choosing a PRO?
   ○ Clinical utility, validity/reliability, MID, other
3. When reviewing studies like this, done by physiotherapists who are using conservative measures (not drugs), do you consider using similar PROs based on their results?
4. Based on the information derived from this study, which PRO (I-QOL or OAB-q-SF) would you consider for clinical application?
5. Are you familiar with the TBS outcome (ref #15 Colman 2008)?
   ○ What about PGI-I (Patient Global Impression of Improvement) (Yalcin 2003)
     i. The PGI-I is a transition scale that is a single question asking the patient to rate their urinary tract condition now, as compared with how it was prior to before beginning treatment on a scale from 1 = very much better, 4 = no change, to 7 = very much worse
   ○ Do you use a scale like this?
6. The authors conclude that at the end of treatment a high % of men and women in both groups were “very satisfied or satisfied with the therapeutic response obtains” (page 6). Is “satisfaction” the same as “improvement” per TBS?
7. There was no difference in improvement in either group based on BMI. What are your thoughts on this finding?
8. Regarding cost, consider the breakdown below. Thoughts?
   ○ 2012 data for tolterodine (Detrol) - $1200/year, mirabegron (Mybetriq) - $200/month ( - $2400/year)
   ○ PTNS - $3500/year (based on 12 visits for procedure and 5 office visits)
   ○ TENS - $29.99 to $49.99 for a medical grade device (one that has adjustable frequencies and pulse width)
i. PT visit -$125-400/visit (varies based on PP vs hospital-based and w/ or w/o insurance)

Supporting Articles:

