FULL TITLE: Factors influencing return for maintenance treatment with Percutaneous Tibial Nerve Stimulation for the management of the overactive bladder

AUTHORS:

Janek Salatzki [*], Martina D. Liechti [*], Eleonora Spanudakis, Gwen Gonzales, Joanne Baldwin, Collette Haslam, Mahreen Pakzad, Jalesh N. Panicker

*Shared first authorship

AFFILIATIONS:

From the Department of Uro-Neurology, The National Hospital for Neurology and Neurosurgery and UCL Institute of Neurology, Queen Square, London WC1N 3BG United Kingdom (JS, MDL, ES, GG, JB, CH, MP, JNP), Department of Cardiology, Angiology and Pneumology, Heidelberg University Hospital, Heidelberg, Germany (JS)

DISCLOSURES:

The authors have no potential conflicts of interest to disclose.

CORRESPONDENCE:

Department of Uro-Neurology, The National Hospital for Neurology and Neurosurgery and UCL Institute of Neurology, Queen Square, London WC1N 3BG United Kingdom, e-mail: janek.salatzki@posteo.de

ABSTRACT:

Objectives:

To identify factors influencing return for maintenance Percutaneous tibial nerve stimulation (PTNS) treatment after successful completion of a 12-week course of treatment for the overactive bladder (OAB).

Patients and Methods:

Patients with OAB symptoms referred for PTNS treatment underwent twelve sessions of weekly PTNS treatment and evaluated at baseline and week 12 using the International Consultation on Incontinence Questionnaire on OAB (ICIQ-OAB), lower urinary tract symptoms related quality of life questionnaire (ICIQ-LUT symptoms QOL) and bladder diary (BD). Responders to treatment, evaluated using two patient-reported outcome measurements, were invited to return for maintenance treatments when symptoms returned. A PTNS Service Evaluation Questionnaire (PTNS-SEQ) was used to evaluate factors influencing return for maintenance treatment.

Results:

79 patients were evaluated (mean age 58.9 ($\pm$14.7), female 72.6%) and clustered into three groups - group 1 (n=28) did not respond to 12 weekly sessions of PTNS treatment; group 2 (n=28) responded to treatment but did not return for maintenance treatment and group 3 (n=31) responded to treatment and returned for maintenance treatment. There were no significant differences in demographic characteristics, diagnosis, baseline symptom scores and BD parameters between the three groups. Patients belonging to groups 2 and 3 experienced a significant improvement from baseline to week 12 in total OAB scores (group 2: -1.54 $\pm$ 1.85; group 3: -1.85 $\pm$ 2.28, $p<0.05$). However, patients returning for maintenance treatment reported significant improvements specifically in nocturia (BD difference = -0.4 $\pm$ 0.7, $p<0.05$ and ICIQ-LUT symptoms QOL difference -0.48 $\pm$ 0.94, $p<0.05$), and perceived benefits of the treatment on their OAB symptoms compared to those not returning for maintenance treatment (difference between the two groups = 25.6%, p=0.030). Improvements in nocturia and perceived benefits predicted return for maintenance treatment through a logistic regression analysis. Factors related to the need for attending repeat clinic visits such as transportation, distance and time commitment were not found to differ between the two groups.

Conclusions:

Twelve-session weekly PTNS is a safe and effective treatment for OAB. Responders to treatment returning for maintenance PTNS more often reported significant improvements in nocturia and perceived benefits over time, compared to those not returning for

maintenance treatment. The bladder diary provides a more objective assessment of treatment outcome following PTNS treatment.

Key Words:

Percutaneous Tibial Nerve Stimulation, Overactive Bladder, Maintenance Treatment, Follow-Up, Nocturia

Introduction

Overactive bladder (OAB) symptoms have a tremendous impact on health-related quality of life (QOL), posing a significant economic and societal burden [1-3]. Antimuscarinic agents are the first line treatment; however, patients often experience side effects or a lack of effect, which often results in the discontinuation of treatment [1]. Side effects can range from dry mouth, constipation to cognitive impairment due to the effects on the central nervous system [4]. About one in five responders who discontinue antimuscarinic treatment state side-effects as primary reason [5]. Hence, there is a need for alternative treatments for OAB symptoms. In recent years, percutaneous tibial nerve stimulation (PTNS) has been demonstrated to be a safe and effective treatment for OAB [6, 7]. A phase III multicenter, double-blind, randomized controlled study (SUmiT) in a cohort of patients with idiopathic OAB, demonstrated efficacy over sham stimulation [8]. Patients with neurological disease have also shown a favourable response [9, 10]. National Institute for Health and Care Excellence (NICE) has issued guidance for using PTNS for the treatment of OAB in patients for whom conservative treatment has been unsuccessful [11]. This minimally invasive treatment typically consists of a fixed frequency electrical stimulation of the tibial nerve for 30 minutes sessions over 12 weeks.

Long-term efficacy of PTNS has been shown in studies evaluating patients returning for maintenance treatment after the initial 12-session treatment with a median maintenance “top-up” treatment once every 1.1 months [12, 13]. A considerable number of patients however discontinue treatment over time. In the Overactive Bladder Innovative Therapy Trial (OrBIT), 28% of patients withdrew within one year [14]. In the Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation (STEP) trial, 29 of 50 patients of the SUmiT study received maintenance treatment and 42% of patients dropped out over the course of 3 years [12]. A similar drop-out rate of 38% was reported in patients with Multiple sclerosis (MS) who were followed up with maintenance treatment after initial success with 12 weeks of treatment [15]. The reason for a high drop-out rate, despite successful initial treatment, may be due to the perceived lack of benefit at follow-up. However, difficulties in keeping to a program of repeat clinic visits because of logistics issues around travel, appointment booking and time commitments may also contribute to this. These factors have been poorly explored, and the aim of this study was to evaluate factors that influence adherence to PTNS maintenance treatment in patients reporting a beneficial response to PTNS treatment.

Patients and Methods

The study was performed as a cross-sectional analysis on the basis of a prospectively evaluated cohort in a tertiary-level teaching hospital where adult patients underwent PTNS treatment for OAB symptoms has been established since 2012. Patients underwent a standard urological assessment and were referred for PTNS treatment if first line conservative treatments were either ineffective or intolerable.

The following assessments were performed:

- International Consultation on Incontinence Questionnaire on OAB (ICIQ-OAB): validated 4-item questionnaire used to assess OAB symptoms, i.e. nocturia, daytime frequency, urgency and urge urinary incontinence over the previous 4 weeks and scores range from 0-16; higher scores indicate worse OAB symptoms [16].
- ICIQ-LUT symptoms QOL: 20-item validated questionnaire designed to evaluate LUT symptoms-related QOL [17].
- Three-day bladder diary (BD) completed by the patient prior to attending and providing information about fluid intake, number and timing of voids, voided-and residual volume (ml), number of episodes of urinary urge incontinence and severity.
- Bladder scan measuring the post-void residual volume.
- PTNS Satisfaction Survey: This patient-reported outcome measure (PROM) inquired about comfort and satisfaction of treatment, improvement of bladder symptoms and if patients would recommend PTNS using a rating scale from 1 (strongly disagree) to 7 (strongly agree) (supplementary figure 2). In addition, they were also asked if they would like to continue PTNS treatment.
- PTNS Service Evaluation Questionnaire (PTNS-SEQ): this explores different factors that may influence the decision to return for maintenance PTNS treatment. As such a questionnaire does not exist, this was designed following a review of the literature of long-term PTNS studies evaluating patient follow up [6, 8, 12, 18-21] and covered different factors that could influence adherence to maintenance treatment including PTNS treatment (lack of treatment effect and side effects), Clinic (clinical environment, scheduling difficulties, lack of reminder and treatment regime), Travel and Organization (travel difficulties) and Personal Reasons (health-conditions) (Table 2; supplementary Figure 1). In addition, an open question asked about the main reasons for not returning for maintenance treatment. Patients were also asked whether they might consider alternatives to PTNS. Furthermore, overall satisfaction with PTNS clinic was asked. The questionnaire was reviewed by five patients attending the PTNS clinic and amended according to feedback received. This was then uploaded onto an

online survey portal (SurveyMonkey.com) and patients were contacted with a request to fill in the survey. Patients with incomplete data, inconsistent decision about returning for treatment, or those who had recently completed treatment within 6 weeks, were excluded.

Patients contacted the department when they experienced a reoccurrence of OAB symptoms and returned for single session treatment. The frequency at which they returned was dependent upon the patient's perception of recurrence of symptoms; however, patients requesting maintenance sessions more often than once every 6 weeks were moved onto other treatments [12]. Patients not experiencing an improvement following 12 weeks of treatment were offered alternative treatments for managing OAB. Patients were included into the analysis of the PTNS-SEQ if they were aged ≥ 18, attended 10-12 weeks of PTNS baseline treatment and completed the PTNS-SEQ at least 6 weeks after their final session of PTNS baseline treatment. The service evaluation received approvals from the Hospital's Quality and Clinical Governance Department.

Data Analysis

BD scores were calculated as mean values over three days. Treatment response was calculated as difference scores between week-12 and 0. PTNS-SEQ questions 3-10 and 12-16 were merged under items, and questions were clustered into categories according to themes (Table 2). Missing week 0 or week 12 values were assumed to be equal for the respective sub score. If more than 50% of data was missing for a score, the score itself was defined as missing. If patients stated in the PTNS Satisfaction Survey that they would like to continue with PTNS treatment, they were classified as "responders" (binary PROM). Responders were invited to return for maintenance PTNS treatment. Exploratory analyses were performed using a rating scale PROM inquiring about improvement of bladder symptoms. Patients with a score 4-7 were defined as responders and patients with score 1-3 as non-responders.

Statistical Analysis

Statistical analysis was performed using the SPSS version 24, with $p<0.05$ considered as statistically significant for all statistical tests. For parametric testing, ANOVA tests were calculated, followed up by Bonferroni post-hoc pairwise group comparisons. Categorical-data were compared using chi-squared tests. Within-group differences were investigated using paired one-sample t-tests. All clinical scores are reported as the mean±standard deviation (SD) for consistency. For statistically significant results of non-normal distributed continuous data, median (minimum-maximum) values were provided in-text. Individual ICIQ-OAB and ICIQ-LUT symptoms QOL questions as well as BD parameters

were compared between different groups. Categorical data from the PTNS-SEQ were stated as absolute values and percentages.

To distinguish group 2 and 3, binomial logistic regression analyses were performed. The confidence intervals were 95%. Variables from treatment response (BD parameters, OAB and LUT symptoms QOL scores) and categories from PTNS-SEQ were selected a priori to identify predictor models. A Nagelkerke´s R^2>0.40 was defined as a large effect size, while a Nagelkerke's R^2>0.25 was defined as a medium effect size [22]. In addition to the binary PROM, PTNS-SEQ outcomes were compared between responders, who did not return for maintenance PTNS (group 2) and responders, who returned maintenance PTNS (group 3) using the rating scale PROM.

Results

Figure 2 provides an outline of patients included in the study. Of the 103 patients meeting the criteria, 83 completed the PTNS-SEQ. Patients were categorized into one of three subgroups; Group 1 (N=28) were non-responders to treatment and therefore were not offered maintenance treatment (based on the binary PROM); Group 2 (N=24) were responders to treatment, who were offered maintenance treatment, but never returned; Group 3 (N=31) were responders to PTNS who were offered maintenance treatment and did return (Figure 2). Reasons why patients in group 2 did not return for maintenance treatment included: insufficient response to treatment in hindsight according to PTNS-SEQ (N=11), loss to follow up (N= 5) and travel difficulties (N=1). Members in group 2 stated in an open question in the PTNS-SEQ the following reasons for not returning for maintenance treatment; ineffectiveness of treatment for their bladder symptoms (N=9), uncertainty about effectiveness of treatment (N=1), long-time delay of improvement (N=1) and depression and fatigue (N=1).

In group 3, patients returned for a first top-up treatment after the last PTNS treatment after a median period of 39 (55) days, and the longest period was 204 days. No serious adverse effects were reported. There were no significant differences in demographics, diagnosis or baseline questionnaire or BD parameters between the three groups (Table 1 and supplementary table 1).

Treatment responses differed significantly between the three groups (Table 1 and supplementary table 2). Group 2 and 3 patients experienced a highly significant improvement in total OAB scores (according to questionnaire) compared to patients in group 1 (supplementary table 2). In general, patients with idiopathic (non-neurological) OAB had a significant higher OAB score than patients with neurological disease

(p=0.048). The BD values (number and timing of voids, instances-of urinary urge incontinence, and their severity) improved only in group 3 patients (Table 1, supplementary table 2). Group 3 patients experienced a significant greater improvement in nocturia, which was questioned using ICIQ-LUT symptoms QOL (p=0.036) and BD (p=0.046) (table 1). There were no significant differences between group 2 and 3 regarding PTNS Satisfaction (PTNS Satisfaction Survey) when asked after 12 sessions of treatment (supplementary table 3). Interestingly, group 2 patients were significantly more satisfied with their experience at the PTNS clinic compared to group 3 (p=0.031) (supplementary table 4). Group 2 patients more often reported that the treatment never had any effect on their symptoms in the PTNS-SEQ compared to group 3 patients (p=0.030) (Table 2). In correspondence, the rating scale PROM revealed that group 2 patients in the PTNS-SEQ significantly more often reported that the treatment never had any effect on their symptoms (p=0.026). There were no other significant differences in the results of the PTNS-SEQ between group 2 and 3 neither by using the binary nor the rating scale PROM. Group sizes in the rating scale PROM were smaller compared to the binary PROM (group 1: N=17, group 2: N=14 and group 3: N=20).

To identify variables that could predict return for maintenance treatment, logistic regression analysis using the a priori variables 3-day average nighttime voids, daytime voids, number of leakages, ICIQ-OAB Score and ICIQ-LUT symptoms QOL Score was successful to distinguish between group 2 and 3 (Chi-Square 11.23, p=0.047). Nagelkerke's R^2 [23] was 0.443 and the model correctly classified 83.3% of cases. A second model using all categories of statements of the PTNS-SEQ was also successful to predict group membership (Chi-Square 16.25, p=0.039, Nagelkerke's R^2=0.395). The second model correctly classified 75.0% of cases. An increase in categories "lack of treatment effect" was associated with an increased likelihood of membership to group 2. In the PTNS-SEQ patients were asked whether they might consider alternatives to PTNS during the maintenance phase. These included transcutaneous tibial nerve stimulation using a TENS (transcutaneous electrical nerve stimulation) machine (N=28), performing PTNS at home (N=25), implanted tibial nerve stimulator (N=20) and PTNS delivered at general practitioners´ clinics (N=20).

Discussion

Patients attending a standard 12 session course of PTNS treatment showed significant improvements in symptoms as well as QOL and did not experience significant side effects, which confirms the findings from previous studies demonstrating safety and

efficacy of PTNS for the management of OAB [2, 7, 10]. After successful 12 week treatment, OAB symptoms recur after variable periods of time [18], however maintenance treatment sustains the beneficial effects of the treatment [12, 14, 15], either by tapering with wider intervals between fixed sessions [12], or ad hoc treatments offered at patient request [24]. The median interval until first maintenance treatment was similar as previously reported in the SUmiT study [12]. 48 patients (66%) in this cohort of predominantly neurological patients reported successful outcomes following PTNS treatment; however, despite reporting significant improvements in LUT symptoms and QOL using validated questionnaires and the bladder diary, 17 (35%) did not return for maintenance treatment.

Patients belonging to group 2 present a conundrum as they are similar to group 3 patients in that they have indicated benefit to PTNS, report a significant improvement in OAB symptoms according to validated questionnaires and a wish to return for maintenance treatment. However, despite this, they do not return for maintenance treatment. This is a commonly encountered scenario in PTNS clinics and we attempted to prospectively identify factors that could influence adherence to maintenance treatment and compared groups 2 and 3. There were no significant differences in demographic characteristics, and although group 2 had more patients with Parkinson's Disease, this difference was not statistically significant. While significant improvements in overall LUT symptoms and LUT-related QOL were seen in responders as a whole, when comparing individual symptoms of the OAB, improvements in nocturia were significantly greater in group 3 compared to group 2 and therefore was a factor that influenced return for maintenance PTNS treatment. This improvement was observed using a 3-day bladder diary, as well as from a retrospective assessment from questionnaire data. This is an important finding for clinicians as it helps to individually respond to patients during PTNS sessions in order to ensure their return for maintenance treatment. Nocturia is highly prevalent in neurological disorders such as MS [25] and this finding is likely to reflect the effect nocturia has on quality of sleep [26] and impact on overall QOL [27]. Moreover, the resulting sleep fragmentation is associated with diabetes [28] and a higher incidence of cardiovascular morbidity [29]. Nocturia has been shown to improve consistently across different trials evaluating percutaneous and transcutaneous tibial nerve stimulation in cohorts of patients reporting OAB symptoms [8, 12, 30, 31]. Notably, improvements according to bladder diary significantly differed between the 2 groups and this suggests that a real-time assessment of LUT symptoms using a bladder diary provides a more accurate

assessment of success following PTNS treatment. The bladder diary should therefore be used as the criterion for determining success following PTNS treatment.

Furthermore, the findings of the PTNS-SEQ suggest that the apparent perception of benefit reported at the completion of treatment changes over time. Responders returning for maintenance treatment reported more often that PTNS had a beneficial effect according to PTNS-SEQ. An open question in the PTNS-SEQ confirms that a majority of patients in group 2 felt that PTNS was ineffective for their bladder symptoms and therefore did not return for maintenance treatment. However, the perception of satisfaction was greater amongst patients in group 2. This suggests a mismatch between improvements in objective measures at the end of 12 weeks of treatment and a perception of improvement afterwards in group 2 patients. The study was not designed to evaluate the reasons for this mismatch, however group 2 patients never received maintenance treatments and when patients were contacted at a later date they reported a short-lived initial benefit, or a reconsideration over time of the benefits that the treatment provided. Moreover, the benefits of treatment, when viewed in the larger social context of daily living may only become apparent over time. The presence of OAB symptoms can make patients feel uncomfortable in social situations [32], and group 3 patients reported their OAB symptoms having less impact on their ability to socialise with friends compared to patients in group 2. It is possible that the greater satisfaction rate reported at week 12 is influenced by the close care received through regular weekly visits to hospital and access to a new technology, rather than improvements in OAB symptoms alone.

Surprisingly, factors around the conduct of the PTNS service and organisation of the clinic itself were not found to influence return for maintenance treatment. We were expecting logistical issues such as difficulties in travel and travel expenses as important factors. Inconsistent findings have been observed in previous studies and whereas Zimmern et al. demonstrated that participants found travel time to clinic bothersome [33], Sirls et al. showed no relationship between travel distance to clinic and failure to complete 12-week PTNS treatment [34]. While more than one third of patients in group 2 and 3 stated in this study that they experienced travel difficulties, it did not seem to influence patients' decision to return for maintenance treatment. Previous studies have reported a withdrawal rate of 28% to 42% from maintenance sessions [12, 14, 15]. Reasons for withdrawal cited were loss to follow-up, unknown reasons, ineffectiveness of therapy, logistical issues attending appointments, non-urinary health issues, other neurological and non-neuro-urological health problems, switch to drug treatment and refusal of further treatment [12, 14, 15]. In this study we could identify ineffectiveness of therapy (N=11)

and loss to follow-up (N=5) as the main reasons for withdrawal. Travel difficulties were only stated by one subject as the main reason for withdrawal from maintenance treatment. The flexible nature of appointments also facilitate return for regular maintenance treatment. Patients who did not return for maintenance treatment experienced a lack of treatment efficacy, which is consistent with the findings from Sirls et al. which identified poor response to treatment as the main reason for not returning [34]. Irrespective of the PROM used to define responders and non-responders, the PTNS service, organization of clinics and travel issues did not seem to have an influence on patients´ decision to return for maintenance treatment.

In order to predict return for maintenance treatment, logistic regression analysis was performed. Two models using a priori variables were found to predict return to the PTNS clinic. The first included selective items from the BD - daytime and nighttime voids and number of leakages - as well as sum scores of ICIQ-OAB and ICIQ-LUT symptoms QOL. The model correctly classified 83.3% of cases and has more power to predict return compared to the second model, that used categories composed of statements from the PTNS-SEQ. In the second model the categories of statements addressing lack of treatment efficacy was significantly associated with an increase in likelihood in failure to return for maintenance treatment. Lack of treatment efficacy may reflect inadequate dosing of nerve stimulation. PTNS treatment available for at-home use or at the local general practitioners´ clinic as well as the use of a TENS machine or implanted devices, may improve efficacy.

In this study we aimed to evaluate factors influencing adherence to maintenance treatment following 12 sessions of PTNS treatment. A limitation of this study is the small cohort of patients and the unbalanced subgroups. In addition, the results are applicable to a specific health care model, whereby the NHS as a public-health care system, which provides universal and free treatment including PTNS for patients at the point of delivery. The results may not be applicable to other health care models such as in the private sector, where health insurance premiums and self-paying might be an important factor for patients to consider before returning for maintenance treatment. Regional differences in travel time and expenses as well as patients´ income might impact adherence to PTNS maintenance treatment. This should be investigated in a larger prospective multi-centre study across different regions and health care systems in order to generalize the findings of this study.

Furthermore, different PROMs have been used do evaluate success of PTNS treatment, which are subjective measurements. Previous studies have used bladder diary and OAB

questionnaire to define responders [6, 7]. Primary aim of this study was not to evaluate success of 12 session PTNS treatment. However, using two different PROMs, similar results were obtained. This interesting result emphasizes the importance of including apparent satisfaction with the PTNS treatment as a PROM for determining return for maintenance treatment. The size of the subgroups evaluated using the rating scale PROM limits its power. Future prospective studies will need to be designed to compare the two PROMs and to confirm these results. Different maintenance schedules are followed across different centres [24, 35] and validating the PTNS-SEQ would facilitate the establishing of a larger multicentre study to prospectively evaluate the optimal regimen post treatment, to assess factors influencing adherence to treatment in a larger cohort of patients and address limitations of this study including the limited numbers and unbalanced groups. The wide range of retreatment intervals for patients in group 3 (up to 204 days) might have contributed to the change of perceived satisfaction over time. A study with a standard retreatment time may provide additional clarification of the impact of satisfaction with PTNS on return for treatment. Furthermore, group 2 was a heterogeneous group of patients with idiopathic and neurogenic OAB, and the study was not designed to compare these two groups. Patients with idiopathic OAB had a significant higher OAB score than patients with neurological disease. A study of patients with neurogenic OAB should assess the impact neurological disability has on returning for maintenance treatment, as it is possible worse disability and increasing travel difficulties may be a barrier for returning for maintenance treatment.

Conclusions

In conclusion, 12-session PTNS is a safe and effective treatment for OAB. A beneficial response to PTNS and improvement in nocturia predicted return for maintenance treatment. Logistic factors around travel and clinic organization did not predict return. Responders returning for maintenance PTNS more often reported significant improvements in nocturia and perceived benefits over time, compared to those not returning for maintenance. The bladder diary provides a more objective assessment of treatment outcome following PTNS treatment.

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Legends to Figures

Figure 1 Schedule of assessments and treatments

Patients assessment at weeks 0 and 12. The PTNS Service Evaluation Questionnaire (PTNS-SEQ) was completed during the maintenance phase 6 weeks after the end of the initial 12 once-weekly sessions. ICIQ - International Consultation on Incontinence Questionnaire, OAB - Overactive Bladder, LUT symptoms QOL - Lower Urinary Tract Symptoms Quality of Life, 3-day BD – three-day bladder diary, Bladder Scan - measuring the post-void residual volume, PTNS - Percutaneous Tibial Nerve Stimulation, SEQ - Service Evaluation Questionnaire.

Figure 2 Flowchart of patients in the study

Patients completing PTNS treatment were grouped according to response to treatment and return for maintenance top-up sessions. *10 patients were not consistent with their group allocation and excluded.

Figures

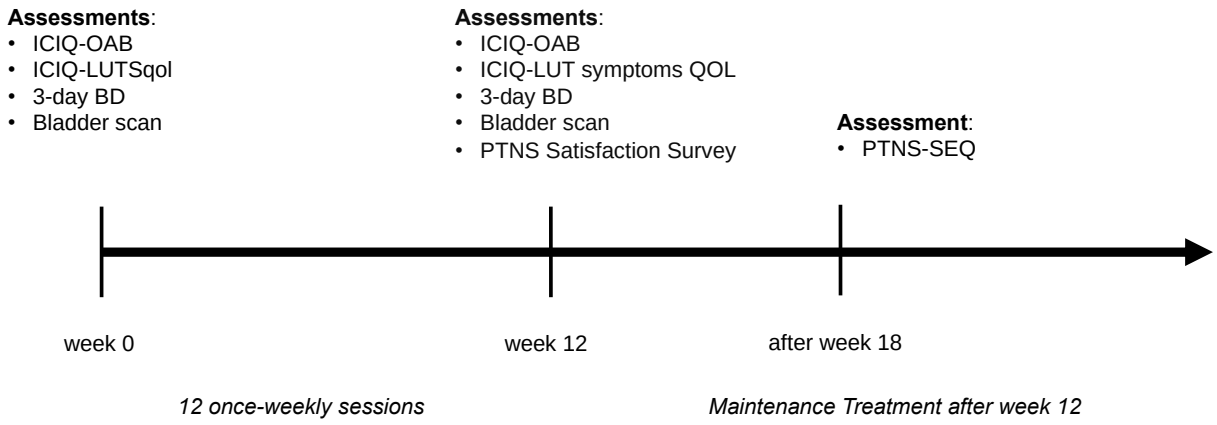

Figure 1 Schedule of assessments and treatments

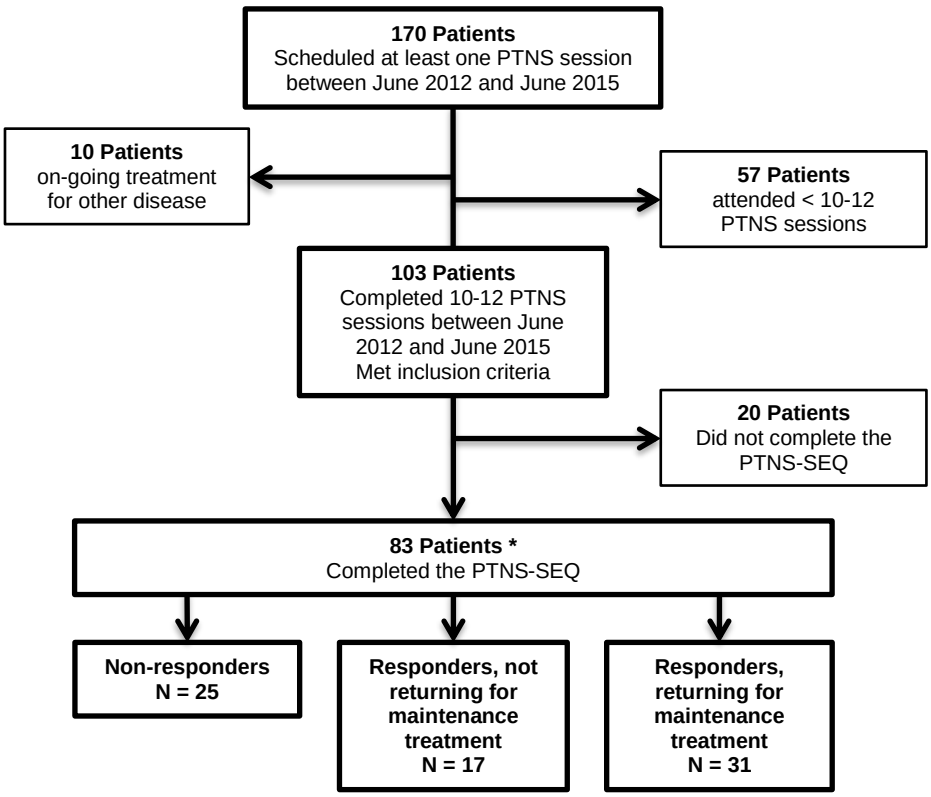

Figure 2 Flowchart of patients in the study

Legends to Tables

Table 1 Baseline Characteristics and Treatment Response between week 0 and week 12 per group of 73 patients undergoing PTNS treatment

Baseline Characteristics (Age and Gender); * T-Test - no sig. differences between the groups. Diagnosis (number of Patients) [#] Chi-Square Test – no sig. differences between groups. [$] Other neurological diagnoses: adrenomyeloneuropathy (n=3), carnitine palmitoyltransferase II (CPT II) deficiency (n=1), limbic encephalitis and subdural hematoma (n=1), cauda equina lumbar decompression (n=1), cervical and lumbar stenosis (=1), peripheral neuropathy and lumbar canal stenosis (n=2), pure autonomic failure (n=1), familial dysautonomia (n=1), Friedreichs ataxia (n=1), spinal cerebellar ataxia type 3 (n=1), alpha-actin deficiency (n=1), myasthenia gravis (n=1), fowlers syndrome (n=3), poliomyelitis (n=1), epilepsy (n=1), traumatic brain injury/whiplash injury (n=1), chronic urinary retention (n=1). Changes within groups were calculated using T-Test, * $p<0.05$. Differences between all three groups were calculated using 2-way ANOVA, Bonferroni-Posttest between group 2 and group 3, ** $p<0.05$.

Table 2 Categories (bold) according to themes with statements from PTNS Service Evaluation Questionnaire (PTNS-SEQ) and comparison between group 2 and group 3

Patients were asked to select all items that apply with a binary response (Yes / No). Differences between groups were calculated using Pearson Chi-Square Test (* $p<0.05$).

Tables

Table 1 Baseline Characteristics and Treatment Response between week 0 and week 12 per group of 73 patients undergoing PTNS treatment

Group	**1**		**2**		**3**		Group effect based on 2-way ANOVA	Bonferroni-Posttest between group 2 and 3
	Non-Responders		Responders, not returning for maintenance treatment		Responders, returning for maintenance treatment			
N =	25		17		31			
Baseline Characteristics								
Age (Mean (SD)) *	58.4 (13.2)		64.7 (15.2)		56.1 (15.1)			
Gender (female%) #	64.0		70.6		80.6			
Diagnosis (No. of Patients) #								
Multiple Sclerosis	9		5		13			
Parkinson's Disease	2		3		1			
other neurological disorders problems $	9		6		9			
Idiopathic OAB	5		3		8			
Treatment Response (between week 12 and week 0)								
	N	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**	**p**	**p**
ICIQ-OAB Score	16	0.09 (1.71)	13	*** -1.54 (1.85)**	27	*** -1.85 (2.28)**	**** 0.012**	1.000
ICIQ-LUT symptoms QOL Score	14	*** -4.07 (4.1)**	15	-4.27 (10.98)	26	*** -5.35 (6.9)**	0.852	1.000
ICIQ-LUT symptoms QOL "Does your urinary problem limit your ability to see/visit friends?"	15	-0.47 (2.45)	15	-0.6 (3.54)	27	*** -2.93 (2.63)**	**** 0.01**	**** 0.043**
ICIQ-LUT symptoms QOL "Does your urinary problem affect your sleep?"	14	0.00 (0.39)	15	0.13 (0.52)	27	*** -0.48 (0.94)**	**** 0.023**	**** 0.036**
3-day avg. Mean Voided Volume	16	17.73 (42.52)	12	-3.85 (47.18)	25	2.34 (49.17)	0.437	1.000
3-day avg. # voids in 24h	17	-0.63 (3.59)	12	1.67 (6.25)	26	*** -1.78 (3.02)**	0.062	0.057
3-day avg. daytime voids	17	-0.51 (3.35)	12	1.17 (5.65)	26	*** -1.4 (2.94)**	0.163	0.174
3-day avg. nighttime voids	17	0.27 (1.14)	12	0.39 (0.93)	26	*** -0.4 (0.7)**	**** 0.016**	**** 0.046**
3-day avg. mean urgency	16	0.32 (0.7)	11	0.11 (0.66)	22	*** -0.33 (0.67)**	**** 0.017**	0.274
3-day avg. # of leakages	17	-0.06 (2.14)	12	0.28 (2.76)	26	*** -0.75 (1.06)**	0.244	0.370

Table 2 Categories (bold) according to themes with statements from PTNS Service Evaluation Questionnaire (PTNS-SEQ) and comparison between group 2 and group 3

Categories and statements of PTNS-SEQ	**Group 2**		**Group 3**		**p**
	N	**% group**	**N**	**% group**	
"Lack of treatment effect"	12	70.6	13	41.9	0.325
- "I experienced good results at first; however the treatment stopped being effective."	1	5.9	6	19.4	0.206
- "I experienced some improvement in my symptoms but my treatment goals were not met."	6	35.3	6	19.4	0.223
- "The treatment never had any effect on my symptoms."	6	35.3	3	9.7	*** 0.030**
"Side effects"	0	0	1	3.2	n.a.
"Difficulties with clinical environment and hospital staff"	0	0	3	9.7	n.a.
"Scheduling difficulties"	2	11.8	4	12.9	0.495
"Lack of reminder"	1	5.9	0	0	0.157
"Travel difficulties"	6	35.3	13	41.9	0.412
- "It took me a long time to reach the clinic."	5	29.4	8	25.8	0.788
- "It was too expensive to travel to the clinic."	1	5.9	2	6.5	0.938
- "It was difficult for me to reach the clinic for mobility reasons."	1	5.9	5	16.1	0.08
- "It was difficult for me to reach the clinic for transport reasons."	1	5.9	3	9.7	0.649
"Difficulties with treatment-regime"	2	11.8	3	9.7	0.439
"Health-condition prevented return to clinic"	2	11.8	2	6.5	0.361

Abbreviations and Acronyms

BD = three-day bladder diary

ICIQ-OAB = International Consultation on Incontinence Questionnaire on OAB

LUT = lower urinary tract

OAB = overactive bladder

PROM = patient-reported outcome measure

PTNS = percutaneous tibial nerve stimulation

PTNS-SEQ = PTNS Service Evaluation Questionnaire

QOL = quality of life

TENS = tibial nerve stimulation