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Long-Term Effects of Percutaneous Tibial Nerve Stimulation Treatment for Neurogenic Overactive Bladder Due to Multiple Sclerosis: 24-Month Results

Multiple Skleroza Bağlı Gelişen Nörojenik Aşırı Aktif Mesane Tedavisinde Kullanılan Perkütan Tibial Sinir Stimülasyonunun 24 Aylık Uzun Dönem Sonuçları

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Abstract

Objective: In this study, it was aimed to determine the effectiveness of percutaneous tibial nerve stimulation (PTNS) treatment in neurogenic overactive bladder (NOAB) due to multiple sclerosis (MS) by extending the application interval for 24 months from the beginning.
Materials and Methods: Patients completed the PTNS treatment with tapering protocols applied for 6, 9, 12, and 24 months. After 12 weeks of therapy, PTNS was applied at 14 day intervals for 3, at 21 day intervals for 3, and at 28 day intervals for 3 months. The patients completed a 3-day voiding diary at the 3rd, 6th, 9th, 12th, and 24th months. The patients were requested to complete validated questionnaires (ICIQ-SF, OAB-V8, OAB-q SF) within 3-month intervals thereafter during their enrolment in the study.
Results: The mean age of 57 patients who completed the PTNS treatment protocol and were included in the study was 42.6 ± 8.2 (23-64) years. Fifteen (26.3%) patients were male and 42 (73.6%) were female. The improvements for all voiding diary parameters were significant at 3rd, 6th, 9th, 12th, and 24th months when compared with the baseline. After 24 months, the daily frequencies of voiding decreased by 6.7 ($p<0.001$), urge urinary incontinence by 4.2 ($p<0.001$), urge by 8.4 ($p<0.001$), nocturia by 2.2 ($p<0.001$), and the mean voiding volume increased by 85.8 cc ($p<0.001$). No treatment-related side effects were reported in the patients for 24 months.
Conclusion: This study showed that the symptoms of the patients with NOAB due to MS improved after 24 months of PTNS treatment.

Keywords: multiple sclerosis, percutaneous tibial nerve stimulation, neurogenic overactive bladder, detrusor overactivity, posterior tibial nerve

Öz

Amaç: Bu çalışmada multiple skleroz (MS)'a bağlı gelişen nörojenik aşırı aktif mesanede (NAAM) perkütan tibial sinir stimulasyonu (PTNS) tedavisinin başlangıçtan itibaren 24 ay boyunca uygulama süre aralığının uzatılarak etkinliğinin belirlenmesi amaçlanmıştır.
Gereçler ve Yöntemler: PTNS tedavisinde 24 aylık tedavi protokolü başlangıçta 12 hafta süresince her hafta, sonraki 3 ay boyunca 14 günde bir, devam eden 3 ay boyunca 21 günde bir uygulandıktan sonra 24 aya kadar 28 günde bir olacak şekilde uygulandı. Hastalar 3 günlük işeme günlüğü ile gündüz işeme sıklığı, sıkışma, sıkışma tipi idrar kaçırma, noktüri, işeme hacimlerini belirlemek için başlangıçta ve daha sonra 3, 6, 9, 12 ve 24'üncü aylarda değerlendirildiler. Ayrıca hastalar başlangıçta ve 3 aylık aralıklarla valide edilmiş anketler (ICIQ-SF, OAB-V8, OAB-q SF) ile değerlendirildiler.
Bulgular: PTNS tedavi protokolünü tamamlayan ve çalışmaya dahil edilen 57 hastanın yaş ortalaması 42.6 ± 8.2 (23-64) idi. Çalışmadaki hastaların 15'i (%26,3) erkek, 42'si (%73,6) kadındı. İşeme günlüğü parametrelerindeki başlangıç, 6, 9, 12 ve 24'üncü aylardaki iyileşmeler anlamlı olarak gözlendi. Başlangıç değerine göre 6, 9, 12 ve 24'üncü aylardaki ICIQ-SF, OAB-V8 ve OAB-q'da gösterilen semptom şiddetinde ve sağlıkla ilişkili yaşam kalitesinde istatistiksel olarak anlamlı iyileşmeler görüldü. 24 ay sonunda işeme sıklığı günlük 6.7 ($p<0.001$), sıkışma tipi idrar kaçırma 4.2 ($p<0.001$), sıkışma 8.4 ($p<0.001$), noktüri günlük 2.2 ($p<0.001$) azalmış ve işeme hacmi ortalama 85.8 cc ($p<0.001$) artmıştır. Hastalarda 24 ay boyunca tedaviye bağlı yan etki bildirilmemiştir.
Sonuç: Bu çalışma, MS hastalığına bağlı gelişen NAAM'ye sahip hastalarda, 24 aylık PTSS tedavileriyle semptomlarında iyileşme gözlendiğini göstermiştir.

Anahtar kelimeler: multiple skleroz, perkütan tibial sinir stimülasyonu, nörojenik aşırı aktif mesane, detrüsör aşırı aktivitesi, posterior tibial sinir

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Introduction

Multiple sclerosis (MS) is a chronic young adult disease that shows its effect in the central nervous system (CNS) and manifests itself with attacks. It is an autoimmune and demyelinating disease. The disease mainly affects the brain and spinal cord, and is characterized by the accumulation of demyelinating plaques in the white and gray matter. In addition, atrophy and irreversible axonal degeneration can also be observed [1]. Demyelinated lesions and plaques eventually cause lower urinary tract dysfunction (LUTD) during the progressive course of the disease, depending on their localization in the CNS. LUTD may present in 5-10% of MS patients as the first symptom, but neuro-urological symptoms occur in 80% of patients 10 years later during the course of the disease. Depending on the location of the lesion, detrusor overactivity (DO), detrusor sphincter dyssynergia (DSD), or hypocontractility may occur during the course of the disease [2].

There are many medical and surgical treatment options for DO, but their therapeutic success is controversial. The first-line treatment of DO includes bladder training, pelvic floor muscle training, and anticholinergics. Since side effects of anticholinergic drugs which are among effective treatment options for DO such as dry mouth and constipation are common, only 20% of patients continue to take these drugs after 6 months [3,4]. Treatment options such as neuromodulation, intravesical botulinum toxin injection, bladder augmentation, detrusor myomectomy and urinary diversion are available for patients who discontinue the treatment due to its side effects, do not want to use drugs, or do not benefit from medical treatment.

Percutaneous tibial nerve stimulation (PTNS) can be preferred as a safe and effective treatment option for the patients with DO symptoms who have not benefited from conservative and medical therapy or did not respond to treatment with at least two oral anticholinergic drugs [2,5-8]. It has been reported that neuromodulation of the sacral nerve plexus (S2-4 roots) can be achieved by stimulating the posterior tibial nerve (PTN). The PTN contains mixed motorsensory fibers that originate from L5 through S3 in the spinal cord. It modulates the innervation to the bladder, urinary sphincter, and pelvic floor. The mechanism of PTNS in attenuating lower urinary tract symptoms (LUTS), however, is not yet fully understood [2,5,8].

The effectiveness of PTNS for LUTS in overactive bladder (OAB) has been demonstrated in several studies [9]. It has been also reported that interruption of PTNS treatment may result in the reappearance of OAB symptoms [10]. Therefore, the introduction of maintenance therapy for PTNS is important for the treatment plan. Our study aims to reveal the changes in LUTS after 24 months of maintenance PTNS therapy in MS patients.

Materials and Methods

This study protocol, which has a prospective design, was started with the approval of local ethics committee with the decision dated 05.08.2015 and numbered 2015-13. Written informed consent was obtained from the participants. Patients diagnosed with MS in the neurology outpatient clinics of our hospital were screened and the patients with neurogenic overactive bladder (NOAB) due to MS were included in the study.

Inclusion Criteria

The volunteer MS-linked NOAB patients aged 18-65 years with neurogenic LUTS for more than 3 months, and did not receive medical treatment including antimuscarinic drug(s) for more than two weeks or tried useless conservative treatment modalities without obtaining any therapeutic benefit were included in the study.

Exclusion Criteria

Patients with DSD, peripheral nerve lesions, serious secondary metabolic disease, prostate enlargement and/or bladder stone, diabetes mellitus, severe cardiopulmonary complaints, urinary system or vaginal infection, bladder malignancy or high-grade dysplasia. Patients who had undergone continence surgery, neuromodulation therapy applied from a different site or PTNS treatment, botulinum toxin injection therapy for neurogenic OAB in the last year or those using a pacemaker or implantable defibrillator, pregnants or those planning to become pregnant were not included in the study.

Urinalysis was performed at the start of the therapy and at each visit to exclude the possibility of urinary tract infection from all patients. The expanded disability status scale (EDSS) was used to assess disability due to MS. Patients with a higher EDSS score (>7) were excluded from the study. Overactive Bladder Questionnaire Short Form (OAB-q SF), Overactive Bladder Questionnaire (OAB-V8), and International Continence Interrogation Questionnaire Short Form (ICIQ-SF) were used to determine the levels of discomfort before, and after treatment of NOAB.

PTNS Technique

PTNS was performed with a 26G or 34G concentric needle (Medtronic, Denmark) inserted into the posterior side of the medial malleolus. The PTN is most easily accessible from the posterior side of the medial malleolus. Following the finding of the correct point reaching the nerve via the percutaneous route, electrical stimuli are delivered by observing action potential traces on the screen or the rhythmic digital plantar flexion in the toe. Electrical stimulation is delivered for a duration of 200 μs and at a frequency of 10-20 Hz, 1.5 times the amplitude of the motor response or at the level that the patient can withstand (average 0.5-9.0 mA). The electrical excitation generator can be supplied with portable devices or via an EMG device. EMG device was used in our study (Medtronic Key Point Net, Denmark).

Application Protocol

The treatment was initially administered once a week for 30 minutes for 12 weeks. In this study, the treatment protocol was extended up to 24 months from the beginning with longer intervals between PTNS sessions. This protocol is based on previous studies of PTNS on the treatment of idiopathic OAB [11].

PTNS was administered at the beginning of treatment every 7 days for 12 weeks, every 14 days for the next 3 months, every 21 days for the next 3 months and then every 28 days for 24 months. Patients were evaluated using a 3-day voiding diary, ICIQ-SF, OAB-V8, and OAB-q SF questionnaires at baseline and at the 3rd, 6th, 9th, 12th, and 24th months. Neurological and urological evaluations were performed at each session to determine any side effects, emergency medical conditions, or diagnoses.

Table 1. Change of voiding diary parameters during treatment and comparison with 3rd, 6th, 9th, 12th and 24th months according to baseline

	Baseline	3rd	% change from baseline	6th	% change from baseline	9th	% change from baseline	12th	% change from baseline	24th	% change from baseline	*P*-value*
Frequency mean±SD	13.31±1.97	7.42±1.89	44.3	7.28±1.81	45.3	7.19±1.90	45.9	7.05±1.96	43.7	6.54±2.02	50.1	**<0.001**
Nocturia mean±SD	3.77±1.63	1.12±0.70	70.3	1.19±0.61	68.4	1.63±1.45	56.7	1.64±1.20	56.5	1.50±1.07	60.2	**<0.001**
Urgency mean±SD	10.52±3.80	2.89±2.38	72.5	2.43±1.73	76.9	2.56±1.82	75.6	2.31±1.33	72.5	2.07±1.01	80.3	**<0.001**
Urge incontinence mean±SD	5.12±2.99	1.07±0.90	79.1	1.47±1.39	71.2	0.89±0.74	82.6	1.24±1.00	75.8	0.92±0.72	82	**<0.001**
Voided vol mean±SD	125.85±70.83	224.73±72.79	78.6	200.01±54.7	58.9	204.40±56.75	62.4	209.87±66.50	66.8	211.71±52.63	68.2	**<0.001**

* Repeat measurement ANOVA

Statistical analysis

The results were evaluated in Statistical Package for Social Sciences (SPSS) 22.0 (SPSS Inc, Chicago, IL, USA) program. Descriptive statistical methods (number, percentage, mean, standard deviation) were used in the analysis of the data. In the comparison of quantitative data between two groups, t-test was used for independent groups and paired t-test for dependent variables. The repeated measurement ANOVA test was used to compare the treatment success rates of the groups. Results were considered statistically significant at $p<0.05$ within a 95% confidence interval.

Results

Seventy-one patients who met the inclusion criteria were included in the study. During the study, patients started to take their previous medical treatment on their own will (n=3), didn't want PTNS treatment because of social reasons (n=4), withdrew due to non-compliance with the follow-up protocol (n=5) and 2 patients were excluded from the study and consequently, 57 patients were included in the study. The mean age of the patients was 42.6 ± 8.2 (23-64) years. Fifteen (26.3%) male and 42 (73.6%) female patients participated in the study. The patients had the diagnosis of MS for a mean period of 8.72 ± 3.8 years, and the mean duration of urinary complaints was 4.5 ± 1.4 years. The mean EDSS score of the patients included in the study was 4.3 ± 1.6 (2-7).

According to the voiding diary parameters, the improvement in neurogenic overactive bladder symptoms including the frequency of voiding, nocturia, urgency, urinary incontinence, and voiding volume was statistically significant at the third month of treatment in patients receiving PTNS. Improvements in all voiding diary parameters first started to be observed at the 3rd month and the recovery was statistically significant at the 3rd, 6th, 9th, 12th, and 24th months compared to baseline. However, there was no significant difference between the 3rd month and the subsequent visits in terms of these parameters ($p>0.001$). At the end of the 24th month, daily frequencies of voiding (6.7) ($p<0.001$), urinary

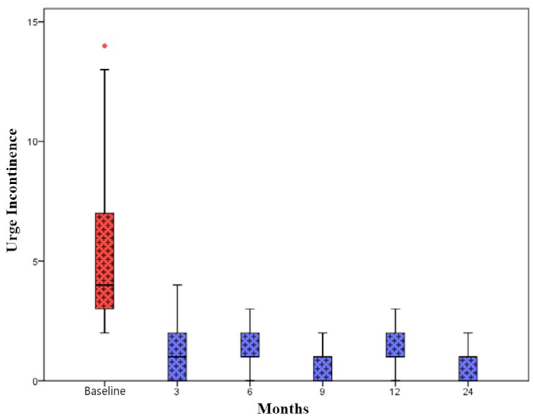

Figure 1. Change of urinary incontinence according to months before and after PTNS treatment

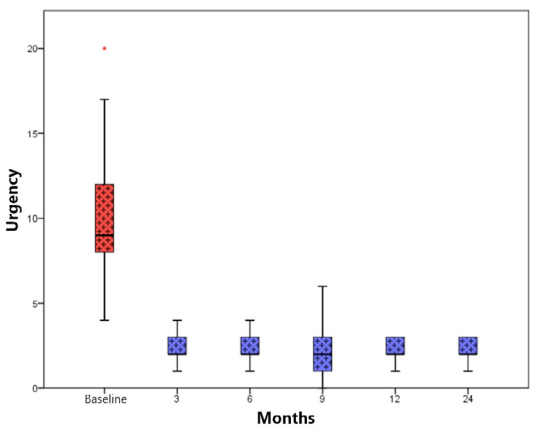

Figure 2. Change in the complaints of urgency before and after PTNS treatment according to months

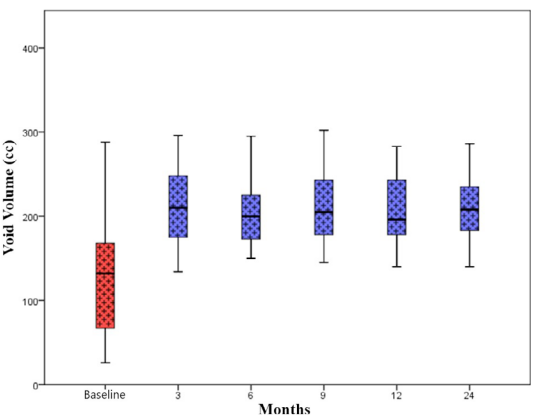

Figure 3. Variation of voiding volume by months before and after PTNS treatment

Table 2. Change of ICIQ-SF, OABv8 and OAB-q scores during treatment and comparison with 3rd, 6th, 9th, 12th and 24th months according to baseline

	Baseline	3rd	% change from baseline	6th	% change from baseline	9th	% change from baseline	12th	% change from baseline	24th	% change from baseline	*P*-value*
OAB-q	60.21+12.01	20.19+5.07	66.5	20.33+6.09	66.2	20.80+5.27	65.4	20.36+4.70	66.2	20.28+5.02	66.3	**<0.001**
ICIQ-SF	17.49±2.18	6.36+1.54	63.6	6.47+1.50	63.0	6.08+ 1.50	65.2	6.12+1.48	65	6.12+1.52	65	**<0.001**
OABV8	28.40+8.65	9.73+3.34	65.7	9.82+3.16	65.4	9.66+3.18	66	10.26+2.95	63.9	8.36+2.89	70.6	**<0.001**

* Repeat measurement ANOVA

incontinence (4.2) (p<0.001), urgency (8.4) (p<0.001) and nocturia (2.2) (p<0.001) were as indicated and voiding volume increased by an average of 85.8 cc (p<0.001) (**Table 1**), (**Figure 1-4**). According to the OAB-V8 questionnaire, there was a statistically significant improvement in symptom severity at the 3rd, 6th, 9th, 12th and 24th months compared to baseline (p<0.001) (**Table 2**), (**Figure 5**). According to the OAB-q questionnaire, there was a statistically significant improvement in symptom severity and health-related quality of life (HRQOL) at the 3rd, 6th, 9th, 12th, and 24th months compared to baseline (p<0.001) (**Table 2**), (**Figure 6**). The ICIQ-SF questionnaire showed a significant improvement in the severity of symptoms at 3rd, 6th, 9th, 12th, and 24th months compared to baseline (p<0.001) (**Table 2**), (**Figure 7**). No side effects related to treatment were reported for 24 months. Five patients (8.7%) had mild to moderate pain at the needle insertion site, cramps and tingling in the legs of unknown association with PTNS.

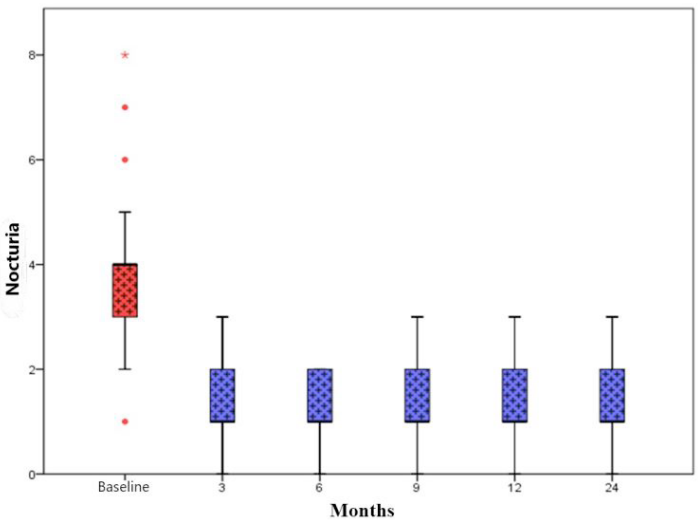

Figure 4. Changes of nocturia complaints before and after PTNS treatment according to months

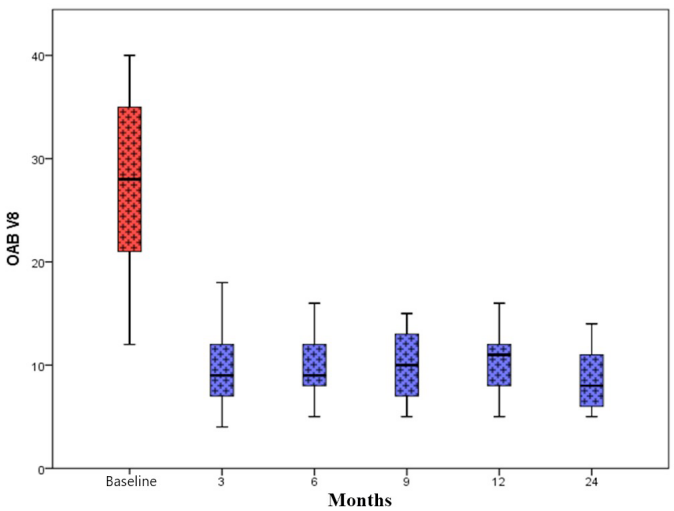

Figure 5. Change in OAB-V8 months before and after PTNS treatment

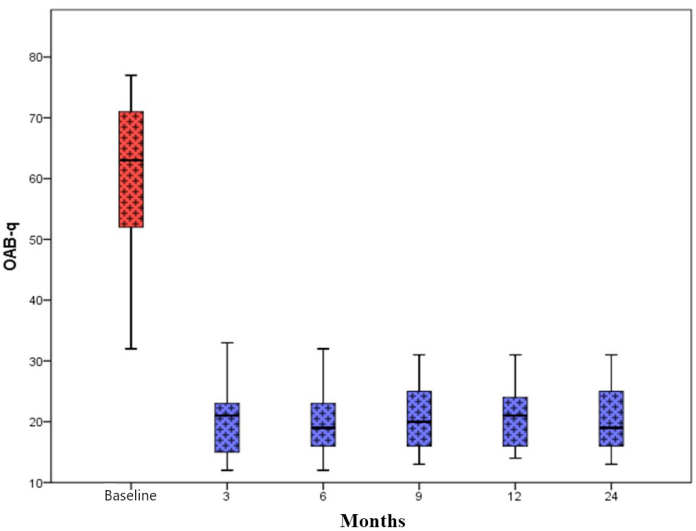

Figure 6. Variation of OAB-q months before and after PTNS treatment

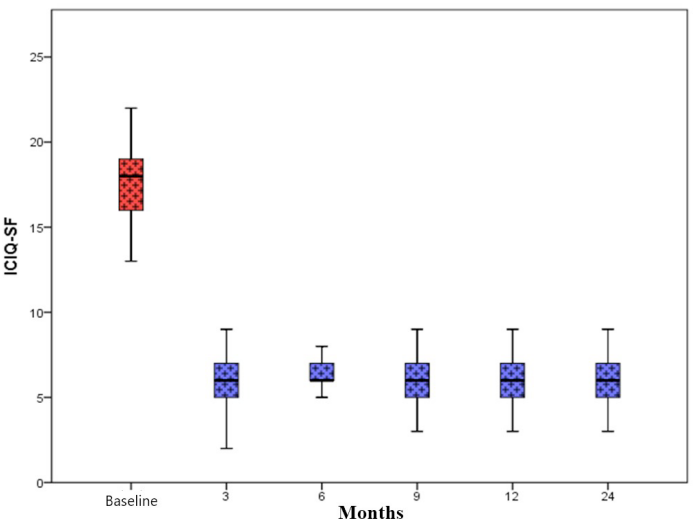

Figure 7. ICIQ-SF change before and after PTNS treatment

Discussion

Urological symptoms are common in MS patients. Symptoms and severity of complaints may vary. The most common symptoms in MS patients are urinary incontinence, increased urinary frequency and nocturia. DO, DSD and/or decreased detrusor activity are urodynamic findings. These symptoms may cause urinary retention, recurrent urinary tract infection, voiding dysfunction, hydroureteronephrosis, pyelonephritis with the progression of MS, and a group of these patients need clean intermittent or permanent catheterization. Although the mechanism of neuromodulation used in the treatment of these disorders is not known exactly, it causes rebalancing of inhibitory and excitatory impulses that control the bladder in the CNS. Afferent nerve stimulation provides direct, central inhibition of preganglionic bladder motor neurons in the sacral cord [12].

Neuromodulation can be applied in many different ways including direct bladder stimulation, intravesical electrical stimulation, pelvic nerve stimulation, sacral spinal stimulation, pudendal nerve stimulation, electrical stimulation of thigh muscles, transcutaneous or percutaneous stimulation of PTN [13,14]. Among these techniques, PTNS is a minimally invasive technique with greater treatment efficacy than other techniques. It is an alternative treatment for patients with OAB [3,4].

PTNS was first described by McGuire et al. who placed the transcutaneous electrode on PTN and grounding electrode on the corresponding contralateral side for the treatment of incontinence. [15]. In another study, Stoller et al., performed this method by placing a percutaneous needle electrode on the ipsilateral side [16]. Since then, there have been many studies investigating the efficacy of intermittent PTNS treatment of OAB.

Although many studies have been conducted in NOAB, the effective mechanism of action of PTNS is still unclear. Danisman et al. showed that after PTNS, the number of mast cells in the bladder of female rats decreased [17]. Finazzi-Agro et al. demonstrated a significant increase in the amplitude of delayed somatosensory evoked potentials for 24 hours at the end of a 12-session PTNS treatment and indicated that it exerts its effect on supraspinal centers [5]. This finding may lead to a change in our understanding of mechanism of sensory stimuli, suggesting a possible reorganization of cortical stimulation after PTNS treatment [18].

Vandoninck et al. demonstrated the effects of PTNS in a study involving 35 women with refractory idiopathic DO. They reported that 71% of patients responded to PTNS treatment and there was a greater than 50% reduction in the frequency of urge incontinence in the patient group compared to placebo ($p<0.001$) [19]. A multicenter study of 53 female patients with refractory idiopathic OAB has shown that 71% of the patients had significant improvement in their complaints, with 35% improvement in urinary incontinence, 20% in QoL, and 30% reduction in pain [20]. In their study, MacDiarmid et al., reported its therapeutic effectiveness in patients with idiopathic OAB who completed a 12-week session consecutively and the persistent PTNS treatment for 1 year. They showed that after 12 weeks of treatment, it was an effective treatment in decreasing symptoms of voiding frequency, nocturia, urgency, and urinary incontinence, and increasing voiding volume with resultant persistent improvement of symptoms during 12 months of prolonged treatment [21]. In another study, patients receiving PTNS and PTNS + low-dose oxybutynin were compared and their response rates were reported as 61.6% and 83.2%, respectively [22]. In another study conducted with MS patients with refractory LUTS, the symptoms of 89% of the patients who received PTNS treatment had improved at a rate of 70% with a significant improvement in their QoLs [7]. De Seze et al. published 3-month results of TTNS administered transcutaneously to 70 MS patients and showed that more than 80% of patients had congestive urinary incontinence and clinical improvement in urinary frequency [23]. TTNS was also shown to be effective in the review by Tu et al. [24]. Similarly, in our study, we have seen an improvement in all of these parameters thanks to PTNS treatment starting from the 3rd month compared to the baseline.

Kabay et al. investigated the acute urodynamic effects of PTNS in MS and Parkinson's disease patients [3,4]. These studies showed an increase in voluntary detrusor contractions and cystometric capacity. Another study demonstrated the efficacy of 12-week PTNS treatment in clinical and urodynamic parameters in MS patients with LUTS. This study also reported that 12-month treatment of PTNS in MS patients with NOAB was effective and safe [25].

The improvement achieved as a result of the first 12 weeks of treatment was maintained for patients who received this treatment for 12 months. It has been reported that the frequency of voiding, voided urine volume, nocturia, urinary incontinence, and urgency symptoms improved significantly compared to baseline and this improvement lasted for 12 months during treatment. Consistent with voiding diary results, ICIQ-SF, OAB-q, and OAB-V8 scores confirmed sustained improvement over 12 months, reflecting the clinical significance of symptomatic improvement in patients [25,26]. In our study, we observed an improvement in ICIQ-SF, OAB-V8, and OAB-q scores starting from the 3rd month compared to the baseline, and this improvement continued similarly during the treatment.

In our study, in accordance with the literature, a significant improvement was observed in all parameters of the voiding diary starting from 3 months, and extending up to 24 months. This improvement continued until 24 months with maintenance therapy. However, there was no statistically significant change in the effectiveness of symptomatic treatment after 3 months. In our study, we observed an improvement in ICIQ-SF, OAB-V8, and OAB-q scores starting from the 3rd month compared to the baseline, and this improvement was maintained during the 24-month treatment. We think that this improvement, which was observed starting from the 3rd month of the treatment did not show any significant change during the ongoing controls which indicates limited effectiveness of PTNS. However, it also signifies that long-term effectiveness of PTNS has not regressed and continues to be effective thanks to this treatment protocol.

The limitation of this study is that it was conducted with a small number of patients. In addition, urodynamic examination was not performed during the follow-up of the patients after the diagnosis of NOAB was made. The reason why we could not perform urodynamic examination during follow-up in our study was that most of the patients did not accept urodynamic examination. In this case, we thought that the decrease in the number of patients we followed and included in the study would make it impossible to carry out the study further.

Conclusion

PTNS is a valuable treatment option for NOAB symptoms. It should be considered as a long-term well-tolerated treatment option, especially in patients with NOAB who are refractory to medical therapy. In this study, improvements in voiding frequency, nocturia, urgency, and urinary incontinence were observed after 12 weeks of PTNS treatment, and then the significant efficacy of the treatment was maintained during the application of 24-month protocol. However, we think that further prospective randomized multicenter studies should be performed to generalize the results of our study.

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of Canakkkale Onsekiz Mart University with the decision dated 05.08.2015 and numbered 2015-13.
Informed Consent: Written informed consent was obtained from patients who participated in this study.
Publication: The results of the study were not published in full or in part in form of abstracts.
Peer-review: Externally and internally peer-reviewed.
Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept – M.S., S.K., S.C.K.; Design – M.S., B.A., S.K., S.C.K.; Supervision – S.C.K., S.K., B.A.; Resources – M.S., S.K., B.A.; Materials – M.S., S.C.K., S.K.; Data Collection and/or Processing – M.S., S.K., B.A.; Analysis and/or Interpretation – M.S., B.A., S.K., S.C.K.; Literature Search – M.S., B.A.; Writing Manuscript – M.S., B.A., S.K., S.C.K.; Critical Review – M.S., S.K., B.A., S.C.K.
Conflict of Interest: The authors declare that they have no conflict of interest.
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References

[1] Lublin FD, Häring DA, Ganjgahi H, Ocampo A, Hatami F, Čuklina J, et al. How patients with multiple sclerosis acquire disability. Brain 2022;145:3147-61. https://doi.org/10.1093/brain/awac016

[2] Taylor R. Rehabilitation of persons with multiple sclerosis. Physical Medicine and Rehabilitation. Philadelphia, PA: Saunders; 1996.

[3] Kabay SC, Yucel M, Kabay S. Acute effect of posterior tibial nerve stimulation on neurogenic detrusor overactivity in patients with multiple sclerosis: urodynamic study. Urology 2008;71:641-5. https://doi.org/10.1016/j.urology.2007.11.135

[4] Kabay SC, Kabay S, Yucel M, Ozden H. Acute urodynamic effects of percutaneous posterior tibial nerve stimulation on neurogenic detrusor overactivity in patients with Parkinson's disease. Neurourol Urodyn 2009;28:62-7. https://doi.org/10.1002/nau.20593

[5] Finazzi-Agrò E, Rocchi C, Pachatz C, Petta F, Spera E, Mori F, et al. Percutaneous tibial nerve stimulation produces effects on brain activity: study on the modifications of the long latency somatosensory evoked potentials. Neurourol Urodyn 2009;28:320-4. https://doi.org/10.1002/nau.20651

[6] Peters KM, Carrico DJ, MacDiarmid SA, Wooldridge LS, Khan AU, McCoy CE, et al. Sustained therapeutic effects of percutaneous tibial nerve stimulation: 24-month results of the STEP study. Neurourol Urodyn 2013;32:24-9. https://doi.org/10.1002/nau.22266

[7] Gobbi C, Digesu GA, Khullar V, El Neil S, Caccia G, Zecca C. Percutaneous posterior tibial nerve stimulation as an effective treatment of refractory lower urinary tract symptoms in patients with multiple sclerosis: preliminary data from a multicentre, prospective, open label trial. Mult Scler 2011;17:1514-9. https://doi.org/10.1177/1352458511414040

[8] de Sèze M, Ruffion A, Denys P, Joseph P-A, Perrouin-Verbe B, group IFN-Ues. The neurogenic bladder in multiple sclerosis: review of the literature and proposal of management guidelines. Mult Scler 2007;13:915-28. https://doi.org/10.1177/1352458506075651

[9] Kabay S, Kabay SC, Yucel M, Ozden H, Yilmaz Z, Aras O, et al. The Urodynamic Effect of a 3-Month Percutaneous Posterior Tibial Nerve Stimulation Treatment in Patients With Multiple Sclerosis-Related Neurogenic Bladder Dysfunction. Neurourol Urodyn 2009;28:964-8. https://doi.org/10.1002/nau.20733

[10] van der Pal F, nan Balken MR, Heesakkers JP, Debruyne FM, Bemelmans BL. Percutaneous tibial nerve stimulation in the treatment of refractory overactive bladder syndrome: is maintenance treatment necessary? BJU Int 2006;97:547-50. https://doi.org/10.1111/j.1464-410X.2006.06055.x

[11] Peters KM, MacDiarmid SA, Wooldridge LS, Leong FC, Shobeiri SA, Rovner ES, et al. Randomized trial of percutaneous tibial nerve stimulation versus extended-release tolterodine: results from the overactive bladder innovative therapy trial. J Urol 2009;182:1055-61. https://doi.org/10.1016/j.juro.2009.05.045

[12] Soomro NA, Khadra MH, Robson W, Neal DE. A crossover randomized trial of transcutaneous electrical nerve stimulation and oxybutynin in patients with detrusor instability. J Urol 2001;166:146-9. https://pubmed.ncbi.nlm.nih.gov/11435843/

[13] van Rey FS, Heesakkers JP. Applications of neurostimulation for urinary storage and voiding dysfunction in neurological patients. Urol Int 2008;81:373-8. https://doi.org/10.1159/000167831

[14] Sarmento ALC, Sá BS, Vasconcelos AG, Arcanjo DDR, Durazzo A, Lucarini M, et al. Perspectives on the Therapeutic Effects of Pelvic Floor Electrical Stimulation: A Systematic Review. Int J Environ Res Public Health 2022;19:14035. https://doi.org/10.3390/ijerph192114035

[15] Mcguire EJ, Zhang SC, Horwinski ER, Lytton B. Treatment of motor and sensory detrusor instability by electrical stimulation. J Urol 1983;129:78-9. https://doi.org/10.1016/s0022-5347(17)51928-x

[16] Stoller ML. Afferent nerve stimulation for pelvic floor dysfunction. Eur Urol 2000;37(Suppl.2):33.

[17] Danisman A, Kutlu O, Akkaya E, Karpuzoglu G, Erdogru T. Tibial nerve stimulation diminishes mast cell infiltration in the bladder wall induced by interstitial cystitis urine. Scand J Urol Nephrol 2007;41:98-102. https://doi.org/10.1080/00365590600911233

[18] Vodusek DB, Light JK, Libby JM. Detrusor inhibition induced by stimulation of pudendal nerve afferents. Neurourol Urodyn 1986;5:381-9. https://doi.org/10.1002/nau.1930050404

[19] Vandoninck V, Van Balken MR, Finazzi Agró E, Petta F, Caltagirone C, Heesakkers JP et al. Posterior tibial nerve stimulation in the treatment of urge incontinence. Neurourol Urodyn 2003; 22:17-23. https://doi.org/10.1002/nau.10036

[20] Govier FE, Litwiller S, Nitti V, Kreder KJ Jr, Rosenblatt P. Percutaneous afferent neuromodulation for the refractory overactive bladder: results of a multicenter study. J Urol 2001;165:1193-8. https://pubmed.ncbi.nlm.nih.gov/11257669/

[21] MacDiarmid SA, Peters KM, Shobeiri SA, Wooldridge LS, Rovner ES, Leong FC, et al. Long-term durability of percutaneous tibial nerve stimulation for the treatment of overactive bladder. J Urol 2010;183:234-40. https://doi.org/10.1016/j.juro.2009.08.160

[22] Karademir K, Baykal K, Sen B, Senkul T, Iseri C, Erden D. A peripheric neuromodulation technique for curing detrusor overactivity: Stoller afferent neurostimulation. Scand J Urol Nephrol 2005;39:230-3. https://doi.org/10.1080/00365590510031147

[23] de Sèze M, Raibaut P, Gallien P, Even-Schneider A, Denys P, Bonniaud V, et al. Transcutaneous posterior tibial nerve stimulation for treatment of the overactive bladder syndrome in multiple sclerosis: results of a multicenter prospective study. Neurourol Urodyn 2011;30:306-11. https://doi.org/10.1002/nau.20958

[24] Tu H, Li N, Liu W, Fan Z, Kong D. Effects of transcutaneous tibial nerve stimulation on females with overactive bladder syndrome in multiple sclerosis a protocol for a systematic review and meta-analysis. PLoS One 2022;17:e0269371. https://doi.org/10.1371/journal.pone.0269371

[25] Canbaz Kabay S, Kabay S, Mestan E, Cetiner M, Ayas S, Sevim M, et al. Long term sustained therapeutic effects of percutaneous posterior tibial nerve stimulation treatment of neurogenic overactive bladder in multiple sclerosis patients: 12-months results. Neurourol Urodyn 2017;36:104-10. https://doi.org/10.1002/nau.22868

[26] Kabay S, Canbaz Kabay S, Cetiner M, Mestan E, Sevim M, Ayas S, et al. The Clinical and Urodynamic Results of Percutaneous Posterior Tibial Nerve Stimulation on Neurogenic Detrusor Overactivity in Patients With Parkinson's Disease. Urology 2016;87:76-81. https://doi.org/10.1016/j.urology.2015.09.026