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FEMALE UROLOGY

Original Article

Role of percutaneous posterior tibial nerve stimulation either alone or combined with an anticholinergic agent in treating patients with overactive bladder

Aşırı aktif mesaneli hastaların tedavisinde, tek başına ve antikolinerjik ajanla kombine edilerek kullanılan perkütan posterior tibial sinir uyarımının rolü

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ABSTRACT

Objective: To evaluate the efficacy of percutaneous tibial nerve stimulation (PTNS), either alone or combined with an anticholinergic agent, in treating patients with an overactive bladder (OAB) in whom previous conservative treatment failed.

Material and methods: In this study, we included a total of 30 female patients with OAB in whom all conventional therapies failed between January 2010 and April 2011. Patients were randomly divided into three groups: Group 1, PTNS group; Group 2, patients receiving an anticholinergic agent; and Group 3, patients receiving both PTNS and anticholinergic agent. PTNS treatment continued for 12 weeks with each session lasting 30 min.

Results: All parameters of the bladder diary significantly improved in all groups ($p<0.05$). Similarly, all scores measured by questionnaires (UDI-6, IIQ-7, and OABSS) revealed significant improvements in all groups. When the improvements in symptoms were compared among the groups, there was a statistically significantly higher improvement in groups 1 and 3 than in Group 2.

Conclusion: PTNS is a safe, simple, and minimally invasive treatment modality in patients with OAB, and it may be suggested either alone or in combination with anticholinergics when conventional treatments fail.

Keywords: Anticholinergic; overactive bladder; percutaneous tibial nerve stimulation; treatment.

ÖZ

Amaç: Konservatif yaklaşımlar ile tedavide yeterli yanıt alınamayan aşırı aktif mesaneli (AAM) hastalarda, perkütan tibial sinir stimülasyonunun (PTSS) tek başına ya da antikolinerjik ilaç uygulamaları ile kombine edilerek kullanımının, tedavideki etkinliğini değerlendirmek.

Gereç ve yöntemler: Ocak 2010 ile Nisan 2011 tarihleri arasında konvansiyonel tedavi yöntemlerinden fayda görmeyen AAM'li 30 kadın hasta çalışmaya alındı. Hastalar randomize olarak 3 eşit gruba ayrıldı. Grup 1; yalnızca PTSS uygulanan grup, Grup 2; yalnız antikolinerjik kullanan (günde bir kez Tolterodine 4 mg SR kapsül) hastalar ve Grup 3; PTSS ve antikolinerjik tedavisi uygulanan hastalar. PTSS, 12 hafta boyunca haftada 30 dakika uygulandı.

Bulgular: Tüm gruplarda işeme günlüğü parametrelerinde istatistiksel olarak anlamlı iyileşmeler saptandı ($p<0,05$). Benzer şekilde (UDI-6, IIQ-7, AAMSS) değerlendirmesinde ise her 3 grupta da istatistiksel olarak anlamlı iyileşmeler saptandı. Her 3 grupta tedavi sonrası elde edilen verilerin karşılıklı değerlendirmesinde ise; PTSS ve PTSS+AKK tedavisi uygulanan gruplardaki iyileşmenin yalnız AKK uygulanan gruba oranla daha yüksek olduğu saptandı.

Sonuç: PTSS AAM'li hastalarda minimal invaziv, kolay uygulanabilir ve ciddi yan etkisi olmayan bir tedavi seçeneği olup dirençli olgularda tek başına ya da antikolinerjik ajanlarla kombine olarak kullanılabilir.

Anahtar kelimeler: Antikolinerjik; aşırı aktif mesane; perkütan tibial sinir stimülasyonu; tedavi.

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Introduction

Overactive bladder (OAB) is a disturbing symptom complex characterized by urgency, frequent urination, and nocturia with/without urge incontinence.[1] OAB has a high prevalence and affects millions of people worldwide. It has been reported that 6% of the adult population in Europe and the United States is affected.[2] All previous epidemiological studies have reached a consensus that OAB prevalence increases with increasing age.[3]

Overactive bladder has a significant impact on the quality of life, quality of sleep, sexual activity, mental health, work productivity, and healthcare costs.[4,5] Conservative and medical treatments, including bladder training, pelvic floor muscle training, and antimuscarinic medication are frequently used; however, the results can be disappointing. It was reported that after 6 months, only 18% of patients continued antimuscarinic medications because of their adverse effects and insufficient symptom improvement.[6] Modulation of bladder reflex pathways has been acknowledged as the next logical step in the algorithm of care when conservative and medical treatments have failed.[7] Neuromodulation may be either invasive when implantable electrodes are used, such as in sacral nerve stimulation (SNS), or noninvasive when removable devices, such as transvaginal or transanal electrostimulation, magnetic stimulation, or percutaneous tibial nerve stimulation (PTNS), are used. Despite effectiveness of SNS, the use of sacral nerve stimulation is limited in clinical practice because of several factors, including invasiveness, associated costs, and its limitations in older adults and those who are frail or who have several medical comorbidities.[8] Some randomized controlled studies compared PTNS and anticholinergic drugs (ACDs).[9,10]

This study aimed to investigate efficacy and safety of PTNS alone or together with an anticholinergic agent in patients who were diagnosed with OAB and did not respond sufficiently to previous conservative treatment options.

Material and methods

Design of the study

Firat University Medical Faculty Ethics Committee approved the study (date: Jan 13, 2010, no: 247). Written informed consent was obtained from patients who participated in this study. Between January 2010 and April 2011, a total of 30 women patients who were admitted to Firat University Hospital's Urology Clinic with complaints of lower urinary tract symptoms (LUTS), OAB symptoms (urgency, urge incontinence, nocturia, and frequent urination) for at least 6 months and who did not sufficiently respond to previous conservative treatment options were included in this study. The mean age of patients was 39 years, with a range of 20–59 years. A detailed history for LUTS was obtained from all patients, and biochemical analyses, radiological imaging, and urodynamic tests were conducted. Their medical and surgical histories were obtained, and urogynecological and short neurological examinations were performed.

Patients included in the study had OAB symptoms (frequent urination, urgency, and/or urge incontinence) for at least 6 months. Their 3-day voiding diary revealed ≥8 micturitions/24 h and ≥1 micturitions/night, urgency with or without urge incontinence in a 24-h period, and a previous conservative medical treatment without any satisfactory response. Exclusion criteria included any known or determined urinary retention or urinary tract obstruction; history of bladder augmentation surgery; presence of a metabolic disease; any neurogenic disease causing urinary incontinence, refractory, or recurrent urinary tract infection; interstitial cystitis; bladder cancer; spinal cord injury; Alzheimer's disease or dementia; neuropathic disorders; uncontrolled narrow-angle glaucoma; permanent pacemaker; bleeding diathesis; presence, suspicion of, or planning pregnancy; hypersensitivity to tolterodine and its contents; and superficial and/or deep skin infection where intervention is required.

Patients were provided with a 3-day voiding diary before and after treatment, and they were asked to record all fluid intake, micturitions, number of voiding in the daytime and night, incontinence episodes, and what they were dealing with during incontinence episodes. The patients were asked to complete the Urinary Distress Inventory (UDI-6) (appendix 1), Incontinence Impact Questionnaire (IIQ-7) (appendix 2), and Overactive Bladder Symptom Score (OABSS) (appendix 3) questionnaires, which were validated in Turkish, before and after treatment to determine how patients were affected by the disease and the impact of the disease on the quality of life. In all groups, questions 2, 3, and 4 in UDI-6 were only asked to patients who had incontinence. In addition, all patients had uroflowmetry before and after treatment to determine whether the treatment had any effect on speed of voiding and residual urine volume, and their residual urine volumes were analyzed by ultrasonography.

Group Definitions

The patients included in the study were randomized into three groups with equal number of patients in each with respect to the PTNS and ACD [tolterodine 4 mg SR capsule (Detrusitol; Pfizer, İstanbul, Turkey), once a day] treatments as follows:

Group 1 (n=10): These patients had PTNS alone for 30 min/week for 12 weeks.

Group 2 (n=10): These patients were administered only anticholinergic agent treatment, i.e., tolterodine 4 mg SR capsule (Pfizer) once a day for 12 weeks.

Group 3 (n=10): These patients had a combination of PTNS and ACD. They had PTNS for 30 min/week for 12 weeks and tolterodine 4 mg SR capsule (Pfizer) once a day for 12 weeks.

PTNS technique

Percutaneous tibial nerve stimulation was performed using a low-voltage electrical stimulator (Urgent PC; Uroplasty, Minnetonka, MN, USA) and a 34-gauge acupuncture needle. The patient was asked to sit with legs slightly bent, and the 34-gauge needle was percutaneously inserted 60° to the horizontal plane, approximately 5 cm cephalad to either the right or left medial malleolus. A surface electrode was placed on the medial surface of the ipsilateral calcaneum and both the needle and electrode were connected to the 9-V electrical stimulator (Urgent PC). The stimulation current (0–10 mA) with a fixed frequency of 20 Hz and a pulse duration of 200 μs was increased until flexion of the big toe was noticed. Stimulation sessions lasted for 30 min weekly in an outpatient setting.

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Statistical analysis

Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) for Windows 12.0 was used for statistical analyses. Pre- and post-treatment values were provided as mean±standard deviation. Intragroup pre- and post-treatment comparisons were done with paired samples t-test. One-way ANOVA test was used for intergroup comparisons, and Tukey's test was used as a post-hoc test. The results were analyzed with a 95% confidence interval, and $p<0.05$ was regarded as statistically significant.

Results

The ages of 30 patients included in the study ranged between 20 and 59 years. The mean age was 41.00±14.49 (20–59) years in PTNS, 36.30±6.11 (28–47) years in ACD, and 38.00±9.6 (23–55) years in PTNS+ACD groups, and there were no significant differences among the groups.

PTNS Group

The data obtained from pre- and post-treatment voiding diaries of the group that had PTNS alone are presented in Table 1.

Post-treatment mean urine volume was significantly higher than pre-treatment mean urine volume ($p<0.05$) (Table 1). This demonstrates an increase in the bladder capacity. Similarly, comparison of void frequency during daytime, nocturia, number of urge incontinences, and total number of voids revealed significant reductions after treatment ($p<0.05$) (Table 1).

The results of IIQ-7 test that determines the negative impact of incontinence on daily life and mood revealed that scores significantly decreased after treatment ($p<0.05$) (Table 2). When total scores of the first and second questions of UDI-6 test concerning urge incontinence were compared before and after treatment, it was observed that mean post-treatment score demonstrated a highly significant reduction when than mean pre-treatment score ($p<0.001$) (Table 2).

ACD Group

When frequency volume chart was examined, it was found that patients who used anticholinergic agent demonstrated significant reductions in void frequency, nocturia, urgency, and total voids ($p<0.05$) (Table 3).

The mean scores of UDI-6, IIQ-7, and OABSS demonstrated significant reductions after treatment than pre-treatment scores ($p<0.05$) (Table 4).

PTNS+ACD Group

The data obtained from pre- and post-treatment voiding diaries of the group that had PTNS+ACD are presented in Table 5. There were significant improvements in all parameters except mean PMR or Qmax parameters ($p<0.001$) (Table 5).

Pre-and post-treatment mean scores of UDI-6, IIQ-7, and OABSS are presented in Table 6. Post-treatment scores reveled significant reductions than pre-treatment scores ($p<0.05$).

Table 1. Voiding diary data of PTNS group

PTNS group (n=10)	Pre-treatment	Post-treatment	p
Total urine (cc)	1293±33.7	1473±90.6	0.02*
Void frequency (daytime)	10.1±0.88	8.9±0.880	0.011*
Nocturia	5.3±0.90	2.03±0.50	0.007**
Urge incontinence (n=4)	1.2±1.60	0.13±0.23	0.003**
Total voids (mL)	15.7±0.67	11.3±0.67	0.001***
PMR (mL)	58.8±14.41	25.5±8.90	0.283
QMAX (mL/sec)	16.4±1.710	22.6±2.63	0.211

PTNS: percutaneous tibial nerve stimulation; PMR: post-micturition residual volume; QMAX: maximum flow rate. Data are presented as mean±standard deviation. Paired T test was used. *p<0.05, **p<0.01, ***p<0.001

Table 2. Analysis of UDI-6, IIQ-7 and OABSS scores in PTNS group

PTNS group (n=10)	Pre-treatment	Post-treatment	p
UDI-6	8±1.5	2.9±1.59	0.001***
UDI-6 (Questions 1 and 2)	03.60±1.07	01.30±0.82	0.001**
IIQ-7	17.5±1.73	5.75±0.95	0.039*
OABSS	20.5±4.6	6.5±2.83	0.001***

PTNS: percutaneous tibial nerve stimulation; UDI-6: urinary distress inventory; IIQ-7: incontinence impact questionnaire; OABSS: overactive bladder symptom score. Data are presented as mean±standard deviation. Paired T test was used. *p<0.05, **p<0.01, ***p<0.001

Table 3. Voiding diary data of ACD group

ACD group (n=10)	Pre-treatment	Post-treatment	p
Total urine (cc)	1353±37.8	1362±37.5	0.298
Void frequency (daytime)	11.27±0.44	10.57±0.5	0.024*
Nocturia	5.9±0.47	4.93±0.49	0.008**
Urge incontinence (n=9)	2.43±1.05	1.93±0.86	0.02*
Total voids (mL)	18.26±1.18	17.37±1.12	0.019*
PMR (mL)	102.2±40.43	84.5±40.1	0.932
QMAX (mL/sec)	15.4±1.64	17.5±1.58	0.415

ACD: anticholinergic drug; PMR: post-micturition residual volume; QMAX: maximum flow rate. Data are presented as mean±standard deviation. Paired T test was used. *p<0.05, **p<0.01, ***p<0.001

Analysis of post-treatment percent change of the quality of life score in PTNS+ACD group revealed a high decrease, as observed in the PTNS group (54% in UDI-6, 65% in IIQ-7, and 42% in OABSS).

Comparison of the groups

Analysis of voiding diary

Comparisons of the groups revealed that urine volume significantly increased after treatment in PTNS and PTNS+ACD groups (Figure 1). Comparison of PTNS and PTNS+ACD

groups revealed that the increase in PTNS+ACD group was more significant than PTNS group ($p<0.05$ in PTNS group, $p<0.001$ in PTNS+ACD group, and $p>0.05$ in ACD group).

Frequency of voiding during daytime significantly decreased in all three groups. Decrease in PTNS group was more significant than ACD group; however, decrease in PTNS+ACD group was more significant when compared with that in the other two groups ($p<0.05$ for PTNS and ACD groups, $p<0.01$ for PTNS+ACD group).

As mentioned before, comparisons of pre- and post-treatment nocturia revealed significant reductions after treatment in all of three groups. However, decrease in PTNS group was significantly more than in ACD group ($p<0.05$). Similarly, decrease in PTNS+ACD group was statistically significant ($p<0.01$ in PTNS and ACD group, $p<0.001$ in PTNS+ACD group).

Comparison of the groups for the number of urge incontinence episodes demonstrated that reduction in PTNS group was more significant than in ACD group and reduction was most significant in PTNS+ACD group ($p<0.01$, $p<0.05$, and $p<0.001$ for PTNS, ACD, and PTNS+ACD groups, respectively).

Decrease in the mean number of total voids after treatment was more significant in PTNS and PTNS+ACD groups than in ACD group ($p<0.001$ for PTNS and PTNS+ACD groups, $p<0.05$ for ACD group).

Differences of treatment response rates in voiding diary parameters among the groups

The parameters of voiding diary demonstrated differences among the groups. Pre- and post-treatment response rates of these parameters are shown in Figure 1.

The maximum increase in total void volume was observed in Group 3 (PTNS+ACD) (Figure 1). When parameters of voiding diary were analyzed, most significant changes in all parameters were observed in Group 3. When Groups 1 and 2 were analyzed together, response rates in parameters were higher in Group 1 (PTNS) than in Group 2 (ACD) (Figure 1).

Table 4. Evaluation of UDI-6, IIQ-7 and OABSS scores in ACD group

ACD group (n=10)	Pre-treatment	Post-treatment	p
UDI-6	9.7±2.58	7.6±2.95	0.002**
UDI-6 (Questions 1 and 2)	04.50±1.08	03.10±0.73	0.001**
IIQ-7	14.6±5.19	13±4.74	0.016*
OABSS	21.2±2.61	17.4±3.47	0.005**

ACD: anticholinergic drug; UDI-6: urinary distress inventory; IIQ-7: incontinence impact questionnaire; OABSS: overactive bladder symptom score. Data are presented as mean±standard deviation. Paired T test was used. *p<0.05, **p<0.01, ***p<0.001

Table 5. Analysis of voiding diary data in PTNS+ACD group

PTNS+ACD group (n=10)	Pre-treatment	Post-treatment	p
Total urine (cc)	1221±80.3	1532±97	0.001***
Void frequency (daytime)	10.8±0.9	8.03±1.07	0.009**
Nocturia	5.3±0.67	2±0.66	0.001***
Urge incontinence (n=4)	1.33±1.77	0.33±0.57	0.001***
Total voids (mL)	16.1±0.77	10.07±1.07	0.001***
PMR (mL)	76±20.42	65.1±18.13	0.053
QMAX (mL/sec)	15.3±1.57	16.3±2.86	0.293

PTNS: percutaneous tibial nerve stimulation; ACD: anticholinergic drug; PMR: post-micturition residual volume; QMAX: maximum flow rate. Data are presented as mean±standard deviation. Paired T test was used. *p<0.05, **p<0.01, ***p<0.001

Table 6. Analysis of UDI-6, IIQ-7, and OABSS scores in PTNS + ACD group

PTNS+ACD group (n=10)	Pre-treatment	Post-treatment	p
UDI-6	8.2±2.74	3.8±2.57	0.001***
UDI-6 (Questions 1 and 2)	03.40±1.17	01.60±0.96	0.001***
IIQ-7	14±2.58	4.75±1.70	0.047*
OABSS	23.3±3.4	16.5±5.33	0.001***

PTNS: percutaneous tibial nerve stimulation; ACD: anticholinergic drug; UDI-6: urinary distress inventory; IIQ-7: incontinence impact questionnaire; OABSS: overactive bladder symptom score. Data are presented as mean±standard deviation. Paired T test was used. *p<0.05, **p<0.01, ***p<0.001

Discussion

For the first time in 1983, McGuire et al.[11] described electrical stimulation of the tibial nerve in a mixed group of patients with detrusor instability, multiple sclerosis, spinal cord injury, and interstitial cystitis. After treatment, 55% of patients were dry, and 32% of them had improvement. In 1987, Stoller et al.[12] described a new technique in pig-tailed monkeys: Stoller afferent nerve stimulation (SANS), in which electrical stimulus was percutaneously applied with an acupuncture needle inserted near the tibial nerve. The mechanism of the bladder neuromodulative action is unclear. The effect is possibly mediated through a combination of increase in cerebral endorphins, stimulation of somatic sacral and lumbar afferent fibers, and activation of efferent fibers to the striated urethral sphincter. These possible mechanisms result in inhibition of the detrussor activity.[13] More than 30 studies regarding PTNS have been published. The earliest ones are case series or single-arm efficacy studies,[14-16] three are randomized, controlled trials,[9,17,18] and two are long-term follow-up studies of patients who were responders in the overactive bladder innovative therapy (OrBIT) and sham effectiveness in the treatment of overactive bladder symptoms (SUmiT) trials.[19, 20] Over half of the patients receiving PTNS therapy in the SUmiT trial, a randomized, double-blinded,

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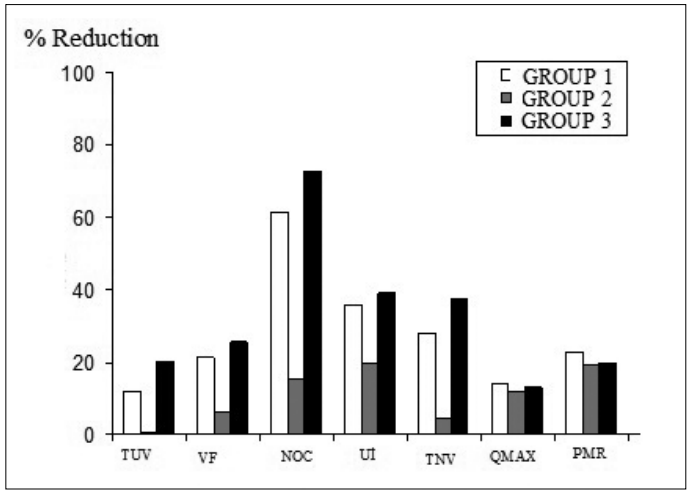

Figure 1. Treatment response rates in voiding diary parameters

sham controlled study, reported moderate or marked improvement in bladder symptoms (54.5% in PTNS patients vs. 20.9% in sham, p<0.001). In addition, PTNS reduced the number of voids per day from 12.3 at baseline to 9.8 at 12 weeks, a mean reduction of –2.4 vs. a reduction of –1.5 in the sham group (p<0.001). Urge incontinence episodes per day decreased from 3/day at baseline to 0.3/day at 12 weeks vs. 1.8/day at baseline to 1.0/day for sham (p<0.001).[19] In a randomized, controlled study, Finazzi-Agro et al.[17] reported that PTNS significantly increased voided volume than sham treatment (150–186 mL in the PTNS treatment group vs. 146–150 mL in the sham group, p<0.001). In a urodynamic study, Klingler et al.[21] reported that PTNS increased the mean total bladder capacity from 197 mL at baseline (range 35–349 mL) to 252 mL (range 78–384 mL, p<0.01) after 12 weeks of therapy. When PTNS was compared with tolterodine extended release in the OrBIT study, both therapies demonstrated statistically significant improvements in incontinence episodes, voids per day, and nocturia.[9]

In our study, analysis of 3-day voiding diary parameters revealed a 25%, 21%, and 6% decrease in the number of total voids during daytime in PTNS+ACD, PTNS, and ACD groups, respectively. The reduction in nocturia was 72% in PTNS+ACD group, 61% in PTNS group, and 15% in ACD group. Decrease in urge incontinence episodes was 39% in PTNS+ACD group, 35% in PTNS group, and 19% in ACD group. All groups included in our study demonstrated statistically significant decreases in frequency of urination during daytime, nocturia, and urge incontinence after treatment. Comparison of our results with literature revealed that the rates of decrease in frequency during daytime, nocturia, and urge incontinence in PTNS and PTNS+ACD groups were consistent with the literature; however, the rate of decrease in ACD group was smaller. Post-treatment urine volumes in our groups revealed that increase in urine volume after treatment was statistically significant in PTNS+ACD and PTNS groups but not significant in ACD group. Increase in urine volume in the groups that had PTNS (PTNS and PTNS+ACD) was in accordance with the literature.

We used IIQ-7, UDI-6, and OABSS questionnaires before and after treatment in our study. Although we found significant changes after treatment in all three groups included in our study, the success rate was higher in the groups that had PTNS (PTNS and PTNS+ACD), and this result was consistent with the literature. Analysis of quality of life measures indicated the most significant improvement in the first and second questions of (frequency and urge incontinence) of UDI-6 and all questions of OABSS (frequency during daytime, nocturia, urge incontinence, etc). The quality of life studies demonstrated that frequency, nocturia, urgency, and urge incontinence were primarily improved after treatment, and they were the parameters that affected the psychological status of the patients the most. In our study, our patients reported that improvement in these parameters affected their social lives, and our data indicated that the most significant improvements after treatment were observed in these parameters.

Similar to our study, Karademir et al.[22] performed a study on 43 patients, divided them into two groups, and the patients in Group 1 were administered only SANS treatment and the ones in Group 2 were administered SANS+5 mg oxybutynin for 8 weeks. The treatment response rate was 61.6% and 83.2% in Groups 1 and 2, respectively. In both groups, the best symptomatic improvements were obtained in patients with urge incontinence. The percentage decreases in the mean number of symptoms of frequency and urgency were 36.7% and 46.1%, respectively, in Group 1 and 44.2% and 61.1%, respectively, in Group 2. However, there were no statistically significant differences in the effects on frequency and urgency between the two groups.[22]

Similarly, in our study, the treatment response rate was higher in PTNS+ACD (tolterodine 4 mg SR capsule) group than in PTNS group; however, statistical analysis did not yield a significant difference between the two groups. Literature data and data obtained in our study suggests that we may consider PTNS as a new treatment modality in patients who do not benefit from traditional treatment modalities of OAB; however, simultaneous use of anticholinergic agents does not cause a significant additional benefit even when different agents are used or they are administered for extended periods. Studies have demonstrated that the success of PTNS is approximately 60%, and our results are in accordance with the literature.

In female patients having urge urinary incontinence (UUI) and who did not respond to antimuscarinics, PTNS therapy may be used with a grade of recommendation as optional by guidelines. Because of the side effects of the antimuscarinics, their use is limited; therefore, we consider PTNS as an optional therapy alternative since no major side effects are reported by this technique.

Although there is no report regarding a stronger therapeutic effect of PTNS compared with tolterodine on patients with UUI by guidelines, our results revealed that there is an improvement in the

number of micturition, nocturia, and urge incontinence per day; furthermore, improvement in the quality of life may be observed by single use of PTNS than single ACD and/or ACD+PTNS combination therapy. Scaldazza et al.[10] have reported results of a better response in patients treated with PTNS than in patients treated with solifenasin. In our study, we aimed to evaluate the efficacy of the combination therapy in contrast to the current literature. The small number of patients is a limitation of our study. We assume that there is a need for future studies with long-term, large, randomized, and controlled series for the comparison of PTNS and ACD therapy in patients with UUI.

Ethics Committee Approval: Ethics committee approval was obtained.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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Appendix

Appendix 1. Urogenital distress inventory short form (UDI-6)

Do you experience, and if so, how much are you bothered by	Not at all	Slightly	Moderately	Greatly
Frequent urination	0	1	2	3
Leakage related to feeling of urgency	0	1	2	3
Leakage related to physical activity, coughing, or sneezing	0	1	2	3
Small amounts of leaka.ge (drops)	0	1	2	3
Difficulty emptying bladder	0	1	2	3
Pain or discomfort in lower abdominal or genital area	0	1	2	3

Appendix 2. Incontinence impact questionnaire-short form (IIQ-7)

Has urine leakage affected your	Not at all	Slightly	Moderately	Greatly
1. Ability to do household chores (cooking, housecleaning, laundry)?	0	1	2	3
2. Physical recreation such as walking, swimming, or other exercise?	0	1	2	3
3. Entertainment activities (movies, concerts, etc.)?	0	1	2	3
4. Ability to travel by car or bus more than 30 min from home?	0	1	2	3
5. Participation in social activities outside your home?	0	1	2	3
6. Emotional health (nervousness, depression, etc.)?	0	1	2	3
7. Feeling frustrated?	0	1	2	3

Items 1 and 2=physical activity; Items 3 and 4=travel
Item 5=social/relationships; Items 6 and 7=emotional health
Scoring: Item responses are assigned values of 0 for "not at all," 1 for "slightly," 2 for "moderately," and 3 for "greatly."

Appendix 3. Overactive bladder symptom score (OABSS)

	Score	Frequency
How many times do you typically urinate from waking in the morning until sleeping at night?	0	7 or less
	1	8–14
	2	15 or more
How many times do you typically wake up to urinate from sleeping at night until waking in the morning?	0	0
	1	1
	2	2
	3	3 or more
How often do you have a sudden desire to urinate, which is difficult to defer?	0	Not at all
	1	Less than once a week
	2	Once a week or more
	3	About once a day
	4	2–4 times a day
	5	5 times a day or more
How often do you leak urine because you cannot defer the sudden desire to urinate?	0	Not at all
	1	Less than once a week
	2	Once a week or more
	3	About once a day
	4	2–4 times a day
	5	5 times a day or more