

Effects of Transcutaneous and Percutaneous Tibial Nerve Stimulation in Bosnian Female Patients with an Idiopathic Overactive Urinary Bladder

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Abstract

Objective. The purpose of this study was to evaluate the efficacy of daily transcutaneous tibial nerve stimulation (TTNS) versus weekly percutaneous tibial nerve stimulation (PTNS) on the quality of life of patients with idiopathic overactive bladder (OAB). **Patients and Methods.** The study was designed as a randomized controlled trial. The diagnosis of OAB was made on the basis of clinical symptoms, and urodynamic tests were performed to check whether uncontrolled contractions of the detrusor during bladder filling were responsible for the OAB symptoms. The tests used to assess symptoms and quality of life were Overactive Bladder Questionnaires (OAB-q) SF. The patients were divided into 2 groups of 30 patients each. The first group was treated with TTNS every day for 3 months and the second group with PTNS once a week, also for 3 months. **Results.** Stimulation with both TTNS and PTNS led to the reduction of all clinical symptoms of OAB and improved quality of life, with statistical significance ($P < 0.05$) and with no side effects. When comparing these two groups, the improvement was statistically more significant in the group treated with PTNS. When the quality of life scores and symptoms were compared to the type of treatment, it was found that the improved quality of life parameters and the reduced OAB symptoms were more statistically significant in the treatment with PTNS than TTNS therapy ($P < 0.001$). **Conclusion.** The results of the study suggest good efficacy of both TTNS and PTNS in the treatment of OAB. Better effects are achieved with weekly PTNS, as it leads to a statistically significant reduction in symptoms as well as an improvement in quality of life, without side effects.

Key Words: Overactive Bladder ■ PTNS ■ TTNS.

Introduction

The International Continence Society (ICS) defines an overactive urinary bladder (OAB) as an urge with or without urinary urge incontinence, and with increased frequency during the day and night (1). These symptoms greatly affect the patient's quality of life. In order for patients to be treated as adequately as possible, it is necessary to first make an accurate diagnosis, which is most safely done through urodynamic examination. Due to the presence of urgent incontinence,

the overactive bladder can be divided into the so-called "wet type" with urge incontinence and the so-called "dry type" without incontinence, which is more common and present in about 63% of patients (2). The excessive activity of the detrusor is associated with the excessive activity of the bladder. The ICS states that the hyperactive detrusor is characterized by the presence of unwanted contractions of the detrusor, which is diagnosed with urodynamics (3). However, the link between an overactive bladder and hyperreflexia of the detrusor is not completely clear. It is reported that in

urodynamic examinations, hyperreflexia of the detrusor is only found in 54% of women who have symptoms of an overactive bladder (4).

The emptying of the urinary bladder occurs as soon as a small amount of urine has accumulated in it. Usually the sphincter muscle function is preserved. With regard to etiology, the cause may be neurological or idiopathic. OAB prevalence differs between individual studies. According to the ICS, the incidence in the general female population is about 13-17% and increases with age. In women under the age of 35, the prevalence is up to 5%, while in women over the age of 65 the prevalence is 20-30% (5-7). There are several ways to treat a hyperactive bladder, from behavioral treatment, medication, by injecting botulinum toxin, electrostimulation, and surgical treatment. Success depends on an adequate diagnosis and a well-chosen treatment. Modern therapeutic methods achieve the best treatment outcomes and improve the quality of life. In the treatment of OAB, electrical nerve stimulation is also used. It is a non-invasive method which uses exponential current (low frequency current) to effectively suppress excessive bladder activity.

In the late 1990s, Dr. Marschall Stoller presented tibial nerve stimulation, first known as the SANS (Stoller Afferent Nerve Stimulator) protocol like promising therapy for nonneurogenic lower urinary tract dysfunction (8). The term percutaneous or transcutaneous tibial nerve stimulation is now used, depending on which electrodes are used. If an acupuncture needle is inserted into or near SP 6, connected to a stimulator and then the tibial nerve is stimulated, this is called percutaneous tibial nerve stimulation (PTNS), and, if self-adhesive electrodes are used, this is called transcutaneous tibial nerve stimulation (TTNS). In most studies, in which PTNS or TTNS stimulation were used, improvements were demonstrated in terms of a significant reduction in symptoms and an improvement in the quality of life of patients with OAB, without side effects (9-11). So far, no such studies have been carried out in Bosnia and Herzegovina.

The aim of this study was to evaluate the efficacy of daily TTNS versus weekly PTNS on the quality of life and clinical symptoms of patients with an idiopathic overactive bladder (OAB).

Patients and Methods

The study was a randomized controlled trial. Participants were enrolled consecutively during their visits to the Urodynamics unit of the Physical Medicine and Rehabilitation Clinic, University Medical Center Tuzla (Bosnia and Herzegovina) for a period from January 2016 until December 2019. The inclusion criteria were female patients who presented with clinical symptoms, and urodynamic testing that showed an OAB with maximum bladder capacity of less than 300 ml.

Each patient had to have a normal urine sample before the urodynamic testing. Exclusion criteria were symptoms lasting less than 6 months, pregnancy, sacral peripheral nerve lesion, urinary tract infection confirmed by microbiological analysis, serious secondary illnesses (such as renal failure, nephrolithiasis, bladder and kidney tumors..) and detrusor-sphincter dyssynergia confirmed by a urodynamic investigation. 62% of patients had used anticholinergic drugs for at least 3 months without improvement, 11% of patients had discontinued anticholinergic therapy after a short time due to side effects, and 27% of patients had refused anticholinergic treatment.

Randomization was based on a single sequence of random assignments. The first group (30 patients) was treated with TTNS with TENS every day for 3 months, while the second group (also 30 patients) had PTNS with TENS once a week for a total of 3 months. The assessment of symptoms and quality of life was completed immediately after detecting OAB, as well as before and after treatment.

TTNS stimulation of the tibial nerve was performed using two 50×50 mm self-adhesive electrodes, with one electrode placed behind the medial malleolus and the other electrode approximately 10 cm above. The current intensity, frequency, and pulse duration were set on each apparatus at a frequency of 10 HZ, pulse duration of 200 µs and du-



Figure 1. Stimulation with transcutaneous tibial nerve stimulation.

ration of stimulation of 30 min. The intensity level was immediately above the threshold determining a net perception of the current, without induced pain. Medio Tens devices (Iskra Medical device) were used, which were given to patients to use at home daily for 3 months (Figure 1). Detailed instructions were given to the patients on how to operate the device at home with the specified parameters set.

For PTNS stimulation we placed an acupuncture needle, 0.25×25 mm in size, above the medial malleolus directly into the acupuncture point SP 6 located near n. tibialis three cun (cun is a traditional Chinese measure of thumb width, used to map acupuncture points on the human body) or a distance of four transverse toes above the medial malleolus and behind the posterior edge of the tibia and one self-adhesive electrode was placed on the medial plantar part of the right foot (Figure 2). The needle was placed at an angle of 90 degrees, on the right leg 2 cm deep. The frequency was 10Hz, with pulse duration of 200 μ s and stimulation length of 30 minutes. We decided to place electrodes and an acupuncture needle in the right leg because, according to Chinese traditional medicine (acupuncture), the points for solid organs (in this case the spleen) that belong to the yin are on the right side of the body. In addition, the rules state that when the needles are inserted in only one side, in women it should be in the right side of the body.



Figure 2. Stimulation with percutaneous tibial nerve stimulation.

OAB-q SF (OAB-S=Overactive bladder S-symptoms, OAB-Q=Overactive bladder Q-quality of life), a specific questionnaire that consisted of two subscales, was used to assess the frequency of hyperactive bladder symptoms and the quality of life of patients with urinary disorders. The symptom subscale contained six questions rated separately from 1 to 6 and quality of life subscale included 13 questions rated from 1 to 6. The lowest score for symptoms is 6, and the highest is 36. A lower score is a better finding that indicates less pronounced symptoms. To assess the quality of life, the lowest score is 13 and the highest is 78. The higher score shows a better finding, i.e. a better quality of life. It was validated, culturally adapted and translated for use in the population of Bosnia and Herzegovina. The symptoms which were monitored and affected the quality of life are: urgency (>than 3 to 24 h), daily voiding (frequency >8 in 24 h), nocturia and urge incontinence. The OAB-q SF questionnaire was completed before treatment and 3 months after treatment.

Statistical Analysis

All statistical analyses have been done by MedCalc software (ver.12.1.4.0 for Windows; MedCalc, Mariakerke, Belgium). The differences between the groups in categorical variables, Wilcoxon sum rank tests were done as well as one-way ANOVA test. $P < 0.05$ was considered significant.

Results

Sixty female patients who had symptoms of OAB were examined. Urodynamic testing proved detrusor overactivity in 72% of women who had symptoms of an overactive bladder. Patients who had electrostimulation with TTNS were on average 47.4±8.0 years old, and patients who had electrostimulation with PTNS were on average 49.0±6.9 years old. The groups were homogeneous in age and baseline clinical characteristics (Table 1). Stimulation with TTNS has shown a statistically significant reduction in all clinical symptoms of the bladder and improved quality of life (Table 2). The

symptom score before treatment with daily TTNS was 61.2±14.6 and decreased after treatment to 50.8±12.3 ($P<0.0001$). The quality of life score increased from 28.5±12.6 after treatment with daily TTNS to 38.3±11.4 ($P<0.0001$). Stimulation with PTNS has shown a statistically significant reduction in all clinical symptoms of the bladder and improved quality of life. The symptom score before treatment with weekly PTNS was 54.3±14.9 and decreased after treatment to 26.8±15.3 ($P<0.0001$). The quality of life score increased from 35.3±16.8 after treatment with weekly PTNS to 64.9±16.9 ($P<0.0001$) (Table 3).

Table 1. Demographic and Basic Clinical Parameters

Variable	Groups		P
	TTNS	PTNS	
Age (years)	47.4±8.0	49.0±6.9	<0.41
Daily micturition number	12.9±4.4	14.1±3.9	0.27
Night micturition number	3.8±1.9	4.3±2.6	0.46
Daily incontinence number	3.8±1.8	3.3±2.4	0.436
Night incontinence number	1.9±1.4	1.7±1.3	0.706
OAB-Q	28.5±12.6	35.3±16.8	0.085
OAB-S	61.2±14.6	54.3±14.9	0.074

TTNS=Transcutaneous tibial nerve stimulation; PTNS=Percutaneous tibial nerve stimulation; OAB-Q=Overactive bladder quality of life; OAB-S=Overactive bladder symptoms.

Table 2. OAB-S Clinical Symptoms and OAB-Q Quality of Life in the TTNS Group before and after Treatment

Clinical symptoms	Treatment		P*
	Before	After	
Daily micturition number	12.9±4.4	9.4±3.4	<0.0001
Night micturition number	3.8±1.9	2.4±1.4	<0.0001
Daily incontinence number	3.8±1.8	2.4±1.4	<0.0001
Night incontinence number	1.9±1.4	1.3±1.0	0.0002
OAB-Q	28.5±12.6	38.3±11.4	<0.0001
OAB-S	61.2±14.6	50.8±12.3	<0.0001

OAB-Q=Overactive bladder quality of life; OAB-S=Overactive bladder symptoms; TTNS= Transcutaneous tibial nerve stimulation; *Paired t test.

Table 3. OAB-S Clinical Symptoms and OAB-Q Quality of life in the PTNS group before and after Treatment

Clinical symptoms	Treatment		P*
	Before	After	
Daily micturition number	14.1±3.9	6.8±2.8	<0.0001
Night micturition number	4.3±2.6	1.5±1.2	<0.0001
Daily incontinence number	3.3±2.4	1.2±1.0	<0.0001
Night incontinence number	1.7±1.3	0.6±0.7	<0.0001
OAB-Q	35.3±16.8	64.9±16.9	<0.0001
OAB-S	54.3±14.9	26.8±15.3	<0.0001

OAB-Q=Overactive bladder quality of life; OAB-S=Overactive bladder symptoms; PTNS=Percutaneous tibial nerve stimulation; *Paired t test.

Table 4. Comparison of Clinical Symptoms and Quality of Life after Treatment with TTNS and PTNS Stimulation

Clinical symptoms	TTNS	PTNS	P
Daily micturition number	9.4±3.4	6.8±2.8	0.02
Night micturition number	2.4±1.4	1.5±1.2	0.016
Daily incontinence number	2.4±1.4	1.2±1.0	<0.001
Night incontinence number	1.3±1.0	0.6±0.7	0.004
OAB-Q	38.3±11.4	64.9±16.9	<0.001
OAB-S	50.8±12.3	26.8±15.3	<0.001

TTNS=Transcutaneous tibial nerve stimulation; PTNS=Percutaneous tibial nerve stimulation; OAB-Q=Overactive bladder quality of life; OAB-S=Overactive bladder symptoms.

Comparing the quality of life scores and symptoms measured by the OAB-q SF questionnaire, in relation to the type of treatment, statistically significantly improved quality of life parameters and statistically significantly reduced symptoms were found in favor of PTNS treatment compared to TTNS therapy ($P<0.001$) (Table 4).

It is possible that the localization of the right leg and use of the acupuncture point SP 6 itself led to extremely good results. There were no side effects after treatment with both TTNS and PTNS therapy.

Discussion

The results of our study showed good effectiveness of TTNS in reducing all clinical symptoms of a hyperactive bladder, and all this had a positive effect on quality of life. The TTNS treatment also showed good tolerability, without side effects. The effectiveness of the treatment was already evident in the second week of treatment and did not change significantly during the 3 months of the treatment. The efficacy of the treatment, as well as treatment tolerance, makes the treatment suitable for patients, especially if they have other diseases or symptoms due to which they would not be able to use anticholinergic drugs.

Voorham et al. (12) demonstrated the acute effect of a single application of TTNS in patients with OAB symptoms using urodynamic parameters. The results of urodynamic parameters for a group of 20 patients without stimulation were almost unchanged, and in the group after stimula-

tion there was a statistically significant improvement in bladder capacity, micturition volume and first detrusor contraction. The study was done as a diagnostic procedure, not a treatment. A multicenter study was conducted in France by De Seze et al. (9), where 70 patients treated with the TTNS technique who suffered from MS were followed. Stimulation with TTNS lasted 3 months, and the duration of therapy was 20 minutes per day. After treatment, 83.3% of patients had a statistically significant improvement in clinical symptoms as well as quality of life (9). Booth et al. (13) used a systematic literature review of four databases between 1980 and 2017 to evaluate the efficacy of transcutaneous tibial nerve stimulation (TTNS) for the treatment of adults with a hyperactive bladder (OAB) of idiopathic or neurogenic origin. Ten randomized controlled trials and three prospective cohort studies were reviewed, involving 629 participants. A meta-analysis of two trials comparing TTNS with a placebo showed a mean reduction in the total ICIQ Urinary Incontinence Short Form (ICIQ-UI SF). A review of 4 studies showed that TTNS and antimuscarinic treatment were equally effective. In two trials, TTNS provided greater benefits for OAB symptoms than behavioral therapy. The stimulation of the tibial nerve and sacral foramen were equally effective, but combined stimulation was the most effective (single study). No adverse events were reported. Martin-Garcia and Crampton (14) demonstrated the efficacy of TTNS stimulation in maintaining symptom improvement over a 6-month period in women with idiopathic OAB who responded positively to 12-week PTNS treatment.

PTNS is a minimally invasive procedure used to treat OAB. The Urgent® PC Neuromodulation System is usually used for stimulation, but we used a TENS device with a modified acupuncture needle outlet in our research. Stimulation with PTNS led to a statistically significant reduction in all clinical symptoms of a hyperactive bladder and improved quality of life. Gaziev et al. (15) investigated papers related to the effect of PTNS on lower urinary tract dysfunction using MEDLINE and ISI web databases. PTNS stimulation was effective in 37-100% of patients with OAB, in 41-100% in patients with nonobstructive urinary retention and up to 100% in patients with painful bladder syndrome. In a multicenter study, involving 53 patients who did not respond to conventional therapy, Govier et al. (16) used PTNS for 12 weeks, where a 0.22 mm wide acupuncture needle was placed near the tibial nerve, three fingers above the ankle. In 71% of patients there was a decrease in the frequency of day and night urination ($P < 0.05$). Urge incontinence was reduced by an average of 35% ($P < 0.05$). Statistically significant improvements were noted in the quality of life. No significant treatment-related adverse events were reported in any of the patients. It was concluded that PTNS is a safe, effective and minimally invasive method. In a multicenter study, Van Balken et al. (17) examined the effect of PTNS as a neuromodulatory treatment of lower urinary tract dysfunction in 37 patients with OAB symptoms and in 12 patients with non-obstructive urinary retention. A positive outcome was noted in 60% of all patients. In patients with OAB, a statistically significant decrease in incontinence, frequency of urination, and equal increases in medium and low volume were observed. Improvements have also been seen in patients with non-obstructive urinary retention. Only mild side effects were observed. Vandoninck et al. (18) assessed urodynamic changes in 90 patients, after 12 sessions of PTNS stimulation, and showed an increase in cystometric capacity and a delay in the onset of detrusor instability. De Wall LL and Heesakkers (19) investigated the efficacy studies of PTNS on symptoms of OAB and pelvic organ disorders, pain, and quality of life in the MEDLINE,

CINAHL, and EMBASE databases. Five randomized controlled trials showed improvement (range 36.7-80%) in HAB symptoms, frequency, urgency, nocturia, and incontinence. Peters and colleagues (20) examined a 12-week PTNS stimulation in a multicenter, double-blind, randomized controlled trial comparing it to placebo stimulation. A total of 220 patients were included. Patients receiving PTNS for 12 weeks showed a 55% moderate or marked improvement in frequency, nocturia, discharge with moderate/severe urgency, compared with an improvement of 21% in the placebo group. Finazzi et al. (21) analyzed the effect of PTNS stimulation frequency and concluded that stimulation three times per week gave the same results as once per week.

In our study, it was proven that PTNS stimulation once a week, for a total of 3 months, i.e. 12 treatments, gave excellent results in the treatment of OAB, where the parameters of quality of life and clinical symptoms significantly improved. Bhide et al. (22) reviewed papers related to n. tibialis stimulation techniques in the treatment of OAB, as well as their efficacy. PTNS stimulation of the tibial nerve was done by inserting a 22-mm profile needle, 3 to 4 fingers above the medial malleolus. The most commonly used current stimulation was 20 Hz, with intervals of 200 μ s. The intensity of the current was also set to the highest level the patient could tolerate. The main side effect of PTNS was pain at the site of needle insertion. The simulations usually lasted 30 min. The use of PTNS in patients with OAB showed improvement in symptoms, as seen in the two studies comparing PTNS with placebo treatment. However, studies, where a combination of treatment with PTNS and antimuscarinic drugs were used, showed a greater improvement in symptoms. However, TTNS showed similar results to PTNS.

Results of our study show better effectiveness of the process with PTNS versus TTNS. In each, the parameters of stimulation are the same and the only difference consists of the placement of the electrode. The use of an acupuncture needle placed in the acupuncture point SP6 has to be discussed. Acupuncture might have an effect in decreasing

the number of micturition episodes, incontinence episodes, and nocturia episodes. A lot of studies investigate the effects of acupuncture and/or electro-acupuncture (EA) on an overactive bladder (Mo Q 2015, Wen Q 2020, Zwang J 2018). However, the evidence is insufficient to show the effect of using acupuncture alone or the additional effect to drugs in treating OAB (23).

Padilha et al. (24) published a study protocol to be conducted as a randomized controlled clinical trial and to include 99 women with OAB and urgency. The aim of this study was to provide evidence for a more detailed discussion of electrostimulation electrode positioning for 2 TTNS and PTES (parasacral transcutaneous electrical stimulation) treatments as an option in terms of the positioning of electrodes relative to the tibial nerve region in specific populations, such as amputees or people with severe sensory damage to the lower limbs. Slovak M and al.'s (25) review of research on Pub Med found differences in descriptions of stimulation intensity, therapy strategy and electrode position, as well as in different symptoms and pathology of patients. Limited data on long-term follow-up have been published in the literature, so the treatment regimen that brings lasting benefits is unclear. The different effects shown in the studies can be explained by different stimulation parameters and electrode placement. We used a TENS device with a modified acupuncture needle outlet for PTNS stimulation. It is possible that the localization or use of the acupuncture point itself led to extremely good results, as well as the parameters used. Weaker results with TTNS stimulation may possibly be explained by insufficient stimulation intensity via electrodes. The drawback of this treatment is the need for daily stimulation of the n. tibialis, and for that reason patients have to be trained on how to use the device at home. The disadvantage of the study could be the inability to monitor patients to check if they are doing daily stimulation. Further large placebo-controlled studies are needed to obtain a solid evidence base.

Little is known about the underlying mechanism for efficacy of the procedures. Finazzi (26) studied long-latency somatosensory evoked poten-

tials providing information on the function of somatosensory cortical structures. Mean amplitude of P80 and P100 waves increased significantly after PTNS and might reflect long-term modifications in synaptic efficiency through the somatosensory pathway. The plastic reorganization of the cortical network triggered by peripheral neuromodulation can be hypothesized as a mechanism of the action of PTNS. However, the evidence does not support the efficacy of electro-acupuncture (EA) alone in the treatment of OAB. EA is similar to PTNS in some ways; however, the type of EA treatment used in this trial could stimulate not only the tibial nerve (through the acupoint of SP6) but also the 3 sacral (through the acupoint of BL33) and pudendal nerves (through the acupoint of BL35). Integrating PTNS and SNS stimulation points may have good benefits (27).

Conclusion

There are several ways to treat an overactive bladder, and pharmacological treatment is still the first line in the management of patients with OAB symptoms. In addition to pharmacological therapy, electrical tibial nerve stimulation is used in the treatment of OAB, which is a non-invasive method of exponential current (low-frequency current) which suppresses excessive bladder activity. Adequate diagnosis and treatment can improve bladder control in patients with OAB symptoms. In this study, we confirmed the positive effects of two different electrical tibial nerve stimulation methods used for the treatment of OAB: the transcutaneous method with two self-adhesive electrodes and the percutaneous method of acupuncture electrostimulation. Our recommendation is to use PTNS stimulation with acupuncture needle and point SP6 on a right leg, once a week, for a total of 3 months, i.e. 12 therapies, because it is easily implemented. A TENS device with a modified needle outlet can be used and it is more effective than TTNS (which involves a total of 90 individual treatments) in improving quality of life and clinical symptoms.

What Is Already Known on This Topic:

There are a number of ways to treat OAB and electrical tibial nerve stimulation is used, which is a non-invasive exponential current (low-frequency) method that suppresses excessive bladder activity. We evaluated the efficacy of daily transcutaneous tibial nerve stimulation (TTNS) versus weekly percutaneous tibial nerve stimulation (PTNS) on the quality of life of patients with idiopathic overactive bladder (OAB).

What This Study Adds:

In this study, we confirmed the positive effects of two different electrical tibial nerve stimulation methods used for the treatment of OAB: the transcutaneous method with two self-adhesive electrodes and the percutaneous method of acupuncture electrostimulation. Our recommendation is to use PTNS stimulation (which is a minimally invasive procedure) with acupuncture needle and point SP6 on a right leg, once a week, for a total of 3 months, i.e. 12 therapies, because it is easily implemented, a TENS device with a modified needle outlet can be used and it is more effective than TTNS (which involves a total of 90 individual treatments) in improving quality of life and clinical symptoms. There were no side effects after treatment with either TTNS or PTNS therapy.

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Conflict of Interest: The authors declare that they have no conflict of interest.

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