Comparison of Transcutaneous Tibial Nerve Stimulation (TTNS) Protocols for Women With Refractory Overactive Bladder (OAB), a Prospective Randomised Trial

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Abstract

Objectives: Transcutaneous Tibial Nerve Stimulation (TTNS) is a non-invasive method used in OAB treatment. We aimed to compare the effectiveness of the once a week and three times a week TTNS procedure in women diagnosed with wet type refractory OAB. Methods: A total of 60 patients diagnosed with wet type OAB was refractory to medical treatment included in the study. Participants were equally and randomly divided into two groups: TTNS treatment was performed with a time duration of 30 minutes for 12 weeks, once a week to Groıp-I and three times a week to Group-II. Pre and post-treatment OAB-V8/ICIQ-SF scores and voiding frequencies recorded in the bladder diary were compared between groups. Results: Four patients in Group-1 and eight in Group-2 left the study without completing the treatment. TTNS was performed in both groups for 12 weeks. There was a significant decrease in the voiding frequency, OAB-V8, ICIQ-SF scores in both group-1 and group-2 ($p<0.001$). A significant decrease in the OAB-V8 score was observed in the 5th week in Group-1, and on the 3rd week in group-2. Complete response was observed in 6 patients (23.1%) in Group-1 after 12 weeks of TTNS procedure. In group-2, 10 patients (45.5%) had a complete response. After the 12-week TTNS procedure, no significant difference was observed between the groups in terms of treatment response. Conclusion: TTNS can be safely used before invasive treatments in resistant OAB. TTNS procedure three times a week seems more effective than performing it once a week.

Introduction

Overactive bladder syndrome (OAB) is a symptomatic diagnosis consisting of urinary frequency, urgency and nocturia, with or without urge urinary incontinence (1). Lifestyle changes and behavioral therapy are recommended as the first-line treatment in OAB. Anticholinergics, which are second-line treatment modalities, are recommended for patients who do not respond to behavioral therapy. In patients who do not respond to medical treatment, posterior tibial nerve stimulation (PTNS), botulinum toxin injection, sacral neuromodulation, and pelvic floor rehabilitation are used as the third step treatment method (2).

In the literature, PTNS, one of these 3rd step treatment methods, has been observed to improve symptoms over 50% in refractory OAB (3, 4). PTNS can be applied percutaneously with a needle electrode or transdermally with an adhesive surface electrode. This method is very advantageous because it is not invasive, it can be performed easily, the patient feels less pain, is cheaper, and no side effects (5). Besides, transcutaneous tibial nerve stimulation (TTNS) can be performed by the patient in the home environment by providing the necessary training. Along with these advantages, it has been reported that its efficacy is similar to PTNS in the literature (6, 7). The TTNS protocol is generally performed as weekly 30-minute sessions for 12 weeks. (8). However, there are different protocols in the literature regarding the frequency of TTNS treatment. (9, 10, 11, 12).

There is only one study comparing the number of PTNS sessions in resistant OAB treatment (13). However, there is no comparative study on the number of TTNS sessions in refractory OAB. There is a study comparing the effectiveness of the number of sessions of TTNS only in fecal incontinence (14). Based on this evidence, we aimed to find the ideal frequency of the TTNS procedure in the treatment of refractory OAB in women.

Materials-methods

The current study was designed as a prospective and randomised experimental study. The study was approved by Kutahya Health Sciences University Ethical Committee on 08.07.20 with 2020-04/10 decision number.

Patients diagnosed with refractory OAB-wet type were included study according to inclusion and exclusion criteria (Table-1). Sixty patients included in the study were randomly divided into two groups using a simple random number table after informed consent form as established for each participant. Our study was prepared in accordance with the CONSORT guide (15). The CONSORT study flow chart was prepared (Figure-1).

Transcutaneous tibial nerve stimulation procedure

TTNS was performed with a transcutaneous electrical nerve stimulation device (NeuroTrac®, Verity Medical, UK) and electrode pads. One of the electrode pads was positioned approximately 5 cm above and posterior the medial malleolus. The other electrode pad placed medial to the foot (figure 2). Electrodes were connected to the stimulator. Bipolar continuous stimulation was set to a frequency of 10 Hz and a pulse width of 200 μs. Each session was performed for 30 minutes at the hospital with a researcher. Treatment sessions were administered to both groups for 12 weeks.

Measurements

Patients in TTNS group-1 were administered once a week, and in group-2 three times a week for 12 weeks. A daily bladder diary, as well as Turkish-validated OAB-V8 and ICIQ-SF questionnaires were filled for whole participants on the first day of each week during the treatment and after treatment. Daytime voiding frequency and nocturia numbers were noted from the bladder diary of the patients. During the procedure, the patients were questioned about the effectiveness of the treatment, side effects and patient satisfaction. The patients who wanted to leave the study before the treatment was completed were asked why they stopped working and their reasons were noted. The reduction in OAB-V8, ICIQ-SF scores and nocturia counts were compared between groups after treatment. Treatment success was determined as follows; Patients with more than 50 percent reduction in urge incontinence frequency were considered as "responders". Patients with less than 25 percent reduction in urge incontinence frequency were accepted as non-responders to the treatment. Whereas, other patients were considered as those with partial response. There are no serious side effects reported in the literature for the TTNS procedure. Patients who experienced any unexpected serious side effects in the procedure were excluded from the study.

Statistical analysis

Statistical analyses were performed using the SPSS software vesion 26 (IBM SPSS Corp.; Armonk, NY, USA) program. The variables were investigated using visual (histograms) and analytical methods (kolmogorov-Simirnov/Shapiro-Wilk's test) to determine whether or not they are normally distributed. Descriptive analyses were presented using means and standard deviations for normally distributed and medians and minimum-maximum values for the non-normally distributed and ordinal variables. The Mann-Whitney U-test was used for comparisons between 2 groups for parameters without a normal distribution, and Student t-test was used for parameters with a normal distribution. TTNS treatments were given using cross tables according to their success results. Whether there was a difference between the TTNS treatment groups in terms of treatment success was compared using the Chi-square test. The effect of TTNS treatments applied on the change in OAB-V8 score, ICIQ-SF score and Urinary frequency by time was investigated using repeated measures analysis of variance. Greenhouse-Geisser correction was used when the sphericity assumption was violated. An overall %5 type-I error was used ton fer statistical significance.

Results

In our study, sixty patients were randomly divided into two groups. There were thirty patients in each group. Three patients from Group-1 left the study, stating that they did not benefit from the treatment. One of the patients could not complete the treatment due to a COVID-19 infection. Seven patients in Group-2 left the study because they did not benefit from the treatment, while one patient could not complete the treatment due to the COVID-19 infection. The data of 26 patients in Group-1 and 22 patients in Group-2 were analyzed. The mean age of group 1 was 51.04±14.25 years, and the mean age of group 2 was 51.64±13.52 years ($p>0.05$). There was no difference between the groups in terms of BMI. The pre-treatment OAB-V8, ICIQ-SF scores, and urinary frequency, nocturia numbers of the groups were evaluated and presented in Table-2. The groups were similar in terms of pre-treatment OAB-V8, ICIQ-SF scores, and urinary frequency and nocturia counts ($p>0.05$) (Table-2).

When we examine the change in OAB-V8 scores in Group-1 and Group-2; There was a statistically significant decrease in OAB-V8 scores following the treatment ($p<0.001$). Although a greater decrease was observed in OAB-V8 scores in patients who underwent TTNS three times a week, no statistically significant difference was found ($p=0.094$). When the weekly change in OAB-V8 score after pretreatment and treatment in Group-1 was examined, it was found that the statistically significant response difference started at the 5th week of the treatment ($p=0.005$) and that in Group-2, it occurred in the third week of the treatment ($p=0.017$). Weekly OAB-V8 score changes of the groups before and after treatment are shown in Figure-3.

It was found that ICIQ-SF scores in Group-1 and Group-2 decreased statistically significantly after the treatment ($p<0.001$). Although there was a greater decrease in ICIQ-SF scores in Group-2, no significant difference was found between the groups in terms of ICIQ-SF score change ($p=0.118$). When the ICIQ-SF score change after pretreatment and treatment was examined in Group-1, it was found that the statistically significant response difference started at the sixth week of the treatment ($p<0.001$), and that in Group-2, it occurred in the fifth week of the treatment ($p<0.001$). Weekly ICIQ-SF score changes of the groups before and after the treatment were shown in Figure-4.

It was found that the frequency of urination decreased statistically significantly in group-1 and group-2 after treatment ($p<0.001$). Although there was a greater decrease in the frequency of urination in Group-2, no significant difference was found between the groups in terms of the change in urination frequency ($p=0.118$). When the change in urination frequency after pretreatment and treatment is examined; It was found that a statistically significant difference in response in both groups started in the fourth week of the treatment (Group-1 $p=0.018$, Group-2 $p=0.003$). Weekly voiding frequency changes of the groups before and after treatment are shown in Figure-5.

The results established from the evaluation of treatment protocols in terms of unresponsiveness, partial response, and complete response after the 12-week TTNS procedure were given in Table-3. After the 12-week TTNS procedure, no statistically significant difference was observed between the groups in terms of treatment response ($p = 0.203$).

Discussion

In the literature, TTNS treatment has been performed with different protocols and the number of sessions. Souto et al. performed TTNS twice a week for 12 weeks while Booth et al. performed the procedure for six weeks (9, 16). Svihra et al. performed it once a week for 12 weeks while Sillén et al. performed TTNS every day, and Lordêlo et al. three times a week (10, 11, 12). Finazzi et al. 35 patients with resistant OAB performed PTNS once a week and 3 sessions a week. They reported that the procedure performed once a week and 3 times a week did not change the effectiveness. But, that many sessions enabled the early onset of the treatment effect. (13). Thomas et al. reported that TTNS performed every day in fecal incontinence gave better results than twice a week (14). Also, we performed TTNS once a week and three times a week for 12 weeks in two different groups. We have demonstrated that three times a week sessions increased the treatment response and improves the symptoms earlier. Our study showed that we achieved a similar success rate to literature with three sessions per week in refractory OAB.

TTNS, PTNS, and other electrical stimulation methods, Botulinum toxin-A (BoNT / A) and sacral neuromodulation (SNM) are frequently used in OAB patients who do not respond to behavioral therapy and anticholinergic therapy. Although BoNT / A and SNM are more effective methods, they have more side effects. (17, 18). However, TTNS has no side effects. Also, TTNS has been used in many studies in the literature due to its ease to perform, being feeled less pain and low cost (19).

TTNS showed similar effectiveness with PTNS in studies (19, 20). Urge and voiding frequency, number of nocturia, frequency of incontinence, OAB scores were used to evaluate the effectiveness in related studies (19, 20, 21). Also, more than 50% reduction in urge incontinence episodes was accepted as the complete response in studies. (22, 23, 24). Very different success rates have been reported in the literature. Ammi et al. showed 53% success after one month of TTNS in resistant OAB cases (23). Welk et al. found success in only 15% of patients with OAB (24). Considering this wide range of outcomes, we achieved a complete response in the groups with 23.1% and 45.5% success rates, respectively. We think that the difference between our study and the literature in terms of complete response rates may be related to the small size of the study groups, the different characteristics and symptom severity of the patients in the study groups. The complete response to treatment may increase if anticholinergic treatment is given together with TTNS. Randomized double-blind placebo-controlled studies with a high number of patients are needed to evaluate the true success of TTNS treatment. Welk et al. also pointed out the high risk of bias in the studies in the literature and stated that studies with high evidence levels are needed (24).

This is the first study comparing the number of TTNS sessions in refractory OAB in the literature. We have demonstrated that as the number of sessions per week increases, TTNS is more beneficial. According to outcomes of our study, TTNS can be tried especially before invasive procedures in cases that do not respond to first-line treatment in OAB. We think that the patient-based treatment scheme, which is performed by reducing the number of sessions according to the symptom status, may be more beneficial after providing early benefits with more sessions in the first weeks. Besides, TTNS can also be performed by the patient at home (14, 23). On the other hand, we conducted our study in the hospital with a single stimulator due to budget constraints. This situation created difficulties for the patients due to the obligation to come to the hospital for 12 weeks. The ideal practice for TTNS would be to have the first session is performed in the hospital in the presence of a specialist and then the patient continues to be treated at home. Thus, patient satisfaction will increase and the loss of time and money will decrease.

In our study, the low number of patients, the absence of a urodynamic study for objective comparison before and after treatment, and the absence of a placebo control group are limitations. Also, we evaluated treatment success subjectively with symptom scores and satisfaction questionnaires. However, the voiding frequency, the number of urge incontinence episodes, and the frequency of nocturia in the voiding diary were considered objective data. Also, there are no criteria based on objective data regarding the duration of treatment and the number of sessions per week. We also think that our study contributes to the literature to determine the ideal treatment protocol of TTNS. Also, randomized, placebo-controlled studies with large patient groups evaluated with urodynamic data are needed to develop an ideal treatment scheme.

Conclusion

We have shown that women with refractory OAB are observed to early improvements in the symptoms as the number of sessions increases. However, it did not change the final treatment success. In the future, we think that TTNS may become widespread as a method that can be applied easily and at a low cost at the home of patients before invasive procedures in refractory OAB.

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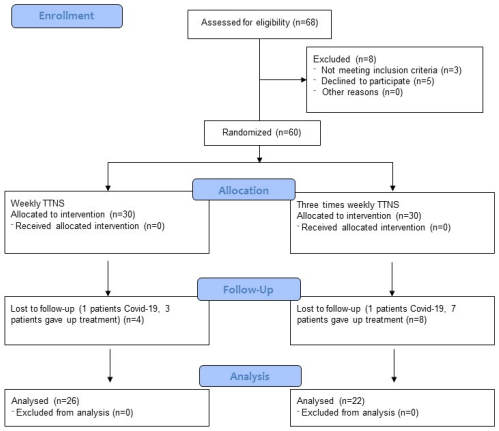
Figure 1. The CONSORT study flow chart.

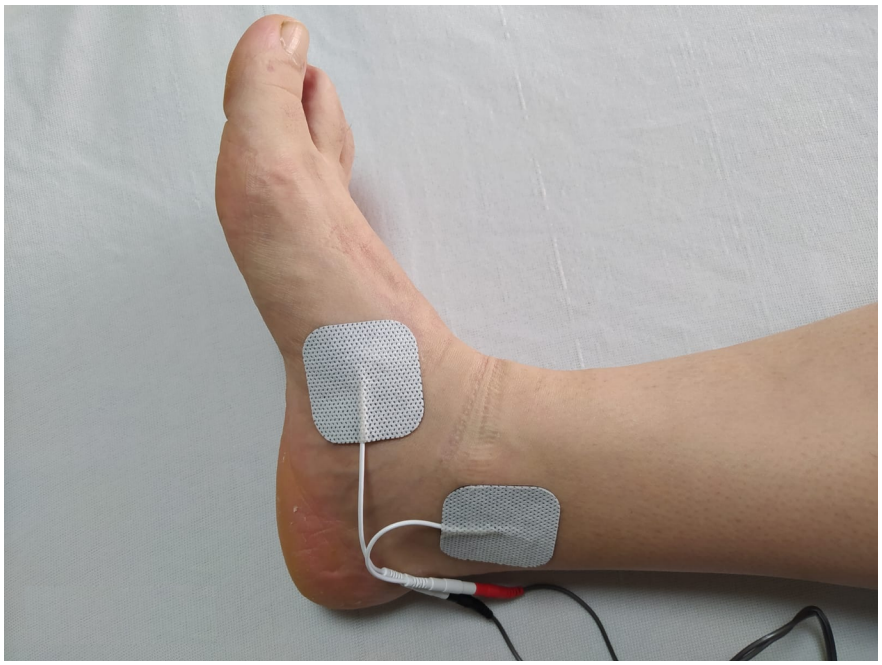
Figure 2. Placement of surface electrodes.

Figure 3. Change of OAB-V8 scores within and between groups before and during treatment.

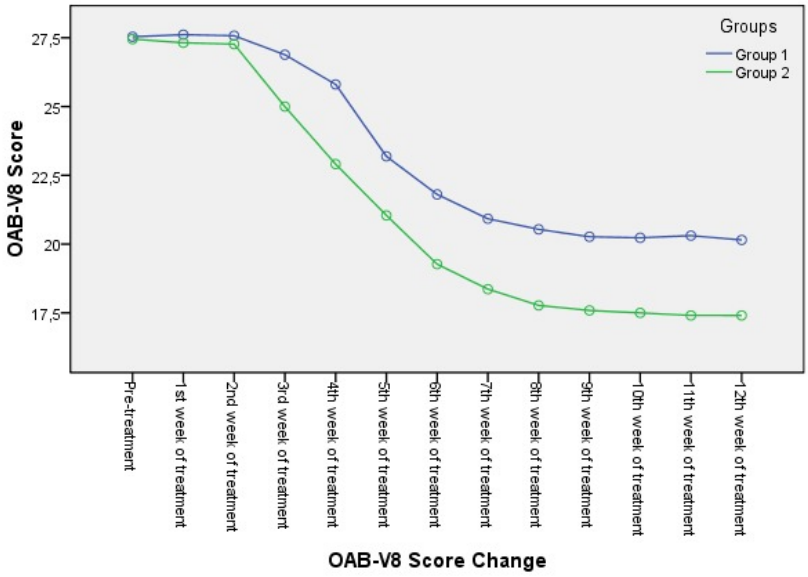
Figure 4. Change of ICIQ-SF scores within and between groups before and during treatment.

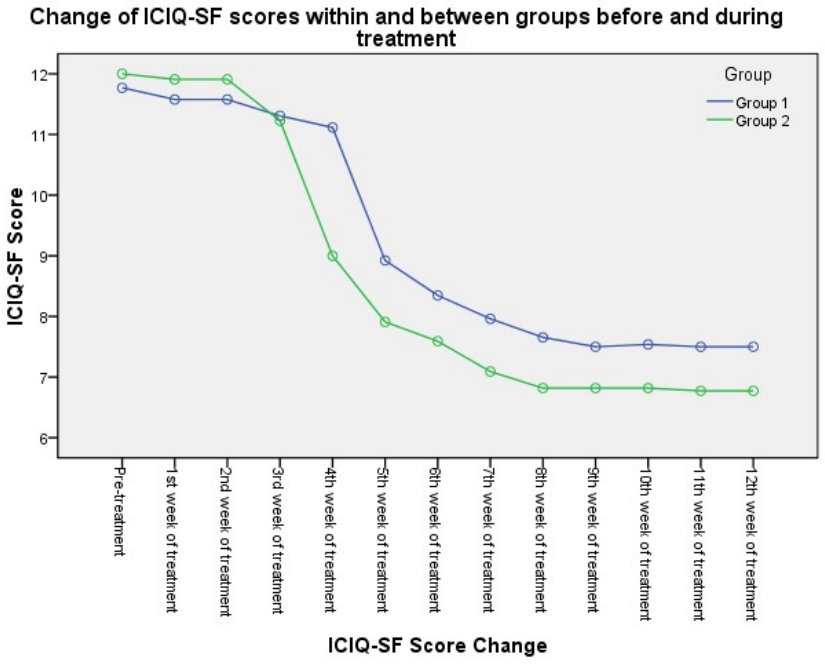
Figure 5. Change of urinary frequency within and between groups before and during treatment.

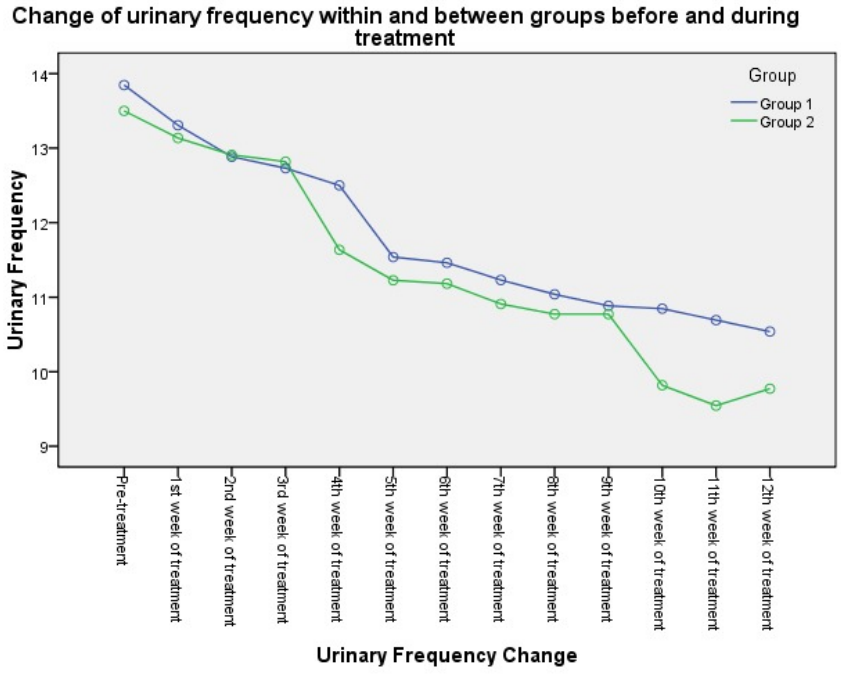




Change of OAB-V8 scores within and between groups before and during treatment







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