



Comparison of the Effect of Percutaneous Tibial Nerve Stimulation (PTNS) with Medical Treatment in Patients with Overactive Bladder

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Overactive bladder (OAB) is a common problem that involves therapeutic challenges. Therefore, finding new and effective treatment modalities in these patients is essential. The aim of this study was to compare the therapeutic effect of percutaneous tibial nerve stimulation (PTNS) with drug therapy in patients with OAB.

Methods: In this randomized controlled clinical trial, 74 patients with OAB were randomly divided into two groups: PTNS (twice a week for 12 weeks) and drug treatment (Solifenacin 10 mg daily for 12 weeks). OAB Symptom Score, q-OAB and Health-Related Quality of Life Questionnaire (HRQL) were completed and then compared at the beginning and end of the study for the two groups. Findings were analyzed using SPSS software version 20.

Results: The drug intervention group consisted of 33 (89.2%) females and 4 males (10.81%), and

PTNS group consisted of 31 females (83.8%) and 6 males (16.21%), (P = 0.496). Mean quality of life score, mean OABSS score, OAB screening score and urinary incontinence in both groups before the intervention did not show a statistically significant difference. After treatment, the mean quality of life in both groups increased significantly compared to before the intervention, but this increase was significantly higher in PTNS when compared with other group (74.2±6.9 vs. 68.9±7.3). The mean OABSS score, OAB screening score and urinary incontinence in both groups decreased significantly compared to before treatment, but the mean OABSS score and OAB and urinary incontinence screening scores showed a significant decrease in PTNS group compared to drug treatment.

Conclusion: Based on the findings, PTNS was found to be more effective than drug treatment in increasing the quality of life and controlling symptoms of OAB.

Keywords: Hyperactive bladder; percutaneous tibial nerve stimulation (PTNS); drug treatment.

1. INTRODUCTION

Overactive bladder (OAB) syndrome is a chronic medical condition characterized by *involuntary detrusor contractions* (IDC), urinary urgency, frequency and nocturia with or without urgency incontinence as updated by the International Continence Society [1-2], but its etiology is unknown.

OAB, an embarrassing and debilitating condition, has a significant impact on the quality of life of these patients with considerable health (e.g., social, psychological, occupational, and physical problems, as well as sleep, and sexual function) and economic consequences [2-3].

The prevalence of OAB is dependent on age and among women 65 years and older, the prevalence of OAB has been reported to be about 30% [1,4]. The OAB International Assessment Program (NOBLE) estimated the overall prevalence of an OAB at 16.9% for women and 16% for men [1]. The total cost of OAB in the United States in 2000 was estimated at more than \$ 12 billion [4,5]. Findings from a large demographic study in six European countries revealed a prevalence of 16.6% for OAB in people over 40 years of age. The most commonly reported symptoms are frequent urination with a prevalence of 85%, followed by urinary urgency (54%) and urinary Incontinence (36%), [6-7].

Although the main goal of treatment is to improve symptoms, the concurrent improvement of objective parameters supports the effectiveness of the modality used [8]. It should be noted that the diagnosis of an OAB is symptomatic and, according to the ICS definition, does not require

cystometric confirmation or urodynamic tests. However, some physicians have expressed concern about the neglect of the correct diagnosis in many patients, thus they will not receive appropriate therapeutic strategy due to the unreliability of the bladder as a witness [9,10].

Pelvic floor muscle exercises, lifestyle interventions and bladder training are the conservative and primary treatments for this disorder, which effectively improve the signs and symptoms of the disease. The first line of drug treatment for OAB are oral anticholinergics and antimuscarinics, and anticholinergics are generally the basis of drug treatment for this disease [11] However, their administration has caused some adverse effects, including dry mouth, headache, blurred vision constipation and blurred vision [12-16].

Oxybutynin is currently used as the first line drug in the treatment of OAB in Iran and several other countries. According to statistics, 76% of patients cannot tolerate the side effects of oxybutynin at the therapeutic dose. Complications of dry mouth and bad taste affect the reception of the drug and a significant number of patients refuse to treatment [17].

In some cases, an OAB does not respond to medication. Therefore, the use of other therapeutic modalities in these patients is necessary. The tibial nerve is derived from the tibial portion of the *sciatic nerve*, being composed of *fibers* from L4 to S3, involving in stimulation of the bladder and pelvic floor muscles. Therefore, environmental stimulation of this nerve can play a role in the treatment of these patients. Percutaneous Tibial Nerve Stimulation (PTNS) has been shown to be a safe

and effective treatment comparable to medication [18].

Given that insufficient national studies have been performed on the effect of PTNS in patients with OAB, this clinical trial study intends to compare the effect of this modality with drug therapy.

2. MATERIALS AND METHODS

2.1 Sampling

This randomized controlled clinical trial was performed on 74 patients with hyperactive bladder referred to Fatemieh, Shahid Beheshti hospitals and clinics affiliated to Hamadan University of Medical Sciences in 2020. Random sampling method was used to select patients \geq 18 years of age. Inclusion criteria included: Clinical diagnosis of OAB in patients aged 18 years or older who had a negative urine culture.

Exclusion criteria were: Pregnant patients, patients with pacemaker, symptoms suspected of inflammatory or neurological origin, spinal cord trauma, central nervous system lesions, metabolic disease or genetic syndromes, history of abdominal surgery, pelvic fractures, urogenital abnormalities and psychological disorders.

The samples of drug and PTNS groups are calculated by considering $p < 0.05$ and 95% power. In order to randomly assign the drug and PTNS groups, the method of block random division with quadruple blocks was used. In the present study, patients were aware of which group they were assigned to due to their clinical condition, but the data collector and statistical analyst were not aware of the assignment of the groups. After the preparation period for participating in the study, patients were randomly divided into 2 groups.

2.2 Procedure

The first group received 10 mg E.R.O (solifenacin) daily for 12 weeks and the other group received PTNS twice a week for 12 weeks. PTNS was performed by TENS (20 Hz, 200 cycles/s) through normal stimulation for 30 minutes per session. PTNS was done by a superficial electrode on the skin 5 cm above the medial and posterior ankle relative to the tibia. In this intervention, a neutral electrode was placed on the arches of the foot. At each session, patients received a 'motor response' that

included plantar flexion of the thumb. Preliminary results were recorded as a report of 3 days of urination in the hyperactive bladder questionnaire (q-OAB). The q-OAB questionnaire was used to prepare a report of urination including the urinary *urgency*, frequency, and incontinence for 3 days. Q-OAB is a quality-of-life questionnaire designed to assess symptoms and health-related quality of life (HRQL) in patients with or without incontinence and OAB. q-OAB has four subscales measuring *coping*, *concern*, *sleep*, and *social interaction*.

2.3 Data Analysis

SPSS software version 20 was used to analyze the data. Data were described using descriptive statistics (mean and standard deviation) for quantitative variables and ratio and percentage for qualitative variables. Furthermore, test was applied to compare quantitative variables, and chi-square test was used to compare qualitative variables. $p < 0.05$ was considered to be statistically significant.

3. RESULTS

The drug intervention group consisted of 33 (89.2%) females and 4 males (10.81%), and PTNS group consisted of 31 females (83.8%) and 6 males (16.21%). There was no statistically significant difference between the two groups in terms of gender (Fig. 1).

On average, both groups of patients were 40 years old, which was not significantly different (Table 1).

Independent t-test showed that the mean score of quality of life in the two groups of drug therapy and PTNS at the beginning of the study was 59.2 ± 4.7 and 57.8 ± 4.8 , respectively, which no statistically significant difference was found between the two groups ($P = 0.191$).

In terms of subscale, both groups did not have a statistically significant difference before the intervention based on independent t-test. After the intervention, the mean score of quality of life in the PTNS group increased to 74.2 ± 6.9 . Furthermore, the mean quality of life score increased to 68.9 ± 7.3 in the drug treatment group. The quality-of-life score in the PTNS group showed a significant increase compared to the drug group ($P = 0.001$).

Paired t-test was performed to compare each group before and after the intervention. The

results showed that the mean quality of life and its subscale increased significantly compared to

the beginning of the study in both groups (Table 2 and Fig. 2).

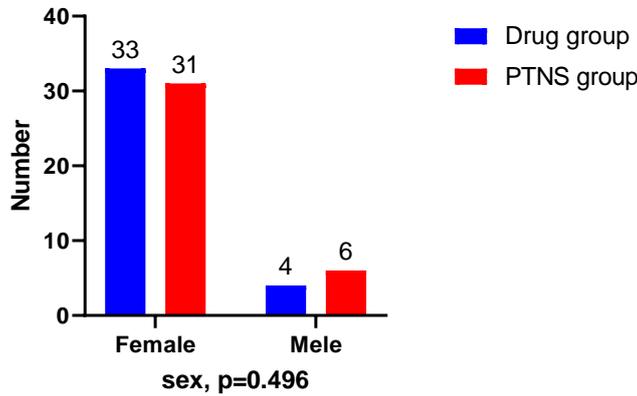


Fig. 1. Comparison of patients in two groups based on gender

Table 1. Comparison of the mean age of the two groups of patients

Variable	Drug Group· n=34	PTNS Group·n=34	P(independent-t-test)
Age (Years)·M±SD	1.2 ±5.39	4.2 ± 4.40	367.0

Table 2. Comparison of the mean score of quality of life of patients with OAB before and after treatment in the two groups

Variable	Time	Drug· n=34	PTNS·n=34	P(independent-t-test)
Limiting behavior	Start	1.9 ±3.21	9.7 ± 2.21	716.0
	Finish of study	7.3 ± 5.26	4.1 ±5.28	161.0
	P-value	001.0	001.0	-
Psychosocial impacts	Start	8.4 ±3.26	3.8 ± 4.24	095.0
	Finish of study	1.1 ± 5.28	9.1 ±4.30	097.0
	P-value	001.0	045.0	-
Social	Start	1.9 ± 2.10	1.3 ±2.11	482.0
	Finish of study	.44 ± 3.14	8.9 ±3.15	092.0
	P-value	001.0	001.0	-
	Start	7.2 ±4.59	8.8 ± 4.57	191.0
	Finish of study	3.9 ± 7.68	9.1 ±6.74	002.0
	P-value	001.0	001.0	-

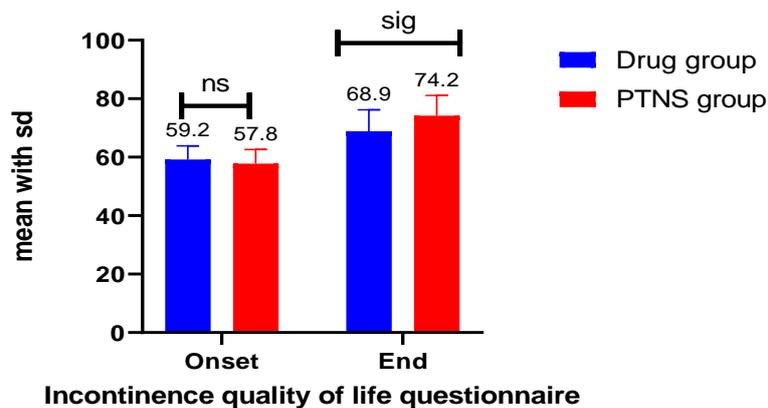


Fig. 2. Comparison of quality-of-life scores in the two groups before and after the intervention

The results revealed that the mean score of OABSS in the pharmacotherapy and PTNS groups was 10.6 ± 1.4 and 10.7 ± 1.7 , respectively ($P = 0.824$). After the intervention, the severity of symptoms decreased significantly in the PTNS group ($P = 0.023$). Paired t-test also showed that the severity of symptoms in both groups decreased significantly compared to before the intervention ($P = 0.001$).

The results showed that the mean screening scores in the drug and PTNS groups were 25.6 ± 5.4 and $24.7. 5.8$, respectively. Independent t-test showed no statistically significant difference between the two groups in terms of symptoms of OAB before the intervention ($P = 0.482$). After the intervention, the severity of symptoms decreased significantly in the PTNS group ($P = 0.016$). Paired t-test also showed that the

severity of symptoms in the two groups decreased significantly compared to before the intervention ($P = 0.001$), (Table 3, Figs. 3 and 4).

4. DISCUSSION

The aim of this clinical trial study was to evaluate the therapeutic effect of effect of PTNS in patients suffered from OAB in comparison with drug therapy.

The results of our study demonstrated that drug treatment with solifenacin and PTNS were both effective in reducing the symptoms of this disorder and increasing the quality of life of patients. However, PTNS showed a better therapeutic response and quality of life among patients with OAB.

Table 3. Comparison of the mean score of OAB and screening before and after treatment in the two groups

Variable	Time	Drug group (n=34)	group PTNS:n=34	P(independent-t-test)
OABSS	Start	4.6 ± 1.10	7.7 ± 1.10	824.0
	Finish of the study	2.1 ± 1.6	9.5 ± 0.5	023.0
	P-value	001.0	001.0	-
Screen	Start	4.6 ± 5.25	8.7 ± 5.24	482.0
	Finish of the study	8.3 ± 3.12	3.5 ± 2.10	016.0
	P-value	001.0	045.0	-

OABSS :Overactive Bladder Symptom Score

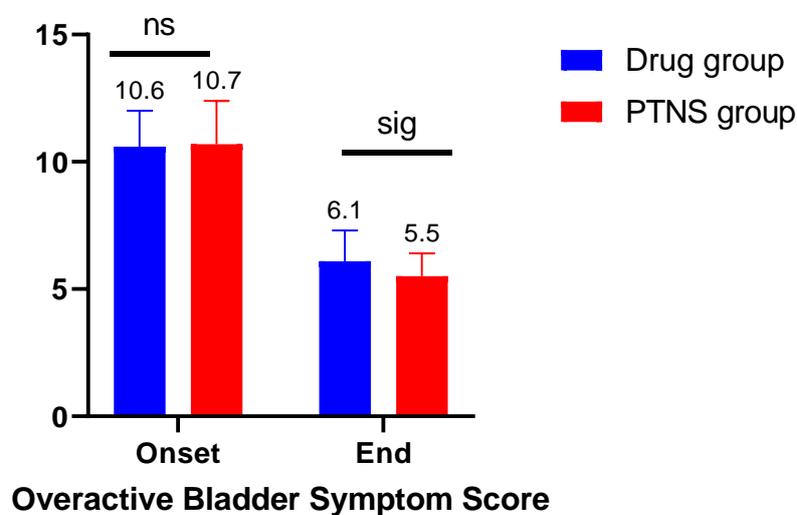


Fig. 3. Comparison of OABSS score in two groups before and after the intervention

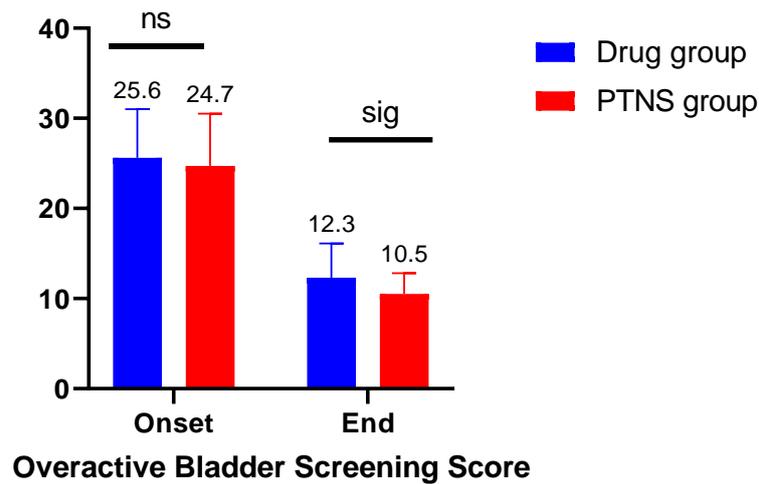


Fig. 4. Comparison of OAB screening score and urinary incontinence in the two groups before and after the intervention

The total cost of OAB in the United States in 2000 was estimated at more than \$ 12 billion [4-5]. These costs have been previously estimated to be comparable to those of osteoporosis and gynecological cancers [4-5].

The prevalence of hyperactive has been described to be increased with age. In the present study, more than half of the patients were over 40 years old. The symptoms of OAB have a significant negative impact on the quality of life of these patients with considerable health and physical problems (e.g., social, psychological, and occupational levels, as well as quality of sleep, and sexual function), [1-3]. One of the reasons for the decrease in quality of life in these patients is waking up, insomnia and nocturnal enuresis.

OAB is a common disease in both men and women. Most of the patients in the present study were female. However, for anatomical and physiological reasons, men and women may differ in the prevalence of hyperactive bladder and its symptoms [19]. Old age, genetics, female gender, pregnancy, childbirth, stress and strenuous physical activity are among the risk factors for it. Limited understanding or appreciation of the morbidity may lead to underreporting of OAB in women when women see OAB as a normal part of aging and develop coping mechanisms [3,5].

Non-invasive methods for treating an OB patient are considered and agreed upon by specialists.

The two main receptors in the bladder are calcium channel receptors and muscarinic receptors. Antimuscarinics act on M1 and M2 receptors, crossing the blood-brain barrier and exerting their effect. Although anticholinergics and antimuscarinics are the first line of treatment for OAB, the results of studies have shown that a high percentage of patients are not satisfied with their treatment and experience treatment failure [11] However, their administration has caused some adverse effects, including dry mouth, headache, blurred vision constipation and blurred vision [12-16].

Therefore, alternative therapies such as botulinum toxin type A injection, sacral neuromodulation and PTNS have been introduced. PTNS is known as a lower urinary tract neuromodulation method described by Stoller in the late 1990s for the treatment of OAB [20]. This therapeutic modality has attracted more attention due to its less invasive nature than other *neurostimulation techniques*. PTNS is a safe, minimally invasive, and effective form of *neurostimulation technique* that is capable of treating the symptoms of OBA.

Many studies have considered this method a successful treatment in improving symptoms and urodynamic observations [21-24]. Although the definition of "success" varies between studies, from the use of urodynamic data to clinical parameters and quality of life criteria. In particular, many of them came from a group of patients who had not previously responded to

conventional therapies [18]. Positive findings on the efficacy of PTNS in OAB are available from randomized controlled trials [25-27]. Our findings demonstrated that PTNS was an effective and safe option to treat OAB patients, resulting in a better quality of life among these patients.

Based on the findings of a meta-analysis study published by Wang et al. (2020), from 28 studies with a population of 2461 OAB patients, the findings revealed a significant effect of PTNS on the voiding frequency, nocturia frequency, urgency episodes, incontinence episodes, maximum cystometric capacity and compliance (the success rate: 0.68 [95% CI 0.59, 0.78]) [28]. Other meta-analytic studies, including those of Tutolo et al. (2018) and Wibisono et al. (2015), have shown that PTNS is a safe, with no major complications, and effective treatment for patients with OAB [29,30].

PTNS has been more effective than the drug therapy or was comparable to the drug strategy as reported by some authors. In consideration of these potentialities, PTNS could be suggested as the first line of treatment in these patients with no major complications.

Findings from a study in Turkey by Kızılyel et al. (2015) showed that PTNS was an effective technique for OAB patients nonresponding to conservative therapies as recommended either alone or in combination with anticholinergics [31]. A study by Manriquez et al. (2016) showed the similar effectiveness of both T.C. PTNS and extended release oxybutynin (E.R.O.) in patients suffered from OAB. SANS is an easy and inexpensive therapeutic method with low morbidity in patients with an overactive bladder. Combination with a low-dose anticholinergic increases the success rate without causing any significant side-effects [32].

In the studies of Karademir et al. (2005) on 43 patients, it was observed that the combination of a low-dose anticholinergic (oxybutynin hydrochloride) with SANS had a higher therapeutic response rate (83.2 vs. 61.6%) in patients with OAB, without causing any significant complications [24].

5. CONCLUSION

Based on the findings presented herein, PTNS was found to be more effective than drug treatment in increasing the quality of life and controlling symptoms of OAB. Further investigations are required to evaluate the effect

of PTNS on the remaining indications. The long-term durability of PTNS in the treatment of OAB was reported where results revealed sustained improvement from 12 weeks at 6 and 12 months. However, further investigations are required to assess the long-term durability of PTNS.

CONSENT AND ETHICAL APPROVAL

This study was performed with the approval of the Hamadan University of Medical Sciences after obtaining the code of ethics IR.UMSHA.REC.1398.237. Informed consent was obtained from patients before participating in the study. No additional costs were imposed on patients and patient personal details remained confidential.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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