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Transcutaneous posterior tibial nerve stimulation versus extended release oxybutynin in overactive bladder patients. A prospective randomized trial

Valentín Manríquez [a,*], Rodrigo Guzmán [a], Michel Naser [a], Amalia Aguilera [a], Simonie Narvaez [a], Ariel Castro [b], Steven Swift [c], G. Alessandro Digesu [d]

[a] Pelvic Floor Unit, Obstetrics and Gynecology Department, Clinical Hospital, Universidad de Chile, Chile
[b] Clinical Investigation Support Department, Clinical Hospital, Universidad de Chile, Chile
[c] Division of Urogynecology & Incontinence, Medical University of South Carolina, United States
[d] Imperial College Healthcare NHS Trust, Academic Department of Obstetrics & Gynaecology, United Kingdom

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ABSTRACT

Introduction and hypothesis: The aim of this study was to evaluate the effectiveness of transcutaneous posterior tibial nerve stimulation (T.C. PTNS) versus extended release oxybutynin (E.R.O.) in patients with overactive bladder.
Materials and methods: Seventy female patients were randomized to receive either 10 mg E.R.O. daily or T.C. PTNS, using a TENS machine program with the 20 Hz, 200 cycles/s, and normal stimulation setting for two 30-min sessions, each week for a 12-week period. Pre-treatment and after the 12-week intervention, each patient completed a 3-day voiding diary and a self-report quality of life questionnaire (OAB-q). Statistical analysis was performed using Stata V12.1.
Results: Sixty-four patients completed the treatment protocol. There were no significant differences between study groups in terms of age, body mass index, past hormone replacement therapy, smoking habits, menopause status, and parity. Prior to treatment, there were also no significant differences in the analysis of the 3-day voiding diary or in the OAB-q questionnaire results. Following the 12-week study, there was a statistically significant reduction in frequency of urination, urgency episodes, and urge incontinent episodes compared to pre-treatment values. However, there were no significant differences in these values between intervention groups after 12-weeks of therapy. There was a similar improvement in OAB-q scores in both treatment groups following therapy, and the T.C. PTNS group showed a statistically significant improvement over the E.R.O. in domain 2 of the OAB-q questionnaire. The other two domains showed similar improvement in both study groups.
Conclusion: T.C. PTNS and E.R.O. demonstrated similar improvements in subjects with OAB in a 12-week study.

Brief summary

Transcutaneous posterior tibial nerve stimulation is as effective as extended release oxybutynin as a treatment option to control overactive bladder symptoms and improve patient quality of life.

Introduction

Overactive bladder syndrome (OAB) is a common and debilitating condition that is increasingly seen by gynecologists, as a result of growing patient awareness, improved understanding of the condition, the introduction of new treatment modalities, patients' increased desire for improved quality of life, and changing demographics, as the global population ages. The condition is defined by the International Continence Society (ICS) as "urgency, with or without urge incontinence, usually with frequency and nocturia, in the absence of local or metabolic factors explaining these symptoms" [1]. Although the exact prevalence of OAB is unknown, since investigators have used varied definitions of OAB in epidemiologic studies and clinical trials, two large

* Corresponding author at: Hospital Clínico Universidad de Chile, Santos Dumont 999 oficina 209-A, Independecia, Santiago, Chile. Tel.: +56 22297882879; mobile: +56 984391865.
E-mail address: valentinmanriquez@gmail.com (V. Manríquez).

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population-based surveys using the 2010 ICS definition for OAB have reported prevalences of 9.4% and 16.9% [2,3]. Extrapolated to the population in Chile, where the current study was conducted, nearly 2 million adults could suffer from OAB. With demographic changes, gynecologists can expect to see an even greater number of individuals seeking medical attention, for OAB symptoms in the future.

Pharmacotherapy has long been the mainstay for OAB treatment, and a variety of newer drugs have recently been introduced. These drugs – anticholinergic/muscarinic receptor antagonists – have demonstrated efficacy, with varying dosing schedules, side-effect profiles, and biochemical properties. Gopal et al. studied the discontinuation rates of female patients treated with anticholinergic medication, due to concerns of poor tolerability or suboptimal success rates. The authors found that the average 6-month incidence of discontinuation was 58.8%, with discontinuation rates ranging from 54% to 71%, depending on the medication used [4]. Moreover, a study by Kay et al. has shown that 30% of OAB patients do not respond to antimuscarinics, and that there are often several co-morbidities that prevent the use of this class of drug [5].

In light of the above, there is a growing need for therapeutic options that are as effective as antimuscarinics, but which have fewer side effects and contraindications and are available at a lower cost. Since 1999, posterior tibial nerve stimulation (PTNS) has had demonstrated efficacy in controlling symptoms and improving quality of life in OAB patients, with approximately 70% of patients achieving at least a 50% reduction in incontinence episodes, and with 40–50% achieving complete dryness [6]. A few trials have compared the effectiveness of PTNS and antimuscarinic drugs, showing similar responses for both treatments [7]. Traditional PTNS treatment, however, is costly and requires direct professional supervision for the placement of needles.

Transcutaneous tibial nerve stimulation (T.C. PTNS), on the other hand, uses a surface electrode, instead of a needle, to stimulate the nerve, making it a less expensive and less invasive treatment option, which could be self-applied by patients. Recently, research has shown that T.C. PTNS has proven to be an effective treatment option in managing refractory OAB patients [8]. Nevertheless, to our knowledge, there are no published trials comparing the effectiveness of T.C. PTNS versus antimuscarinic drugs for patients with OAB.

The aim of our study was to compare the effectiveness of transcutaneous posterior tibial nerve stimulation (T.C. PTNS) versus extended release oxybutynin (E.R.O.), an antimuscarinic drug, in OAB symptom control and quality of life improvement.

Materials and methods

Between November 2010 and December 2013, 70 female patients recruited from the Pelvic Unit of the Clinical Hospital of Universidad de Chile in Santiago were randomized by permuted blocks to either 10 mg E.R.O. daily or twice a week T.C. PTNS. T.C. PTNS was applied using a TENS machine program, with 20 Hz, 200 cycles/s normal stimulation for 30 min each session, and voltage was regulated by patients, each time they achieved motor response (plantar flexion of the big toe and/or toe fanning) (Fig. 1). As previously reported [9], the more frequent the stimulation, the earlier the clinical response. Although stimulation could, ideally, be performed daily, the study participants had to travel to the hospital for applications of T.C. PTNS, to ensure that stimulation was applied in concordance with protocol. Thus, to reduce subjects financial burden, and prevent drop-out, yet still receive an earlier response than would be seen by once a week stimulation, we decided to apply T.C. PTNS twice a week.

Primary outcomes were the results of a 3-day voiding diary and the results of the OAB-q questionnaire. Each participant completed a 3-day voiding diary, which recorded urinary frequency, urgency episodes, and urge incontinence episodes, and filled out the OAB-q self-report questionnaire before randomization and at the end of the 12-week intervention period. The OAB-q questionnaire is a quality of life questionnaire, developed to assess symptom bother and health-related quality of life (HRQL) among patients with either continent or incontinent overactive bladder. It has an 8-item symptom bother scale and four HRQL subscales (coping, concern, sleep, and social interaction), which are derived from 25 items. Successful responders were defined as participants who demonstrated a $\geq$50% reduction in urinary frequency, based on the 3-day voiding diary, compared to pre-treatment values.

Inclusion criteria were the following: clinical diagnosis of OAB (as defined by IUGA/ICS 2010 guidelines), being 18 years of age or older permanent residence in the Metropolitan Region of Santiago for the subsequent 6 months, and having a negative urine culture within 2 weeks of randomization. Pregnant women, pacemaker users, and those whose symptoms were suspected to be neurological or inflammatory in origin were excluded.

In the E.R.O. group, 29 out of 34 patients, and 31 out of 36 patients in the T.C. PTNS group, were naive to treatment options regarding overactive bladder. Previously treated participants were asked to follow a 2-week wash-out period, if they were undergoing antimuscarinic treatment.

The study was approved by the local ethical committee of the Clinical Hospital of Universidad de Chile (IRB: 225/07), and written informed consent was obtained from all patients.

Sample size

The Arcsine method was used to calculate sample size, based on the assumption of E.R.O. achieving a 40% reduction in urinary frequency and T.C. PTNS a 70% reduction, with 5% alpha error and 20% beta error. The allocation ratio was 1:1, with a replacement rate of 5%, in the case of loss of participants to follow-up. A sample size of 70 participants was calculated.

Statistical analysis

Statistical analysis was conducted using Stata V12.1, licensed to author A. Castro. Data were presented with summary measures of central tendency (average and median) and dispersion (standard deviation and range).

The T-test and Wilcoxon test were used for continuous normally distributed and non-normally distributed data, respectively. Normality was checked using the Kolmogorov–Smirnov method, and the comparison test of proportions was also used. A p-value of <0.05 was considered statistically significant, with a 95% confidence interval (CI 95%).

Results

Of the 70 enrolled participants, 34 were randomized to receive 10 mg E.R.O., and 36 to T.C. PTNS. Four women in the antimuscarinic (E.R.O.) group were lost to follow-up, due to adverse effects (dry mouth) and pregnancy, and two women were lost to follow-up in the neuromodulation group (T.C. PTNS), one becoming pregnant and the other changing her city of residence (Fig. 1). No adverse events were reported in the T.C. PTNS group, while 9 patients in the E.R.O. group reported dry mouth. There were no significant differences between treatment groups in terms of age, body mass index, past hormone replacement therapy, smoking status, menopause status, and parity (Table 1).