

Neuromodulation with microcurrents versus posterior tibial nerve stimulation in the treatment of overactive bladder: a prospective comparative study

Miguel Arrabal-Martin,^{1,2} Maria Isabel Martinez-Sanchez,¹
Laura Jerez-Fernandez,¹ Marta Sacristan-Ruiz,¹ Maria Jose Garcia-Ortega,¹
Andrea Maria Hernandez-Perez,³ Miguel Angel Arrabal-Polo,^{1,2*}
Alberto Zambudio-Munuera,¹ Mercedes Nogueras-Ocaña¹

¹Department of Urology, San Cecilio University Clinical Hospital, Granada, Spain

²Biomedical Research Institute IBS Granada, University of Granada, Granada, Spain

³Faculty of Health Sciences, University of La Laguna, Tenerife, Spain

ARRABAL-MARTIN M, MARTINEZ-SANCHEZ MI, JEREZ-FERNANDEZ L, SACRISTAN-RUIZ M, GARCIA-ORTEGA MJ, HERNANDEZ-PEREZ AM, ARRABAL-POLO MA, ZAMBUDIO-MUNUERA A, NOGUERAS-OCANA M. Neuromodulation with microcurrents versus posterior tibial nerve stimulation in the treatment of overactive bladder: a prospective comparative study. *Can J Urol* 2026;33(5):1285–1294.

Background: Posterior tibial nerve stimulation (PTNS) using the Urgent PC device has been shown to improve symptoms of overactive bladder (OAB). In this context, non-invasive autonomic nervous system neuromodulation using microcurrents (NESA), delivered via the NXsignal device, has emerged as a potential alternative therapy. The study aimed to evaluate the initial efficacy of NESA in patients with an overactive bladder.

Methods: We conducted a prospective, non-randomized study comparing microcurrent neuromodulation (NESA) with PTNS in 60 consecutively recruited patients, evaluating changes in clinical bladder diary parameters and urodynamic findings after 12 treatment sessions. The main variables measured were clinical (collected from a 3-day bladder diary), including: daytime urinary frequency (DUF); nocturnal urinary frequency (NUF); urgency episodes (EU); urgency urinary incontinence episodes (UUI) and urodynamic (first

urge to void; maximum bladder capacity; urgency-related voiding; detrusor overactivity). Various parametric and non-parametric statistical tests were used, and statistical significance was considered at $p < 0.05$.

Results: Favorable outcomes were observed across all clinical and urodynamic variables with both treatments (NESA vs. PTNS). A significant reduction in urgency episodes (EU) was observed in patients treated with PTNS ($p = 0.006$), while a significant reduction in detrusor overactivity was found in patients treated with NESA ($p = 0.008$). In the NESA group, the bladder tolerated a greater urine volume before the first desire to void, whereas significant differences in increased bladder capacity were observed in patients treated with PTNS. No adverse effects were detected in either treatment group.

Conclusion: Both treatments were effective, with no statistically significant differences between NESA and PTNS in the management of OAB. Further studies are warranted to investigate the long-term effects of microcurrent neuromodulation, as well as to better define its optimal, patient-specific application.

Key Words: overactive bladder, posterior tibial nerve stimulation, non-invasive autonomic nervous system neuromodulation using microcurrents, urinary urgency

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*Corresponding Author: Miguel Angel

Arrabal-Polo. Email: arrabalp29@gmail.com

Introduction

Overactive bladder (OAB) syndrome has a multifactorial etiopathogenesis and may have a neurogenic, urothelial, myogenic, or idiopathic origin. According to the International Continence Society, OAB is defined as urinary urgency, usually accompanied by daytime and nocturnal frequency, with or without urgency urinary incontinence, in the absence of urinary tract infection or other identifiable pathology. When detrusor muscle activity is normal on urodynamic evaluation, this condition is considered sensitive urgency. OAB is a highly prevalent health problem that significantly interferes with daily activities and represents a chronic medical condition that markedly impairs patients' quality of life.^{1,2}

The therapeutic strategy for Overactive Bladder (OAB) is traditionally organized into a tiered framework, prioritizing non-invasive interventions such as behavioral therapy, pelvic floor rehabilitation, and dietary or lifestyle adjustments as the primary line of care.³ Second-line treatment includes β 3-adrenergic agonists and antimuscarinic agents, which are the most commonly used pharmacological therapies; however, their use is often limited or discontinued due to frequent adverse effects.³ When conservative measures fail, third-line interventions encompass a range of specialized modalities, including intradetrusor onabotulinumtoxinA injections, posterior tibial nerve stimulation (PTNS), and sacral neuromodulation.⁴

Neuromodulation has shown encouraging results with few or no adverse effects and is therefore currently an accepted therapeutic modality. Depending on the technique employed, long-lasting effects have been reported, particularly in reducing daytime and nocturnal urinary frequency.⁵ Subsequent investigations should focus on elucidating the underlying autonomic nervous system mechanisms involved in bladder dysfunction and urinary incontinence. Furthermore, there is a critical need to refine neuromodulation protocols and explore synergistic combination therapies to optimize clinical outcomes for patients suffering from urgency urinary incontinence.⁶

Sacral neuromodulation requires a specific implantable device and a costly surgical procedure. PTNS represents an alternative technique that has also been shown to be effective in improving urinary continence in patients with OAB and/or sensitive urgency. Its immediate effect has been demonstrated through inhibition of detrusor muscle activity and elevation of the threshold for the first desire to void.⁷ Moreover, treatment effects lasting up to 24 months

have been reported, particularly in the control of daytime and nocturnal frequency.^{5,8}

The convergence of the autonomic and somatic nervous systems at the lumbosacral level and their functional interaction may partially explain the effects of PTNS in controlling detrusor overactivity.⁹ Current understanding of the role of interneurons in somato-autonomic interactions within the central nervous system suggests that the antidromic impulse generated by PTNS exerts an inhibitory effect on the detrusor muscle via spinal interneurons. Central nervous system plasticity may further explain the sustained effects of PTNS and other neuroelectrostimulation techniques in the treatment of OAB.^{8,9}

The Hodgkin–Huxley model of nerve impulse conduction^{10,11} postulates the existence of action potentials in nerves and the coordination of electrical impulses by the central nervous system through ion channel activity. In this context, non-invasive autonomic nervous system neuromodulation using microcurrents (NESA) delivered via the NXsignal device is proposed as an alternative therapeutic approach. By leveraging global neuromodulation, this technique triggers modulatory responses—specifically via orthodromic impulses—that engage descending inhibitory pathways.¹² Consequently, this intervention counteracts several of the core etiological drivers underlying OAB symptomatology.

Microcurrent neuromodulation is therefore proposed as a technological alternative to existing electrostimulation therapies. Unlike conventional techniques, it is non-invasive, does not induce muscle contraction or movement, and delivers imperceptible microcurrents with physiological intensity and frequency.

Materials and Methods

Primary objective

The primary objective of this prospective study was to evaluate the effectiveness and safety of microneuromodulation with microcurrents using the NXsignal device compared with PTNS in patients with OAB, including those presenting with detrusor overactivity (involuntary detrusor contractions) during the filling phase on urodynamic study (UDS) and those without detrusor contractions (sensitive urgency). The study was designed as a prospective observational comparative study of NESA versus PTNS.

Secondary objectives

The secondary objectives was to assess the safety of NESA compared with PTNS in patients with OAB

and/or sensitive urgency and to evaluate improvements in quality of life and sleep quality assessed using the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF)¹³ and the Pittsburgh Sleep Quality Index.¹⁴

Study design

A prospective study was conducted in women and men aged ≥ 18 years attending the Functional Urology outpatient clinic of San Cecilio University Clinical Hospital. Eligible patients presented with symptoms consistent with OAB or sensitive urgency and were considered candidates for treatment with NESA or PTNS.

The study protocol (Code: FIB-NES-2024-11) was approved by the Provincial Clinical Research Ethics Committee of Granada (Comité de Ética de la Investigación con Medicamentos and Comité de Ética de la Investigación, Granada, Spain) on 25 June 2024. Patients signed informed consent to participate in the study. Register code: 202499906944178.

Patients were classified into two main groups according to urodynamic findings. Group A comprised 30 patients diagnosed with overactive bladder, of whom 15 with detrusor overactivity during the filling phase were treated with NESA (subgroup A1) and 15 with similar urodynamic findings were treated with PTNS (subgroup A2). Group B included 30 patients with sensitive urgency and normal detrusor activity on urodynamic study; within this group, 15 patients received NESA (subgroup B1) and 15 received PTNS (subgroup B2).

Sample size

Participants were recruited consecutively from the Functional Urology clinic after diagnosis of OAB or sensitive urgency, following provision of study information and written informed consent. For a reference population of 500,000 inhabitants, with a 90% confidence interval and a 10% margin of error, a sample size of 60 patients was estimated. A total of 60 patients were included and consecutively assigned to each subgroup.

Eligible participants were adults aged ≥ 18 years with a diagnosis of overactive bladder or sensitive urgency who had undergone urodynamic evaluation and provided written informed consent. Exclusion criteria included prior posterior tibial nerve stimulation within the preceding 12 months, the presence of any implanted electrical device (such as a neuromodulator or pacemaker), and current pregnancy or risk of pregnancy.

Study variables

Clinical urological parameters were collected from a 3-day bladder diary and included daytime urinary frequency (DUF), nocturnal urinary frequency (NUF), urgency episodes (EU), and urgency urinary incontinence episodes (UUI). Urodynamic parameters were assessed based on urodynamic study data and in accordance with International Continence Society (ICS) definitions, and included first desire to void, maximum bladder capacity, urgency-related voiding, and the presence of detrusor overactivity.¹⁵ Patient-reported outcomes were evaluated using validated questionnaires, specifically the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF)¹³ and the Pittsburgh Sleep Quality Index.¹⁴

Treatment protocol

After urodynamic evaluation, patients were consecutively assigned to one of the four subgroups for treatment with PTNS (using the Urgent PC device) or NESA (using the NXsignal device). Patients were informed about the treatment protocol and the starting date. All participants completed a bladder diary and the ICIQ-SF and Pittsburgh questionnaires at baseline and at the end of treatment. Urodynamic studies were performed before and after treatment.

NESA treatment lasted five weeks. During weeks 1 and 2, three sessions per week were administered; during weeks 3 to 5, two weekly sessions of 60 min were performed, for a total of 12 sessions (Figures 1 and 2). Treatment was delivered with patients in the supine position, using gloves and ankle straps connected to a total of 24 electrodes, along with an additional directional electrode for global neuromodulation.

The NESA device delivers low-frequency microcurrents (1.3–14.28 Hz, depending on the program), low intensity (0.1–0.9 mA), and low voltage (± 3 V), organized in 130-ms pulses, which are imperceptible to the patient. During the first four sessions, programs P1 (30 min), P7 (15 min), and P8 (15 min) were applied, with the directional electrode positioned at the cervical level (C7). During sessions five to eight, programs P2 (15 min) and P7 (45 min) were used, with the directional electrode placed at L3. During the final four sessions, programs P3 (15 min) and P7 (45 min) were applied, with the directional electrode positioned at S1–S2.

For PTNS, stimulation intensity (pulse amplitude) was adjusted to achieve an adequate patient response, defined by plantar tingling and toe flexion. Treatment duration was six weeks, with two 30-min sessions per week, totaling 12 sessions (Figure 3).

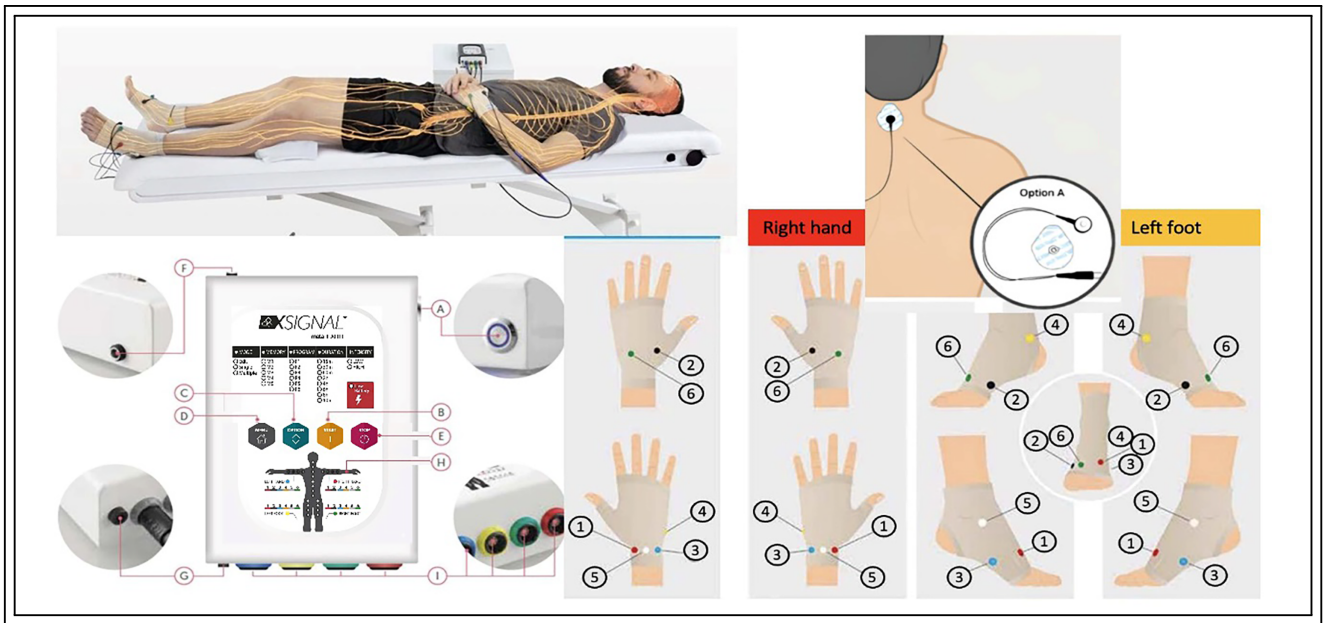


FIGURE 1. Six semi-electrodes are placed on each glove and ankle strap and connected to the NXsignal device. The directional electrode is positioned at the cervical, lumbar, or sacral spine level

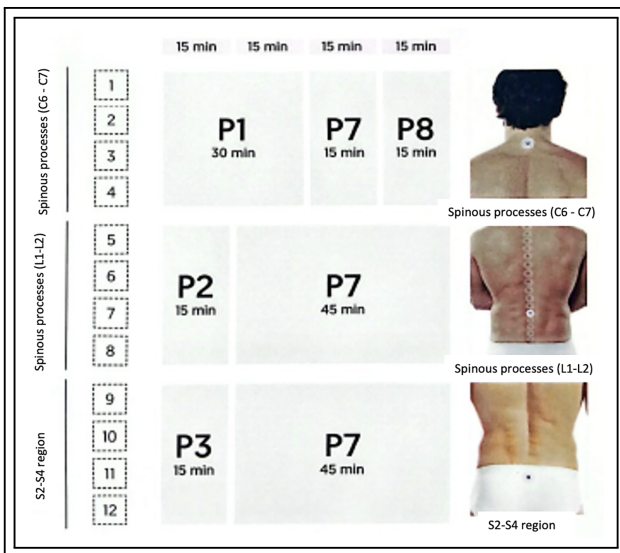


FIGURE 2. Selection of the combination of programs applied during each treatment block on the NXsignal device, with predefined intensity and frequency parameters and a fixed voltage of 3 volts

Statistical analysis

The Kolmogorov–Smirnov test was used to assess the normality of the distribution of the main outcomes. To quantify treatment effects of NESA and PTNS, univariate analyses were performed using ANOVA,

Wilcoxon test, Mann–Whitney U test, Student's *t*-test for independent samples, McNemar test, and Fisher's exact test, as appropriate. Baseline characteristics were included in all models, and the interaction between treatment type and stratification variables was assessed using the likelihood ratio test. Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). A two-sided *p*-value of <0.05 was considered statistically significant.

Results

Between November 2024 and May 2025, a total of 29 patients were treated with microcurrents using the NXsignal device [NESA WORLD. Version 1. NGS Health and Mind SL. Parque Empresarial Zuatzu. San Sebastian. Spain], and 30 patients were treated with posterior tibial nerve stimulation (PTNS) using the Urgent PC device. Patients were allocated to two treatment groups (Table 1), comprising 50 women and 9 men aged between 34 and 72 years. No statistically significant differences were observed in baseline characteristics between groups.

Table 2 summarizes the percentage of favorable outcomes obtained with PTNS and NESA for each analyzed variable in patients with OAB and sensitive urgency.



FIGURE 3. Posterior tibial nerve stimulation was performed using the Urgent PC device with a percutaneous electrode

TABLE 1. Baseline characteristics of patients treated with PTNS and NESA

Characteristic	PTNS (n = 30)	NESA (n = 29)	p-value
Sex, n (%)			0.064
Women	28 (93.3)	22 (75.9)	
Men	2 (6.7)	7 (24.1)	
Age, years, median (range)	64 (34–72)	63 (34–71)	0.813
Body mass index, kg/m ²	24.0 (22.0–39.0)	27.0 (22.0–38.0)	0.848
Diagnosis, n (%)			0.796
Overactive bladder	15 (50.0)	16 (55.2)	
Sensitive urgency	15 (50.0)	13 (44.8)	
Smokers, n (%)	12 (40.0)	11 (37.9)	0.791
Diabetes mellitus, n (%)	6 (20.0)	3 (10.3)	0.278
Antidepressant treatment, n (%)	2 (6.7)	4 (13.8)	0.389
Significant postvoid residual, n (%)	3 (10.0)	2 (6.9)	0.640
Maximum flow rate (Qmax), mL/s	15.0 (5.4–33.0)	16.4 (2.5–48.6)	0.756
Bladder capacity, mL, median (range)	310 (81–354)	309 (35–383)	0.604
Daytime frequency, median (range)	10 (5–22)	8 (5–14)	0.121
Nocturnal frequency, median (range)	1 (0–8)	2 (0–5)	0.680
Urgency episodes, median (range)	6.5 (0.0–24.0)	6.0 (0.0–19.0)	0.573
Urgency urinary incontinence episodes, median (range)	3 (0–14)	2.5 (0–9)	0.759
Urgent voids per day, median (range)	10 (4–14)	11 (3–15)	0.861
ICIQ-OAB score, median (range)	15 (2–20)	16 (4–18)	0.760
Pittsburgh sleep quality index, median (range)	14 (3–20)	12 (2–21)	0.879

Notes. Data are presented as median (range) unless otherwise specified. Categorical variables are reported as a number (percentage). Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the chi-square test or Fisher’s exact test as appropriate. A two-sided *p*-value < 0.05 was considered statistically significant. PTNS = posterior tibial nerve stimulation; NESA = neuromodulation with microcurrents; ICIQ-OAB = International Consultation on Incontinence Questionnaire–Overactive Bladder.

TABLE 2. Percentage of favorable outcomes observed for each clinical, urodynamic, quality-of-life, and sleep-related variable in patients with OAB and sensitive urgency

Favorable results treatment	Sensitive urgency NESA	Sensitive urgency PTNS	Sensitive urgency NESA + PTNS	Overactive bladder NESA	Overactive bladder PTNS	Overactive bladder NESA + PTNS
	13 cases	15 cases	28 cases	16 cases	15 cases	31 cases
DUF	38.5%	60.0%	50.0%	18.8%	46.7%	32.3%
NUF	15.4%	26.7%	21.4%	31.3%	40.0%	35.5%
EU	38.5%	50.3%	46.4%	37.5%	66.7%	51.6%
UII	38.5%	26.7%	32.1%	31.3%	53.3%	41.9%
Bladder capacity	38.5%	33.3%	35.7%	50.0%	60.0%	54.8%
1st urination desire	46.2%	46.7%	46.4%	56.3%	53.3%	54.8%
Urination by urgency	−15.4%	−20.0%	−17.8%	25.0%	26.7%	25.8%
Detrusor overactivity	−23.1%	−20.0%	−21.4%	56.3%	33.3%	43.4%
Detrusor overactivity/drain	−15.4%	−20.0%	−17.8%	25.0%	26.6%	25.8%
ICIQ-SF	46.2%	40.0%	42.9%	50.0%	73.3%	61.3%
PITTSBURGH	53.8%	46.7%	50.0%	56.3%	66.7%	61.3%

Note. NESA, Non-invasive autonomic nervous system neuromodulation using microcurrents; PTNS, Posterior tibial nerve stimulation; DUF, Daytime urinary frequency; NUF, Nocturnal urinary frequency; EU, Urgency episodes; UII, Urgency urinary incontinence; ICIQ-SF, International Consultation on Incontinence Questionnaire–Short Form.

Group A: overactive bladder

In Group A (patients with OAB), improvement in DUF was observed in 32.3% of patients, NUF in 35.5%, EU in 51.6%, and UII in 41.9%. Improvements in both the ICIQ-SF score and the Pittsburgh Sleep Quality Index score were observed in 61.3% of cases.

Statistical analysis comparing NESA and PTNS demonstrated no significant differences between treatments, except for urgency episodes, which showed a significant reduction in favor of PTNS (Mann–Whitney U test, $p = 0.006$).

Regarding urodynamic outcomes in Group A, bladder capacity improved in 54.8% of patients, first desire to void improved in 54.8%, detrusor overactivity without leakage improved in 43.4%, detrusor overactivity with leakage in 25.8%, and urgency-related voiding in 25.8%.

In subgroup A1 (patients treated with NESA), the bladder tolerated a greater urine volume before the first desire to void, and 56.25% of patients showed complete resolution of detrusor overactivity after treatment, with no new cases of detrusor overactivity with leakage observed (McNemar test, $p = 0.008$).

In subgroup A2 (patients treated with PTNS), a significant increase in bladder capacity was observed (Mann–Whitney U test, $p = 0.040$). However, no

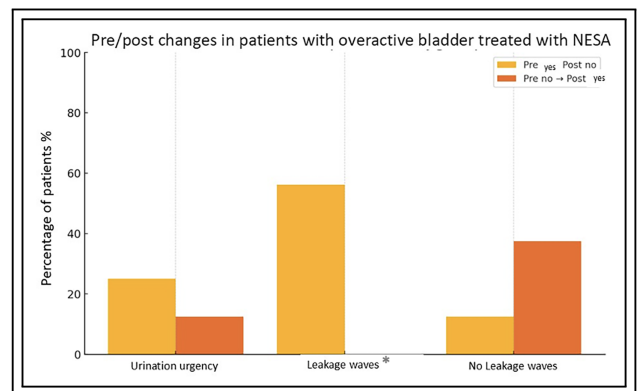


FIGURE 4. After treatment with NESA, 56.25% of patients with overactive bladder showed complete resolution of detrusor overactivity. No new cases of detrusor overactivity with leakage were observed (McNemar test, $*p = 0.008$)

statistically significant differences were found when directly comparing both treatment subgroups (NESA vs. PTNS), and no differences were observed for the first desire to void between treatments (Figures 4 and 5).

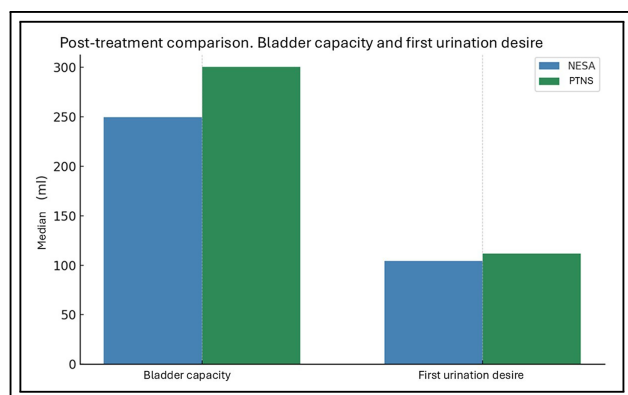


FIGURE 5. Non-significant differences were observed in bladder capacity increase between subgroups A1 and A2 in patients with overactive bladder. No significant differences were found for the first desire to void between treatments in the overactive bladder group (subgroups A1 and A2) (Mann–Whitney U test)

Group B: sensitive urgency

In Group B (patients with sensitive urgency), improvement in DUF was observed in 50% of patients, NUF in 21.4%, EU in 46.4%, and UII episodes in 32.1%. Improvement in ICIQ-SF scores was observed in 42.9% of patients, while improvement in the Pittsburgh Sleep Quality Index score was observed in 50% of cases.

In subgroup B2 (patients treated with PTNS), a trend toward statistical significance was observed for the reduction in urgency episodes (Mann–Whitney U test, $p = 0.064$). Post-treatment DUF in this subgroup also showed a trend toward improvement with PTNS, although statistical significance was not reached ($p = 0.072$). However, comparative analysis revealed no significant differences in any of the analyzed variables between NESa and PTNS in Group B (Figure 6).

In Group B overall, bladder capacity improved in 35.7% of patients, and first desire to void improved in 46.4%. In 21.4% of patients, detrusor overactivity appeared that had not been present in the baseline urodynamic study.

In subgroup B1 (patients treated with NESa), the bladder tolerated a greater volume before the first desire to void. In subgroup B2 (patients treated with PTNS), a significant increase in bladder capacity was observed (Student's t -test, $p = 0.020$). Nevertheless, comparative analysis showed no significant differences between treatments (NESa vs. PTNS) regarding bladder capacity, first desire to void,

urgency-related voiding, or the appearance of detrusor overactivity.

Safety

Both treatments were well tolerated, and no adverse events were observed during treatment administration or throughout the follow-up period.

Overall findings

Overall, no significant differences were observed between the two treatments, except for a greater reduction in urgency episodes in patients with OAB treated with PTNS ($p = 0.006$) and a greater reduction in detrusor overactivity in patients with OAB treated with NESa ($p = 0.008$) (Figure 4). Additionally, a significant increase in bladder capacity was observed in patients with sensitive urgency treated with PTNS ($p = 0.020$).

Discussion

In the present study, we compared NESa microcurrent neuromodulation with posterior tibial nerve stimulation (PTNS) in 59 patients diagnosed with overactive bladder or sensitive urgency. Our results indicate that, regarding improvements in clinical variables derived from the bladder diaries, no significant differences were observed between NESa and PTNS, except for a greater reduction in urgency episodes (EU) in patients with overactive bladder treated with PTNS ($p = 0.006$). Patients treated with NESa showed a significantly greater reduction in detrusor overactivity compared with those treated with PTNS ($p = 0.008$). However, 21.4% of patients initially classified as having sensitive urgency based on pre-treatment urodynamic evaluation developed detrusor overactivity on post-treatment urodynamic studies, with associated leakage in 17.8% of cases. These findings suggest that initial discrimination between OAB and sensitive urgency using urodynamic studies may not be necessary when indicating non-invasive neuromodulation in patients with overactive bladder. A greater increase in bladder capacity was observed in patients treated with PTNS, while no significant differences were found for the remaining urodynamic parameters. No significant differences were observed between treatments regarding improvement in voiding-related quality of life or sleep quality, and no adverse effects were detected. Overall, our findings indicate that there are no significant differences between NESa and PTNS in the treatment of patients with overactive bladder or sensitive urgency, so NESa could be

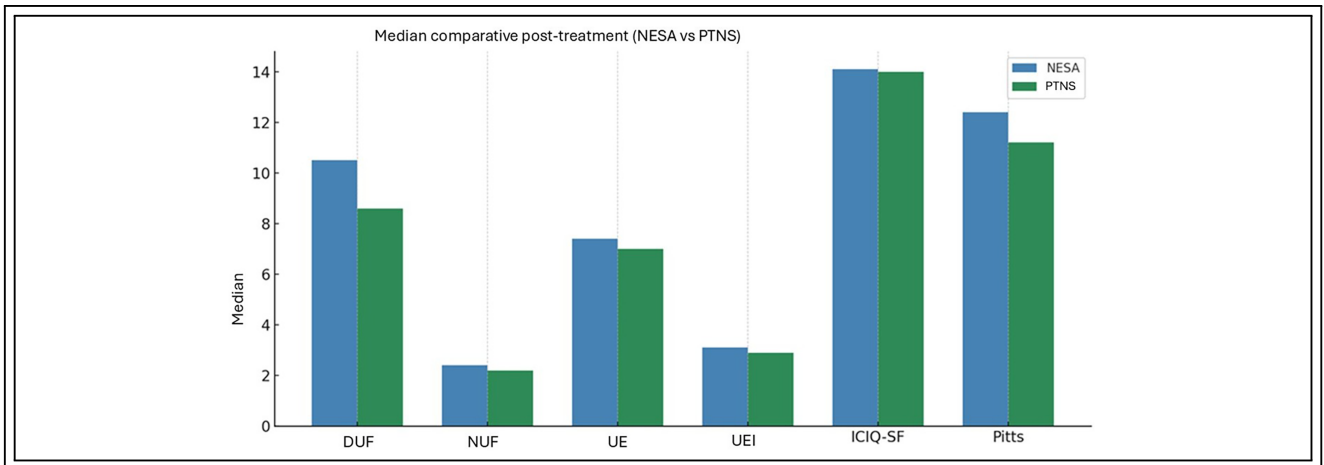


FIGURE 6. No statistically significant differences were observed between treatments for any of the analyzed variables (Mann–Whitney U test)

offered as a third line of treatment in patients with overactive bladder.¹⁶

The Hodgkin–Huxley model of nerve impulse conduction¹⁰ demonstrated the existence of neuronal action potentials and established that electrical impulses can be coordinated by the central nervous system through ion channel activity.¹¹ Since then, the application of electricity in medicine has expanded substantially and remains a continuously evolving field. The development of a new microcurrent-based application known as NESA represents a further step forward in the field of physical medicine. This technique provides global neuromodulation, meaning that it acts through modulatory mechanisms such as orthodromic impulses that activate descending inhibitory pathways, afferent regulatory mechanisms, and efferent regulation of neuromodulatory systems.¹²

NESA is a superficial electrostimulation system that delivers external, pulsed electrical stimulation that is imperceptible and closely resembles endogenous physiological electrical signals. Its mechanism of action is based on Wilder’s law, which states that the body’s response depends on its prior functional state, and on the principle of hormesis, whereby low doses of a stimulus may produce beneficial or adaptive effects¹⁷. The system is applied to the extremities using gloves and ankle straps connected to electrodes linked to a control console. This type of technology is currently used in the fields of physiotherapy and sports medicine, with favorable outcomes. Using the NXsignal device, imperceptible sensations are delivered through areas of low electrical impedance.

The treatment is based on the application of a low-frequency biphasic current with parameters below those used in conventional electrotherapy.^{18,19} Current intensity ranges from 0.1 to 1 mA, with frequencies between 1.14 and 14.28 Hz, while voltage remains fixed at 3 V. These parameters vary according to the specific programs integrated into the NXsignal device.^{20–22}

Electrical information is generated and introduced into the patient’s circuit through 24 semi-electrodes placed on the distal nerve endings of the hands and feet, along with a directional electrode. The anatomical positioning of these semi-electrodes is critical for treatment effectiveness, as they target areas of low electrical impedance.²² Each set of six semi-electrodes functions as a single electrode, resulting in a total of four electrodes, one for each limb. The electrical algorithm generated by the device is transmitted to the body through metal-to-skin contact of the semi-electrodes applied to clean skin. A series of intermittent and cyclical stimuli enters through low-impedance zones associated with peripheral nerve endings. Once introduced, autonomic nerve pathways may serve as conduits for signal propagation, converging toward the directional electrode, which acts as a guiding electrode.²³

Preliminary studies have demonstrated evidence of autonomic nervous system regulation and modulation of neuropathic pain, including conditions such as complex regional pain syndrome (Sudeck’s dystrophy), trigeminal neuralgia, fibromyalgia, and chronic post-surgical pain, with positive results in pain reduction and improvement in sleep quality.²³ Additional effects have been explored in the field of neurology,

including multiple sclerosis,²⁴ stroke, and in institutionalized older adults or patients with cognitive impairment, where microcurrent neuromodulation with NESA has been shown to improve quality of life, daytime somnolence, sleep quality, and cognitive function.^{25,26} One of the most promising areas within health sciences,^{26,27} where other electrostimulation therapies are already routinely applied, is the treatment of chronic pain and overactive bladder syndrome.^{20,28,29} Conde Santos et al., in a clinical trial evaluating non-invasive NESA neuromodulation in 46 patients with overactive bladder syndrome, reported a reduction in the number of voids over 24 h and a significant improvement in sleep quality, concluding that NESA microcurrent neuromodulation may be an effective treatment for patients with overactive bladder, although larger studies are required.³⁰ Recently, Blasco-Bonora et al. demonstrated in a small pilot study that NESA has similar results to PTNS but with better results in quality of life.³¹

Among the limitations of this study are its observational, non-randomized design, the relatively small sample size distributed across four subgroups, its single-center nature, and the short follow-up period. These limitations highlight the need for multicenter clinical trials with longer follow-up to further explore the long-term outcomes of NESA microcurrent neuromodulation and to better define its optimal, patient-specific application.

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Author Contributions

Miguel Arrabal-Martin, study design and writing; Laura Jerez-Fernandez, application of treatment and figures; Maria Isabel Martinez-Sanchez, application of treatment and writing; Marta Sacristan-Ruiz, figures and application of treatment; Maria Jose Garcia-Ortega, application of treatment and bibliographic review; Andrea Maria Hernandez-Perez, statistical analysis; Miguel Angel Arrabal-Polo, writing and bibliographic review; Mercedes Nogueras-Ocaña, final approval and

review; Alberto Zambudio-Munuera, statistical analysis and manuscript corrections. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials

Data are available upon request.

Ethics Approval

Protocol Code: FIB-NES-2024-11, approved by the Clinical Research Ethics Committee of Granada (Spain).

Informed Consent

All patients who participated in the study provided signed informed consent.

Conflicts of Interest

The authors declare no conflicts of interest.

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