University of Valencia and University of Las Palmas de Gran Canaria

NON-INVASIVE NESA NEUROMODULATION VERSUS TRANSCUTANEOUS POSTERIOR TIBIAL NERVE STIMULATION FOR THE TREATMENT OF OVERACTIVE BLADDER

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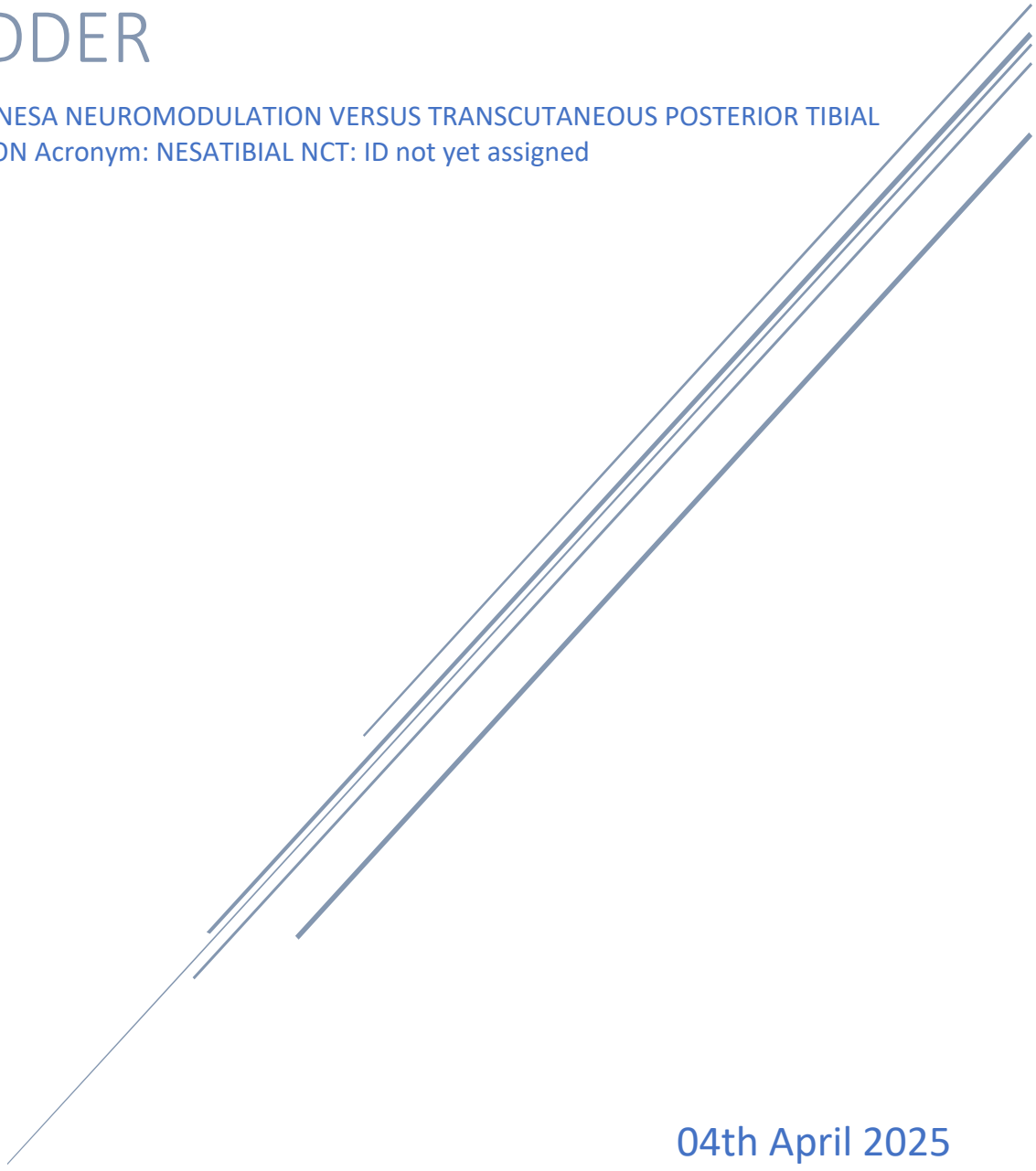

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Paloma Blasco-Sonora; Laura Fuentes-Aparicio; Raquel Medina-Ramírez

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(NESATIBIAL)

ABSTRACT

Objectives: To evaluate the effect of non-invasive NESA neuromodulation compared to posterior tibial stimulation in patients with overactive bladder. compared to posterior tibial stimulation, with same-day exercises and patient education on quality of life, symptoms, discomfort and sleep. day of the session and patient education on quality of life, symptoms, discomfort and sleep.

Methods: Twenty-four patients (24 women), aged 38-85 years with overactive bladder were included in this experimental clinical study. Each patient attended ten sessions two days a week. Patient health was measured using SF-36, sleep quality using the Pittsburgh questionnaire, perception of UI symptoms and patient quality of life using the ICIQ-SF questionnaire. All these variables were measured before, immediately after the ten sessions and at two months after the end of treatment.

Results: Mann-Whitney U test where, in general, improvements were obtained in all the variables, although not significantly in the variables, although not significant over time in both groups, except in the assessment of discomfort assessment (CACV) and the SF-36, which only showed an improvement in the non-invasive group, NESA vs. Tibial group in the quality of health, with a P-value of P=0.035.

Conclusion: The two treatments generated an improvement in quality of life, symptoms, discomfort and quality of life, discomfort and in the quality of sleep in the short term; obtaining better results in the non-invasive NESA group in the quality of health, with a P value of 0.035. group in quality of life and discomfort in women with overactive bladder.

INTRODUCTION

La vejiga hiperactiva (VH) es un síndrome caracterizado por un aumento de la frecuencia miccional acompañado de urgencia miccional y asociado en ocasiones con incontinencia urinaria de urgencia. Es un proceso crónico que tiene un importante impacto en la calidad de vida de los pacientes que lo padecen, con una prevalencia que aumenta a medida que se envejece, llegando al 22% en las mujeres. La Incontinencia Urinaria es un padecimiento que producen escapes involuntarios de orina. Existen dos tipos de incontinencia, la asociada a los esfuerzos y la incontinencia asociada a la sensación de micción urgente no relacionada con los esfuerzos. Este segundo tipo de incontinencia es el que se asocia al Síndrome de Vejiga Hiperactiva. El tratamiento de la VH es escalonado, con un tratamiento inicial basado en el cambio en el estilo de vida, reeducación vesical, ejercicios de suelo pélvico y farmacológico. La neuroestimulación forma parte del algoritmo terapéutico recomendado en casos rebeldes al tratamiento inicial. NXSignal (www.nesaworld.es) es un sistema de electroestimulación de aplicación superficial que administra una estimulación eléctrica pulsátil externa, imperceptible y de características similares a las que produce el cuerpo humano. Se aplica sobre las extremidades, mediante guantes y tobilleras conectados con electrodos a una consola de control. Este tipo de tecnología se usa en la actualidad en el sector de la fisioterapia y el deporte con excelentes resultados. Diferentes estudios clínicos han demostrado que las terapias de electroestimulación tienen aplicación rutinaria en el tratamiento del Síndrome de vejiga hiperactiva. Se propone, por tanto, una alternativa tecnológica a las terapias ya existentes, que a diferencia de las técnicas convencionales no es invasiva, no produce contracción muscular ni movimiento y emite una microcorriente de intensidad y frecuencia fisiológica no perceptible. Este estudio se ha diseñado para valorar de manera objetiva la eficacia de la tecnología NXSignal en el Síndrome de Vejiga Hiperactiva con tratamientos ya existentes como la estimulación del Tibial posterior con gran evidencia científica en estos últimos años.

El formato de ensayo clínico nos permite dar validez científica a los resultados obtenidos y poder confirmar de forma rigurosa su beneficio. Si el resultado de la investigación demuestra que el nuevo sistema de neuromodulación es eficaz para tratar el síndrome de vejiga hiperactiva, además de la estimulación del Tibial posterior, beneficiaríamos a un porcentaje de pacientes que en este momento no responden al tratamiento farmacológico y que son candidatos a otros tratamientos más invasivos.

Los sujetos de este estudio participarán en un ensayo clínico aleatorizado doble ciego para demostrar la eficacia de la neuromodulación NXsignal frente la neuromodulación transcutánea del Tibial posterior.

METHODS

General hypothesis: The use of the low frequency electrotherapy system of non-invasive Neuromodulation NESA, could neuromodulate the nervous system allowing to regulate the physiopathological mechanism of overactive bladder, improving the symptoms of quality of life, discomfort and quality of sleep of patients suffering from overactive bladder..

Objectives: To evaluate the effect of non-invasive NESA neuromodulation compared to posterior tibial stimulation in patients with overactive bladder. compared to posterior tibial stimulation, with same-day exercises and patient education on quality of life, symptoms, discomfort and sleep. day of the session and patient education on quality of life, symptoms, discomfort and sleep.

Ethic

The methodology of the clinical trial has been specifically designed to obtain answers to the stated objectives. The study will be conducted in accordance with the standard code of good clinical practice, respecting the current regulations for this type of study and the recommendations of the Declaration of Helsinki. Informed consent will be given to all patients and the study is approved by the ethics committee of the University of Valencia (Cod. 2025-FIS-3870878).

Subjects and Recruitment: Subjects will be recruited at the physiotherapy office of the L'Estiuet clinic in Valencia. After obtaining consent, the patient will be scheduled for the application of the intervention two days a week, for 5 weeks for a total of 10 sessions in both treatments. Patients who agree to participate will be randomly assigned to one of the 2 treatment groups (NESA is the NNG group and tibial stimulation is the NTPG group). The study will be single-blinded, blinding the allocation of the intervention to which the patients have been assigned and to the specialist who collects the information and performs the follow-ups. Data analysis will also be performed in a blinded manner.

Inclusion Criteria:

- Minimum criteria for a primary diagnosis of overactive bladder who have or have not received active/alternative treatments for this pathology.
- Patients with previous pharmacological treatments that have not obtained an adequate clinical response.
- Patients whose cognitive abilities are competent to participate in the study and are able to complete the study questionnaires and have given written consent to participate in the study.
- Without further contraindications for electrotherapy treatment such as serious use of pacemakers, pregnancy, internal bleeding, poor skin condition (ulcerations, wounds...) and/or phobia of electricity.

Participants will be excluded if they had any of the following criteria:

- Presence of urinary fistula.
- Infections in the last 12 months.
- Haematuria during the trial period.
- Pregnancy or plans to become pregnant during the study.
- Pathology of the central or peripheral nervous system (multiple sclerosis, Parkinson's disease, etc.).
- Uncontrolled diabetes.
- Currently treated with Botox injections for the bladder or within the last year.
- Current treatment with interstim or currently implanted interstim device.
- Bladder outlet obstruction.
- Urinary retention.
- Treatment with more than two antidepressants and/or multiple benzodiazepines, as well as antiepileptics.
- Contraindications for electrotherapy treatment. All patients signed an informed consent form prior to inclusion.

Patients were randomised into each of the groups:

Group1: NESA non-invasive neuromodulation (NNG) using the NESA XSIGNAL device with exercises on the same day of the session and education providing common written instructions not individualised, such as dietary and social advice.

NNG was performed with the patient supine, using NESA technology with gloves and anklets, with a total of 24 electrodes plus a directional electrode performing global neuromodulation; NESA is a non-invasive monitoring device, which emits low frequency microcurrents (1.3-14.28 Hz, depending on the programme), low intensity (0.1-0.9 mA), and low voltage (±3 V) and therefore imperceptible to the patient. Each day a different programme was applied. On the first three days, programme 1 (P1) 15 min, programme 2 (P2) 15 min and programme 7 (P7) 30 min were applied. From the fourth to the sixth day, P2 30 min and P7 30 min were applied, ending the rest of the days with P3 30 min and P7 30 min. At the same time, SP exercises were performed (on the same day of the treatment with a duration of 30 min of the 60 min session), all of this accompanied by advice. Programme 1, uses a maximum frequency 7.69 Hz and a minimum frequency of 3.85 Hz to adapt to the patient and modulate the CNS centrally. Programme 2 and 3 used a maximum frequency of 1.96 Hz and a minimum frequency of 1.14 Hz to focus the treatment on the ventral and dorsal area and programme 7 used a maximum frequency of 14.29 Hz and a minimum frequency of 1.92 Hz to focally inhibit the tone and achieve a modulation of the parasympathetic autonomic nervous system.

Group 2: Non-invasive posterior tibial neuromodulation (NTPG) with same-day exercises and education through common, non-individualised written instructions.

NTPG was performed by posterior tibial application plus SP exercises (same day of treatment) and advice, with the patient supine, using NEUROTRAC MYOPLUS PRO to perform TENS for 30 minutes. An electric current with a frequency of 10 Hz and pulse duration of 200μs was applied. The intensity was adjusted according to the patient's tolerance, with thumb flexion perceptible to visual inspection by the therapist. Two 50 x 50 MM electrodes were placed along the posterior tibial nerve pathway, one on the sole of the foot and the other near the medial malleolus on one leg. The exercises in both groups consisted of abdomino-diaphragmatic breathing through tonic contractions (taking air, blowing, contracting the pelvic floor while bringing the navel inwards and upwards for approximately 7 seconds during the contraction, relaxing the pelvic floor without pushing, with a rest time of approximately 4 seconds), and phasic (short but fast contractions, 1 second contraction, 5-10 repetitions, with a rest time greater than and equal to the work, 10 seconds) during these 30 minutes. The sets and repetitions of the exercises were performed depending on the physical condition of each patient. All patients performed ten sessions two days a week.

Measure tools

Both groups will be provided with a set of reliable and validated questionnaires. All these variables will be assessed before treatment, immediately after the treatment is finished and at two months later (follow-up) by a blinded assessor.

The patient's perception of quality of life will be measured using SF-36, which is composed of 36 items that assess both positive and negative states of health by asking about: Physical Function, Physical Role, Bodily Pain, General Health, Vitality, Social Function, Emotional Role and Mental Health. Additionally, the SF-36 includes a transition item that asks about change in general health status from the previous year. This item is not used for the calculation of any of the scales, but provides useful information about the perceived change in health status during the year prior to the administration of the SF-36. 10

Sleep quality using the Pittsburg questionnaire, consisting of 19 items that analyse 7 different components of sleep (subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction). Each item is scored from 0 to 3. The total score of the scale ranges from 0 to 21 points where the lower end represents good sleep quality, and the upper end represents poor sleep quality.11.

Perception of frequency, severity of UI and patient quality of life will be assessed using the International Consultation on Incontinence Questionnaire (ICIQ-SF) validated questionnaire, where the individual's daily experience of urination and incontinence is answered with three scored items and one unmarked self-diagnostic item.12

Bladder symptoms and discomfort will be assessed using the Bladder Control Self-Assessment Questionnaire (B-SAQ), a validated questionnaire consisting of 8 questions grouped into two scales, each with a scale of 0 to 3 points, giving a maximum score of 24 points (12 in each group).13

They will be also asked after two months about their satisfaction with the treatment received (numerical scale NSR 0 not satisfied -10 very satisfied), whether they continued to perform the exercises and whether they had any side effects after the treatment.

Data analysis

The statistical data analysis will be performed using statistical SPSS software version 25.0 (SPSS Inc., Chicago, IL, USA). The normality of the variables will be evaluated by the Shapiro–Wilk test. Descriptive statistics are presented as to as mean (standard deviation),median (25-75th percentile) or frequencies (percentage), as appropriate. For the inferential analysis to compare among the groups and three different times (T0, T1 and T2) three-factor ANOVA with repeated measures will be conducted. When the ANOVA models indicate significant differences in the main effects, Bonferroni's correction will be applied to avoid type I errors in the multiple comparisons. The α level will be set at 0.05 for all tests.

Effect sizes for the study variables will be measured using Cohen's d and r. According to Cohen's d, the effect sizes could be categorized as small (0.20 to 0.49), medium (0.50 to 0.79), or large (greater than 0.80). For the "r" measure, effect sizes will be classified as low (0.10), moderate (0.30), large (0.50), and very large (greater than 0.80).

Timing and supervision

This project is part of a master's thesis. It is estimated to last a total of 8 months, with 1 month of recruitment, 4 months of treatment, and then 3 months to analyse and prepare the article or scientific communication. This project is supervised by two directors who will ensure the application of good practices, its registration in the clinical trial and its execution.

Contact

Central Contact Person: Raquel I Medina-Ramírez , PhD. Physiotherapist 0034 665265685 Ext. 0034 raquel.medina@ulpgc.es

Central Contact Backup: Laura FUENTES-APARICIO , PhD. Physical Therapy 669682391 Ext. 0034 Laura.Fuentes@uv.es

Overall Study Officials:

Principal Investigator: Paloma Blasco-Sonora , Physical Therapy University of Valencia
Study Director: Laura FUENTES-APARICIO , PhD. Physical Therapy University of Valencia
Study Director: Raquel Medina-Ramírez , PhD. Physical Therapy University of Las Palmas