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Research Article

Rehabilitation in Sleep, Pain, and Bladder Symptoms of NESA Neuromodulation Application in Multiple Sclerosis Patients: A Innovative Treatment

Marina Contreras-Polo[1], Raquel Medina-Ramirez[2*], Esther Teruel-Hernández[3], Martín Vilchez Barrera[2], Aníbal Báez-Suárez[2] & David Álamo-Arce[2]

[1]*Clínica Sinapsis Fisioterapia, Illes Balears, Spain*

[2]*SocDig Research Group, University of Las Palmas de Gran Canaria, Las Palmas, Spain*

[3]*University of Las Palmas de Gran Canaria, Las Palmas, Spain*

[*]**Correspondence to:** Dr. Raquel Medina-Ramirez, SocDig Research Group, University of Las Palmas de Gran Canaria, Las Palmas, Spain.

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Abstract

Introduction: Multiple sclerosis is an autoimmune demyelinating inflammatory disease of unknown cause and chronic progression caused by damage to myelin, which impairs the nerves' ability to conduct electrical impulses. This results in a variety of symptoms including spasticity, fatigue, neuropathic pain and/or urinary incontinence. As they often do not remit and respond poorly to conventional medical treatment, recent attention has focused on novel interventions for bladder, pain and sleep control. Non-invasive superficial neuromodulation using the NESA device can help restore the body's electrical balance by regulating the autonomic nervous system and is beginning to show promising results in patients with sleep disorders. It may therefore provide an opportunity for an autonomous approach to sleep, bladder, and pain management. The aim of the

study was to improve sleep quality, urinary incontinence control and pain perception in patients treated with NESA technology alone.

Material and Methods: A quasi-experimental randomized prospective study will be conducted with patients diagnosed with multiple sclerosis. They were divided into two non-invasive neuromodulation treatment groups with different treatment programs (Combination A and Combination B). Data on sleep quality, urinary incontinence and pain will be measured using different rating scales at three different points in the study.

Results: The analysis of the variables of urinary incontinence and pain show significant and favourable data in the treatment group with combination A, with a positive improvement throughout the 3 weeks of treatment. The variable sleep quality shows a significant improvement in both experimental groups, with a more favourable score in the Combination A treatment group.

Conclusion: This first study using the Nesa non-invasive neuromodulation device in patients with multiple sclerosis reveals its efficacy in improving urinary incontinence, pain, and sleep quality.

Abbreviations

MS= Multiple Sclerosis
SNM= Sacral Neuromodulation
PTNS= Percutaneous Tibial Nerve Stimulation
NNT= Non-invasive Neuromodulation Technique
NESA= Neuromodulación Superficial Aplicada
PSQI= Pittsburgh Sleep Quality Index
B-SAQ= Overactive Bladder Control Self-Assessment Questionnaire
ICIQ_UI SF= International Consultation on Incontinence questionnaire on incontinence
VAS= Visual Analogue Scale
SPSS= Statistical Package for the Social Sciences

Introduction

Multiple sclerosis (MS) is defined as a progressive disease that occurs with the appearance of focal inflammatory lesions (plaques) in the cerebral white matter, in which the most striking is the loss of myelin (demyelination), with relative preservation of the axons in the early phase, although they may be severely affected in the later stages [1]. Multiple sclerosis has an unknown cause and chronic course caused by damage to myelin Damage to myelin generates an alteration in the ability of the nerves to conduct electrical impulses to and from the brain and this produces various symptoms, including spasticity, fatigue, neuropathic pain and / or urinary incontinence [2]. All these factors directly influence the quality of life and sleep of the patient, getting worse every time an outbreak of this pathology appears. Due to the involutional nature of MS, any improvement in symptoms will also improve quality of sleep and state of health [3].

MS symptoms are often unremitting and respond poorly to conventional medical management. Recently, attention has focused on novel interventions for bladder, pain, and sleep management. Among these, medical cannabis therapy, targeted physiotherapy and neuromodulation are showing promising results [4]. There are different types of non-pharmacological treatment that are getting importance as a second line treatment. Nowadays, there are available studies that suggest that sacral neuromodulation (SNM) and percutaneous tibial nerve stimulation (PTNS) may be helpful in the neuromodulation of MS-related overactive bladder symptoms [5]. These techniques may not only reduce the severity of symptoms, but also significantly improve the quality of life of those affected. Investigating the role of implantable tibial nerve stimulation devices in people with MS may open new doors in the management of urgency and urge incontinence in this patient group [6]. However, it is crucial to find new types of non-invasive neuromodulation techniques (NNT). Actually, there are a new way of NNT such us NESA neuromodulation (NESA is a Spanish name; Neuromodulación superficial aplicada) which may help regulate the Autonomic Nervous System [7]. NESA NNT is a non-invasive and painless electrotherapy, based on low frequency microcurrents (less than 1 mA). Previous studies indicate that it improves sleep quality [8] and it seems to be a new opportunity for neurogenic bladder [9] by providing electrical signals that are imperceptible and slow to the autonomic nervous system, normalising its functions. Thus, the NESA NNT could be an opportunity for an autonomic approach to the treatment of sleep, bladder and pain.

The main objective of this study is to improve the quality of sleep of Multiple Sclerosis patients. The secondary objective was to enhance the control of urinary incontinence due to neurogenic bladder and pain perception.

Materials and Methods

Design and Context

This research was a prospective randomised quasi experimental study. The study was situated in a private clinic in Spain, with a collaboration with a Multiple Sclerosis local association (ABDEM).

Participants

Female patients from a local multiple sclerosis association were invited to participate. After an online meeting, potential patients were invited openly. All participants gave written informed consent before being allocated to a group and assessment, and the rights of all participants were protected. A university clinical research ethics committee approved the experimental procedures of the study.

Intervention

The NESA neuromodulation technique was the unique treatment developed and it was carried out over 3 weeks with 15 sessions (one session per day). All participants attended an initial visit with an experienced physiotherapist to verify the inclusion criteria. The inclusion criteria were an MS diagnosis of more than ten years, full cognitive abilities and to belong to the local MS association chosen. The exclusion criteria were the presence of some of the contraindications for treatment with NESA non-invasive neuromodulation:

cardiac pacemakers, internal bleeding, not applying electrodes to skin in poor condition, with ulcers or wounds, acute febrile processes, acute thrombophlebitis and/or electricity phobia; not having signed the informed consent.

NESA neuromodulation is a coordinated NNT through 24 electrodes, modulating the autonomic nervous system through ultralow-frequency electrical signals. The action on the different areas of the body is through the circulating bioelectricity current. The technology is minimally invasive; as a surface-based application. The characteristics of the current are an emission of low-frequency pulses oscillating from 1.3 Hz to 14.28 Hz (depending on the program), pulse emission at an intensity of 0.1–0.9 milliamps with a potential difference of ±3 V, with coordination between 24 electrodes (6 electrodes per limb, situated in both wrist and both ankles) stimulated simultaneously. The effect is not in a local muscle or nerve area activation, the effect is systemic due to the 24 electrode and the microcurrent produced by the ultra-low electrical parameters [7]. (See figure 1).

Figure 1: *A diagram representing the electrode located in wrist and ankles. The NESA NNT device can be seen in the background.*

Once the participants (n=11) were accepted, the sample was randomly divided into two groups using digital software. Each group had a different programme application (see Figure 2):

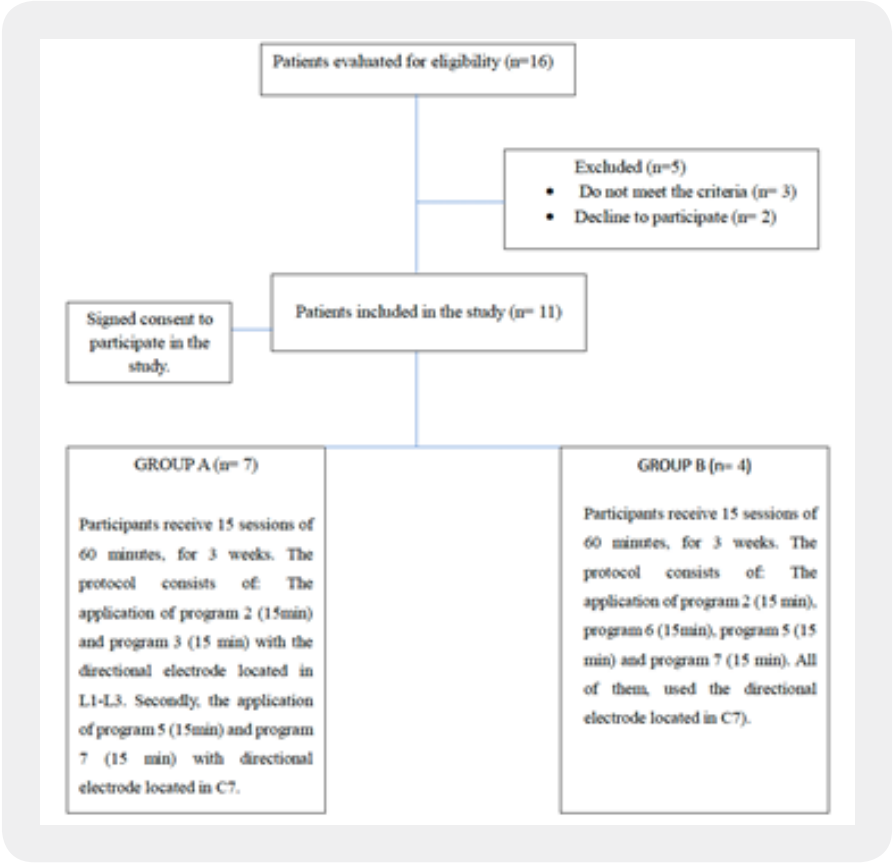

Figure 2: *Flowchart of the intervention process developed.*

- Group A(n=7): with NESA NNT based on: firstly, the application of program 2 (15min) and program 3 (15 min) with the directional electrode located in L1-L3. Secondly, the application of program 5 (15min) and program 7 (15 min) with directional electrode located in C7.

- Group B (n=4): with NESA NNT based on: firstly, program 2 (15 min), program 6 (15min), program 5 (15 min) and program 7 (15 min). All of them, used the directional electrode located in C7).

The results measurements were assessed at the beginning (moment 1), session 7 (moment 2) and after session 15 (moment 3).

Measures

Sleep Quality

Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI) [10]. It consists of 19 items that analyse 7 different sleep components (subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, sleep efficiency, use of sleep medications and daytime dysfunction). Each item is scored

from 0-3. The total scale score ranges from 0-21 points where the lower end represents good sleep quality, and the upper end represents poor sleep quality. Cronbach 's a of 0.83 obtained for the PSQI components indicates a high degree of internal homogeneity. Therefore, the clinical and clinical properties of the PSQI suggest its usefulness in both psychiatric clinical practice and research [11].

Urinary Incontinence

It has been evaluated using the Overactive Bladder Control Self-Assessment Questionnaire (B-SAQ and CACV in Spanish) [12]. We used the Spanish validated questionnaire of symptoms and quality of life specific to overactive bladder, consisting of 8 items scored from 0 to 3, grouped into two scales (discomfort and symptoms). In the B-SAQ, the emotional state of the patient is considered in each of the situations of the questionnaire, and it makes more reference to the stage prior to the loss of urine [13].

We also used the International Consultation on Incontinence questionnaire on incontinence in its reduced format (ICIQ_UI SF) (22), which consists of identifying people with urinary incontinence and the impact on quality of life by means of 3 items (frequency, quantity and impact). The score is obtained by the sum of these items, ranging from 0 to 21 points.

Pain Perception

A visual analogue scale (VAS) is one of the pain rating scales first used by Hayes and Patterson in 1921 [14]. It is widely used in epidemiological and clinical research to measure the intensity or frequency of different symptoms. The Pain VAS is a unidimensional measure of pain intensity and is used to record the progression of pain in patients or to compare pain severity between patients with similar conditions [14].

Analysis

All statistical analyses were performed using SPSS statistical program version 22. Descriptive results were expressed as mean ± standard deviation. The differences between the initial, intermediate and final scores were analysed using the Friedman test. 95% confidence interval. We also analysed the differences between the combinations of the two programmes using non-parametric tests such as the Mann-Whitney test. We used the SPSS-22 statistical programme.

Results

Sample

Fourteen participants (n=14) were finally included and randomised in group A (n=7) and group B (n=7). After the first week we lost three patients for group B (n=4) due to the COVID infection. The sample mean age was +-51.8 years.

Assessment Among Weeks

In the analysis of sleep quality between weeks in each group, we found significant differences in group A (p-value = 0.019) and for group B (p-value = 0.030). In group A, the Pittsburgh score started with a mean of 7.85 points, and had a better evolution trough the weeks, 4.85 points for the last week (figure 3).

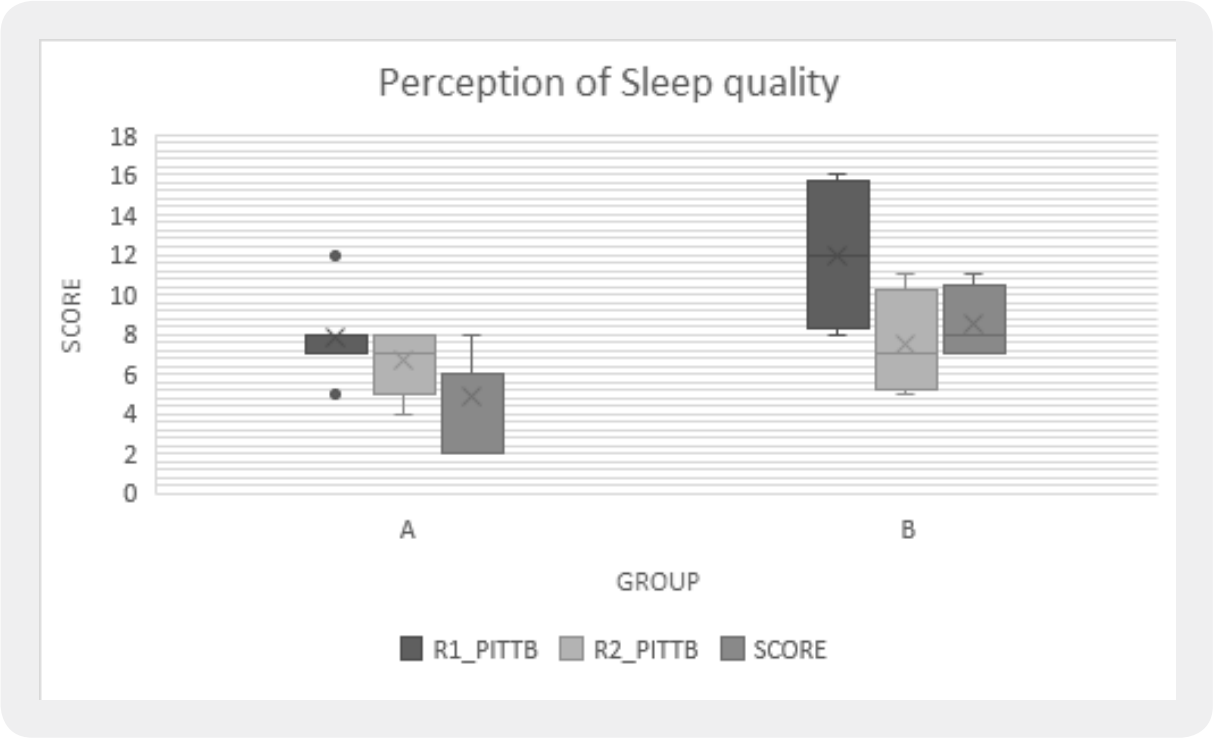

Figure 3: *The Pittsburgh test results for each group are shown in a scatter plot with boxes. The results for group A are statistically significant.*

Regarding incontinence assessment, we found significant differences between weeks in the B-SAQ test in the symptom (p-value=.008) and incontinence (p-value=.046) domains only for group A, with a positive improvement throughout the 3 weeks of treatment. In addition, significant differences between treatment weeks were observed in the results of the ICIQ_SF test only for group A (p-value=.013), with an improvement. For group B, no significant differences were found between the weekly assessments. (figure 4).

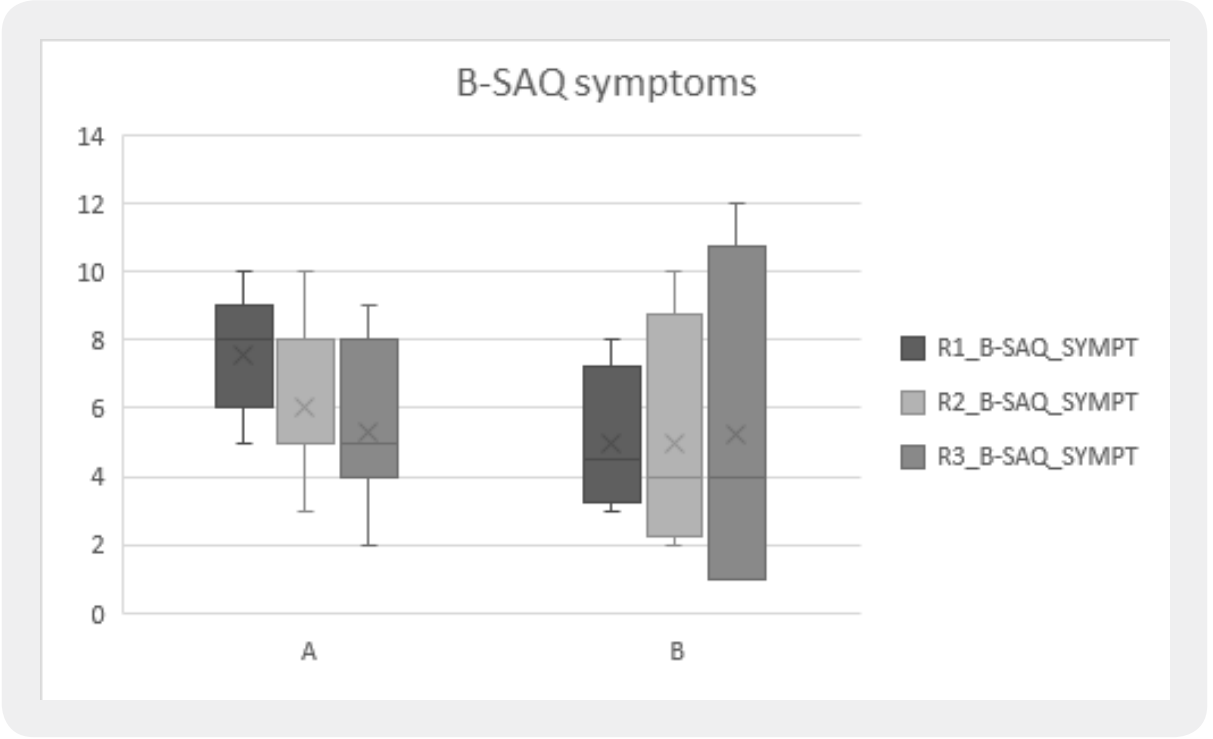

Figure 4: *The results obtained in each group for the B-SAO test are shown in a scatter plot with boxes. The results for group A are statistically significant for the symptom area. The B-SAQ questionnaire is named CACV in the Spanish version.*

Finally, only in group A were significant differences observed in pain scores between weeks (p-value = 0.022), being lower at the end of treatment with a mean of 2 points on the VAS scale.3.3

Assessment Between Groups

The differences between the beginning and end of treatment were analysed by group to see if one group was more effective than the other. We found significant differences in sleep quality between the groups (p-value =.024). Group A had a better improvement after the treatment. There were no significant differences between the groups for urinary incontinence or pain.

Discussions

The results of this first study using NESA Non-invasive neuromodulation in MS symptom has shown that is effective to enhance sleep quality for both programs combination, which is it always very poor and fragmented in these patients. This research has also demonstrated an improvement in urinary incontinence due to neurogenic bladder just for programming A. In addition, a reduction in pain perception it was observed just for group A. We could suggest that both programs combination was useful for sleep quality, however the combination for the group A was more effective in incontinence and pain too.

It is important to stress that the autonomic system (parasympathetic and sympathetic) participate actively in the bladder function. The parasympathetic nervous system mediates contraction of the detrusor muscle (i.e. micturition) [6]. The improvement of the bladder symptoms has a strong relationship with the autonomic function. Some studies have attempted to document the prevalence of bowel and bladder dysfunction in MS populations, few have explored the possible relationship between bladder and bowel problems and other concurrent MS symptoms such as disability and fatigue [15]. Therefore, the non-invasive neuromodulation NESA offers an opportunity to neuromodulate the autonomic nervous system of patients with Multiple Sclerosis, leading to changes in incontinence and pain symptoms.

It is well known that the prevalence of sleep disorders in individuals with multiple sclerosis (MS) is 3-5 times higher compared to the general population [16]. For this reason, there is recent concern about treatments that may help to improve sleep in these patients. There are treatments such as cannabinoid therapies or traditional pharmaceuticals, which often have undesirable side effects [17,18]. One of the tools that is proving successful is cognitive behavioural therapy, but it allows for a variety of approaches and good adherence to treatment is necessary [16]. The results of the present study on the improvement in sleep quality of the patients in this study open a window for new neuromodulation treatments (NNT) such as Neuromodulation NESA. It also opens up the possibility of combining it with other sleep treatments in clinical practice. In fact, improving sleep may be a way to improve mental health or physical symptoms of MS.

This research has some limitations, such as the small sample size, and future studies based on clinical trials are needed to generalise the results and to investigate other variables such as fatigue in people with multiple sclerosis. Studies using more objective sleep variables such as actigraphy are also recommended. However, the improvement seen in this preliminary research is an opportunity for people with multiple sclerosis to improve their symptoms and live a better life.

Conclusions

This study has demonstrated that non-invasive neuromodulation NESA may be an effective innovative NNT to improve perceived sleep quality, neurogenic bladder and pain in patients with multiple sclerosis using the combination programme A.

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Conflicts of Interests

The authors declare no conflict of interest.

Bibliography

1. Zurawska, A. E., Mycko, M. P., Selmaj, I., Raine, C. S. & Selmaj, K. W. (2021). Multiple Sclerosis: CircRNA Profile Defined Reveals Links to B-Cell Function. *Neurology - Neuroimmunology Neuroinflammation, 8*(5).

2. Martinez-Altarriba, M. C., Ramos-Campoy, O., Luna-Calcaño, I. M. & Arrieta-Antón, E. (2015). A review of multiple sclerosis (2). Diagnosis and treatment. *Semergen, 41*(6), 324-328.

3. Sakkas, G. K., Giannaki, C. D., Karatzaferi, C. & Manconi, M. (2019). Sleep Abnormalities in Multiple Sclerosis. *Current Treatment Options in Neurology, 21*(1), 4.

4. Urits, I., Adamian, L., Fiocchi, J., Hoyt, D., Ernst, C., Kaye, A. D. & Viswanath, O. (2019). Advances in the Understanding and Management of Chronic Pain in Multiple Sclerosis: A Comprehensive Review. *Current Pain and Headache Reports, 23*(8), 59.

5. Araiza Navarro, J. J., Sánchez, R., Uscanga, O., Sosa, M., Reyes, F. & Barbabosa, J. (2018). Refractory hyperactive bladder treated with sacral neuromodulator: Case report and literature review. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 7*(7), 2937.

6. Rahnama'i, M. S. (2020). Neuromodulation for functional bladder disorders in patients with multiple sclerosis. *Multiple Sclerosis Journal, 26*(11), 1274-1280.

7. Medina-Ramírez, R., Molina-Cedrés, F., Báez-Suárez, A. & Álamo-Arce, D. (2021). Nesa Non-Invasive Neuromodulation; A New Frontier of Treatment of the Autonomous Nervous System in Physiotherapy. *CPQ Orthopaedics, 5*(4), 1-4.

8. García, F., Fernández, D., Vázquez-Guerrero, J., Font, R., Moreno-Planas, B., Álamo-Arce, D., Medina-Ramírez, R. & Mallol-Soler, M. (2022). Recovery of the physiological status in professional basketball players using NESA neuromodulation treatment during different types of microcycles in season: A preliminary randomized clinical trial. *Frontiers in Physiology, 13*.

9. Contreras, M., Medina-Ramírez, R. & Molina-Cedrés. (2022). Nesa Non-invasive neuromodulation; a chance to approach Sclerosis Multiple symptoms. The International Society for Physical Rehabilitation Medicine Conference. The International Society for Physical Rehabilitation Medicine, Lisbon, Portugal.

10. Mollayeva, T., Thurairajah, P., Burton, K., Mollayeva, S., Shapiro, C. M. & Colantonio, A. (2016). The Pittsburgh sleep quality index as a screening tool for sleep dysfunction in clinical and non-clinical samples: A systematic review and meta-analysis. *Sleep Medicine Reviews, 25,* 52-73.

11. Buysse, D. J., Hall, M. L., Strollo, P. J., Kamarck, T. W., Owens, J., Lee, L., Reis, S. E. & Matthews, K. A. (2008). Relationships Between the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and Clinical/Polysomnographic Measures in a Community Sample. *Journal of Clinical Sleep Medicine, 04*(06), 563-571.

12. Espuña Pons, M., Puig Clota, M. & Rebollo Álvarez, P. (2006). Validación de la versión en español del "Cuestionario de Autoevaluación del Control de la Vejiga (CACV): Un nuevo instrumento para detectar pacientes con disfunción del tracto urinario inferior. *Actas Urológicas Españolas, 30*(10), 1017-1024.

13. Booth, L., Skelton, D. A., Hagen, S. & Booth, J. (2020). Identifying the most reliable and valid bladder health screening tool: A systematic review. *Disability and Rehabilitation, 42*(17), 2451-2470.

14. Delgado, D. A., Lambert, B. S., Boutris, N., McCulloch, P. C., Robbins, A. B., Moreno, M. R. & Harris, J. D. (2018). Validation of Digital Visual Analog Scale Pain Scoring with a Traditional Paper-based Visual Analog Scale in Adults. Journal of the American Academy of Orthopaedic Surgeons. *Global Research & Reviews, 2*(3), e088.

15. Lin, Y. N., Liu, Z. R., Li, S. Q., Li, C. X., Zhang, L., Li, N., Sun, X. W., Li, H. P., Zhou, J. P. & Li, Q. Y. (2021). Burden of Sleep Disturbance During COVID-19 Pandemic: A Systematic Review. *Nature and Science of Sleep, 13,* 933-966.

16. Drerup, M., Roth, A., Kane, A. & Sullivan, A. B. (2021). Therapeutic Approaches to Insomnia and Fatigue in Patients with Multiple Sclerosis. *Nature and Science of Sleep, 13,* 201-207.

17. Haddad, F., Dokmak, G. & Karaman, R. (2022). The Efficacy of Cannabis on Multiple Sclerosis-Related Symptoms. *Life, 12*(5), 682.

18. Zielińska-Nowak, E., Włodarczyk, L., Kostka, J. & Miller, E. (2020). New Strategies for Rehabilitation and Pharmacological Treatment of Fatigue Syndrome in Multiple Sclerosis. *Journal of Clinical Medicine, 9*(11), 3592.