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EFFECT OF NON-INVASIVE NEUROMODULATION ON BLADDER FUNCTION IN SPINAL CORD INJURY PATIENTS: A SYSTEMATIC REVIEW

Neurophysiotherapy

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ABSTRACT

Background: Individuals with SCI are challenged with various problems, including motor, sensory impairments, neurogenic respiratory dysfunction, cardiovascular autonomic dysfunction &bladder and bowel dysfunction, which frequently result in limitations in activities and participation like immobility, in self-care, in communication and in domestic life. The purpose of this article is to report the non-invasive neuromodulation methods to treat the overactive bladder or incontinence with urodynamics, electromyography as outcome measures in various conditions. **Methods:** PubMed, Cochrane, Scopus, EMBASE, CINAHL database were searched from 2010 to 2023 using terms Genital nerve stimulation, dorsal penile nerve stimulation, dorsal clitoral nerve stimulation, magnetic stimulation in neurogenic bladder, non-invasive neuromodulation. Studies were included with selection criteria of original publications including RCTs and cross over trials published in peer-reviewed journals focused on neurogenic bladder in SCI. Adult Participants irrespective of gender, Age, Initial level of Impairment, Duration of SCI, and Level of Injury and, the Mechanism involved. Study quality was evaluated with Physiotherapy Evidence Database (PEDRO). **Results:** 13 articles met the inclusion criteria with information about the improvment in the bladder outcome measures as Urodynamics, cyctseometry, Perineal muscle Electromyography, Video urodynamic and bladder dairy. No studies had critical methodologies flaws. Clinical utility varied in time to complete and bladder capacity and decreased contraction of the detrusor muscle. **Discussion And Conclusion:** Linear correlation between stimulation & bladder capacity gain in SCI individuals. There was significantly improvement in bladder function, symptoms and quality of life and decreased bladder detrusor pressure, frequency of incontinence.

KEYWORDS

Neurogenic bladder, Urodynamics, Neuromodulation

INTRODUCTION

Spinal Cord Injury (SCI) refers to the damage to the neural elements of the spinal cord due to traumatic or non-traumatic lesions which lead to dysfunction in various aspects of human functioning and participation (1). SCI results from traumatic or non-traumatic causes and incidence of non-traumatic injury was higher in developed countries than traumatic spinal cord injury (24). In SCI, some motor or sensory function preserved below the injury level including voluntary anal contraction (sacral sparing), deep anal pressure, palpable or visible muscle contraction below injury level or presence of peri-anal sensation (3). Individuals with SCI are challenged with various problems, including motor, sensory impairments, neurogenic respiratory dysfunction, cardiovascular autonomic dysfunction &bladder and bowel dysfunction, which frequently result in limitations in activities and participation like immobility, in self-care, in communication and in domestic life (25).

As per Global Burden Disease 2019, 0.9 million incident cases and 6.2 million of total SCI were Years Lived with Disability (YLD). Males had higher rate of incidence and prevalence with Age Standardized Incidence Rate, Age Standardize Year Lived Disability Rateand prevalence, and rate of incidence, YLD increased with age (10) .Individuals with spinal cord injury, face barriers to social and economic participation due to high rate of unemployment for SCI survivors. The spinal cord injury not only affect quality of life and life span of individuals but also lead to psychological, mental & emotional disturbance with huge impact and economic burden on both care givers as well as on social health system (31). SCI has devastating impact on the quality of life with a significant effect on bladder and bowel function, sexual function of affected individuals (9).

The bowel & bladder dysfunction is one of the most common impairment reflected in individuals following SCI. Damage in the spinal cord leads to neurogenic lower urinary tract dysfunction which removes the voluntary control of micturition (30).The pattern of neurogenic lower urinary tract dysfunction was Overactive bladder combined with voiding dysfunction and urinary retention. The overactive bladder with symptoms of frequency, urgency, urges incontinence and nocturia affects performance of daily activities and social function such as sleep, physical exercise and sexual function(19). The negative impact of neurogenic bladder on psychological and social domains, which affects quality of life and social participation of individual (4).

The bladder rehabilitation is essential for individual with SCI to reduce social, mental & emotional baggage and to improve the participation of individual after SCI and enhance quality of life. There has been rapid drift of rehabilitation professionals from traditional therapeutic strategies such as electrical stimulation i.e., Transcutaneous Electrical Nerve Stimulation (TENS) (29), posterior tibial nerve stimulation, pelvic floor exercises, crede'smanoeuvre, Clean Intermittent Catheterization (CIC) (21) to the clinical use of technology aided electrical intervention in the form of repetitive trans-magnetic stimulation (rTMS) and genital nerve stimulation with the aim to optimize the recovery.

Hence, there is strong need to adopt the methods to restore the bladder function which are endurable, easy to administer, non-invasive and are cost effective. According to international neuromodulation society, neuromodulation therapy may come up with alternative to long term drug therapy for the symptomatic relief of persistent or chronic condition like spinal cord damage to urinary incontinence. It can provide better degree of therapeutic control for both affected individuals and therapists. rTMS is one of the non-invasive neuromodulation therapies which might be a novel approach for management of neurogenic lower urinary tract dysfunction in SCI. Genital nerve stimulation is non-invasive electrical stimulation technique which is effective, tolerable and helps in reducing the symptoms of urinary incontinence (7).

Systematic Review

Types Of Study Included:

INCLUSION CRITERIA	EXCLUSION CRITERIA
• Literature published in English language • Original publications including RCTs and cross over trials published in peer-reviewed journals focused on neurogenic bladder inSCI. • A key literature search adopted, for a more targeted search the following terms were used: genital nerve stimulation, dorsal penile nerve stimulation, repetitive magnetic stimulation, transcutaneous electrical stimulation in neurogenic detrusor overactivity in SCI survivors. Non-invasive interventions mainly	• Non-Experimental Studies such as review articles, editorials, letters to editors, commentaries, protocols or book chapters were excluded. • Duplicate studies those with insufficient data for pooling and inaccessible full text articles. • Non-SCI participants i.e. able-bodied individuals, other neurological conditions/diseases. • Peripheral Neuromodulation i.e. Functional Electrical Stimulation, Transcutaneous Electrical Nerve Stimulation. Brain Computer Interfaces,

electrical stimulation and non-invasive neuromodulation. • Adult Participants irrespective of gender, Age, Initial level of Impairment, Duration of SCI, and Level of Injury and, the Mechanismsinvolved.	pharmacological additions. Involve invasive interventions (epidural spinal stimulation).

Randomized Control Trials, case control study, cross over trial, quasi experimental trials.

SEARCH STRATEGY:

DATABASE	YEAR	SEARCH FOCUS
•PubMed • Cochrane • Scopus • EMBASE • CINAHL	2010-2023	• General Information • Participant Information • Trial Information • Intervention Information • Outcomes

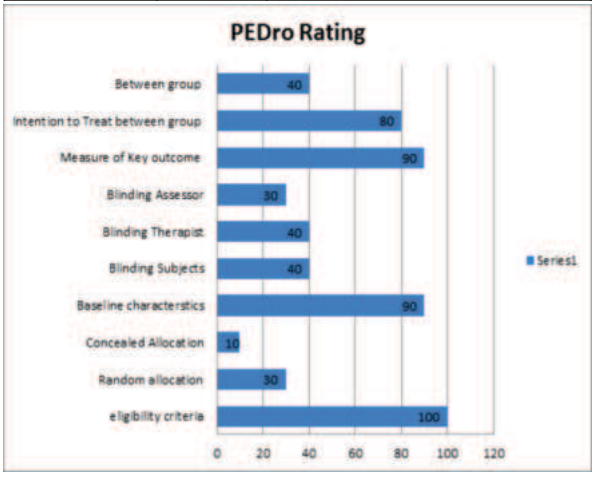

Figure 1: PEDro rating -Flow Diagram

Medical Subject Headings and Keywords:
Genital nerve stimulation, dorsal penile nerve stimulation, dorsal clitoral nerve stimulation, magnetic stimulation in neurogenic bladder, non-invasive neuromodulation.

Quality Assessment and Data Extraction (Assessment of Risk of Bias)- Physiotherapy Evidence Database (PEDRO)

ANALYSIS OF RISK OF BIAS-(PEDro Rating)
8 Trials (6-8)- Good Quality & 1 Trial (4-5)-Fair Quality of Evidence

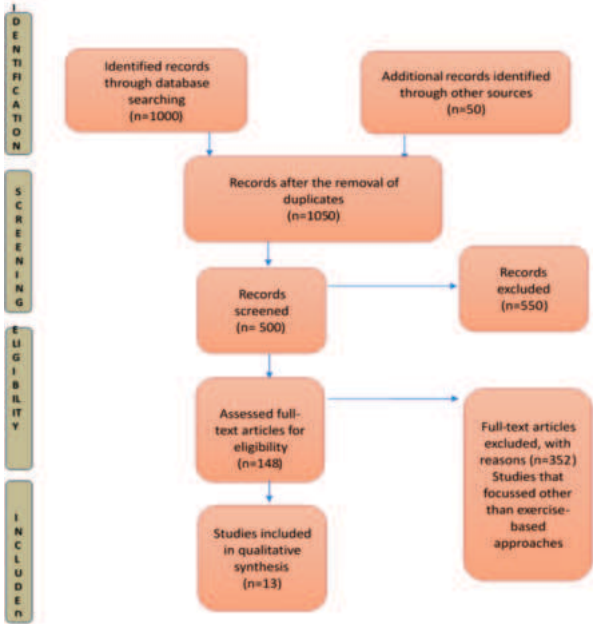

Figure 2: PRISMA-Flow Diagram

Author	Aim of the study	Intervention	Outcome	Conclusion
Li *et al.,* 2023	To evaluate the efficacy of repetitive functional magnetic stimulation in the sacral nerve in patients with neurogenic detrusor overactivity (NDO) after suprasacral spinal cord injury and to provide more options for treating NDO after suprasacral injury.	One group received repetitive functional magnetic stimulation treatment for sacral nerve at 100% stimulation intensity, 5 Hz, 20 min. 5 times a week and second group received sham repetitive functional magnetic stimulation. N= 66 (n=33 each group)	Bladder compliance and pudendal nerve electromyography, SCI-QOL, NBSS	Bladder function, symptoms and quality of life might be significantly improved.
Peng, 2020	To investigate the feasibility and therapeutic effect of percutaneous electrical stimulation of dorsal penile/clitorial nerve in the treatment of neurogenic bladder after SCI.	1 session per day for 14 days 14 days stimulation & 2 rounds of urodynamics examination N=10 Experimental group: Electrical stimulation	Urodynamic parameters: bladder capacity, bladder detrusor pressure (Pdet), and bladder compliance.	Improved bladder compliance Decreased bladder detrusor pressure Decreased frequency of incontinence
Doherty *et al*., 2020	To assess the effect of dorsal genital nerve stimulation on urine storage parameters in participants with spinal cord injury and neurogenic detrusor overactivity during natural bladder filling.	7 days intervention N=5 Experimental group: Dorsal genital nerve stimulation	Urodynamics test included Average peak detrusor pressure (APDP), maximum detrusor pressure (MDP), maximum cystometric capacity (MCC).	Increased bladder capacity Decreased maximum detrusor pressure, Average peak detrusor pressure Increased in the number of detrusor contraction from the first involuntary detrusor contraction to a strong desire.
Yeh *et al.,* 2019	The effects of genital nerve stimulation amplitude on bladder capacity in spinal cord injured participants	Each subject received a sequence of 5-6 cystometric trials. N= 10 Experimental group Genital nerve stimulation with cystometric trial.	Urodynamic test: bladder capacity	Increased bladder capacity Linear correlation between stimulation & bladder capacity gain in SCI individuals.

Doherty *et al.,* 2019	To assess and compare the effect of Dorsal genital nerve stimulation (DGNS), Tibial nerve stimulation (TNS), Sacral nerve stimulation (SNS), Spinal stimulation (SS) on neurogenic detrusor overactivity and bladder capacity	5 days of each experimental session, N=10 Experimental group Dorsal genital nerve stimulation (DGNS) Tibial nerve stimulation (TNS) Sacral nerve stimulation (SNS) Spinal stimulation (SS)	Cystometry test: bladder capacity	Dorsal genital nerve stimulation acutely suppress detrusor contractions & increased bladder capacity than TNS, SNS, SS.
Niu *et al.,* 2018	A proof of concept study of Transcutaneous Magnetic Spinal Cord Stimulation for neuorgenic bladder.	3 phase study 24 weeks study 16 weeks treatment period N=5 3 phase study: 2 weeks- assessment phase 16 weeks- treatment phase 6 weeks- follow up	Perineal muscle Electromyography Video urodynamic	Improved bladder function Increased voluntarily volume of urine produced Decreased self catheterization frequency
Brose *et al.,* 2017	Genital nerve stimulation is tolerable and effective for bladder inhibition in sensate individuals with incomplete SCI.	N=24 Experimental group GNS to tolerable threshold	Urodynamics Sensation threshold & tolerable stimulation amplitude	Genital nerve stimulation is tolerable at amplitudes that effectively inhibit neurogenic detrusor activity Increased the bladder capacity.
Bourbeau *et al.,* 2017	Aim of the study was to quantify the amount and variance that genital nerve stimulation increases bladder capacity in individual with neurogenic detrusor overactivity and determines which subject and study factors affect improvement in bladder capacity.	N= 33 Genital nerve stimulation Both conditional and continuous stimulation	Bladder capacity	Variance of the bladder capacity gain significantly increased with increasing infusion rate. Acutely increases bladder capacity.
Breda *et al.,* 2016	To evaluate the effect of subject controlled, on demand, dorsal genital nerve stimulation to treat urgency urinary incontinence.	N= 7 (4 males/3 females) 1 week intervention. Subject controlled, on-demand Dorsal genital nerve stimulation	Pad test Void volume	participant controlled, on demand dorsal genital nerve stimulation using a surface placed electrode is possible over a long period, in home setting, with a positive effect on non-neurogenic overactive bladder symptoms
Ojha *et al.,* 2014	To demonstrate reduction in detrusor overactivity using surface electrical stimulation of posterior tibial nerve or dorsal penile nerve in patients with spinal coed injury.	1 session per day for 14 days N=15 Experimental group 1: Posterior tibial nerve stimulation Experimental group: Dorsal penile nerve stimulation	Cystometrogram	reduction in the frequency of leaks and improvement in bladder capacity.
Opisso*et al*., 2013	To investigate the effect of Subject controlled stimulation of dorsal genital nerve to treat neurogenic detrusor overactivity at home.	5 days dorsal genital nerve stimulation with pre & post urodynamic study N= 11 Experimental group: Dorsal genital nerve stimulation.	Urodynamic test Bladder diary	increase in bladder capacities Mean volume per day voided significantly Increased
Lee *et al.,* 2012	The effect of semiconditional dorsal penile nerve electrical stimulation on capacity and compliance of the bladder with deformity in spinal cord injury patients	1 session/ day for 28 days N=6 Experimental group: Dorsal penile nerve stimulation	Urodynamic study	Improved bladder capacity and compliance as well as the bladder wall deformity
Horvath *et al.,* 2010	To measure changes in maximum cystometric capacity (MCC) evoked by electrical stimulation of the dorsal genital nerve (DGN) delivered either continuously or conditionally (only during bladder contractions) in persons with SCI.	N= 9 Experimental protocol: Two repetitions of three treatment types (no stimulation, continuous stimulation, and conditional stimulation).	Cystometric capacity electromygraphy	Conditional stimulation increased cystometric capacity Conditional and continuous stimulation equally effective in increasing MCC

DISCUSSION

Total articles searched from various search engines were 1050 and after removal of duplicated articles & others, 13 articles were qualitatively synthesized for this review. PEDro scale was used for analysis of risk of bias. The articles had score between 4-5 was considered in review. The strongest domain was eligibility criteria, baseline characteristics, measure key outcome followed by intention to treat, between group and weakest domain of PEDro analysis was

concealed allocation followed by random allocation and blinding assessor.

This study included a review of 201 patients who had neurogenic overactive bladder due to spinal cord injury. The outcome measure were urodynamics parameters included bladder capacity, bladder detrusor pressure (Pdet), and bladder compliance, pudendal nerve electromyography, Spinal Cord Injury- Quality Of Life (SCI-QOL), Neurogenic Bladder Symptom Score (NBSS), Pad test, Void volume, Bladder diary. All these studies resulted in increase in baseline bladder capacity, bladder compliance as well as the bladder wall deformity. These studies checked the feasibility and therapeutic effect on genital nerve stimulation on bladder. One study resulted in application of repetitive trans magnetic stimulation on bladder function whether it lead to increase in bladder capacity or not.

Trials based studies revealed that both type of stimulation is non-invasive neuromodulation and provide a new prospective on the role of treating the overactive bladder which is feasible, easy to administer and easy tolerable to the patients. Extensive variability was observed in terms of duration of applicability, tolerance, long term use, and follow up, variability in duration of stimulation. The difficulty in generalizability of results due to small sample size and variable duration.

CONCLUSION

This review concluded that genital nerve stimulation and repetitive trans magnetic stimulation are non-invasive neuromodulation method to treat the neurogenic overactive bladder in spinal cord injury survivors. Future research should be done by the gaps indentified in this review, as more study need to done to treat overactive bladder which inhibit the detrusor overactivity and reduce the symptoms of incontinence. By this review we further recommended that these methods can be used in clinical set up as a protocol in bladder rehabilitation.

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