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PERIPHERAL NEUROMODULATION USING DIRECT CUTANEOUS EXTERNAL PUDENDAL NERVE STIMULATION MAY IMPROVE NEUROGENIC DETRUSOR UNDERACTIVITY- A CASE REPORT

*Dr. Akmal Hafizah Zamli, Dr. Sumayya Shaharom, Dr. Sharifah Aminah Az Zahrah Md Isa

Department of Rehabilitation Medicine, Hospital Sungai Buloh, Selangor, Malaysia.

*Corresponding Author: Dr. Akmal Hafizah Zamli

Department of Rehabilitation Medicine, Hospital Sungai Buloh, Selangor, Malaysia.

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ABSTRACT

Neurogenic bladder dysfunction ranged from detrusor acontractility, underactivity or over activity, depending on the site of neurologic insult. The urinary sphincter also may be affected, resulting in sphincter loss of activity, underactivity, overactivity or loss of coordination with bladder function. Available evidence suggest the use of peripheral neuromodulation (PNM) using tibial nerve or dorsal penile nerve stimulation as an alternative method of non-invasive option for the management of neurogenic bladder dysfunction refractory to other conservative management. However, the application of PNM using direct cutaneous external pudendal nerve stimulation for neurogenic bladder dysfunction remains unexplored, thus the objective of this study. We report on the application of PNM using cutaneous external pudendal nerve stimulation using a neuromuscular electrical device in a 31 year old man with residual neurogenic bladder dysfunction 4 years following transverse myelitis. Intervention protocol involved placement of four external electrode pads over the perineal region. Stimulation applied with starting magnitude of 15 mA with gradual increased until perianal contraction observed. Duration of stimulation was 1 hour for 3 sessions per week until completion of 12 sessions. Post intervention, he reported subjective and objective improvement in symptoms and improved Part I Kings Quality of Life score. There was also Urodynamic evidence of detrusor contraction at 175 mls infusion with Pdet of 15 cmH₂0 which was absent pre-intervention. Consistent cough induced detrusor contraction with Pdet ranged between 20 - 40 cmH₂0 was also evident postintervention. At voiding phase pre-intervention, he was only able to void few drops of urine with post void residual (PVR) volume of 640 mls. Post intervention, he was able to void 140 mls with PVR of 430 mls. Our findings have demonstrated that PNM using external cutaneous pudendal nerve stimulation may be effective in improving detrusor function in a patient with neurogenic detrusor underactivity.

KEYWORDS: Neurogenic bladder, peripheral neuromodulation, pudendal nerve.

INTRODUCTION

Malfunctioning of the urinary bladder due to damage or diseases of the central, peripheral, and autonomic nervous systems is termed neurogenic bladder[1]. It is a impairment seen in rehabilitation setting especially among patients with spinal cord injury. Spinal cord injury (SCI) alters the dynamics of voiding as the lower urinary tract is regulated by the brain and lumbosacral segment of the spinal cord. [2] The type of neurogenic bladder dysfunction ranged from detrusor acontractility, underactivity or over activity, depending on the site of neurologic insult. The urinary sphincter also may be affected, resulting in either loss of activity, underactivity, overactivity or loss of coordination with bladder function. [1-3] Impaired coordination between detrusor contraction and external sphincter relaxation termed detrusor external sphincter dyssinergia (DSD) is also common post SCI, with an estimate of 75% of patients with suprasacral injury. [4] Serious urological complications such as reduced bladder compliance, elevated upper tract pressures, hydronephrosis, vesicoureteral reflux and in the extreme situation renal failure complications may result from improperly managed DSD condition. [1,3,5] Neuromodulation involved alteration of nerve activity through the delivery of electrical stimulation to targeted sites of the body. Sacral neuromodulation (SNM) using an implantable device has been regarded as an established treatment option for severe idiopathic and neurogenic bladder dysfunction. [6-7] However, its use is extremely limited due to its high cost; requirement of specialized surgical and technological expertise; need for major surgery and risk of serious complication. So far, its use has never been reported in Malaysia. Current available evidences also suggest the use of peripheral neuromodulation (PNM) using tibal stimulation either percutaneously transcutaneously as one of the promising non-invasive, effective and safe option for the management of

neurogenic and non-neurogenic bladder dysfunction refractory to other conservative management. [8,9] An initial study on application of PNM for neurogenic bladder dysfunction using cutaneous stimulation of the dorsal penile nerve has also shown to be promising. [10] In all of these studies involved subjects with neurogenic detrusor overactivity diagnosis. The application of PNM using direct cutaneous external pudendal nerve stimulation is lacking and its use for bladder retention symptoms remains unexplored, thus the objective of this study.

CASE REPORT

Clinical history

A 31 year old man was referred to us with a background four years history of cervical transverse myelitis. His initial presentation was of ascending weakness and numbness of all four limbs associated with both bladder and bowel involvement. At four years post event, he had regained remarkable neurological recovery and attained full functional independence. Presently, he regained normal gait, able to perform all aspects of activities of daily living independently and is presently employed.

However, he reported persistence of bladder storage and emptying symptoms characterized by daytime frequency of 12 times/day, nocturia with average of 3 times/night, hesitancy and incomplete voiding sensation. There was episodes of urge urinary incontinence especially with high fluid intake, however he never reported stress urinary incontinence episodes. He emptied his bladder

using Valsalva manoeuvre combined with clean intermittent self-catheterization 8 hourly and when he feels his voiding was incomplete. He experiences an average of 2-3 times urine tract infection with systemic manifestation per year requiring antibiotic treatment as outpatient. He was commenced on Ciprofloxacin 250 mg prn prophylaxis.

Clinical examination

On examination, he has intact motor function with normal gait pattern. Sensory examination showed patchy impaired sensation from T10 onwards. Per rectal examination showed intact anal tone. However, S2-S5 dermatome function was impaired. His deep anal sensation was present, and there was intact voluntary anal contraction. Perianal, bulbocavernosus and cremasteric reflexes were present.

Investigation

His renal function surveillance study On 2.2.2016 showed normal findings with Urea 7.1 mmol/L and Serum Creatinine 83.1 Umol/L. His ultrasound KUB done on 7.11.2014 showed trabeculated bladder wall with maximum thickness of 0.6 cm, however no evidence of calculi or hydronephrosis. CT Urethrography done for a single haematuria episode on 9.2.2015 was unremarkable. Urodynamic study using Mediwatch® device done on 8.12.2015 showed findings consistent with neurogenic detrusor underactivity.



Figure 1: Ultrasound KUB and CT Urethrography images showing bladder trabeculation with maximal thickness of 0.6 cm.

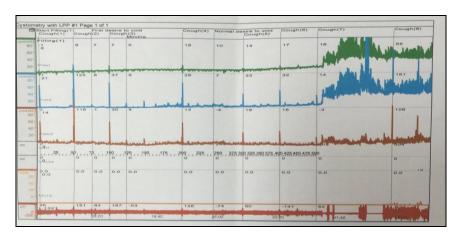


Figure 2: Pre-intervention Urodynamic study graphs done on 8.12.2015 with features consistent with a diagnosis of neurogenic detrusor underactivity.

INTERVENTION

Intervention protocol involved direct cutaneous external pudendal nerve stimulation using four external electrode pads placed over the perineal region between the scrotal region and anus. Stimulation were performed using a programmable neuromuscular electrical stimulation (NMES) device – Model Cefar Rehab ®, manufacturer DJO, LLC, USA. (Picture 1). The device was pre-programmed at P8. The amplitude was applied from starting magnitude of 15 mA with

gradual increased until perianal contraction was observed; or maximum of 25 mA; or discomfort experience. Duration of stimulation was 1 hour per session. The frequency of treatment were 3 sessions per week until completion of 12 sessions from 9.12.2015 – 8.1.2016. Outcome measurement involved in this study included patient's subjective report, Urodynamic parameters and King's Quality of Life Questionnaire Part 1 total score.



Picture 1: Programmable neuromuscular electrical stimulation device (Cefar Rehab ®) used in this study.

RESULTS

Post intervention, this patient reported persistent hesitancy and continued to require Valsalva manoeuvre to initiate voiding but to a lesser extent. Additionally, he noticed improvement in urine outflow and reduced feeling of incomplete voiding. His daytime frequency had decreased to 8 times/day, while nocturia episodes had reduced to 2 times/night (Figure 3). He also reported regaining early morning spontaneous erection. Objectively, his quality of life had improved as demonstrated by the King's Quality of Life Part 1 increased total score from baseline 92 to 150 (Figure 4).

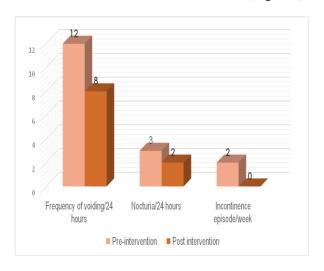


Figure 3: Comparison of lower urinary tract symptoms pre and post-intervention

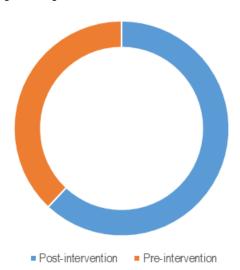


Figure 4: Improvement in King's Quality of Life Part 1 total score

Post-intervention Urodynamic bladder filling phase showed evidence of spontaneous detrusor contraction at 175 mls, consistent cough induced detrusor contraction and evidence of detrusor contraction at first and normal desire to void sensation which was absent previously (Figure 5). At post-intervention Urodynamic voiding

phase, his post voiding residual volume had improved from 640 mls to 430 mls (Table 1).

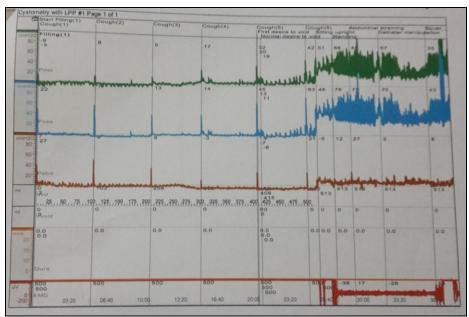


Figure 5: Post-intervention Urodynamic study graphs done on 2.2.2016.

Table 1: Comparison of main Urodynamic parameters pre and post intervention.

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Main Urodynamic parameters	Pre-intervention	Post-intervention
First desire to void volume(mls)/detrusor pressure(cmH ₂ O)	76/7	400/20
Normal desire to void volume(mls)/detrusor pressure(cmH ₂ O)	244/10	409/19
End filling detrusor pressure (cmH ₂ O)	15	11
Bladder compliance (mls/cmH ₂ O)	42.6	51.8
Maximum cystometric capacity(mls)	640	570
Post voiding residual (mls)	640	430

DISCUSSION

This patient was referred to us for neurogenic bladder dysfunction management following a non-traumatic spinal cord injury i.e. cervical transverse myelitis. His presenting clinical features and specific urological investigations were consistent with a diagnosis of neurogenic detrusor underactivity (NDU). The actual incidence of neurogenic bladder dysfunction following transverse myelitis is unknown. However, a fairly recent study by Kalita et al involving 18 patients with confirmed diagnosis of acute transverse myelitis reported 94% of patients have urinary retention symptoms. In ~59% of these patients had urodynamic evidence of neurogenic detrusor acontractility/underactivity. [11] NDU can be defined as detrusor contraction of inadequate magnitude and/or duration to effect bladder emptying in a normal time span. [12] Dysfunction of the central neural control of the voiding reflex may result in NDU by impacting upon key processes in perception, integration, and outflow.[13]

The clinical features of impaired bladder emptying including reduced urinary flow rate, the need for abdominal straining/ Valsalva manoeuvre to initiate

voiding and raised post-void residual [PVR] were often reported^[13], which in this study was the scenario experienced by this patient. Except for recurrent urinary tract infection (UTI), other known complications of NDU such as bladder or renal calculi and hydronephrosis were absent in this patient. Other known complications that may occur in relation to this patient's alternative ways of bladder emptying such as herniation, rectal prolapse, anal fissures were absent.

Compared to neurogenic detrusor overactivity (NDO), the clinical and scientific literatures on NDU management is very scanty and under researched, and there are no validated or effective oral pharmacological agents available. Generally, management of NDU aims to protect the upper urinary tract, and improve continence, Quality of Life (QOL) and, whenever possible, lower urinary tract function. [1,13,14] Patients' preferences, lifestyles and QOL is a prime consideration when making any treatment decision.

Common management options include double void, Valsalva manoeuvre/straining to void and indwelling or intermittent catheterization. [14, 15] Standard

pharmacotherapy such as the use of α -adrenergic blockers to reduce urethral outlet resistance and muscarinic agonists (eg, bethanechol) or choline esterase inhibitors (eg, distigmine) was suggested. However, analyses demonstrate few beneficial effects of these oral drugs, in addition to unfavourable effects. [15]

In the management of NDU, sacral anterior root stimulation (complete lesions) and sacral neuromodulation (incomplete lesions) are effective in certain selected patients. [14, 15] Established evidences had also suggested the beneficial effects of sacral neuromodulation for the management of neurogenic and non-neurogenic detrusor overactivity refractory to measures. [6,7,16-18] conservative The postulated mechanism of action of sacral neuromodulation responsible for its contrasting effects on different bladder dysfunction conditions is complex and not fully understood. This is expected considering the exact pathophysiological mechanisms that underlie bladder dysfunction conditions are themselves not fully understood. However, evidence supports an emerging consensus that it exerts its effect through afferent pathways that modulate the activity in other neural pathways within the spinal cord and higher centres. [16]

Other reported neuromodulation techniques used for the management of neurogenic bladder dysfunction include the stimulation of peripheral nerves. [8-10,19] So far, current evidences suggested its main beneficial outcomes favouring detrusor overactivity conditions refractory to measures.^[8-10,19] conservative Peripheral neuromodulation using posterior tibial nerves stimulation either percutaneously or transcutaneously had been reported to be effective in the management of neurogenic detrusor overactivity refractory to other conservative management. [8-9] The application of cutaneous dorsal penile nerve stimulation had also been reported as effective for neurogenic detrusor overactivity management. [10] The use of pudendal afferent pathway stimulation using cutaneous electrodes has also been reported to be effective in improving bladder compliance and capacity in patients with neurogenic detrusor overactivity. [19] To the best of our knowledge, the use of peripheral neuromodulation using direct cutaneous pudendal nerve stimulation for NDU condition has never been reported.

Our study represented initial review on the potential beneficial effect of direct cutaneous pudendal nerve stimulation in a patient with neurogenic detrusor underactivity. Our study shown positive impacts of its application in minimizing patient's symptoms and thus improved his Quality of Life. This was further supported by the evidences seen in his Urodynamic findings. The additional benefits of interest noted in this study was his report of regaining some degree of erectile function that was absent pre-stimulation. Thus, potential application of PNM using direct cutaneous pudendal nerve stimulation

for neurogenic erectile dysfunction treatment may be worth explored in future.

The exact mechanism of pudendal nerve stimulation remains unknown, however the afferent nerve stimulation is most likely play a major role. [19] Most of the sensory nerves contained in the sacral area of the spine originate from pudendal nerve. Stimulating the pudendal nerve, which controls the pelvic floor muscle, can improve the function of the bladder and pelvic floor muscle groups [19] which may be the determinant factor for the favourable outcome in this study.

CONCLUSIONS

Our findings had demonstrated that acute PNM using direct cutaneous external pudendal nerve stimulation is effective in improving the efficiency of detrusor function in a patient with neurogenic detrusor underactivity. Although its long-term efficacy is unknown, the prominent improvements on the clinical and urodynamic outcome in this study contribute to the evidence that it may be a promising option in conservative management of neurogenic bladder in the future.

IMPLICATION

This initial study findings had demonstrated that peripheral neuromodulation using direct cutaneous external pudendal nerve stimulation is effective, practical and safe in improving symptoms related to neurogenic detrusor underactivity. The fact that it is a non-invasive method, cheap, well tolerated and is a widely available modality makes it a desirable option for conservative management of neurogenic bladder.

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