Effect of Individualized Bladder Rehabilitation Program in Patients with Neurogenic Lower Urinary Tract Dysfunction, a Pilot Study

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Objectives: Neurogenic lower urinary tract dysfunction (NLUTD) is one of the major sequelae after spinal cord injury (SCI) and a cause of increased morbidity and mortality in SCI patients. Current treatment strategies for NLUTD include medication, non-invasive conservative management, minimally invasive therapy, and surgical intervention. However, there are no studies regarding non-invasive conservative management that combines pelvic floor muscle (PFM) exercises and electrical stimulation (ES). This study was designed to evaluate the efficacy of individualized bladder rehabilitation programs, which included education on voiding behavior, PFM exercise training combined with electromyography (EMG) biofeedback, and ES (for bladder inhibition or PFM strengthening), in SCI patients with NLUTD.

Methods: Individualized bladder rehabilitation programs were provided for 2 months for patients with incomplete SCI at the suprasacral level or cauda equina syndrome. The patients were evaluated using post-voiding residual urine (PVR) amounts and the questionnaires of the International Prostate Symptom Score (IPSS), Overactive Bladder Symptom Score (OABSS), Urogenital Distress Inventory-6 (UDI-6), and Incontinence Impact Questionnaire-7 (IIQ-7).

Results: After the individualized bladder rehabilitation programs, the post-voiding residual urine amounts; OABSS, UDI-6, and IIQ-7 scores; and subtotal incontinence score and quality of life (QOL) scores of the IPSS all decreased significantly. These results indicate an improved quality of life and fewer symptoms. However, the changes in the subtotal obstruction score and the total symptom score of the IPSS were not significant.

Conclusion: Selected SCI patients with NLUTD could benefit from individualized bladder rehabilitation programs, which include education on voiding behavior, PFM exercises combined with EMG biofeedback, and ES for bladder inhibition or PFM strengthening. Patients who received bladder rehabilitation programs obtained beneficial effects on reducing PVR amounts and QOL scores related to incontinence. (Tw J Phys Med Rehabil 2015; 43(2): 111 - 120)

Key Words: Spinal cord injury, Neurogenic lower urinary tract dysfunction, Bladder rehabilitation, Pelvic floor muscle exercise, Electrical stimulation
INTRODUCTION

Neurogenic lower urinary tract dysfunction (NLUTD) is one of the major sequelae of spinal cord injury (SCI) and a cause of increased morbidity and mortality in SCI patients. One year after the initial injury, most patients continue to have some degree of bladder dysfunction and may also have urinary tract complications, such as renal failure, renal or bladder calculi, hydronephrosis, and vesicoureteral reflux, which affect the quality of life (QOL). The chief goal of managing NLUTD is to prevent genitourinary complications, especially deterioration in renal function. Other goals include retaining continence, maintaining QOL, restoring self-esteem, and helping patients reintegration into the community.

Currently, the treatment strategies commonly used for NLUTD include medication, non-invasive conservative management, minimally invasive therapy, and surgical intervention. There is no single, most suitable medication for every patient; therefore, combination therapy remains the best policy to achieve maximal beneficial effects. Medications often prescribed in the clinical setting include anti-cholinergic agents (e.g., tolterodine tartrate and oxybutynin chloride) and tricyclic anti-depressants (e.g., imipramine) for neurogenic overactive bladder, cholinergic drugs (e.g., bethanechol chloride) for hypoactive detrusor muscle, α-adrenergic agents for hypotonic sphincter, and α-blocking agents (e.g., phenoxbenzamine, prazosin, and terazosin) and other relaxing agents (e.g., baclofen and diazepam) for spastic sphincter. However, the potential side effects of these medications may limit their application; for example, the side effects of anti-cholinergic agents include blurred vision, dry mouth, constipation, and tachycardia.

Minimally invasive management also has a role in the management of NLUTD and includes intravesical instillation of drugs, injection of botulinum toxin into the sphincter or detrusor muscle, pudendal nerve block, urethral stent or balloon dilatation, and transurethral sphincterotomy. Injection of Botulinum toxin, which has recently gained popularity, is an effective method of treatment; however, it is expensive and usually loses its efficacy in 4-6 months. Repeat injections are inevitable, and some patients may become resistant to botulinum toxin due to the development of antibodies. Although stenting and sphincterotomy also have satisfactory effects, potential complications, such as post-surgical hematuria, stent incrustation, bladder neck obstruction, urethral stricture, and erectile/ejaculatory dysfunction, are limiting factors. Surgical intervention (e.g., bladder augmentation, detrusor myectomy, urinary division, and artificial sphincter) may be the “last-line” therapy if non-invasive therapies fail because it is burdensome and causes the patient to suffer.

Bladder rehabilitation, including pelvic floor muscle (PFM) exercises and electrical stimulation (ES), is a non-invasive conservative management for NLUTD and was proposed for the treatment of NLUTD in the 2011 guidelines of the European Association of Urology. Despite its use in many other conditions, there is little evidence regarding the efficacy of PFM training, with or without biofeedback, in SCI patients. ES, with different stimulation modes, can activate afferent sensory nerves to inhibit detrusor overactivity or can directly induce muscle contraction for the strengthening of the PFM. In NLUTD patients with multiple sclerosis (MS), the combination of these rehabilitation strategies was found to be more effective than any single treatment. There are no studies reporting the efficacy of combined bladder rehabilitation strategies in patients with other forms of NLUTD, including incomplete SCI or cauda equina syndrome in which voluntary control and pelvic floor sensation are thought to be preserved. Furthermore, if combined bladder rehabilitation strategies are prescribed, they should be individualized because SCI patients can have varied presentations of bladder dysfunction.

Here we report the effects of individualized bladder rehabilitation programs, which included education on voiding behavior, PFM training combined with EMG biofeedback, and ES (for bladder inhibition or PFM strengthening), in patients with NLUTD secondary to incomplete suprasacral SCI or cauda equina syndrome. Improvement in the lower urinary tract symptoms and the related QOL were assessed by the post-voiding residual (PVR) urine amounts, International Prostate Symptom Score (IPSS), Overactive Bladder Symptom Score (OABSS), Incontinence Impact Questionnaire Short Form (IIQ-7), and
Urogenital Distress Inventory Short Form (UDI-6).

**METHODS**

The inclusion criteria were patients between 18 and 70 years of age with symptoms of NLUTD, a diagnosis of incomplete SCI at the suprasacral level or cauda equina syndrome, an injury duration of more than 6 months, and a stable neurological and physical condition. The exclusion criteria were any previous genitourinary disease or surgery, current urinary tract infection, a history of cardiovascular disease, complete SCI, and multiple injury levels. All patients underwent a full physical examination and a complete past medical history was taken. Neurological examination and assessment of the completeness of the SCI were based on the American Spinal Injury Association (ASIA) criteria. The Ethics Committee of Chung Shan Medical University Hospital approved the study and informed consents were obtained from all the subjects before the start of the study.

The individualized bladder rehabilitation programs were prescribed by a physiatrist and performed by an experienced physical therapist. These programs included education on voiding behavior, PFM exercise training combined with EMG biofeedback, and ES (for bladder inhibition or PFM strengthening). Education on voiding behavior was given at the first treatment session and during the treatment period as needed. Education on voiding behavior included adequate and controlled water intake, as well as proper voiding posture and behavior. Each subject received bladder rehabilitation two times per week for a period of 2 months. The duration of each treatment session was 30 minutes and included 10 minutes of ES. The training was performed with the patient in the supine position and an EMG surface electrode was placed at the perianal area to record compound muscle action potentials (CMAP) of the PFM. Visual biofeedback was provided when a PFM contraction was recorded and presented on a screen. ES was performed with the same perianal EMG surface electrode. There are two modes of ES: 1) at frequency of 40 Hz and pulse width of 250 ms to strengthen the PFM and 2) at frequency of 10 Hz and pulse width of 450 ms to evoke bladder inhibition. The mode of ES to be used was decided by the physiatrist based on the subject’s bladder dysfunction and the maximum ES intensity that could be tolerated. For patients with upper motor NLUTD (UMNLUTD), the ES mode for bladder inhibition was used. For patients with lower motor NLUTD (LMNLUTD), the ES mode for PFM strengthening was used. For both upper and lower motor neuron pathology associated with detrusor hypoactivity and sphincter hypertonicity (mixed type NLUTD), the treatment option was also the ES mode for PFM strengthening.

Before treatment and after 2 months of treatment, the PVR urine amounts were recorded and the symptoms of voiding were evaluated using the IPSS, OABSS, UDI-6 and IIQ-7. The IPSS is a screening tool for lower urinary tract symptoms and consists of eight questions, including seven symptom questions and one QOL question. The seven symptom questions include the feeling of incomplete bladder emptying, intermittency, weak stream, straining (these four questions are grouped as a subtotal score of “obstruction”), frequency, urgency, and nocturia (these three questions are grouped as a subtotal score of “incontinence”). All of these questions were answered based on the patient’s experience in the previous month, and each question was assigned a score from 1 to 5, making a total maximum score of 35 points (a higher score indicating worsening of symptoms). The eighth question on QOL was assigned a score of 1 to 6 (a higher score indicating worsening of QOL). The OABSS evaluated four symptoms of incontinence, including daytime frequency, nighttime frequency, urgency, and urgency incontinence, with a score of 2, 3, 5, and 5, respectively, and a total maximum score of 15. The Urogenital Distress Inventory-6 (UDI-6) evaluated the impact of symptoms of irritation (items 1 and 2), symptoms of stress (items 3 and 4), and symptoms of obstruction/discomfort or difficulty in voiding (items 5 and 6) on the QOL of subjects with urinary incontinence. The Incontinence Impact Questionnaire-7 (IIQ-7) evaluated the impact of urinary incontinence on daily life including physical activity, travel, social activities, and emotional health. Higher scores of the UDI-6 and IIQ-7 indicated a worsening of QOL.

The difference in all parameters before and after treatment was analyzed using Wilcoxon signed rank test and a p-value of <0.05 was considered to be statistically significant. The statistical software used for analysis was SPSS version 21.
RESULTS

A total of six subjects (four men and two women) with NLUTD were enrolled in this study. They ranged from 22 to 66 years of age (mean age, 41 ± 15.4 years). The post-injury duration ranged from 6 to 192 months (mean duration, 67.7 ± 76.4 months). Out of the six enrolled patients, three had spinal cord injuries with UMNLUTD (one at the cervical spine level with ASIA grade C, one at the thoracic spine level with ASIA grade C, and one at the thoracic spine level with ASIA grade D). The remaining three patients had cauda equina syndrome; two had LMNLUTD and one had detrusor hypoactivity with sphincter hypertonicity (Table 1).

The mean PVR urine amount before treatment was 198.3 ± 74.3 mL, and the mean amount after treatment was 100 ± 50 mL. In all six patients, the PVR urine amount significantly decreased after the individualized bladder rehabilitation program (p < 0.05); the difference ranged from 30 to 200 mL (Table 2 and Figure 1).

The IPSS subtotal score of incontinence significantly changed after treatment (p < 0.05), with the mean declining from 10.8 ± 2.6 to 5.3 ± 1.5 points. However, the change in the IPSS subtotal score of obstruction was not significant. The IPSS total score of symptoms also did not significantly change after treatment. All six patients had significantly lower IPSS scores of QOL after treatment (p < 0.05), with the improvement in scores ranging from 2 to 4 points (Table 2 and Figure 2).

The OABSS, UDI-6, and IIQ-7 scores significantly changed after treatment (p < 0.05). The mean score of the OABSS declined from 10.7 ± 2 to 6.5 ± 2.8 after treatment, indicating symptom improvement. The mean score of the UDI-6 and IIQ-7 decreased from 11 ± 5 to 6.2 ± 2.9 and from 15 ± 3.5 to 7.8 ± 2.2, respectively, indicating improved QOL (Table 2 and Figure 3).

Table 1. Patient demographics

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Age, Years</th>
<th>Gender</th>
<th>Diagnosis</th>
<th>Time since injury, Months</th>
<th>Injury level</th>
<th>ASIA grading</th>
<th>Types of NBD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22</td>
<td>Female</td>
<td>Suprasacral SCI</td>
<td>156</td>
<td>Cervical</td>
<td>C</td>
<td>Upper motor neuron bladder</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>Male</td>
<td>Suprasacral SCI</td>
<td>6</td>
<td>Thoracic</td>
<td>D</td>
<td>Upper motor neuron bladder</td>
</tr>
<tr>
<td>3</td>
<td>66</td>
<td>Male</td>
<td>Suprasacral SCI</td>
<td>14</td>
<td>Thoracic</td>
<td>C</td>
<td>Upper motor neuron bladder</td>
</tr>
<tr>
<td>4</td>
<td>51</td>
<td>Male</td>
<td>Cauda equina syndrome</td>
<td>32</td>
<td></td>
<td></td>
<td>Mixed type Bladder</td>
</tr>
<tr>
<td>5</td>
<td>44</td>
<td>Male</td>
<td>Cauda equina syndrome</td>
<td>6</td>
<td></td>
<td></td>
<td>Lower motor neuron bladder</td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>Female</td>
<td>Cauda equina syndrome</td>
<td>192</td>
<td></td>
<td></td>
<td>Lower motor neuron bladder</td>
</tr>
</tbody>
</table>

Table 2. Parameters before and after individualized bladder rehabilitation programs

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-void residual urine amounts (mL)</td>
<td>198.3 ± 74.3</td>
<td>100 ± 50</td>
<td>0.027*</td>
</tr>
<tr>
<td>IPSS(subtotal score of obstruction)</td>
<td>14.3 ± 6.8</td>
<td>11.7 ± 5.4</td>
<td>0.345</td>
</tr>
<tr>
<td>IPSS(subtotal score of incontinence)</td>
<td>10.8 ± 2.6</td>
<td>5.3 ± 1.5</td>
<td>0.028*</td>
</tr>
<tr>
<td>IPSS(total score of symptoms)</td>
<td>25.2 ± 9.1</td>
<td>17 ± 5.2</td>
<td>0.080</td>
</tr>
<tr>
<td>IPSS(score of quality of life)</td>
<td>5 ± 1.4</td>
<td>2.8 ± 1.5</td>
<td>0.024*</td>
</tr>
<tr>
<td>OABSS</td>
<td>10.7 ± 2</td>
<td>6.5 ± 2.8</td>
<td>0.043*</td>
</tr>
<tr>
<td>UDI-6</td>
<td>11 ± 5</td>
<td>6.2 ± 2.9</td>
<td>0.028*</td>
</tr>
<tr>
<td>IIQ-7</td>
<td>15 ± 3.5</td>
<td>7.8 ± 2.2</td>
<td>0.026*</td>
</tr>
</tbody>
</table>

Note: Values are mean ± standard deviation, * p < 0.05
Abbreviations: IPSS: International Prostate Symptom Score, OABSS: Overactive Bladder Symptom Score, UDI-6: Urogenital Distress Inventory-6, IIQ-7: Incontinence Impact Questionnaire-7
Figure 1. Comparisons of post voiding residual (PVR) urine amount before and after treatment

![Post-Void Residual Urine Volume*](image)

*p <0.05

Figure 2. Comparisons of total and subtotal scores in International Prostate Symptom Score (IPSS) before and after treatment

![International Prostate Symptom Score](image)

*p <0.05
DISCUSSION

In 1948, Kegel first described PFM exercises for the treatment of non-specified urinary incontinence and reported a high response rate of 84%.[16] Several subsequent studies also demonstrated that PFM exercises were effective for women with stress urinary incontinence.[17,18] PFM exercises are often applied in combination with EMG visual biofeedback. In a large prospective study, Dannecker et al. evaluated the efficacy of intensive EMG-biofeedback-assisted PFM exercise training in non-neurogenic patients with incontinence.[19] They reported a significant improvement in stress provocation testing and the EMG-potentials doubled. With a follow-up period ranging from 3 months to 7 years, 71% of subjects reported a persistent improvement in their incontinence symptoms. Other studies, including a Cochrane meta-analysis, also found additional beneficial effects with EMG biofeedback.[19,20] Active contraction and strengthening of the PFM, either through behavioral therapy or ES, were found to inhibit detrusor contraction; therefore, the authors claimed that PFM exercises may be an effective treatment for the overactive bladder.[21,22] Previous studies reporting the training effects of PFM exercises were mostly conducted in non-neurogenic patients. In a 12-week program, Lucio et al. compared the effectiveness of PFM exercises with that of placebo treatment in women with MS, who had lesions either in the brain or spinal cord.[23] The results demonstrated a significant reduction in incontinence-pad weight, the number of incontinence pads used, and nocturia events. The subjects also had significant improvement in PFM strength, endurance, resistance, and rapid contractions.

In the past decades, PFM ES has been shown to have satisfactory effects in the treatment of urinary incontinence related to the overactive bladder. A century previously, Griffiths demonstrated the relaxation of the contracted bladder by stimulation of the pudendal nerve in an animal model.[24] Subsequent research suggested that this was due to the inhibitory spinal reflex mechanism and the possible role of sympathetic inhibitory pathways.[25,26] However, in humans, the exact mechanism remains unclear. It is believed that sensory input through the
pudendal nerve causes PFM contraction accompanied by the inhibition of inappropriate detrusor activity. The earliest study used anal or vaginal plugs for this purpose, and then a non-implantable stimulator for bladder inhibition was developed. [21,27] Previous studies that applied ES for patients with NLUTD following SCI have reported successful results in improving lower urinary tract function, including larger bladder capacity, lower intravesical pressure, and better continence control. Some of these studies even claimed that there was a long-term effect after the completion of the treatment course. [28-30] In addition, when the pudendal efferent nerve or PFM are directly stimulated using an electric current, ES is also effective for PFM strengthening. Previous research has reported that higher frequency stimulation with a shorter pulse width has a better effect on PFM strengthening and that lower frequency stimulation with a wider pulse width is better for bladder inhibition. [13]

McClurg et al. compared the effect of PFM exercises, EMG biofeedback, and neuromuscular ES in patients with MS and concluded that combined treatment was more effective in reducing urinary symptoms. [11] In this study, we evaluated the effect of bladder rehabilitation programs for SCI patients with NLUTD. Their diagnosis was either incomplete SCI or cauda equina syndrome, and their bladder dysfunction was either UMNLUTD or LMNLUTD. Because of the disparity in diagnosis and bladder dysfunction between subjects, we prescribed individualized rehabilitation programs. With an onset of more than 6 months, the subjects included in this study had only limited potential for neurological improvement. However, there remained the possibility that voiding control would improve if they received adequate rehabilitation. Training effects may result from the reserve control of the PFM and bladder sensation, which have previously never been well trained. The subjects’ PVR urine amounts and QOL related to symptoms of incontinence significantly improved after the comprehensive bladder rehabilitation programs. These results are similar to previous studies on patients with MS. [11,13] However, the symptoms related to obstruction in the IPSS questionnaire did not significantly change. This might indicate that PFM rehabilitation has a better or quicker effect on the strengthening of the PFM or the inhibition of the overactive bladder. The underlying mechanism of the treatment effect of PFM exercises in the one patient with detrusor hypoactivity and sphincter hypertonicity may be because PFM exercises not only strengthen the PFM but also enable the muscles to relax more easily.

This study had some limitations. First, only six subjects were studied. In addition, they had two different types of bladder dysfunction (UMNLUTD and LMNLUTD); however, we were unable to separate them into two groups for further stratified analysis. Second, video urodynamic (VUD) data were not included in this study because not all of the patients received VUD before and after treatment. Further study is needed to evaluate VUD changes after bladder rehabilitation. Third, the subjects only received training for 2 months, and the effect of training beyond this period could not be evaluated. Fourth, only subjects with an onset duration of more than 6 months were included to avoid the possibility of spontaneous recovery of the neurological injury. Although some patients with an onset duration of more than 6 months have the potential for neurological recovery, the magnitude of recovery is much less than during the first 6 months post-injury. However, we could not avoid this confounding effect and future studies warrant the inclusion of a control group. Furthermore, it is not clear whether the efficacy of individualized bladder rehabilitation programs would increase if they were administered earlier.

CONCLUSION

Patients with NLUTD resulting from incomplete SCI or cauda equina syndrome could benefit from the individualized bladder rehabilitation programs. These programs included education on voiding behavior, PFM exercise combined with EMG biofeedback, and ES for bladder inhibition or PFM strengthening, all prescribed according to the type of bladder dysfunction. In this study, patients who received individualized bladder rehabilitation programs obtained beneficial effects on reducing PVR urine amounts and QOL related to incontinence.

REFERENCES

61-83.
神經性下尿路功能障礙病人經個人化膀胱復健後效果之
先導性研究

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目的：神經性下尿路障礙(NLUTD)是脊髓損傷後常見的後遺症和致病或致死的主要原因之一。目前治療神經性膀胱的方式包括藥物，非侵襲性保守治療，微創治療及手術治療。然而，目前並沒有研究討論針對綜合骨盆底肌肉運動(PFM exercise)及電刺激(ES)的非侵襲性保守治療。這研究主要是針對脊髓損傷伴隨有神經性下尿路障礙(NLUTD)的病人，提供個人化膀胱復健治療，給予包括排尿行為指導，骨盆底肌肉運動並合併膀胱電圖生理回饋及電刺激(抑制膀胱或強化骨盆底肌肉)治療之後再評估其成效。

方法：提供兩階上不完全脊髓損傷或馬尾束症候群之患者兩個月個人化膀胱復健治療，並在治療前後以解尿後殘尿量和包括國際前列腺症狀積分(IPSS)，膀胱過動症問卷(OABSS)，尿失禁症狀困擾量表(UDI-6)，尿失禁生活衝擊量表(IHQ-7)等問卷加以評估效果。

結果：在治療後，包括解尿後殘尿量，國際前列腺症狀積分中之失禁症狀和生活品質分量表，膀胱過動症問卷，尿失禁症狀困擾量表，尿失禁生活衝擊量表等問卷分數皆顯著下降，代表其生活品質及症狀有改善。不過，國際前列腺症狀積分中之阻塞症狀分量表和總症狀量表分數，在治療前後並未看到顯著差異。

結論：有神經性下尿路障礙的病人在接受包括衛教，骨盆底肌肉運動並合併骨電圖生理回饋及電刺激(抑制膀胱或強化骨盆底肌肉)等個人化膀胱復健治療後將會有所助益。經過此種治療之病人，其解尿後殘尿量及因失禁而受影響之生活品質將因之改善。（台灣復健醫誌 2015；43(2)：111 - 120）

關鍵詞：脊髓損傷(SCI)，神經性下尿路障礙(NLUTD)，膀胱復健(Bladder rehabilitation)，骨盆底肌肉運動(PFM exercise)，電刺激(ES)。