Sacral Neuromodulation in the Treatment of Non-Neurogenic Female Lower Urinary Tract Dysfunction; First Case-series and Systematic Review of Literature

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ABSTRACT

Objective: To demonstrate which types of non-neurogenic female lower urinary tract dysfunction (LUTD) respond to sacral neuromodulation (SNM) after the failure of all non-invasive treatments.

Materials and Methods: Female LUTD performed SNM between 2017 and 2019 were retrospectively reviewed. A case with anatomical or neurological abnormalities were excluded by thorough physical examination and investigations. The specific type of LUTD, including midurethral obstruction (MUO), was diagnosed by videourodynamics (VUDS). Clinical diagnoses, including idiopathic urinary retention (IUR), voiding dysfunction (VD) and refractory overactive bladder (OAB), were used instead of VUDS diagnosis when the result was normal or inconclusive. The International Prostate Symptom Score (IPSS) and Overactive Bladder Symptom Score (OABSS) in Thai version were used to compare between pre and post-treatment. Responder was defined as an IPSS and/or OABSS decreased more than 50% from baseline.

Results: Total 21 cases were performed SNM. The average age was 49.6 (24–80) years. The average pre-treatment IPSS and OABSS were 23.4 and 6.4 as well as average post-treatment IPSS and OABSS were 13.7 and 3.8. Only 9 out of 21 cases (42.9%) showed improvement after SNM. The responders included 7 out of 11 MUO (63.6%), 1 out of 4 IUR (25.0%), and 1 out of 3 OAB (33.3%). None of the VD cases responded to SNM.

Conclusions: SNM is another option for female patients with LUTD who have failed to respond to conservative treatments. After completely excluding anatomical and neurological abnormalities, the types of LUTD having a chance to respond to SNM are MUO, IUR, and OAB.

Keywords: Lower urinary tract dysfunction, Female, Sacral neuromodulation (Siriraj Med J 2021; 73: 732-737)

Abbreviation

LUTD : Lower urinary tract dysfunction
SNM : Sacral neuromodulation
VUDS : Videourodynamics
BOO : Bladder outlet obstruction
MUO : Midurethral obstruction
DU : Detrusor underactivity
IUR : Idiopathic urinary retention
VD : Voiding dysfunction
OAB : Overactive bladder

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INTRODUCTION

Lower urinary dysfunction (LUTD) is a functional problem that mainly causes lower urinary symptoms in women and usually affects their quality of life. Functional abnormalities in each patient may consist of bladder and/or outlet dysfunction. Because LUTD is a dynamic abnormality and changes over time, the appropriate management for LUTD should be conservative treatment and/or medication. However, lower urinary tract symptoms may not properly be alleviated by non-invasive treatment; while invasive surgery will rarely be considered due to the risk of a permanent change of function. Neuromodulation, a treatment using electrical stimulation directly to the nerve in order to modulate the reflexes that influence the bladder, sphincters, bowel, and pelvic floor[1] to restore normal lower urinary tract function, has been widely accepted for treating LUTD and is considered as a non-invasive procedure. Nowadays, there are many neuromodulation procedures that have been used for treating LUTD, but the most popular one is sacral neuromodulation (SNM), which has supported from many scientific studies. The US FDA has approved the use of InterStim™ or SNM for the treatment of urgency-frequency syndrome, urinary urge incontinence, and non-obstructive urinary retention.[2] In Thailand, neuromodulation has been used in many neurological conditions but there has never had a study of neuromodulation for treating LUTD. Consequently, this study aims to demonstrate our experience and to provide the LUTD characteristics of patients who have a chance to obtain a benefit from SNM.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of 21 female patients with non-neurogenic LUTD who were performed SNM between 2017 and 2019 in our hospital. This study was approved by our institute IRB, number 714/2562(IRB2)

Patient selection

The inclusion criteria were female patients with LUTD who had not responded or had an unsatisfactory response to all conservative treatments for more than 6 months. All cases would like to try SNM after counselling and understanding the risks and benefits of procedure. Further, physical and neurological examination must reveal no significant anatomical or neurological abnormality that could probably be a cause of the LUTD. All the cases had videourodynamics (VUDS) performed followed by the International Continence Society (ICS) recommendation[3] in order to diagnose a type of functional abnormality and to get a clear urodynamic diagnosis before SNM was performed. Because surface electromyography during VUDS was unreliable, the result was not considered as a part of diagnosis and fluoroscopic imaging was used instead of it. In cases of normal or inconclusive result due to situational inability to void, clinical diagnosis was used for the grouping instead of urodynamic diagnosis.

Definitions

According to ICS terminology 2010, the definition of characteristics of LUTD consist of an overactive bladder (OAB), defined as urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathology; voiding dysfunction (VD), defined as an abnormally slow and/or incomplete micturition; detrusor underactivity (DU), defined as a detrusor contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span; and bladder outlet obstruction (BOO), defined as a reduced urine flow rate and/or presence of a raised post-void residual urine and an increased detrusor pressure.[4] The urodynamic criteria for the diagnosis of female BOO were described in Blaivas's study.[5] In this group, the point of obstruction could be demonstrated by fluoroscopic examination on VUDS so that specific term, including midurethral obstruction (MUO), was used instead of BOO. Urethral stricture must be excluded by cystourethroscopy in all BOO cases. In cases of normal or inconclusive VUDS, the clinical diagnosis consisted of voiding dysfunction (VD), defined as a maximal urine flow rate equal to or less than 12 ml/sec with or without post-void residual urine; idiopathic urinary retention (IUR), defined as a past or current inability to void; and refractory overactive bladder (OAB), defined as OAB which had failed to respond to conservative treatment and medications or led to intolerable adverse events. Responders were defined as being cured or showed an improvement after SNM.

Measurement

The validated questionnaires in the Thai language, including the International Prostate Symptom Score (IPSS)[6] and Overactive Bladder Symptom Score (OABSS)[7], were used as a symptom measurement tool. Cure was defined as an IPSS and/or OABSS improvement of more than 80% from baseline, while improvement was defined as an IPSS and/or OABSS improvement of between 50% and 80% from baseline within 7-30 days after implantation and the last follow-up for the response cases. Responder was defined as a case who was cure or improvement after SNM.

Procedure

Sacral neuromodulation (SNM) is usually performed in two stages: a test phase and a phase with implantation of an implantable pulse generator (IPG) by using the InterStim II® system (Medtronic). The test phase utilized two techniques: temporary lead implantation, called percutaneous nerve evaluation (PNE), and permanent tined lead implantation, composed of four leads and a hook. The full SNM system consisted of a permanent tined lead and IPG. Lead implantation was performed in the prone position, in a well-prepared sterile field and under local anesthesia with light sedation. Fluoroscopic guidance was used to identify the 3rd sacral foramen in two-dimensions, in the anteroposterior and lateral views. A 20-gauge needle in the set of SNM was used to make a puncture at 2 cm cephalad to the 3rd sacral foramen in the anteroposterior view and at the 45°–60° axis in the lateral view. The needle was passed through the foramen and stopped at the anterior surface. The proximal end of the needle was connected to an external pacemaker and then electrical stimulation was given. The proper position of the needle was defined by the patient reporting feeling a tickling sensation at the perianal area, anus, and/or vagina, called a sensory response and demonstrating anal contraction, called a motor response. If the selected site did not demonstrate any response, the procedure would be repeated at the contralateral site in the same step. The needle stylet was then removed. Either a temporary lead or permanent lead was inserted via the needle and placed in a proper position by checking the sensory and motor responses. For PNE, the lead was fixed directly at the puncture site using a transparent medical dressing. For the permanent lead, a subcutaneous tunnel was created by a trocar with a plastic tube from the puncture site to the subcutaneous pocket at the right buttock and the lead was connected to an extended wire to directly connect to an external pacemaker in order to prevent contamination. Due to the easy displacement of the PNE lead, some cases reporting no response might repeat either PNE or permanent tined lead implantation if the patient agrees. During the test phase, the external pacemaker was used as an electrical generator and the implanted patient could adjust the intensity of the electrical stimulation by monitoring their feeling in the perianal area, anus, and vagina. If the feeling was too much, electrical stimulation could be reduced by remote control. For evaluation, if a patient reported symptoms improvement of more than 50% from baseline by IPSS and OABSS, full SNM system implantation would be performed within 1-4 weeks. Because of the high cost of full SNM system implantation, PNE was considered as a first step in all cases who had unsuccessful VUDS or where there were doubts about the benefit of SNM. All cases of full SNM system implantation were supported by the high cost treatment project of our hospital foundation.

Statistics

The results were presented using descriptive statistics as a frequency and percentage for categorical data, as well as average for continuous data.

RESULTS

In total, 21 cases of female LUTD who had SNM performed. The average age was 49.6 (24 – 80) years. The types of LUTD consisted of MUO 11 cases, IUR 4 cases, VD 3 cases, and OAB 3 cases. MUO and VD cases were treated by non-invasive management including behavioral therapy, pelvic floor muscle rehabilitation and oral medications. IUR cases were initially treated by indwelling catheter and then performed clean intermittent catheterization. OAB cases were treated step by step including first - single oral bladder relaxant, second - combination of oral high dose bladder relaxant and last - 100 unit of intradetrusor botulinum toxin A injection. The average pre-treatment IPSS and OABSS were 23.4 and 6.4 as well as the average post-treatment IPSS and OABSS were 13.7 and 3.8. (Table 1) Only 9 out of 21 cases (42.9%) were cured or improved after SNM. The responders included 7 out of 11 MUO (63.6%), 1 out of 4 IUR (25.0%), and 1 out of 3 OAB (33.3%). None of the VD cases responded to SNM. Twelve of 21 cases had complete VUDS successfully performed. (Table 2) Only 8 out of 9 responders had fully implanted SNM and the average follow-up was 15.4 (4.4 – 32.4) months, while the average IPSS and OABSS were 8.4 and 2.7, respectively. One case decided not to continue with SNM because of an awareness of the foreign body and fear of the long-term consequences (Table 3). In total, 6 out of 8 cases reported and considered themselves cured. No adverse events were reported in all cases.

DISCUSSION

Female LUTD without anatomical and neurologic abnormality is a challenging condition. Importantly, it is not a life-threatening condition but always affects the patient's quality of life. Because of the dynamic changes that can occur, the most appropriate treatment, including conservative and medical treatment, should be reversible over time, meaning that invasive surgery is not an ideal option. However, while most patients are properly treated by conservative and medical treatment, some patients may not achieve their goal. SNM is another treatment

TABLE 1. Comparison between average pre- and post-treatment IPSS and OABSS in each type of LUTD.

Type of LUTD		No.	IPSS		OABSS	
			Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
MUO	Responder	7	23.7	5.4	6.0	1.9
	Non-responder	4	18.3	15.0	3.5	2.6
IUR	Responder	1	34.0	6.0	6.0	3.0
	Non-responder	3	27.3	22.7	4.0	2.7
DV	Responder	0	-	-	-	-
	Non-responder	3	25.3	23.3	8.3	8.3
OAB	Responder	1	15.0	0	9.0	0
	Non-responder	2	15.5	15.5	11.0	11.0

TABLE 2. Case number, diagnosis and videourodynamics parameters in each case.

Case no.	Age	Dx	Group	VV	PVR	Free uroflow	Urodynamic parameters		
						Qmax	Catheter Qmax	Pdet at Qmax	Fluoroscopic findings
1	35	MUO	Responder	178	0	12.9	-	-	Mid
2	54	MUO	Responder	115	155	-	4.2	80	Mid
3	41	MUO	Non-responder	67	0	13.8	4.8	51.5	Mid
4	54	MUO	Responder	40	205	-	2.1	57.5	Mid
5	68	MUO	Responder	81	154	25	4.3	23	Mid
6	53	MUO	Responder	376	0	16	16.4	26.5	Mid
7	53	MUO	Non-responder	144	0	-	10.3	61.2	Mid
8	38	MUO	Non-responder	210	0	18.8	-	-	Mid
9	24	MUO	Responder	65	0	-	8.8	24	Mid
10	76	MUO	Responder	80	96	-	5	25	Mid
11	80	MUO	Non-responder	274	63	11	8.8	37.2	Mid
12	42	IUR	Non-responder	199	202	11.6	-	-	-
13	45	IUR	Non-responder	161	80	6.9	-	-	-
14	31	IUR	Non-responder	126	150	10.2	-	-	-
15	36	IUR	Responder	70	600	4	-	-	-
16	38	VD	Non-responder	592	0	12	-	-	-
17	34	VD	Non-responder	233	200	10	-	-	-
18	65	VD	Non-responder	256	0	11.5	-	-	-
19	76	OAB	Responder	491	0	-	21.9	17.1	No BOO
20	41	OAB	Non-responder	420	0	-	25.5	30	No BOO
21	59	OAB	Non-responder	180	0	-	24.2	28.2	No BOO

Abbreviations: Dx : diagnosis, VV : voided volume (ml), PVR : post-void residual urine (ml), Qmax : maximal urine flow rate (ml/sec), Pdet@Qmax : detrusor pressure at maximal urine flow rate (cmH2O), Mid : midurethral obstruction, BOO : bladder outlet obstruction

TABLE 3. Comparison between pre- and post-treatment IPSS and OABSS in responder group at the last follow up.

Case no.	Age (year)	Diagnosis	Follow time (month)	IPSS Pre-treatment	IPSS Post-treatment	OABSS Pre-treatment	OABSS Post-treatment	Status
1	35	MUO	32.4	31	0	3	0	Cure
2	54	MUO	21.2	40	1	15	1	Cure
4	54	MUO	7.1	22	11	6	2	Improvement
5	68	MUO	13.0	20	8	4	3	Improvement
6	53	MUO	12.7	15	0	2	2	Cure
9	24	MUO	-	19	-	11	-	Not perform
10	76	MUO	4.4	19	1	1	1	Cure
15	36	IUR	7.3	34	4	6	2	Cure
19	76	rOAB	25.2	15	5	9	4	Cure

option and is appropriate for LUTD. In our study, we categorized female LUTD into 4 types based on firstly urodynamic and lastly clinical diagnosis, including MUO, IUR, DV, and OAB.

For female BOO, common locations of obstruction are the bladder neck and midurethral. Bladder neck obstruction is usually treated by an alpha-adrenergic antagonist or transurethral incision bladder neck. On the other hand, most MUO cases are usually treated and respond to SNM. Soumendra et al. reported a 10-year experience of SNM for females with urinary retention secondary to external urethral sphincter overactivity or Fowler's syndrome. The overall success was 72% and the results revealed that females with normal urethral sphincter activity had worse outcomes than those with an abnormal urethral sphincter activity.[8] In our study, female BOO was diagnosed by VUDS according to the criteria in Blaivas's study[5] and we found 11 cases were MUO. In total, 7 out of 11 (63.6%) MUO cases responded to SNM and the success rate was comparable.

In our study, both IUR and DV were clinical diagnoses because of inconclusive VUDS result, such that they might be detrusor acontractility (DAC), DU, BOO, or combined abnormalities. Rademakers et al. performed a study in 18 men with DU, defined as a measurement value less than the 25th percentile in the linear interpolation of a Maastricht–Hannover nomogram, and reported that 50% of the cases responded to SNM.[9] Chan et al. performed a study in 50 women and 19 men with DU, defined as having a bladder contractility index (BCI = Pdet at Qmax + 5Qmax) of less than 100, and reported that 51% of cases had a favorable response to the trial phase, defined by at least a 50% improvement in symptoms, PVR, and voided volume bladder diary. Interestingly, 6 of 18 cases with detrusor acontractility, defined by an absent contractility with failure to empty and absence of EMG abnormalities, had a favorable response to the trial phase. They concluded that patients with preserved detrusor contractility were more likely to respond to SNM.[10] In our study, only one of our IUR cases successfully responded to SNM, which probably meant this patient had enough detrusor contractility or BOO.

Noblett et al. performed a study in patients with OAB, confirmed on a consecutive three-day voiding diary with a minimum of two involuntary leaking episodes in 72 hours and/or ≥ 8 voids per day, where success at 12 months was defined as a ≥50% improvement in average leaks/day or ≥50% improvement in voids/day or a return to normal voiding frequency (<8 voids/day). The responder rate was 85% in overall OAB symptoms. Only 37% of OAB cases with UUI had complete continence.[11] In our study, 1 of our 3 OAB cases gained continence and was cured.

A key strength of our study study is that we tried to identify dysfunctional causes in each case by VUDS in order to make it clear which type of LUTD would benefit from SNM. However, urodynamic diagnosis should be a key tool to predict SNM response, as VUDS could not be successfully performed for most cases. Because the

test is in an unnatural setting, we even tried to perform it in a similar way to mimic a patient's lower urinary tract function. Importantly, strict urodynamic criteria for diagnosing female BOO and DU are inconclusive and difficult to draw conclusions, so that the SNM results of many studies highly depend on patient selection. Lastly, the limitations of this study to note are its small sample size and retrospective design, which prompt the need for further research.

CONCLUSION

SNM is another option for female patients with non-neurogenic LUTD who have failed to respond to all conservative treatments. In our study, after completely excluding anatomical abnormalities, the type of LUTD having the highest chance to respond to SNM was found to be midurethral obstruction (MUO). For idiopathic urinary retention (IUR) and refractory overactive bladder (OAB), only one-third of cases responded. No voiding dysfunction (VD) cases responded to SNM. This information may help urologists to better select patients for SNM.

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