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# The first Iraqi experience in sacral neuromodulation for patients with lower urinary tract dysfunction



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## KEYWORDS

Lower urinary tract dysfunction;  
Overactive bladder;  
Urge urinary incontinence;  
Urinary retention;  
Neuromodulation

## ABBREVIATIONS

IPG, implantable pulse generator;  
NOUR, non-obstructive urinary retention;  
OAB, overactive bladder;

**Abstract Objectives:** To present our experience, in Iraq, with sacral neuromodulation (SNM) in patients with refractory lower urinary tract dysfunction, with discussion of the factors that affect the response rate.

**Patients and methods:** In this prospective, clinical, interventional study, 24 patients were evaluated and treated by a team comprised of a Urologist and a Neurosurgeon with SNM over a 1.5-year period. The gender, age, pathology, and clinical presentation, were all studied and evaluated. Successful clinical response was defined as achieving a  $\geq 50\%$  improvement in voiding diary variables.

**Results:** The mean age of those that responded to SNM was 28 years, with females responding better than males (10 of 14 vs four of 10). The SNM response rate according to presentation was six of 10 in those with overactive bladder/urge urinary incontinence, six of nine of those with urinary retention, and two of five in those with a mixed presentation. The response rate in idiopathic voiding dysfunctions was 11 of 13, whilst for neurogenic dysfunctions it was three of 11. Other

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QoL, quality of life;  
SNM, sacral neuromodulation;  
(U)UI, (urge) urinary incontinence

benefits such as in bowel motion, erectile function, menstruation, power of lower limbs, and quality of life (QoL), were also recorded. The complications were reasonable for this minimally invasive procedure.

**Conclusion:** SNM offers a good and durable solution for some functional bladder problems, if patients are well selected. There may also be additional extra-urinary benefits that contribute to improvements in QoL. SNM was well tolerated by our patients with an encouraging response rate, especially in psychologically stable patients with idiopathic dysfunctions.

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## Introduction

Physiological disorders of bladder function denote problems with either urine voiding, storage, or both. These disorders can be either neurogenic (as in multiple sclerosis, spinal cord injury, etc.) or idiopathic in origin. Patients commonly present with repeated UTIs, obstructive uropathies, problems in urination, or urinary incontinence (UI), resulting in a negative influence on their quality of life (QoL) [1].

The ICS defines OAB syndrome as urgency, frequency and/or nocturia with or without urge UI (UUI) [2]. Non-obstructive urinary retention (NOUR) has a multifactorial aetiology and can be due to detrusor underactivity, detrusor–bladder neck dyssynergia, dysfunctional voiding, detrusor–external sphincter dyssynergia, and non-relaxing urethral sphincter obstruction.

Since the 1990s, sacral neuromodulation (SNM) has been endorsed as a secondary treatment choice, if conservative treatments either fail or cause adverse reactions in patients with overactive bladder (OAB) or NOUR. Treatment success of these storage and voiding dysfunctions is judged by improvement in micturition diaries, subjective personal satisfaction, QoL scores, and symptom score surveys [3].

Consistent improvements in the SNM procedure have been accomplished and it is currently a minimally invasive procedure performed under local anaesthesia, which should be considered before undertaking more invasive reconstructive actions. An electrode is inserted in the S3 or S4 sacral foramen and during a ‘test phase’, enduring for days to weeks, the patient keeps a bladder diary to gauge whether SNM has delivered a significant advantage. If the outcomes of the test phase are positive, a neuromodulator is imbedded in the gluteal area. The mechanism of action of SNM has not been completely elucidated, but afferent nerves most probably play a significant part. It appears that SNM yields a modulation of medullary reflexes and brain centres by peripheral afferents [4]. The technique has been accepted since 1997 by the USA Food and Drug Administration (FDA) and has been effectively used in patients with different types of lower urinary tract dysfunction,

comprising urgency, frequency and UUI, in addition to NOUR [5].

SNM represents a promising choice for treating treatment-refractory neurogenic/idiopathic bladder dysfunction. It remains to be appreciated which kinds of neurogenic bladder dysfunction and which underlying neurological conditions best respond to SNM. The present study represents the first experience of SNM in Iraqi patients with different lower urinary tract dysfunctions, with an assessment of the probable parameters that affected treatment response in our patients.

## Patients and methods

In this prospective clinical interventional study, conducted from August 2015 to December 2016, a cohort of 24 patients with LUTS (storage and/or voiding dysfunction) were treated with SNM, using the InterStim® device with tined-lead (Medtronic Inc., Fridley, MN, USA). All the patients were evaluated and treated by a team consisting of a Urologist and a Neurosurgeon.

Dependent on the treatment success in the test phase, patients received either implantation of the implantable pulse generator (IPG) or the electrodes were removed. The median (range) follow-up was 12 (6–15) months.

The patient selection criteria were as follows:

- Both male and female patients aged  $\geq 16$  years.
- Patients with lower urinary tract dysfunctions that significantly affected their QoL.
- Dysfunctions included were: OAB with or without UUI, poor bladder evacuation or NOUR, and mixed problems (UI and incomplete emptying).
- As to the pathology behind these LUT dysfunctions, both idiopathic and neurological diseases (such as multiple sclerosis and spinal pathology, e.g. trauma in the form of incomplete spinal cord injury, diffused spinal cord compression, failed back surgery) were included.
- There should be a patient desire for an alternative to medication due to side-effects or lack of efficacy.
- Patient acceptance, with a written consent (patient’s signature), after oral and written information about the clinical investigation.

In addition to detailed history taking, a voiding diary, physical/neurological examination, routine laboratory investigations, ultrasonography, MRI study (for neurogenic cases), cystoscopy (to exclude anatomical obstruction), and urodynamic studies, were conducted for all the patients (for preoperative objective diagnosis) and were interpreted by a staff member specialised in neuro-urology and experienced in judging urodynamic measurements. SNM treatment success was defined as a reduction in one or more micturition symptoms of  $\geq 50\%$ , compared to baseline, determined by comparing symptom scores and voiding diaries.

The exclusion criteria were as follows:

- Other forms of UI such as stress UI or fistulae.
- Patients who were unable to operate or accommodate the neuromodulation system.
- Patients who were not appropriate candidates for surgery.
- Urinary retention due to mechanical obstructions such as BPH, prostate cancer, or urethral stricture.
- Pregnancy, risk of pregnancy, lactation, unborn foetus, and delivery during participation in the clinical investigation.
- Paediatric age group (aged  $< 16$  years).
- Military service.
- Severe pelvic organ prolapse.

The following products, all Conformité Européene (CE)-certified and manufactured by Medtronic Inc., were the components of the sets used for the testing and permanent implant phases:

A. Lead introducer kit.

B. Tined lead (33-cm long).

C1. Implantable devices: electrode, percutaneous extension.

C2. Implantable device: InterStim II neurostimulator (model 3058).

D. iCon Patient Programmer: a programmer for patients to turn InterStim II neurostimulator on/off, to change amplitude within physician set limits and/or to switch from four pre-set configuration settings.

#### Mode of application – test-stimulation, IPG implantation and continuous use

The IPG implantation procedure consisted of two steps:

**Step 1** (Evaluation Phase): Test stimulation via stimulation needles to define the best place for electrode implantation (motor response of the pelvic floor), then implantation of one or two tined leads via the Seldinger technique near the nerves of the sacral foramina S3 or S4 (left and right side), and finally temporary connection (through the skin) to an external stimulator and evaluation of therapy success (usually for 2–4 weeks).

**Step 2** (Treatment Phase): In cases with a  $\geq 50\%$  improvement in symptoms, an IPG was implanted in the gluteal region, with subsequent long-term routine

use of the SNM (with follow-up evaluations at 0.5 weeks, 1 month and then every 3 months).

The settings of the SNM parameters were as follows:

- Voltage (mV): range 0.1–10.0 mV, measurement in steps of 0.1 mV.
- Frequency (Hz): range 5–50 Hz, measurement in steps of 5 Hz.
- Pulse width (ms): range 210–450 ms, measurement in steps of 10 ms.
- Pole configuration: range 0–3.

#### Statistical analysis

MedCalc version 14 software was used for the analysis of the data. The categorical data are presented as frequencies and percentages. Pearson's chi-squared test was used for testing the association between the categorical data. Continuous variables are presented as mean and standard deviation (SD). The independent *t*-test was used for assessing the difference in response according to patients' age. Statistical significance was considered at a  $P \leq 0.05$ .

#### Results

For the pathological aetiologies amongst the studied cases, 13 of the 24 patients (54.2%) had an idiopathic aetiology, whilst 11 (45.8%) had neurological problems, with most having spinal cord pathology (seven of the 24 patients, 29.2%). The patients' demographic features, pathology, as well as presentation, are listed in [Table 1](#).

**Table 1** Demographic features, pathology and presentation of the patients.

Variable	Value
Total number of patients	24
Gender, <i>n</i> (%)	
Male	10 (41.7)
Female	14 (58.3)
Age, years, mean (SD)	
Male	32.8 (8.1)
Female	26.6 (11.2)
Total	29.2 (10.3)
<i>N</i> (%)	
Pathology	
Idiopathic	13 (54.2)
Neurological diseases	11 (45.8)
Spinal cord pathology	7 (29.2)
Multiple sclerosis	1 (4.2)
Brain tumour	1 (4.2)
Diabetic neuropathy	1 (4.2)
Neurogenic bladder	1 (4.2)
Presentation	
Detrusor-over activity $\pm$ UUI	10 (41.7)
Poor emptying/urinary retention	9 (37.5)
Mixed	5 (20.8)

There were more female patients (14/24, 58.3%) than male patients (10/24, 41.7%) and the female patients were younger [mean (SD) age 26.6 (11.2) vs 32.8 (8.1) years]. Table 1 also shows that OAB ± UII was the most common presentation amongst the sample group, with a frequency of 41.7% (10/24), followed by poor emptying/NOUR at 37.5% (nine of 24), and 20.8% (five of 24) had a mixed presentation (UI and poor emptying).

Concerning the response of the patients to the test phase and permanent implant; Table 2 shows that there was a better response in the female group, both at the testing phase and throughout the follow-up (12 of 14 females and 10 of 14, respectively) as compared to the male group (five of 10 males and four of 10, respectively). Patients with an idiopathic aetiology showed statistically significant responses throughout the study compared with those who presented with associated neurological diseases (13 of 13 vs four of 11, in the testing period; and 11 of 13 vs three of 11, as a final outcome after IPG implantation). Patients with the lowest

response in the present series were those with multiple sclerosis and brain tumour.

With regard to response to SNM according to patient's presentation, those with NOUR/poor emptying showed better (although statistically non-significant) responses in both periods of examination than those with signs and symptoms of OAB/UII. The least responses were recorded amongst patients of mixed symptoms, again throughout the testing and IPG implantation phases (Table 2).

The parameters monitored using the voiding diaries for each presentation are shown in Table 3, with their mean pre-treatment level and categorisation of the final response for each presentation, with 'positive response' subdivided into either ≥50% improvement in these parameters or complete response with return to almost normal function.

No statistical significance was found regarding response rate with the mean age of patients (Table 2).

Postoperative complications (Table 4) were recorded in six patients during the testing phase, where the most

**Table 2** Response of the patients at test phase and at last follow-up, according to gender, pathology, presentation and age.

Variables	Test phase		<i>P</i>	Final outcome		<i>P</i>
	Positive	Negative		Positive	Negative	
<i>n/N</i>						
Gender						
Female	12/14	2/14	0.058 NS	10/14	4/14	0.124 NS
Male	5/10	5/10		4/10	6/10	
Pathology						
Idiopathic	13/13	0/13	0.001*	11/13	2/13	0.004*
Neurological diseases	4/11	7/11		3/11	8/11	
Presentation						
Overactive bladder/UII	7/10	3/10	0.155 NS	6/10	4/10	0.619 NS
Poor emptying/urinary retention	8/9	1/9		6/9	3/9	
Mixed	2/5	3/5		2/5	3/5	
				Response to SNM treat		<i>P</i>
				Good	Poor	
Age, years, mean (SD)	–	–	–	27.9 (10.3)	31.1 (10.5)	0.46 NS

\* Chi-squared test,  $P \leq 0.05$ ; NS, not significant.

**Table 3** Final outcome of SNM according to the parameters tested for each presentation.

Presentation	No. of patients	Parameter tested	Pretreatment level, mean (SD)	Final response to SNM, <i>n/N</i>		
				Poor response	≥50% improvement	Complete response
Dry OAB	4	No. of voids/day Volume voided/void, mL	17.6 (6.3) 102.5 (43.6)	1/4	2/4	1/4
UII	6	Leakage episodes/day, <i>n</i>	7.8 (5.0)	3/6	1/6	2/6
Urinary retention	9	No. of catheterisations/day Volume/catheterisation, mL	6.2 (2.5) 295 (94.7)	3/9	2/9	4/9
Mixed symptoms	5	All above parameters	As above levels	3/5	2/5	0/5

**Table 4** Postoperative complications amongst the included patients.

Complications, n/N	Test phase	Permanent implant	Total
Infection	3/6	3/9	6
Dislodgment/ break of lead	1/6	1/9	2
Pain	2/6	2/9	4
Drop in response	0/6	3/9	3
Total	6	9	15

frequently encountered complication was infection in three of the six cases. After IPG implantation there were nine complications: three complicated cases showed a drop in SNM response and three had infections, of which two required removal of the device. Additionally, our sample exhibited extra-urinary benefits from SNM, mostly in the form of relief of associated chronic pelvic pain, improvement in erectile function in two patients, improved menstruation in four patients, improvement in bowel motion in five patients, and self-reported improved QoL in all the 14 responders. However, the most important recorded extra-urinary benefit was a dramatic improvement in power grade of the lower limbs (from PG2 to PG5) in a patient with a ballistic incomplete spinal cord injury of 3 years.

## Discussion

This prospective study denotes the first experience and follow-up study of SNM treatment to be conducted and analysed or published to date in Iraq. The results support the persistent clinical advantage of SNM, which has been shown in various patient groups and reported in many studies [6–9]. A problem of any such study is that it cannot evaluate new therapeutic progression that occurs after the study period, which can affect patient assortment and overall patient outcomes. Some lost or incomplete data due to patient's irregular attendance at scheduled visits represent another problem. For such reasons, clinical implications from the present study should be interpreted with caution. However, the present study found that ~58.3% of the treated patients continued to experience therapeutic benefit from SNM after 10 months of treatment as compared to 41.6% who showed a poor response at the end of the study period, supporting results from earlier studies [10,11]. However, this result was significantly lower than the 88% and the 52–77% reported success rates in the Brazzelli et al. [7] and Siddiqui et al. [8] studies, respectively. There are many possible explanations for the treatment failure in the latter group, such as placebo effect of test stimulation, insufficient pre-implantation test stimulation sensitivity, and inadequate patient selection (e.g. disease severity and type, patient mentality, patient's

intelligence and expectations, socio-medical history). This is reflected in the study of Weil et al. [9], who reported a striking association between late loss of therapeutic outcome and the existence of former psychiatric complaints.

More responses amongst our patients with idiopathic bladder disorders as compared to those with neurogenic bladder disorders was to be expected, as SNM has become a well-established and widely recognised management for patients with refractory functional bladder disorders [7,12,13] and it has been incorporated into the guidelines of the European Association of Urology (EAU), the International Consultation on Incontinence (ICI) [14,15], and the National Institute for Health and Clinical Excellence (NICE). SNM was not initially considered for neurogenic bladder dysfunction and still its value in such patients is unclear, although various studies have proposed its effectiveness in neurological patients [16,17], which again is supported by the responses of some well-selected neurogenic cases in the present study. In fact, patients with refractory idiopathic disorders were our initial target at the beginning of the study, but later, patients with disorders of neurogenic origin were also incorporated, as we had a lot of referred cases, especially of those with spinal cord pathologies.

Statistically, the cure rate showed some non-significant association with age and sex, which does not agree with other studies, where a higher cure rate was associated with younger patients [17].

There was significant indication inconsistency and an almost non-significant difference in response rates to SNM in diverse groups of patients with functional bladder disorders included and treated in the present study. This may be attributed to the fact that the indications for SNM are not absolute and depend on the surgeon preference (selection criteria and experience of the surgeon) and patient's desires. However, the highest rate of response was amongst patients with poor emptying, which has been previously reported [18].

As a consequence of being a minimally invasive technique, there were no major complications with SNM. The complications seen in our present series fell in to three categories: infections, mechanical problems, and response-related dysfunction. Such types and rates of complications have been reported before [19]. No clear explanation has been reported for the drop in response over time, apart from IPG dysfunction; however, one interesting study reported that different brain areas were affected during chronic and acute SNM, and this may account for the change in response seen in some patients over time [20]. This could also explain why some of our patients showed a difference in response over time, whether positively or negatively.

With the increased use of SNM, other incidental improvements have been found for other pathological disorders, e.g. off-label use in the treatment of interstitial



cystitis [21]. This agrees with our present results, where some extra-urinary benefits were gained, e.g. improved power grade of the lower limbs in a patient with a ballistic incomplete spinal cord injury, which could offer a base for more studies into these extra-urinary benefits in the future.

## Conclusions

SNM offers a good and durable solution for some lower urinary tract functional problems, if patients are well selected. It is minimally invasive with limited complications and offers a good testing period for evaluation of results. There may also be additional extra-urinary benefits that contribute to improvements in QoL. Despite its recent introduction in Iraq, SNM was well accepted by our patients seeking a minimally invasive and durable treatment option, with an encouraging response rate, especially in psychologically stable patients with idiopathic dysfunctions.

## Conflict of interest

None.

## Funding

None.

## References

- [1] Li LF, Ka-Kit Leung G, Lui WM. Sacral nerve stimulation for neurogenic bladder. *World Neurosurg* 2016;**90**:236–43.
- [2] Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. *Urology* 2003;**61**:37–49.
- [3] Drossaerts J, Rademakers K, van Koevinge G, van Kerrebroeck P. The value of urodynamic tools to guide patient selection in sacral neuromodulation. *World J Urol* 2015;**33**:1889–95.
- [4] Kessler TM, Wöllner J, Kozomara M, Mordasini L, Mehnert U. Sacral neuromodulation for neurogenic bladder dysfunction. *Urologe A* 2012;**51**:179–83 [Article in German].
- [5] Van Kerrebroeck PE, Marcelissen TA. Sacral neuromodulation for lower urinary tract dysfunction. *World J Urol* 2012;**30**:445–50.
- [6] Hassouna MM, Siegel SW, Njeholt AA, Elhilali MM, van Kerrebroeck PE, Das AK, et al. Sacral neuromodulation in the treatment of urgency-frequency symptoms: a multicenter study on efficacy and safety. *J Urol* 2000;**163**:1849–54.
- [7] Brazzelli M, Murray A, Fraser C. Efficacy and safety of sacral nerve stimulation for urinary urge incontinence: a systematic review. *J Urol* 2006;**175**:835–41.
- [8] Siddiqui NY, Wu JM, Amundsen CL. Efficacy and adverse events of sacral nerve stimulation for overactive bladder: A systematic review. *Neurourol Urodyn* 2010;**29**:S18–23.
- [9] Weil EH, Ruiz-Cerdá JL, Eerdmans PH, Janknegt RA, Van Kerrebroeck PE. Clinical results of sacral Neuromodulation for chronic voiding dysfunction using unilateral sacral foramen electrodes. *World J Urol* 1998;**16**:313–21.
- [10] Bosch JL, Groen J. Sacral nerve neuromodulation in the treatment of patients with refractory motor urge incontinence: long-term results of a prospective longitudinal study. *J Urol* 2000;**163**:1219–22.
- [11] Vapnek JM, Schmidt RA. Restoration of voiding in chronic urinary retention using neuroprosthesis. *World J Urol* 1991;**9**:142–4.
- [12] Shaker HS, Hassouna M. Sacral root neuromodulation in idiopathic nonobstructive chronic urinary retention. *J Urol* 1998;**159**:1476–8.
- [13] Amundsen CL, Romero AA, Jamison MG, Webster GD. Sacral neuromodulation for intractable urge incontinence: are there factors associated with cure? *Urology* 2005;**66**:746–50.
- [14] van Kerrebroeck PE, van Voskuilen AC, Heesakkers JP, Lycklama á Nijholt AA, Siegel S, Jonas U, et al. Results of sacral neuromodulation therapy for urinary voiding dysfunction: outcomes of a prospective, worldwide clinical study. *J Urol* 2007;**178**:2029–34.
- [15] Abrams P, Andersson KE, Birder L, Brubaker L, Cardozo L, Chapple C, et al. Fourth International Consultation on Incontinence Recommendations of the International Scientific Committee: evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. *Neurourol Urodyn* 2010;**29**:213–40.
- [16] Wallace PA, Lane FL, Noblett KL. Sacral nerve neuromodulation in patients with underlying neurologic disease. *Am J Obstet Gynecol* 2007;**197**(96):91–5.
- [17] Chartier-Kastler EJ, Ruud Bosch JL, Perrigot M, Chancellor F, Richard F, Denys P. Long-term results of sacral nerve stimulation (S3) for the treatment of neurogenic refractory urge incontinence related to detrusor hyperreflexia. *J Urol* 2000;**164**:1476–80.
- [18] Peeters K, Sahai A, De Ridder D, Van Der Aa F. Long-term follow-up of sacral neuromodulation for lower urinary tract dysfunction. *BJU Int* 2014;**113**:789–94.
- [19] Blandon RE, Gebhart JB, Lightner DJ, Klingele CJ. Re-operation rates after permanent sacral nerve stimulation for refractory voiding dysfunction in women. *BJU Int* 2008;**101**:1119–23.
- [20] Blok BF, Groen J, Bosch JL, Veltman DJ, Lammertsma AA. Different brain effects during chronic and acute sacral neuromodulation in urge incontinent patients with implanted neurostimulators. *BJU Int* 2006;**98**:1238–43.
- [21] Van Kerrebroeck PE. Advances in the role of sacral nerve neuromodulation in lower urinary tract symptoms. *Int Urogynecol J Pelvic Floor Dysfunct* 2010;**21**(Suppl. 2):S467–74.