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Efficacy and Safety of Sacral Neuromodulation in Patients with Lower Urinary Tract Dysfunction: A Five-Year Experience in North Cyprus

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Abstract

BACKGROUND/AIMS: Sacral neuromodulation (SNM) therapy is a well-tolerated treatment modality for voiding dysfunctions. The aim of this study was to evaluate the efficacy and safety of SNM in patients with voiding dysfunction in the Turkish Republic of Northern Cyprus (TRNC) and to share our current experience.

MATERIALS AND METHODS: This retrospective study included a cohort of 39 patients who received SNM treatment between April 2018 and December 2023. Patients diagnosed with urinary retention and bladder overactivity were included in the study. History of the disease and etiologies, urinalysis, residual voiding volume, voiding diaries, global response assessment scale, and complications in response to treatment were analyzed.

RESULTS: The study included 39 participants (27 females and 12 males, with a mean age of 60.2±10.9 years. Overall, the treatment success rate was 65.7%. The average duration for implanting leads was 40.8±7.9 minutes. There were no reported cases of infection. However, electrode migration occurred in 2.8% of cases, and device-related pain occurred in 10.3%. The post-void residual volume in patients with urinary retention decreased from >200 mL to <100 mL following treatment. The typical number of urinary incontinence episodes among patients with OAB was 5±2 per day, which significantly decreased to 2.6±1.27 per day following treatment.

CONCLUSION: SNM is a reliable and safe treatment method for patients who are suitable for this treatment. In TRNC, the necessary infrastructure and technical support are available to treat and monitor patients and manage potential complications. However, to achieve higher success rates and more robustly analyzed treatment outcomes, multicenter randomized trials and studies with larger sample sizes are required.

Keywords: Lower urinary tract symptoms, overactive bladder syndrome, sacral neuromodulation, urinary retention, voiding dysfunction

INTRODUCTION

Sacral neuromodulation (SNM) is an innovative treatment for lower urinary and bowel dysfunction that differs from conventional therapies.[1,2] This minimally invasive treatment involves electrical stimulation of the sacral nerves to restore pelvic organ function. This treatment modality has been successfully applied in the Turkish Republic of Northern Cyprus (TRNC) in the last 5 years, and a patient cohort has been established.

The development of SNM can be traced back to the early 1980s. Tanagho and Schmidt's[3] groundbreaking contributions laid the foundation for this field, showcasing the therapeutic potential of electrical stimulation of sacral nerve roots in treating urinary incontinence. The same stimuli affect neural pathways that govern fundamental processes, including urinary and fecal retention, and have demonstrated efficacy in treating dysfunctional conditions. Nevertheless, the precise mechanism of action underlying SNM remains uncertain despite conjecture and speculation.

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In contrast, rather than directly stimulating the detrusor or urethral sphincter for motor purposes, it is posited to influence spinal cord reflexes and cerebral involvement by modulating afferent signaling. The widely accepted theory suggests that SNM blocks or disrupts afferent input to the sacral spinal cord, thereby inhibiting detrusor overactivity and ultimately relieving urinary frequency and urgency symptoms. Since then, technological advances and clinical research have focused on expanding the efficacy and applications of this method.

Experience in the North Cyprus

SNM therapy has been sanctioned by the Food and Drug Administration (FDA) since 1997, and over two hundred thousand patients have been implanted with it.[4] SNM is a treatment modality that has been used for more than 375,000 patients worldwide. Healthcare advancements in TRNC are commensurate to those in the Republic of Türkiye. Reimbursement approval for SNM was granted to Türkiye's healthcare system in 2007. During the years 2007-2013, there was a transitional period for reimbursement, but the path was subsequently cleared for this treatment approach.[5] In 2016, a local distributor and a medical company providing technical support began operations in the field of SNM in the TRNC, resulting in the establishment of appropriate conditions. Consequently, the first SNM for bladder overactivity was performed in 2018. Subsequently, it was applied in tens of cases of TRNC in the field of urology due to overactive bladder (OAB) and urinary retention, and in the field of general surgery, it was used once in the treatment of fecal incontinence.

Our research focused on patients receiving minimally invasive SNM for urologic problems in TRNC. The aim of our study was to evaluate the efficacy and reliability of SNM in patients with voiding dysfunction and to investigate their concordance with the literature.

MATERIALS AND METHODS

Study Design

This retrospective study included a cohort of 39 patients who received SNM therapy between April 2018 and December 2023 in North Cyprus. The patients were diagnosed with urinary retention and OAB. The study collected a range of information, including a detailed history of the disease, urinalysis, post-voiding residual urine, voiding diary, specific evaluations (such as the OAB symptom score, number of urinary incontinence, number of pads, number of catheterizations, and residual urine amount measured by the catheter), global response assessment scale, and etiologies of all patients.

*Urodynamics study results were not included in the dataset.

*Urodynamic evaluation may help identify and direct therapeutic interventions for patients with OAB and urinary retention. Nevertheless, it is not typically advised before SNM. In our series, urodynamic assessments were not conducted in all patients; thus, their outcomes were not considered in the study.

Eligibility Criteria

Patients without sex discrimination or an age limit were included in the study. The presence of neurogenic disorders or diabetes mellitus did not hinder patient participation. Only patients aged 18 years were excluded. During patient selection, patients with mental and psychological disorders who might have follow-up problems were not offered SNM treatment. For male patients, the exclusion criteria included concurrent or known benign prostatic hyperplasia, as well as active or inactive urinary tract calculi in both sexes. Furthermore, the presence of either functional or anatomical urethral stricture, which represents intravesical obstruction in both males and females, was considered sufficient for the exclusion of participants from the study.

Ethical Considerations

Patients were informed of the surgical procedure and provided consent forms prior to treatment initiation. This study adhered to the ethical guidelines established by the Declaration of Helsinki and was approved by the Ethics Committee of Dr. Burhan Nalbantoglu State Hospital (approval number: 20/24).

Statistical Analysis

Descriptive statistics were used to analyze the characteristic features. Categorical data were expressed as numbers (n) and percentages, whereas quantitative data were presented as mean ± standard deviation. Categorical variables were compared using the chi-square test between groups if the groups were independent. For all statistical analyses, a p-value 0.05 was considered statistically significant. Data analysis was performed using SPSS Windows, version 28.0.

Treatment and Follow-up Protocols

All patients received SNM treatment in two phases, with an Interstim™ II. Before 2021, the tined lead electrode was not MRI-compatible. In the first stage, the treatment effect was evaluated using an external pulse-generating device. The initial test phase was performed using prophylactic antibiotics under sedation and in the prone position. The position and covering of the patient are such that the anus and bilateral feet are clearly visible and observable. For entry, the appropriate entry point is marked bilaterally under 90-degree fluoroscopic guidance. After the most important stage for navigation is achieved, local anesthesia is provided using prilocaine for the marked points (A path is followed in accordance with the H technique described by Matzel).[6] Fluoroscopy (C-Arm) was performed at an angle of 180°, and the access needle was inserted into sacral 3 foramen under sagittal imaging at an angle of 60°. Subsequently, the muscles around the anus were observed to contract simultaneously during plantar flexion or flexion of the thumb on the same side, following external electrical stimulation. In the event of an undesirable response or omission of input, the input point is altered, and the optimal response is pursued. We strived to provide responses below 2 mA in magnitude. After ensuring the location of the needle, the guidewire was sent. Subsequently, the tract was dilated and a 4-pole electrode was inserted. The initial phase, known as the test period, extends over a duration-2-3 weeks. In cases in which patients exhibited a benefit of 50% or more during this phase, the permanent implantation phase commenced. The following implantable pulse generator (IPG) implantation, patients were regularly monitored through clinical evaluations. The occurrence of wound infection, pain at the wound site, reflected pain, electrode migration, and shifts in the benefit rate have all been documented. Therefore, adjustments or complexities that may arise in subsequent appointments could necessitate therapeutic interventions, program alterations, or IPG removal.

RESULTS

The study included 27 female and 12 male patients. The average age was 60.2±10.9 years, with the youngest patient being 33 years old and the oldest being 86 years old. The mean body mass index (BMI) of the participants was 26.96±3.1. Seven patients received treatment for urinary retention and 32 for an OAB. In 31 patients, the underlying etiology was idiopathic, whereas in eight patients, it was neurological (three patients with multiple sclerosis, four patients with spinal cord trauma, and one multiple spinal disc hernia operation). The distribution of leads was 26 on the right side and 13 on the left. The average time for lead placement was 40.8±7.9 minutes, and the first stage assessment was conducted 16.7±3.2 days after placement. Table 1 summarizes the patient characteristics according to indication.

Three patients underwent tined-lead electrode removal due to unsuccessful treatment outcomes. Of the patients who underwent lead electrode removal in the first stage, two had neurologic etiology, and one had idiopathic etiology. In 2 patients with neurogenic etiology, urinary retention was indicated, whereas the other patient received SNM treatment for OAB. The remaining 36 patients were treated with permanent IPG. While monitoring these patients, several complications arose, including battery failure in one patient (2.8%) and restless leg syndrome in another patient, at a rate of 2.8%. Furthermore, four patients experienced pain and discomfort at the time of IPG implantation. The IPG of the patient with battery failure was replaced with local anesthesia. The revised program for patients with restless legs syndrome resolved these complications. Two patients who experienced pain at the IPG site underwent IPG removal. Before treatment initiation, seven individuals diagnosed with OAB exhibited a recurrent history of urinary tract infections. Five of the patients no longer experienced recurrent tract infections after treatment. The remaining two patients are currently receiving antibiotic suppression therapy. The mean number of urinary incontinence episodes in patients with OAB was 5±2 per day, which decreased to 2.6±1.27 per day following treatment. This decrease was statistically significant. According to our data, among patients with urinary retention, two individuals had a post-void residual volume of >200 mL, while two others had a 150-200 mL volume. All patients showed significant improvement after treatment, with a post-void residual volume of 100 mL. No patient required clean intermittent catheterization before or after surgery. One patient who rarely experienced stress incontinence was cured.

The overall success rate was 65.7% for all patients who underwent SNM and were followed up. Of the patients who were followed up and treated with IPG, 30 had OAB and 4 had urinary retention at baseline. The treatment success rates were 65.8% and 65.25% for patients with OAB and urinary retention, respectively. There were no statistically significant differences in the success rates between the diagnoses of OAB and urinary retention. A significant difference ($p<0.05$) was observed in the comparison of the global response assessment before and after treatment between the OAB and urinary retention groups. In the evaluation of the 39 patients included in the study, age (0.07) and indication (0.37) had a significant effect on treatment outcomes, as determined by the linear regression test. Our model indicates that the indications for surgery and age play significant roles in predicting postoperative outcomes, whereas sex, BMI, and etiology did not show a significant effect in our patient cohort.

One patient required battery replacement throughout the monitoring period because of battery depletion at 42 months. One female patient (the youngest among them) turned off her IPG due to pregnancy. The following delivery, she reported no OAB symptoms and continued to be monitored while in the off position.

DISCUSSION

SNM therapy has been approved by the FDA for the treatment of refractory OAB syndrome and urinary retention.[7,8] Additionally, it has been used for off-label purposes, such as chronic pelvic pain and sexual dysfunction.[8,9] SNM therapy is not a conventional treatment method, and as a result, it is both intriguing and controversial for physicians and patients alike. Despite potential complications, SNM therapy is generally well tolerated and has promising success rates compared with medical and surgical treatments. In line with international guidelines, SNM therapy has been used as a third-line treatment for resistant dysfunctional voiding in the TRNC since 2018. Our patient series showed that OAB accounted for 82.1% of the cases and urinary retention accounted for 17.9%. The patient selection tended to follow a ratio of approximately 4:1 for OAB and urinary retention.

The fact that the durability of SNM treatment was extended to 60 months indicates that it is advantageous in terms of cost-effectiveness.[2] In our research, the inability to conduct a 60-month follow-up period

Table 1. Patient characteristics according to indications

Overactive bladder syndrome		**Urinary retention**	
Variable	**Value**	**Variable**	**Value**
Total number of patients			
Sex, n (%)			
- Male	8 (25%)	- Male	4 (57.1%)
- Female	24 (75%)	- Female	3 (42.8%)
Age (years)	59.4	Age (years)	60
BMI (kg/m^2)	26.8	BMI (kg/m2)	27.7
Etiology, n (%)			
- Idiopathic	27 (84.3%)	- Idiopathic	5 (71.4%)
- Neurogenic	5 (15.6%)	- Neurogenic	2 (28.5%)
Follow-up (months)	29 (6-51)	Follow-up (months)	24 (4-35)

BMI: Body mass index.

precluded us from conducting this assessment. Nonetheless, battery replacement was required in one patient (2.9%) during the follow-up period, which lasted for 42 months. Pretreatment anxiety often includes the need for repeated surgical interventions. The integration of long-lasting batteries and wireless charging technologies into these devices will increase their cost-effectiveness and reduce patient anxiety.

In the treatment of OAB, the improvement in symptoms from SNM reported in case series and randomized trials ranges from 64% to 88%.[10] In our study, the improvement in OAB was 65.8%, which is consistent with the findings reported in the literature. However, although recovery rates of 45-50% have been reported for urinary retention,[11] a higher rate of 65.25% was found in our study. The rationale for this conclusion can be defended by the careful selection of indications to identify subgroups. Nevertheless, in our view, the reason lies in the fact that our series consisted of only four patients, leading to a random outcome. It is worth mentioning that most patients who did not show improvement experienced urinary retention.

Infection at the site of IPG is noted in the literature, with a rate ranging between 8-11%.[12,13] The overall complication rate was 17.9%. Pain at the IPG site was 12.8%, whereas infection at the IPG site was not observed. This may be explained by the perioperative use of prophylactic antibiotics and their maintenance during the postoperative period. Technically, no different methods are used during IPG site preparation and IPG implantation.

Tined lead electrode dislocation or migration varies between 12% and 16% in the literature. In this study, tined lead electrode migration requiring revision was observed in only one patient (2.9%). Following a successful revision, the patient who developed complications was still receiving SNM treatment and benefited from this treatment (Figures 1,2). We believe that the disparity with the existing research can be primarily attributed to the small sample size of patients and the use of only tined lead electrodes.

The necessity for revisions during SNM treatment for patients, particularly in extensive series, occurs because of several factors. However, despite its effectiveness, safety, and well-tolerated nature, the need for revisions remains high.[14,15] In our series, revision rates were somewhat lower. The assessment suggests that the rigidity of patient selection and the comparatively shallow depth of patient selection diminish the necessity for revision. Consequently, as the number of our patients increases and our indications broaden, the number of individuals who may require revision may also increase. Hence, the divergence of our findings from the literature, particularly concerning complications, can be attributed to our restricted sample and the criteria employed in patient selection.

Study Limitations

This study has some limitations that should be considered. First, the retrospective study design may have influenced the results. Second, the small sample size and lack of homogeneity among the participants were factors that could affect the outcomes. Moreover, the absence of long-term follow-up and insufficient in-depth patient selection are additional limitations of the present study. The need for larger multicenter studies to further investigate the results and compare them with those of other studies is also highlighted.

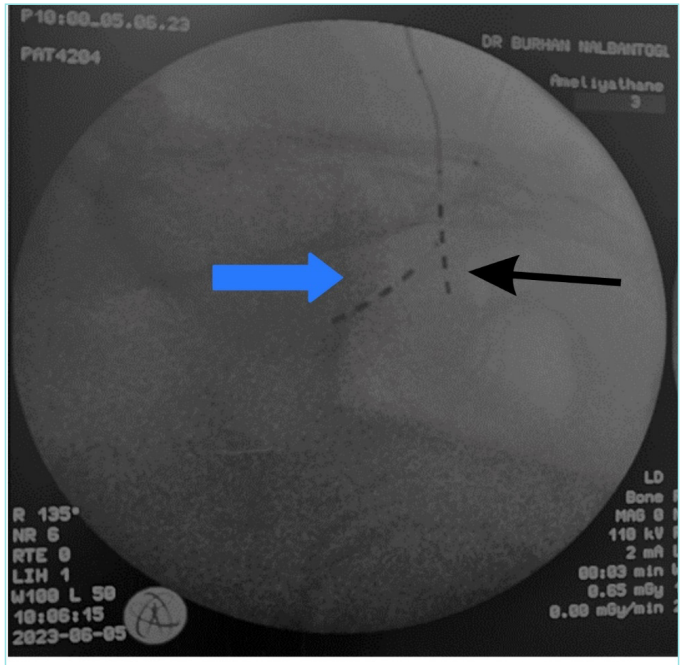

Figure 1. Migration of tined lead electrode. Note: The migration of the tined lead electrode (indicated by the blue arrow) can be visually monitored along with the fluoroscopic image of the newly implanted lead electrode (identified by the black arrow).

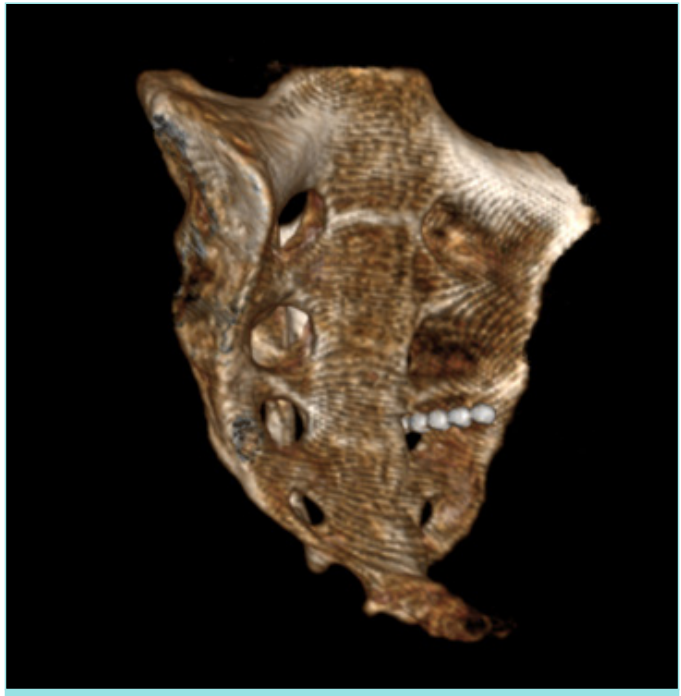

Figure 2. 3D computed tomography images of SNM. Note: 3D computed tomography image showing the appearance following successful lead electrode revision (white).

SNM: Sacral neuromodulation

CONCLUSION

Based on our findings, we conclude that SNM is safe and effective for suitable patients. The necessary infrastructure and technical support required to treat, monitor, and manage potential complications in patients are currently available, and TRNC's success rate for urinary retention is close to the success rate in OAB syndrome, according to our patient series. Undoubtedly, multicenter studies that incorporate control groups and larger sample sizes are necessary to achieve higher success rates and more robust analyses of treatment outcomes.

MAIN POINTS

- Efficacy and safety: Sacral neuromodulation (SNM) has been evaluated as an effective and safe treatment modality for patients with voiding dysfunction in the North Cyprus. The results demonstrate high success rates for managing both urinary retention and overactive bladder, with an overall effectiveness rate of 65.7%.
- Implementation and follow-up: SNM therapy consists of a two-step process: Initially, the effectiveness of the treatment is assessed with the help of an external pulse generator, followed by permanent implantation in patients who show a positive response. Regular follow-up appointments and proper technique programing primarily influence treatment success and the management of complications.
- Infrastructure and technical support: The necessary infrastructure and technical support for SNM are well established in the North Cyprus, facilitating the application of this treatment.
- Recommendations and future research: This study not only represents the first instance of collecting data from patients with voiding dysfunction in the North Cyprus, but it also contributes to the development of future research and patient groups. Furthermore, broadening the scope of the study's indications and conducting joint multicenter research could increase the number of patients who could benefit from these efforts.

ETHICS

Ethics Committee Approval: This study adhered to the ethical guidelines established by the Declaration of Helsinki and was approved by the Ethics Committee of Dr. Burhan Nalbantoglu State Hospital (approval number: 20/24).

Informed Consent: Patients were informed of the surgical procedure and provided consent forms prior to treatment initiation.

DISCLOSURES

Financial Disclosure: The author declared that this study had received no financial support.

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