Neuromodulation – a therapeutic option for refractory overactive bladder. A recent literature review

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Abstract
Overactive bladder (OAB) affects approximately 17% of the population. The treatment of this clinical condition is challenging, especially when conservative therapy is not effective. There are limited options for the treatment of recurrent OAB. Neuromodulation has taken a significant place in the therapy of recalcitrant lower urinary tract dysfunctions over the past 20 years. The aim of this study was to review the literature evaluating the different forms of neuromodulation in various urological clinical conditions and to show the future prospects of this treatment method. Further studies are necessary to determine the effectiveness of neuromodulation and to identify the prognostic factors of therapeutic success. This could be helpful in the selection of patients who will be most likely to respond positively to the treatment.

Key words: urinary incontinence, overactive bladder, sacral neuromodulation, percutaneous tibial nerve modulation, refractory voiding dysfunction.

Introduction
Overactive bladder (OAB) is defined as urinary urgency, usually accompanied by frequency and nocturia, with or without urinary incontinence, in the absence of a urinary tract infection or other obvious pathology [1]. The National Overactive Bladder Evaluation (NOBLE) study showed that the overall prevalence of OAB in the USA was similar between men and women, 16.0% and 16.9%, respectively [2]. The treatment of OAB is usually multi-stage. Behavioral changes such as fluid intake modification, coffee drinking reduction, moderate physical activity, pelvic floor muscle training, and body mass reduction constitute the first line of therapy. Pharmacotherapy is the second line. Anticholinergic and β-adrenergic drugs are the gold standard in the treatment of OAB. However, this kind of therapy is often limited by adverse effects such as dry mouth, constipation, nausea, blurred vision, and cardiovascular disorders. Due to adverse effects, more than 70% of patients cease pharmacotherapy within 6 months to 3 years. Moreover, the same studies show a discontinuation rate of 43–83% within the first 30 days [3–5]. Botulinum toxin A (BTX-A) intra-detrusor injections and neuromodulation are third-line therapies of OAB. Neuromodulation is an alternative therapy for patients who are awaiting for a long-term positive therapeutic response with a reduced risk of difficulties with the emptying of the bladder [6].

Aim
The aim of this study was to review the literature evaluating the different forms of neuromodulation in various urological clinical conditions and to show the future prospects of this treatment method.
Methods

A literature search was performed in December 2018 in the databases MEDLINE and Embase from 1988 to 2018. The search was limited to humans and literature in the English language. The studies evaluating the efficacy and safety of the different forms of neuromodulation for overactive bladder and urinary dysfunction were identified using various MeSH headings.

Results

To evaluate the efficacy of sacral neuromodulation (SNM) and percutaneous posterior tibial nerve stimulation (P-PTNS), a substantial number of studies published after year 2000 were reviewed. Four prospective case series and one retrospective case series were identified with reference to the four SNM randomized trials (Table I), and five randomized trials and one prospective case series were found in relation to the efficacy assessment of the P-PTNS procedure (Table II). The sample size and follow-up periods were heterogeneous with a median sample size of 192 (range: 34–272) and a median follow-up of 21 months (range: 6–114 months) for SNM and with a median sample size of 52 (range: 35–220) and median follow-up of 12 weeks (range: 12–144 weeks) for P-PTNS.

Discussion

The first neuromodulation procedure was performed in 1954 as deep brain stimulation (DBS) for the treatment of chronic pain [7]. In 1988, Tanagho and Schmidt introduced sacral neuromodulation (SNM) for lower urinary tract dysfunction (LUTD) therapy, including OAB treatment [8]. The Food and Drug Administration (FDA) approved SNM for the treatment of refractory OAB, frequency, and non-obstructive post-void residual urinary retention in 1997 and 1999.

The mechanism of action of neuromodulation is still unclear. The stimulation of the afferent pathways probably restores the balance in stimulatory and inhibitory signals going bidirectionally between pelvic organs, sacral neurons, and the CNS [9]. Moreover, some authors suggest that opioid receptors play an important role in inhibiting bladder overactivity during SNM [10]. Al-Shaiji et al. propose three possible mechanisms of action [11]:

1. Stimulation of the pudendal nerve inhibits detrusor activity and increases external anal sphincter tone, thus facilitating urine storage.
2. Stimulation of the sacral nerve causes a rapid contraction of the bladder followed by longer-lasting relaxation; thus, detrusor overactivity can be reduced by repetitive, recurrent electrical impulses.
3. Stimulation of afferent sacral nerves in the pelvis or lower extremities inhibits the signals in the effenter pelvic nerve, thus decreasing detrusor overactivity.

Wenzler et al. [12] described an interesting study that tried to explain the impact of SNM on the bladder. They assessed the current perception threshold (CPT) on the urethra of eight women prior to and after SNM at 5 Hz (C-fibers), 250 Hz (Aδ-fibers), and 2000 Hz (Aβ-fibers). The most detectable reduction of bladder sensitivity was noted at 250 and 2000 Hz, suggesting that they have the greatest impact on large myelinated nerves. Surprisingly, no changes were found in C-fiber CPT measurements, although C-fibers are thought to be involved in the development of OAB. The authors conclude that SNM alters the sensory function of the bladder, activating more than only one nerve type. Other authors have tried to define the role of the urethra in overactive bladder. They assessed the impact of SNM on periurethral sensation and urethral sphincter activity. The study showed no changes in urethral neuromuscular function two weeks after stage 1 implantation; however, the authors conclude that women with more successful urethral reinnervation may be more responsive to neuromodulation [13]. Shalom et al. [14] analyzed urinary nerve growth factor (uNGF) levels in urine as a biomarker useful in the monitoring of OAB therapy. uNGF has been found in the urothelium, the detrusor smooth muscle, and in the urine. The level of uNGF is higher in patients with OAB and its decrease reflects a positive therapeutic response. uNGF affects the expression of Na- and K-ion channels sensitizing afferent C-fibers, and thus is involved in OAB pathophysiology. The authors evaluated urine uNGF levels in 17 women with OAB treated with SNM. A significant decrease of uNGF correlating with signs and symptoms reduction, which was shown in the Incontinence Quality of Life Questionnaire (I-QOL), the Urinary Distress Inventory (UDI-6), and in a micturition diary, was noted in all patients.

The kind of neuromodulation depends on the electrode placement and on the stimulated nerve [15].
### Table I. Efficacy and adverse effects of SNM

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Effectiveness</th>
<th>Quality of life assessment</th>
<th>Adverse effects</th>
<th>Re-interventions</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peeters et al. [39]</td>
<td>Prospective follow-up</td>
<td>217</td>
<td>70% in UUI</td>
<td>Not reported</td>
<td>5% implantation site infection or hematoma</td>
<td>41% overall</td>
<td>Mean of 46.88 months</td>
</tr>
<tr>
<td>Weil et al. [45]</td>
<td>RCT</td>
<td>21 SNM/23 SMT – eligible for crossover to implant after 6 months</td>
<td>88% in UUI</td>
<td>Not reported</td>
<td>42% pain</td>
<td>38% revisions for AE</td>
<td>Mean of 18 months</td>
</tr>
<tr>
<td>Siegel et al. [44]</td>
<td>RCT</td>
<td>70 SNM/77 SMT</td>
<td>71% in UUI</td>
<td>86% improved (ICIQ-OABqol)</td>
<td>30.5% overall</td>
<td>3.9% revision</td>
<td>6 months</td>
</tr>
<tr>
<td>Amundsen et al. [46]</td>
<td>RCT</td>
<td>189 SNM/192 onabotulinumtoxinA</td>
<td>26% in UUI</td>
<td>Improved (OABQ-SF, OAB-STQ, UDI-SF, ICIQ-IIQ-SF)</td>
<td>11% UTI</td>
<td>3% revision or explantation</td>
<td>6 months</td>
</tr>
<tr>
<td>Amundsen et al. [47]</td>
<td>RCT</td>
<td>194 SNM/192 onabotulinumtoxinA</td>
<td>21% in UUI</td>
<td>Improved (OABQ-SF, OAB-STQ, UDI-SF, ICIQ-IIQ-SF)</td>
<td>10.4% UTI</td>
<td>3% revision</td>
<td>24 months</td>
</tr>
<tr>
<td>Noblett et al. [41]</td>
<td>Prospective follow-up</td>
<td>272</td>
<td>74–81% in UUI</td>
<td>Improved (ICIQ-OABqol, HRQoL)</td>
<td>22% change in stimulation</td>
<td>Not reported</td>
<td>24 months</td>
</tr>
<tr>
<td>Jairam et al. [40]</td>
<td>Prospective follow-up</td>
<td>95</td>
<td>59% overall</td>
<td>Not reported</td>
<td>47% revision</td>
<td>Not reported</td>
<td>Mean of 1.77 years</td>
</tr>
<tr>
<td>Siegel et al. [42]</td>
<td>Prospective follow-up</td>
<td>272</td>
<td>67% overall</td>
<td>Improved (HADS, HRQoL, SF-36, ICIQ-OABqol, ICIQ-M/F LUTS)</td>
<td>2% change in stimulation</td>
<td>Not reported</td>
<td>5 years</td>
</tr>
<tr>
<td>Siegel et al. [42]</td>
<td>InSite trial</td>
<td></td>
<td>64% in UUI</td>
<td>84% improved (ICIQ-OABqol)</td>
<td>33.5% battery replacement</td>
<td>30.9% reintervention due to AE</td>
<td>19.9% explantation</td>
</tr>
<tr>
<td>Ismail et al. [43]</td>
<td>Retrospective study</td>
<td>34</td>
<td>63% overall</td>
<td>Not reported</td>
<td>81.8% battery dysfunction</td>
<td>47% revision</td>
<td>Mean of 9.7 years</td>
</tr>
</tbody>
</table>
Table I. Cont.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Effectiveness</th>
<th>Quality of life assessment</th>
<th>Adverse effects</th>
<th>Re-interventions</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Zahrani et al. [61]</td>
<td>Retrospective</td>
<td>96</td>
<td>84.8% in UUI</td>
<td>Not reported</td>
<td>12.5 ineffectiveness</td>
<td>39% revision</td>
<td>Median of 50.7 months</td>
</tr>
<tr>
<td></td>
<td>study</td>
<td></td>
<td>87.5% in IUR</td>
<td></td>
<td>6.3 pain</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Table II. Efficacy and adverse effects of PTNS

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Effectiveness</th>
<th>Quality of life assessment</th>
<th>Adverse effects</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finazzi-Agro et al. [24]</td>
<td>RCT</td>
<td>18 PTNS/17 placebo</td>
<td>71% in UUI/0%</td>
<td>Improved</td>
<td>Occasional transient pain at the stimulation site</td>
<td>Not reported</td>
</tr>
<tr>
<td>Peters et al. [25]</td>
<td>SUmiT trial</td>
<td>110 PTNS/110 sham</td>
<td>54.5% overall/20.9%</td>
<td>Improved (OAB-q HRQoL)</td>
<td>0.9% ankle bruising</td>
<td>13 weeks</td>
</tr>
<tr>
<td>Peters et al. [27]</td>
<td>OrBIT trial</td>
<td>49 PTNS/49 4 mg ER-tolterodine</td>
<td>79.5% overall/54.8%</td>
<td>Improvement (OAB-q)</td>
<td>1.8% discomfort at the needle site 2.7% bleeding 0.9% tingling</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Preyer et al. [28]</td>
<td>RCT</td>
<td>18 PTNS/18 2 mg tolterodine twice-daily</td>
<td>Reduction of incontinence episodes but not micturition frequencies in both groups</td>
<td>Improved (VAS)</td>
<td>17% – pain at puncture site</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Gungor Ugurlucan et al. [29]</td>
<td>RCT</td>
<td>17 PTNS/35 TES</td>
<td>Reduction of incontinence episodes in both groups. Reduction of the mean frequency of daytime micturition more significant in TES group</td>
<td>Improved (KHQ)</td>
<td>Not reported</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Peters et al. [26]</td>
<td>STEP study</td>
<td>50 PTNS</td>
<td>Reduction of median voids per day, nighttime voids and UUI episodes</td>
<td>Improved (OAB-q HRQoL)</td>
<td>4% – bleeding at the needle site 22% – moderate AEs with unknown relation to treatment</td>
<td>36 months – 29 completers</td>
</tr>
</tbody>
</table>

OAB-q – Overactive Bladder questionnaire, HRQoL – Health Related Quality of Life, VAS – Visual Analogue Scale, KHQ – King’s Health Questionnaire, TES – transvaginal electrical stimulation.
In percutaneous stimulation, the electrode perforates the skin, whereas in transcutaneous stimulation, the electrode is on the skin surface only. 

- **T-SNS** – transcutaneous sacral nerve stimulation, 
- **P-SNS** – percutaneous sacral nerve stimulation, 
- **T-PTNS** – transcutaneous posterior tibial nerve stimulation, 
- **P-PTNS** – percutaneous posterior tibial nerve stimulation.

Transcutaneous sacral nerve stimulation – historically, this stimulation refers to TENS (transcutaneous electrical nerve stimulation) in which the sacral surface electrode stimulates sacral roots S2–S4 for 30–45 min. This, in the opinion of the Guideline Development Group, National Collaborating Centre for Women’s and Children’s Health (GDG NCC-WCH) [15], is the less effective method from all the types of neuromodulation in OAB treatment. There were some papers released which showed an improvement in frequency, nocturia, urgency, and urgency urinary incontinence in patients with OAB treated with T-SNS [16, 17]. The study of Fergany et al. [18] showed that TENS was less effective than sacral pulsed electromagnetic field therapy in OAB treatment. The GDG does not recommend T-SNS in OAB treatment.

Transcutaneous posterior tibial nerve stimulation is the stimulation of the posterior tibial nerve using a surface electrode near the medial malleolus. A prospective randomized trial comparing T-PTNS with 10 mg extended release oxybutynin demonstrated similar improvements in subjects with OAB at a 12-week follow-up [19]. A systematic review from 2017 concerning the efficacy of T-PTNS in OAB therapy showed some benefits in terms of subjective outcomes and urodynamical parameters. However, due to the limited quality of evidence, further studies are necessary to determine the optimal stimulation program, the potential sustainability, and the duration of the effects for patients with OAB of idiopathic and neurogenic etiology [20].

Percutaneous posterior tibial nerve stimulation is defined as the stimulation of the posterior tibial nerve using a fine gauge needle electrode above the medial malleolus connected to a low voltage stimulator. The tibial nerve axons originate in the S2–S4 region, similar to the sensitive nerves innervating the pelvic floor muscles, the parasympathetic afferent nerves of the detrusor muscle, and the motor nerves of the pelvic floor muscles. Afferent fiber stimulation activates the suppression of the sympathetic neurons in the sacral spine. Ridout and Yoong [21] suggest that chronic peripheral stimulation of the sacral motor neurons causes the reorganization of neural control of micturition, thus bringing the correct voiding reflex back. P-PTNS in OAB treatment was discovered by McGuire in 1983 [22]. Bernstein et al. [23] extended the indications of neurostimulation to urinary incontinence, fecal incontinence, and sexual dysfunctions. The therapy takes 12 weeks in single, 30-minute sessions performed once a week. The effectiveness of P-PTNS has been compared versus a placebo and sham procedures in two randomized trials (RCTs). The study performed by Finazzi-Agro et al., as well as the SUmiT trial, revealed higher satisfaction of patients in the P-PTNS groups. There was no difference in the reduction of the number of the day/night incontinence episodes and day/night urgency episodes between the groups (high quality evidence). The studies revealed (low-quality evidence) fewer adverse effects in the placebo groups [24, 25]. Subsequently, the STEP study, continuing the follow-up of 50 P-PTNS patients from the SUmiT trial, showed sustained improvements in overactive bladder symptoms at 3 years, with an average of 1 treatment per month [26]. Furthermore, the OrBit trial, comparing P-PTNS to extended-release tolterodine 4 mg, demonstrated higher subjective cure rates and improvement rates in the percutaneous tibial nerve stimulation arm with similar rates of objective improvement [27]. There were no serious adverse events or device malfunctions. On the other hand, another RCT, which compared P-PTNS to tolterodine 2 mg twice daily, showed similar effectiveness of P-PTNS and tolterodine in reducing incontinence episodes and improving quality of life, but no impact on frequency. Moreover, P-PTNS had fewer adverse effects [28]. Finally, Gungor Ugurlucan et al. compared P-PTNS to transvaginal electrical stimulation (TES) and found a similar objective improvement across both groups, although there were significantly more patients who described themselves as cured in the TES arm [29] (Table II). The necessity of needle insertion every time constitutes a significant limitation of patient compliance. Further RCTs comparing different treatment protocols, as well as comparing P-PTNS with other anticholinergics, are needed. Due to the lack of such trials, GDG does not recommend P-PTNS in OAB therapy. However, this method could be reserved for patients with refractory OAB, who
do not agree to other invasive therapy (botulinum toxin intradetrusor injections, P-SNS) as a third line of treatment. In a recent systematic review, P-PTNS therapy has been shown to be effective at short-term follow-ups, with fewer adverse effects [30]. Further trials are necessary to define long-term efficacy and to determine other neurological indications for P-PTNS.

Percutaneous sacral nerve stimulation (sacral neuromodulation) is defined as permanent electric stimulation by an implantable lead at the S3 nerve controlling the bladder and pelvic floor muscles. Light electrical pulses are generated by the pacemaker device (battery) implanted under the gluteal skin. SNM affects the neuronal pathways by both stimulating and inhibiting a detrusor muscle. At first, the lead is secured by fascial fixation in order to prevent migration. In 2002, a self-anchoring tined lead, which decreases the axial movement of the electrode, was approved by the FDA and CE marked [31]. The implantation is performed in two phases. The aim of the first phase is to assess the initial response of the patient with an external electrostimulation device. The testing phase can be performed in two manners. In the first technique, defined as percutaneous nerve evaluation (PNE), which is usually performed under local anesthesia, a temporary unipolar electrode is placed into the S3 foramen. An external neurostimulator is taped to the skin. Good responders (at least 50% symptom improvement from the baseline) are qualified for the second step. The temporary lead is removed and a permanent quadripolar electrode with an implantable neurostimulator (INS) is placed at the same time (one-stage implant). The unipolar electrode is prone to migration, giving a relatively high rate of false negative results of PNE. A two-stage implant procedure is introduced to minimize the drawbacks of PNE and to increase the efficacy of the testing phase. In the initial stage, the permanent lead instead of the temporary lead is implanted to test the patient’s response to neuromodulation. The INS is implanted in good responders in the second stage [31–34] (Figure 1). The lead implantation in the S3 foramen is usually performed under 2D fluoroscopy. The procedure can be challenging in cases of anatomical anomalies and obesity. In such cases, Hellström et al. [35] suggest the use of an O-arm 2D/3D X-ray imaging system instead of the conventional C-arm. In 2017, a pilot study was released [36] concerning the utilization of ultrasound for the placement of the foramen needle to reduce patient and surgeon radiation exposure. An RCT comparing PNE with two-stage implantation in women with urge incontinence revealed better prediction for permanent implantation in the two-stage group [37]. The higher cost of the two-stage procedure as compared to PNE could constitute the limitation of this method. Currently, both these methods are in use. The new neurostimulators are relatively small, allowing for a smaller incision and a shallower pocket, which make implantation much easier. Moreover, the elimination of an extension cable has reduced operative time. Additionally, a small remote control programmer offers the patient the possibility to choose from up to four preset programs to optimize the response rate [38].

![Figure 1. Two-stage implant of SNM therapy. (A) Implant of the permanent lead during the testing phase for selecting responsive patients and (B) implant of the implantable neurostimulator in responsive patients [31]](image_url)
The effectiveness of SNM was confirmed in the prospective follow-up trials in which 59-81% of the main incontinence symptoms of the participants were improved or cured [39-41] (Table I). The InSite trial [42] with a 5-year follow-up reported that 38% of the patients were completely continent and 67% were improved. This is consistent with a long-term retrospective study (median follow-up of 9.7 years) performed by Ismail et al. [43], where the overall improvement was found in 63% of the participants. Jairam et al. [40] evaluated the impact of SNM on quality of life. They observed a significant decrease in depressive symptoms and a substantial increase in the Health-Related Quality of Life Score (HRQL), including the coping, concern, sleep, and social subscales in good SNM responders. In two RCTs comparing SNM versus conservative pharmacological treatment, up to 56% achieved continence and as many as 88% of the patients improved in urgency urinary incontinence (UUI) [44, 45]. On the other hand, the Rosetta trial comparing SNM to onabotulinumtoxinA revealed higher treatment satisfaction and endorsement, and greater improvement in relieving symptoms; however, this group was associated with an increased risk of urinary tract infections and need for transient self-catheterization [46]. Similar results were observed at the subsequent 2-year follow-up assessment [47]. In view of these outcomes, it seems that SNM should be offered as a next line of refractory OAB therapy if an intradetrusor injection of onabotulinumtoxinA cannot be performed.

Patients with Fowler’s syndrome could constitute a very interesting target group for SNM. This syndrome is characterized by excessive myogenic activity of the striated urethral sphincter and increased maximum urethral closure pressure (MUCP), causing urinary retention. The sphincter hyperactivity generates neural impulses that inhibit bladder afferent activity at the sacral level and deactivate the periurethral gray matter (PAG), causing a loss of bladder sensation and ability to void. SNM restores the afferent pathways of the bladder reflex by blocking the inhibition by urethral afferents at the sacral level as well as enhancing the positive response in PAG and higher cortical centers [48]. The other group of special interest is that of patients with neurogenic LUTD. Reports of SNM for neurogenic OAB are limited. It seems that SNM can constitute a safe therapeutic alternative for such patients who have undergone multiple failed treatments in their medical history. A meta-analysis performed by Kessler et al. [49], which included 357 patients with multiple sclerosis, Parkinson’s disease, cerebrovascular accidents, spinal cord injuries, and other neurogenic LUTDs, revealed a success rate of 68% for the test phase and 92% for permanent neuromodulation. Lay and Das [50] highlight that sacral neuromodulation with an implantable pulse generator (IPG) is contraindicated in neurologic disorders when an MRI would be needed. The MRI could cause heating of the leads and affect the IPG. The efficacy of SNM in neurogenic OAB was confirmed by Peters et al. in an 8-year prospective observation on 340 patients with and without neurologic dysfunctions. Both groups experienced similar benefits of treatment [51].

Another group of special interest is that of patients with persistent OAB and de novo OAB after sling surgery. The overall incidence of de novo OAB following mid-urethral sling procedures ranges between 5% and 22%, while the incidence of persistent urgency reaches 30% [52, 53]. There are limited data on the use of neuromodulation in the management of OAB after sling surgery. In the study of Sherman et al. 22 out of 34 patients with refractory UUI responded to the test stimulation and had a permanent lead implanted. The positive predictive factors were: age younger than 55 years, SNM performed within 4 years of the incontinence surgery, and evidence of pelvic floor muscle activity [54]. A similar trial was conducted by Starkman et al. [55] on 25 patients after urogynecologic surgery. The response rate was 88% (22 patients) regardless of the type and number of previous procedures. After a 6-month follow-up, 20 patients maintained > 50% improvement in clinical symptoms.

The next very special group of patients comprises pregnant women with OAB symptoms and/or urinary retention, treated with SNM. The impact of SNM on the fetus and the course of pregnancy has not been established. The ICS Sounding Board does not recommend SNM therapy during pregnancy [56]. In 2014, Mamopoulos et al. [57] reported the first case of a 34-year old pregnant woman with chronic urinary retention after a spinal cord injury. Taking into consideration the increased risk of recurrent urinary retention caused by intermittent self-catheterization, she did not agree to deactivation of the device. The course of pregnancy was uneventful. She delivered a healthy male infant at 39 weeks’ gestation by caesarean section due to breech presentation. A systematic review
published 3 years later included 26 pregnant women treated with SNM due to Fowler’s syndrome, fecal incontinence, urinary urgency and frequency, fecal and urinary urgency, urinary retention, and myelodysplasia. SNM remained active during 8 pregnancies and the next 2 were reactivated at 19- and 20-weeks’ gestation at the patients’ request. Outcomes were reported in 25 pregnancies (one resulted in a miscarriage). There were 18 full-term deliveries and 7 preterm. Caesarean section was performed in 16 cases, in 10 patients due to obstetric indications, and CS was advised in 6 cases because of SNM. Seven pregnancies with a deactivated device were complicated by recurrent urinary tract infections. After delivery, 14 SNM devices were functioning properly, while the others required reprogramming, revision, replacement or removal. Interestingly, two patients with previous OAB remained asymptomatic after SNM deactivation and requested removal of the device. There were no complications observed in the newborns that could be related to SNM. The authors conclude that the decision regarding SNM activation or deactivation during pregnancy should be individualized and all the benefits and risks must be taken into consideration [58].

The SNM procedure in the treatment of OAB has many limitations. Liberman et al. [59] present their skepticism and do not recommend this method in the treatment of overactive bladder. They highlighted the heterogeneity of the treated groups, vague indications for SNM, an overestimation of therapeutic success, as well as clinician and clinical center variability. Liberman et al. challenge the definition of the success rate as an improvement of 50% or more in symptoms during a testing phase. This criterion generates a huge heterogeneous population, including patients who may just reach the threshold while other patients may have an appreciably bigger response. Furthermore, an improvement of 50% could hardly be considered as a therapeutic success for pharmacotherapy of OAB. Thus, a more stringent definition for SNM success should be established. However, the same author predicts the future of SNM in the development of better device options, better software with more programming options, other viable nerve targets, and additional indications [60]. There is a paucity of long-term follow-ups after sacral neuromodulation. Al-Zahrani et al. [61] reported their 14-year experience on 96 patients with SNM. The explantation rate was 20.8% and implant revision was performed in 39% of the patients, mainly due to treatment inefficiency and pain. Other authors report the most frequent adverse events as: an undesirable change in stimulation, implant site pain, lead migration, therapeutic ineffectiveness, and a lower libido and problems with achieving an orgasm [42, 62, 63]. The ICS defines the absolute contraindications for SNM, which include an inadequate clinical response to a therapeutic trial, lack of efficient supportive care, and pregnancy, and the relative contraindications, such as severe or rapidly progressive neurologic disease, established complete spinal cord injury, possible need for MRI, and abnormal sacral anatomy [56].

**Conclusions**

Sacral neuromodulation constitutes an interesting therapeutic option in certain types of lower urinary tract dysfunctions. Further studies are necessary to determine the effectiveness of this method and to identify the prognostic factors of therapeutic success. This could be helpful in the selection of patients who will be most likely to respond positively to the treatment.

**Conflict of interest**

The authors declare no conflict of interest.

**References**


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