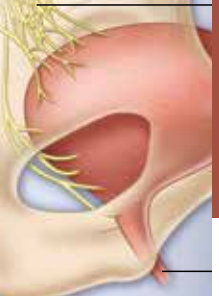

Sacral Neuromodulation for Overactive Bladder

ABSTRACT

Sacral Neuromodulation (SNM) is a FDA-approved minimally invasive surgical therapy offered as a third-line treatment for refractory overactive bladder (OAB). Studies report improvements in continence, mean number of voids/day, quality of life, depression and sexual function in patients receiving SNM compared to medical therapy, with treatment success sustained long-term and with few adverse events. SNM is recommended by CUA and AUA guidelines in the treatment of OAB in carefully selected patients.

KEYWORDS: Neuromodulation, Neurostimulation, Overactive, Bladder, Incontinence

CME Pre-test Quiz

Introduction

Overactive Bladder

Overactive Bladder (OAB) is defined as "the presence of urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of UTI or other obvious pathology".[1]

OAB is prevalent in approximately 18% of men and women aged ≥35 in Canada, and continues to rise with the ageing population.[2] OAB is associated with a reduction in patients' health-related quality of life (HRQOL), increase in healthcare costs, urinary tract infections and increased risk of falls in the elderly.[3,4] Patients may remain untreated as they may be reluctant to discuss their symptoms due to their embarrassing nature.[5]

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Symptoms & Diagnosis of OAB

Symptoms of OAB are neuromuscular in origin and caused inappropriate contraction of the detrusor muscle during bladder filling, referred to as detrusor overactivity (DO). DO may occur as a result of neurological illness or injury, or from idiopathic causes exclusive of underlying neurological, metabolic, inflammatory, obstructive, neoplastic or infectious conditions of the bladder.

ASSESSING THE SEVERITY OF BLADDER SYMPTOMS IN TERMS OF STORAGE, VOIDING AND POST-MICTURITION MAY ASSIST IN ESTABLISHING THE TYPE AND SEVERITY OF INCONTINENCE AND DEGREE OF BOTHER.

CUA and AUA guidelines recommend a detailed history, physical examination and urinalysis as minimum requirements for patients with urinary incontinence (UI) to elicit OAB symptoms and exclude other causes.[6,7] Assessing the severity of bladder symptoms in terms of storage, voiding and post-micturition may assist in establishing the type and severity of incontinence and degree of bother. Urine cultures and/or post-void residual assessment may be performed in some patients, with additional information provided from bladder diaries/symptom questionnaires.[6]

In men with OAB, a symptom and quality of life assessment is recommended together with digital rectal examination (DRE) and prostate-specific antigen (PSA) measurement.[7] Urodynamics, cystoscopy and diagnostic renal and bladder ultrasound are not recommended during initial assessment of uncomplicated cases.[6]

Treatment of OAB

The algorithm of treatment for overactive bladder is shown in figure 1.

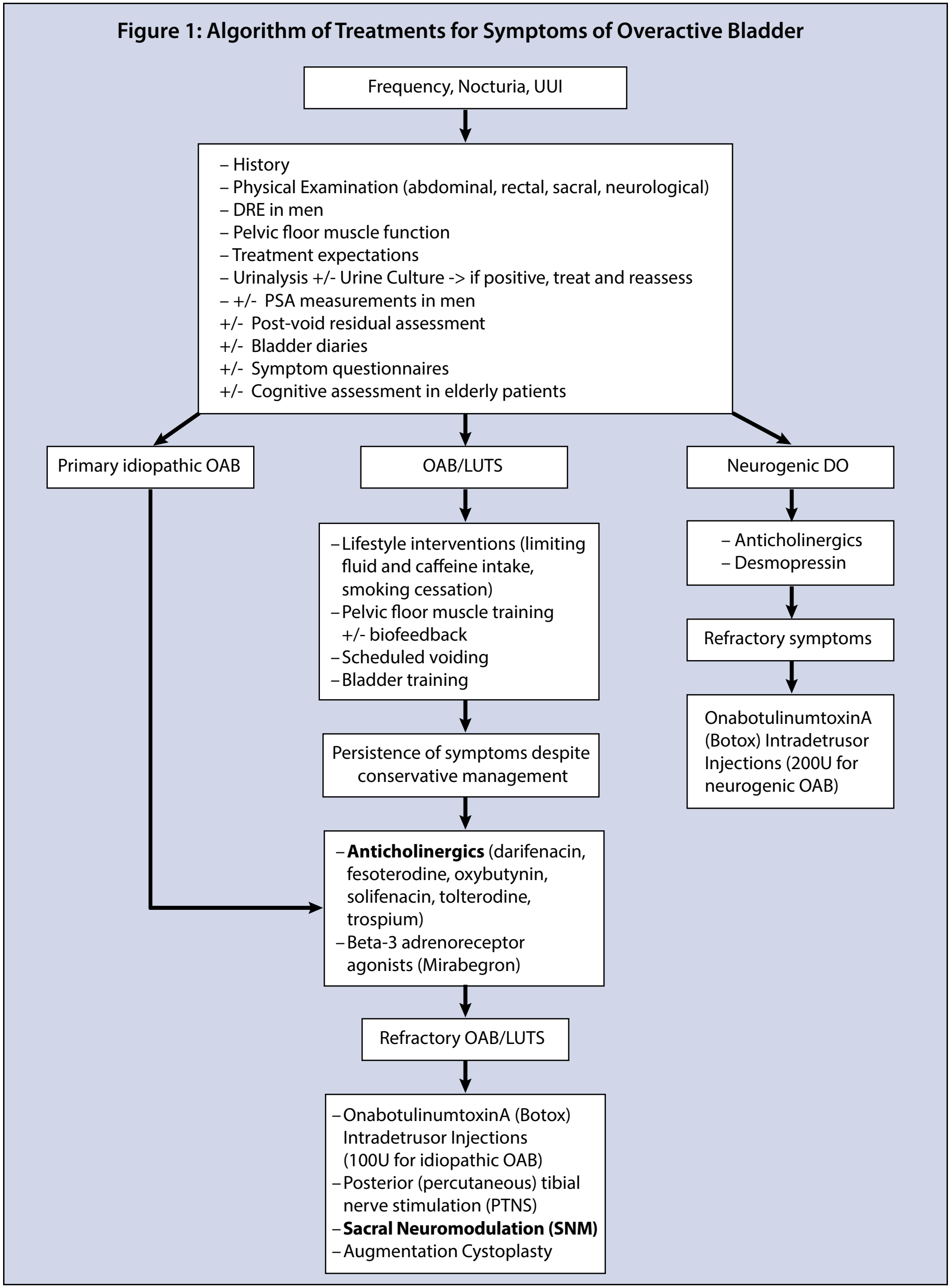
First-line Therapies

Initial treatment of OAB is conservative, using behavioural therapies such as fluid management, limiting caffeine intake, smoking cessation, bladder training, bladder control strategies and pelvic floor muscle training (PFMT).[6,7] In most cases symptoms persist despite conservative treatment, so pharmacological therapies may be used as an adjunct.

Second-Line Therapies

Oral anticholinergics or oral beta-3-adrenoreceptor agonists may be used as first-or second-line treatment for urinary urge incontinence (UUI).[7] Anticholinergics show clinical efficacy in reducing episodes of UI in patients with OAB, but may be discontinued due to side effects of dry mouth and/or constipation,

Figure 1: Algorithm of Treatments for Symptoms of Overactive Bladder



or a lack of clinical efficacy.[7] These side effects should be managed before effective pharmacological treatment is abandoned. Extended release (ER) formulations, if available, should be prescribed in comparison to immediate release (IR) formulations due to lower rates of dry mouth.[6]

Mirabegron, a beta-3-adrenoreceptor agonist offers a similar clinical efficacy to anticholinergics in treating OAB symptoms, without the associated side effects of dry mouth and constipation, but may cause hypertension and tachycardia and should be used with caution in frail and/or elderly patients with OAB.[8-10]

SACRAL NEUROMODULATION IS A MINIMALLY INVASIVE PROCEDURE THAT MAY BE OFFERED TO CAREFULLY SELECTED PATIENTS WITH SEVERE REFRACTORY OAB WHO ARE NOT CANDIDATES FOR SECOND-LINE THERAPY AND ARE WILLING TO UNDERGO A SURGICAL PROCEDURE.

Third-line therapies for refractory OAB

Patients with symptoms refractory to pharmacological therapies (patients that have failed at least 2 treatments of anticholinergics) may require specialist assessment for treatment with third-line therapies, which include OnabotulinumtoxinA injections (Botox), Posterior (percutaneous) tibial nerve stimulation (PTNS) and Sacral Neuromodulation (SNM).

OnabotulinumtoxinA (Botox)

Repeated injections of OnabotulinumtoxinA (100U) show clinical efficacy without increases in adverse events in the management of patients with refractory OAB, and can be offered to carefully selected patients who can return for frequent post-void residual assessment and perform self-catheterization if required.[6,7]

PTNS

PTNS involves electrical stimulation of the posterior tibial nerve using a percutaneous needle placed over the medial malleolus during weekly 30-minute sessions over 12 weeks, with follow-up maintenance therapy.[11] Although PTNS is less invasive than sacral neuromodulation and associated with few adverse events, use is limited to carefully-selected patients due to high costs, labour intensiveness and limited data on long-term outcomes.[7]

Sacral Neuromodulation

Sacral neuromodulation (SNM) is a minimally invasive procedure that may be offered to carefully selected patients with severe refractory OAB who are not candidates for second-line (pharmacological therapy) and

are willing to undergo a surgical procedure.[6]

SNM, first approved by the FDA for urge incontinence in 1997 and for urgency-frequency and non-obstructive urinary retention in 1999, prevents detrusor contraction by activating inhibitory sympathetic neurons using low-amplitude electrical stimulation of S3 afferent nerve roots.[12-14] SNM is approved by Health Canada for refractory UUI.

SNM is performed in a two-stage process. The first (evaluation) stage tests clinical effectiveness by either first-stage lead placement/permanent lead placement (FSLP) in the operating theatre under anaesthesia, or by peripheral nerve evaluation in the clinician's office. The second stage involves implantation of a permanent neurostimulator device.

Evaluation Stage

FSLP is carried out by inserting a needle into the S3 foramen, under fluoroscopic guidance, to stimulate the nerve (confirmed by contraction of the pelvic floor and flexion of the great toe).[12] Then a tined lead of four electrodes is inserted into a subcutaneous pocket over the gluteus muscle of the ipsilateral buttock, where the permanent neurostimulator device may be placed after successful testing. The implanted lead is connected to a temporary impulse generator worn by the patient for 7-14 days during which time OAB symptoms are recorded in a bladder diary.[12]

Peripheral nerve evaluation (PNE) offers a less invasive alternative to FSLP and involves temporary implantation of a single electrode into the eyelet of a needle inserted into the S3 foramen using local anaesthesia, after which the needle is removed leaving the lead in situ.[12] The lead is then taped to the skin and an external temporary generator is attached. The patient then records their symptoms in a bladder diary for 3-7 days.[12]

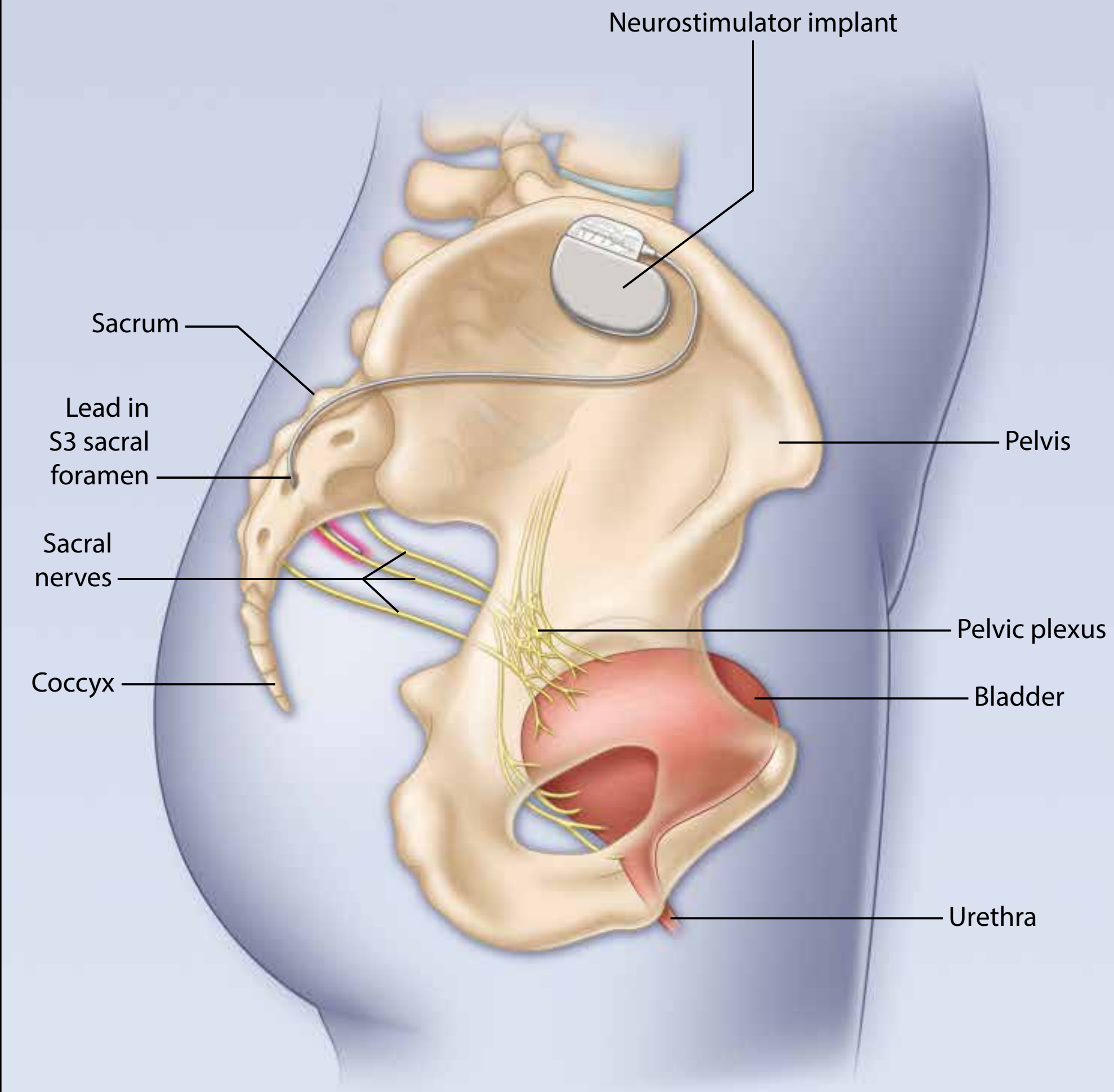
During the evaluation stage, patients may experience pain at the implant site or lead wire migration. Patients with >50% improvement of OAB symptoms during FSLP or PNE may be suitable candidates for insertion of a permanent lead.

Implant procedure

The neurostimulator device and lead can be implanted in a short outpatient procedure, under the skin via a small opening in the upper buttock. One end of the lead is connected to the neurostimulator/generator, and the other is placed in the S3 sacral foramen adjacent to the sacral nerve to stimulate the nerve.

Following the procedure, patients may return to their normal daily activities, but should monitor their symptoms and stimulator and attend regular follow-up appointments where the clinician can check the battery level of the generator.

Sacral Neuromodulation as Treatment for Overactive Bladder



Patients need to proceed with caution when near medical resonance imaging, monitors and diathermy equipment, and inform security staff about their device

NEUROSTIMULATORS MAY AFFECT CARDIAC DEVICES, ELECTROCAUTERY, DEFIBRILLATORS, ULTRASONIC EQUIPMENT, RADIATION THERAPY, MRI, THEFT DETECTORS/SCREENING DEVICES.

in airports and banks, as security scanners in these places may interfere with the neurostimulator settings. Neurostimulators may affect cardiac devices, electrocautery, defibrillators, ultrasonic equipment, radiation therapy, MRI, theft detectors/screening devices.

Contraindications

Contraindications for neurostimulator use include urinary blockage due to mechanical obstruction, as a result of benign prostatic hypertrophy, cancer or urethral stricture.[15] SNM is not appropriate for patients showing limited/no improvement in OAB symptoms after PNE or FSLP screening, inappropriate candidates for surgery, patients unable to use neurostimulation equipment or those predominantly experiencing stress incontinence.[15]

There is limited data available regarding the safety of SNM for bilateral stimulation; pregnancy, unborn fetus, and delivery; pediatric use under the age of 16; or for patients with neurological disease such as multiple sclerosis.[15]

Treatment Outcomes

Several studies have reported on the short and long-term outcomes of SNM use in patients with OAB symptoms.

The InSite trial, a prospective multicentre randomized trial (level 1 evidence), compared 59 patients receiving SNS with 71 patients receiving SMT showed that SNS is superior to SMT in the treatment of OAB.[16] Treatment success (≥50% improvement in average incontinence episodes/day or voids/day or a return to normal voiding frequency of <8 voids/day) was higher in the SNS group vs the SMT group at 6 month follow-up (61% vs 42% respectively, p=0.02).[16] A greater proportion of patients in the SNS group achieved <8 voids/day (p=0.04) and complete continence (p=0.06) compared to those in the SMT group.[16]

In addition, results of quality of life (p<0.001), depression (p=0.01), and sexual function in females (p<0.05) were higher in the SNS group compared to the SMT group.[16] 27.3% of patients in the SMT group suffered from medication-related adverse events, compared to 30.5% of SNS patients who suffered device-related adverse events, which included

SUMMARY OF KEY POINTS

Sacral neuromodulation should be offered as third-line treatment for patients with overactive bladder symptoms refractory to conservative/behavioural and/or pharmacological treatment.

Sacral neuromodulation is a minimally invasive procedure that may be offered to carefully selected patients with severe refractory overactive bladder that are willing to undergo a surgical procedure

Sacral neuromodulation activates inhibitory sympathetic neurons using low-amplitude electrical stimulation of S3 afferent nerve roots to prevent detrusor contraction

A prospective, randomized multi-center trial (level 1 evidence) reported improvements in in continence, mean number of voids/day, quality of life, depression and sexual function in patients receiving sacral neuromodulation compared to standard medical treatment.

Adverse events/complications associated with SNM use include: pain at the implantation site, lead migration, wound-related complications, bowel dysfunction, infection, and generator problems.

an undesirable change in stimulation (10.2%) pain at implant site (8.5%), lead migration (3.4%), and implant site infection (3.4%).[16] A greater number of urinary tract infections was reported in the SNS group compared to the SMT group (p=0.01).[16]

An earlier randomized controlled trial of 51 patients from 21 centers reported statistically significant improvements in the daily number of voids, volume per void and degree of urgency, in patients with an implanted neurostimulator device, compared to controls without the device at 6-month follow-up (P<0.0001).

Results of prospective multi-centre trials reported treatment success in patients 59% of patients with UUI and 56% of patients with urgency-frequency at 2-3 years post-implant,[17] and 68% of patients with urgency incontinence and 56% with urgency-frequency at 5-years post-implant.[14] Prospective single-centre studies also provide evidence for SNM as a suitable therapy for OAB symptoms, with >90% improvement in symptoms in 40% of patients at 47 months[18] and in another study, in 62% of women after 5 years.[19]

Several earlier studies report treatment success in patients with SNM at 1-2 years follow-up[20,21] and one retrospective study reported >50% improvement in symptoms, in 84.8% of patients using SNM for urgency urinary incontinence at 50.7 months follow-up.[22]

Results from observational studies also report testing phase success in patients receiving SNS due to poor medication efficacy and/or intolerable side effects.[23]

In another study, of 20 patients

CME

Post-test Quiz

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that discontinued Onabotulinumtoxin A therapy due to limited efficacy or need for more permanent results, 14 (70%) showed clinical efficacy during the evaluation stage of SNM and received an implant. 5 of 14 patients (36%) showed >90% reduction in leakage episodes and overall 79% of patients were satisfied with SNM at 1-year follow-up.[24]

Alternative therapies

Carefully-selected patients with severe, refractory, complicated OAB and limited success following SNM and other therapies may receive augmentation cystoplasty or urinary diversion as a last resort in treating their symptoms.[6,7]

Conclusion

SNM is an effective short-term and long-term therapy in the management of refractory OAB and is recommended by CUA and AUA guidelines in carefully-selected patients.

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CLINICAL PEARLS

Sacral neuromodulation is a FDA-approved minimally-invasive surgical therapy used as third-line treatment of overactive bladder symptoms/refractory overactive bladder. It is carried out in two stages, the first (evaluation) stage involves insertion of a temporary generator to assess clinical efficacy, and the second stage involves insertion of a permanent neuromodulator implant in patients that have demonstrated >50% improvement in symptoms during the evaluation stage.

Evidence from randomized, controlled trials, prospective multicenter, prospective single-center and retrospective studies demonstrates clinical efficacy of SNM in reducing symptoms of overactive bladder in these patients and therefore SNM is recommended by CUA and AUA guidelines in the treatment of overactive bladder in carefully-selected patients, as the risks of the procedure outweigh the burdens of the overactive bladder syndrome.

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