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REVIEW ARTICLE

Role of sacral neuromodulation in modern urogynaecology practice: a review of recent literature

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Abstract

Sacral neuromodulation (SNM) offers promise in the therapy of many pelvic floor disorders. This innovative treatment has slowly gained popularity. A review of recent literature is presented in relation to its efficacy and complications in various pelvic floor conditions: overactive bladder and urge urinary incontinence, chronic urinary retention, painful bladder syndrome, pelvic pain and double incontinence. It is a minimally invasive, completely reversible safe procedure with good long-term outcomes. However, the treatment is costly, the revision rate is high and patients require life-long follow-up. SNM should always be considered in suitable patients before offering bladder augmentation procedures or urinary diversion or permanent catheterization for bladder dysfunction. SNM should also be considered in patients with double incontinence, after discussion in a urogynaecology/colorectal multidisciplinary team.

Keywords Sacral nerve stimulation · Overactive bladder symptoms · Urinary incontinence · Chronic urinary retention · Bladder pain · Double incontinence

Introduction

Sacral neuromodulation (SNM) is an established treatment for refractory overactive bladder (OAB) syndrome, urge urinary incontinence (UUI) and for non-obstructive voiding difficulty [1–6]. Its use has also been described in bladder pain, pelvic pain, and double incontinence (faecal and urinary). SNM is a minimally invasive, reversible therapy for patients who have failed or could not tolerate more conservative therapy for their symptoms.

SNM was first described in the 1980s by Tanagho and Schmidt for the treatment of refractory lower urinary tract (LUT) dysfunction [7]. Clinical experience with the technique increased with time and it gained Conformité Européenne (CE) approval for the treatment of LUT dysfunction in 1994. The US Food and Drug Administration (FDA) approved SNM in 1997 for the treatment of refractory urge incontinence (UI), and in 1999 for urgency/frequency syndrome and idiopathic, non-obstructive urinary retention (UR). The FDA approvals are for non-neurogenic bladder dysfunction.. In 2005 SNM was included in the International Continence Society (ICS) Recommendations as a treatment option for idiopathic and neurogenic detrusor overactivity (DO). The American Urological Association/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction guidelines on OAB (AUA/SUFU 2015) include SNM and Botox as third-line treatment options for OAB, after failed first-line and second-line treatments (behaviour modification and pharmacotherapy, respectively). The UK National Institute for Health and Care Excellence (NICE) has also supported the use of this procedure for OAB and faecal incontinence since 2004 and non-obstructive UR since 2015.

SNM is a minimally invasive fully reversible therapy that does not preclude further treatment options. The technique has evolved over the years leading to improved efficacy and safety. Although the indications for the use of SNM are growing, there is still significant variability in its use. We present a review of the recent literature in relation to its indications, efficacy, complications and the areas of uncertainty and controversy, and how best to choose and counsel patients for SNM.

Search strategy

We identified published studies evaluating the efficacy and safety of SNM for UUI, UR, urinary dysfunction/disorders,

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bladder pain, pelvic pain, sexual dysfunction and urinary and faecal incontinence using various MeSH headings, by searching major electronic databases and evidence-based reviews and guidelines. The search was limited to humans and literature in the English language. The databases searched were MEDLINE and Embase from 1966 to 2016. Additional searches were performed of the Cochrane Database of Systematic reviews, CINAHL, the Cochrane Central Register of Controlled Trials, the Science Citation Index, the Trip database, and the UK NHS Centre for Reviews and Dissemination Database of Abstracts of Reviews of Effects (DARE). Other sources including Google Scholar, the National Research Register (NRR), the Current Controlled Trials register, and the tables of contents of key journals were searched online. The reference lists of the relevant journal articles identified were hand-searched for additional relevant sources.

Technique

SNM involves the use of mild electrical pulses to stimulate the sacral nerves via an implantable pulse generator (IPG) usually located in the upper buttock. Patients undergo an initial screening phase in which an electrode (a tined lead) is placed in the S3 sacral foramen through the lumbodorsal fascia usually under fluoroscopic guidance and under local or general anaesthesia [8]. Patients monitor their symptoms for 2–4 weeks with a symptom diary. If there is more than 50% improvement, they may proceed to placement of an IPG in the upper buttock. An accurate screening test is crucial in patient selection for SNM.

Contraindications

SNM is not suitable for patients with a sacral deformity, skin conditions at the site of implantation and bleeding disorders/anticoagulant therapy. Presence of the device will preclude the use of diathermy, and it can also be affected by (or can adversely affect) cardiac pacemakers, defibrillators, ultrasonic equipment, radiation therapy, magnetic resonance imaging (MRI), theft detectors and screening devices. If patients suffer from a health condition likely to be monitored by MRI, e.g. some neurological conditions such as multiple sclerosis (MS) and spinal cord diseases. SNM will not be a suitable option.

Mechanism of action

Neuromodulation is a physiological process in which the influence of activity in one neural pathway modulates the pre-existing activity in another through synaptic interaction. Historically, SNM was first described for the treatment of voiding dysfunction after experiments in paraplegic dogs in which electrical stimulation via a sacral electrode resulted in detrusor activation and bladder emptying, and the stimulation was referred to as an ‘electronic bladder pacemaker’ [9]. SNM mainly stimulates the afferent nerves in the pelvis and helps restore the correct balance between excitatory and inhibitory impulses from and to the pelvic organs at a sacral and suprasacral level. The amplitude of the electrical current is lower than the activation threshold of the somatic muscles, it is likely that the electric pulses modulate spinal cord reflexes as well as brain networks. The abnormal reflex arcs that cause DO or sensitivity are interrupted, thus reducing DO, improving pelvic floor coordination and regulating detrusor–sphincter coordination [10]. In patients with UR, SNM is believed to activate the pudendal nerve afferents originating from the pelvic organs into the spinal cord. At the level of the spinal cord, pudendal afferents may turn on voiding reflexes by suppressing exaggerated guarding reflexes, thus relieving symptoms in patients with UR. Prolonged S2-S4 stimulation results in modulation and coordination of the micturition reflex via urethral relaxation [11].

Research comparing positron emission tomography (PET) scans in individuals with UI has shown notable differences between those with long-term SNM use and those who had activation of stimulation for the first time in the PET scanner. In those who have had SNM for at least 6 months, blood flow to areas involved in sensorimotor learning is decreased, suggesting that SNM influences brain areas involved in bladder alertness and awareness [12]. The mechanism of action of SNM is incompletely understood, but voiding dysfunction at both extremes of UI and UR seem to respond well. Neuromodulation has also been employed successfully in chronic pain conditions. Both spinal cord stimulation (SCS), via insertion of electrodes into the epidural space, and peripheral nerve stimulation techniques are widely used by pain physicians.

Chronic pelvic pain (CPP) induces a dysregulated central nervous system response that maintains the perception of pain in the absence of acute injury, and nonpainful stimuli may also be perceived as painful. SNM exerts its effect based on ‘gate control theory’ [13] at the spinal segment level and regulates the interaction between afferent nerve signals and spinal transmission neurons. Impulses from the dorsal horn are controlled by a descending system containing fibres from the brainstem, thalamus and limbic lobes, and thereby SNM controls the pain sensations at the spinal segmental gate and modulates pain sensation at higher brain centres.

Overactive bladder

OAB is defined by the ICS as urgency, with or without incontinence, associated with frequency and/or nocturia, in the

absence of any pathological or metabolic abnormalities [14]. OAB may either be wet or dry, depending on the respective presence or absence of leakage. UUI is the most common form of urinary incontinence and is defined as the involuntary leakage of urine accompanied by, or immediately preceded by, urgency (a sudden desire to void that is difficult to control). OAB is a common condition affecting 38% of women and 19% of men, with a significant effect on their quality of life (QoL) [15]. Its prevalence increases with age. OAB is a key factor in nursing home admission and represents a significant cost to society.

Behavioural interventions and antimuscarinic therapy are the mainstay of treatment for OAB. Both have limited efficacy, and moreover drug therapy has a high discontinuation rate due to side effects [16]. Refractory OAB is considered to be present in a patient who has failed a trial of appropriate lifestyle modifications, bladder training and pelvic floor therapy of sufficient length (8 to 12 weeks), and a trial of at least one anti-muscarinic medication for 4 to 8 weeks [5]. Intravesical Botox and SNM are third-line therapies that are considered before more invasive and irreversible surgical procedures such as bladder reconstruction or urinary diversion in patients who would otherwise be dependent on life-long absorbents. Indwelling catheters are not recommended as a management strategy for OAB, except as a last resort in selected patients, because of the adverse risk/benefit balance. The use of botulinum toxin-A as a third-line treatment has become clinically widespread, but the associated adverse effects of urinary tract infections (UTIs; 20–49%) and intermittent clean self-catheterization (ICSC; 6–16%) may be limiting factors [17].

SNM is a recognised third-line treatment for OAB and UUI. Many randomized controlled trials (RCTs) [18–21], systematic reviews [22–24] and recent case series [25–28] have demonstrated its efficacy. Collectively, higher cure and improvement rates are observed in RCTs than in the compilation of case series, probably due to short follow-up periods and strict inclusion criteria.

In RCTs overall, 50% of patients in the stimulation groups achieved complete continence or greater than 90% improvement in the main incontinence symptoms compared with 1.6% of patients in the delayed implant groups. Another 37% of patients had >50% improvement in the stimulation groups in contrast to 3% in the delayed implant group. Weil et al. [20] also observed that mean bladder capacity assessed by cystometry had significantly increased at 6 months compared with baseline and found a significantly lower mean number of leakage episodes ($p = 0.0005$), lower pad use ($p = 0.0005$) and less severe leakage ($p = 0.047$) in the implanted group than in the delayed implant groups at 6 months. A 50% decrease in the number of voids and an increase in mean volume voided (from 118 ml to 226 ml, $p < 0.001$) and mean bladder capacity (from 234 ml to 325 ml, $p = 0.008$) was found in patients with OAB. Cure was usually defined as no incontinence or greater than 90% clinical improvement, while improvement was defined as a 50% or greater decrease in main incontinence symptoms.

A systematic review [23] found a reported cure rate of 39% of patients (range 7–64%), and 50% or greater improvement in 67% of patients (338 of 501). A significant reduction in the number of daily leakage episodes (53–92%, $p < 0.05$) was found in series in which this outcome was investigated (11 of 14 series). The number of pads used daily was investigated in 14 series, and showed a reduction of 49–94% and the change was significant in ten studies. The severity of incontinence episodes was assessed on a scale of 1 to 3 (*1* mild, *2* moderate, *3* severe) in four studies. Leakage severity was decreased from an average of 1.4–2.0 at baseline to 0.8–1.6 at 18 months or last follow-up (decrease 16–40%). Success seems to be independent of urodynamic evidence of DO [29].

More recent and large series corroborate these findings. In most studies a mixed group of OAB patients was investigated. Peeters et al. [27] reported their results in 217 patients at a mean follow-up of 46.88 months. Success was achieved in 70% of both the wet, and dry OAB groups, and cure in 20% and 33%, respectively. In a more recent study [28] in 255 implanted patients with UI, 77% were successfully treated at 12 months, 60% showed a reduction in the number of leaks per day and 36% showed complete continence. Among patients with dry OAB, 68% were successfully treated and 64% showed a normal voiding pattern (fewer than eight voids per day).

Moon et al. [26] reported outcomes in 61 patients with OAB. The implantation rate was 66% (40 of 61 patients) and 31 patients were available for follow-up at 12 months (18 OAB wet, 13 OAB dry). All patients had urodynamics (UDS) before and 12 months after SNM. Compared with baseline, significant decreases were observed in the number of daily urgency episodes (from 20.2 to 5.7, $p < 0.001$), UI episodes (from 7.3 to 0.2; $p = 0.011$), day-time micturitions (from 21.8 to 9.9; $p < 0.001$), night-time micturitions (from 3.2 to 1.2; $p = 0.006$) and in the severity of urgency episodes (from 3.8 to 2.7; $P = 0.015$). Significant increases were observed in bladder volume at the first unstable contraction (from 182.4 ± 92.7 to 216.8 ± 115.6 ml), bladder volume at the first desire to void (from 150.5 ± 90.8 to 167.8 ± 81.5 ml), maximal cystometric capacity (from 260.7 ± 120.4 to 291.7 ± 124.3 ml) and bladder volume at urgency sensation (from 182.4 ± 92.7 to 208.2 ± 106.6 ml; all $p < 0.05$). Although DO disappeared in only 4 of 20 patients and the group with no DO at baseline tended to have better outcomes at 12 months, patients with evidence of DO on UDS also reported symptomatic improvement, and 65% of patients said they would recommend the therapy to a friend.

Patient satisfaction has been studied in both short-term and long-term studies. In an RCT comparing SNM and standard medical treatment (SMT) [30], patients who had SNM had

greater improvement in their QoL. Leong et al. [31] found that 90% of 207 patients were satisfied with the treatment with a mean follow-up of 77 months.

Although both intravesical Botox and SNM are suitable third-line therapies for OAB, a comparative RCT [32] that included 386 women showed that Botox is more efficacious; however the small improvement in the number of daily incontinence episodes (3.9 to 3.3) was considered to be of questionable clinical significance due to a higher rate of concomitant UTIs and a higher rate of self-catheterization. Moreover, 200 IU Botox was used in this trial, but the recommended dose is 100 IU [1, 5], and an older version of SNM lead, that might have affected the results. Older women with refractory UI, multiple comorbidities and decreased functional and health-related QoL, had a lower treatment response and satisfaction with Botox than with SNM [33].

It would appear that in patients who are unable to self-catheterize or have a coexistent pelvic floor disorder, SNM may be more suitable than intravesical Botox.

Idiopathic chronic urinary retention

Idiopathic chronic UR (CUR; an inability to pass urine [34]), in the absence of anatomical lesions (such as urethral diverticulum, tumour, prolapse and stricture), is not a common complaint in women, but is a difficult problem to manage. Associated pathologies are bladder underactivity, functional urethral obstruction (overactivity of the urethral sphincter) or detrusor sphincter dyssynergia (DSD; see section Bladder dysfunction in neurological conditions for further details on DSD). Pressure flow studies are necessary to identify the underlying pathology that is associated with a low flow rate and high residual. Careful assessment is required to exclude an occult neurological cause. Many patients have a significant history of psychological disorder. On presentation, the condition is usually painless and includes frequency, nocturia, nocturnal enuresis, hesitancy and slow stream. UTIs due to a residual urinary volume and upper tract damage due to back pressure are problems associated with CUR. UR in younger women may be caused by Fowler's syndrome, which is a rare disorder in which the urethral sphincter fails to relax to allow urine to pass normally [35]. Its diagnosis can be confirmed by a characteristic electromyography pattern that demonstrates failure of urethral sphincter relaxation, increased volume of the sphincter on ultrasound scan and increased urethral resting pressure. It is not known if Fowler's syndrome is a subtype of CUR in patients with detrusor underactivity or a distinct clinical entity in young women with CUR.

Because of the ineffectiveness of pharmacotherapy and urethral dilatation [36], catheterization (ICSC or indwelling catheter) is often the mainstay of treatment for CUR. SNM has been recognized as an effective and safe therapy option for restoring bladder function in this difficult to treat group of patients [6]. The evidence for the efficacy of SNM in the treatment of CUR comes from an RCT, several observational studies and case series. A meta-analysis of 14 studies in 2010 [37] analysed the outcomes in the RCT and 13 observational studies (751 patients). The primary outcomes assessed were the change in residual and voided volumes between before and after the procedure. Complete data were available in 478 patients. The mean difference in postvoid residual volume was 236 ml (95% CI 219–253 ml, $p < 0.00001$, $I^2 = 83\%$) favouring SNM. The mean difference in voided volume was 344 ml (95% CI 322–365 ml, $p < 0.00001$, $I^2 = 97\%$) favouring SNM. Both unilateral and bilateral implantation was used in the studies. The follow-up rate was >75% and the minimum follow-up was 6 months in 13 of the 14 studies. The authors concluded that SNM is effective for the treatment of CUR.

An RCT [38] included 177 patients who underwent percutaneous test stimulation for 3–7 days. Of these 177 patients, 68 (38%) qualified for implantation of an IPG (37 early implantation, 31 delayed implantation and SMT). At 6 months follow-up the mean voided volume per catheterization decreased from 339 ml to 49 ml in the implantation group and from 350 ml to 319 ml in the SMT group ($p < 0.0001$). The mean total voided volume per day increased from 722 ml to 1,808 ml in the implantation group and decreased from 560 ml to 488 ml in the SMT group ($p < 0.000$). The mean number of catheterizations per day decreased from 5.7 to 1.4 at 6 months in the implantation group and from 4.0 to 3.9 in the SMT group ($p < 0.0001$ comparing the mean differences). At 18 months, 58% of patients (14 of 24) did not need catheterization, another 13% had a significant reduction in voided volume per catheterization, 25% had minimal or no improvement and 4% had explantation.

In a case series of 40 patients [39] included in the meta-analysis, the mean number of catheterizations per day decreased from 4.3 to 1.0 after a mean follow-up of 41 months ($p < 0.001$) and 55% of patients (11/20) with CUR were able to stop catheterization completely. In a recent case series in 2014 of 93 patients with idiopathic UR [27], the success rate was 73%, and the cure rate (100% success) was 63% in patients with Fowler's syndrome and 54% in patients with non-Fowler's idiopathic UR. Denzinger et al. [40] evaluated outcomes at a median follow-up of 12 months in 20 implanted patients. Voided volumes increased by >50% in 67% of patients, residual volumes significantly increased in 78%, and self-catheterizations reduced from four per day to one per day. Dasgupta et al. [41] reported similar results: >75% of 26 patients had completely stopped self-catheterization at a mean follow-up of 37 months.

Aboseif et al. [42] found that, in 20 implanted patients with non-obstructive CUR, all with detrusor hypoactivity on UDS and relying on ICSC, at a mean follow-up of 24 months, 17

patients were able to void spontaneously with no need for ICSC. One patient required a bilateral implant and at the time of this report was only able to void with both implants on, and two patients continued to use ICSC but less often. An increase in voided volumes was noted from 48 ml to 198 ml and a significant decrease in postvoid residual volume from 315 ml to 60 ml. QoL improvement of ≥50% was seen in 18 patients. All patients were able to void with the device switched on. Pelvic pain was associated with UR in 13 of the 20 patients, and this was also significantly improved (from 6.0 to 2.5).

Urinary hesitancy after hysterectomy is not uncommon especially after radical surgery [43] and UR is reported in up to 0.5% of patients [44]. After hysterectomy patients typically show decreased sensations, increased capacity, slow voiding and large residual volumes. Milder symptoms of deinnervation are more frequent after hysterectomy but are usually temporary. Everaert et al. [45] investigated 13 implanted patients with UR after hysterectomy due to detrusor hypoactivity (mean maximum detrusor pressure 8 cm H_2O, flow rate 7 ml/s and residual volume 582 ml), all of whom were reliant on self-catheterization. At a mean follow-up of 31 months, the maximum flow rate increased to 22 ml/s and residual volume was reduced significantly. Overall the authors concluded that SNM had good efficacy in half of the patients, and partial efficacy in another third of the patients. Three patients had bilateral implants to achieve the effect, and only four patients had to use ICSC during the follow-up period. It has also been reported that in patients with CUR, SNM may have a lower success rate during the initial test phase (<50%), but once implanted has comparable success to that achieved in patients with OAB [46].

Bladder dysfunction in neurological conditions

A disorder of the nervous system can cause problems in storage and voiding of urine by disrupting the coordination of the bladder and bladder outlet activity. The coordination between bladder and bladder neck, and between the urethra and urethral sphincter is regulated by a complex neural control system that is located in the brain, the spinal cord and the peripheral ganglia, and is mediated by autonomic and somatic neural circuits. With a neurological lesion, the type of LUT dysfunction that arises depends on the site, extent and evolution of the lesion, and which part of the nervous system is affected. In suprapontine lesions (stroke, Parkinson's disease, MS), patients usually continue to have reflex detrusor contractions but impaired cerebral regulation/inhibition leads to inappropriate timing of voids, inability to initiate voids, DO and UUI. Suprasacral spinal cord lesions (trauma, tumours, multiple system atrophy) cause DO and UUI, poorly sustained detrusor contractions that may lead to incomplete bladder emptying; reduced compliance, and in some cases DSD resulting in a significant postvoid residual volume and a "high pressure" bladder.

Sacral spinal cord lesions (such as spina bifida and disc prolapse) lead to detrusor areflexia, stress incontinence due to sphincter deficiency, and reduced compliance over time. Subsacral disorders (cauda equina, lumbar disc prolapse, peripheral nerve lesions including diabetic neuropathy, and radical pelvic surgery) cause loss of contractile function and altered reflex activity leading to DO and incomplete emptying; and reduced compliance over time [47]. In addition to LUT symptoms, the dangerous sequelae of renal damage due to a sustained elevated storage pressure due to DO and/or low compliance combined with DSD are carefully evaluated and managed. The lesions commonly associated with DSD are suprasacral infrapontine spinal lesions and meningomyelocele, and in patients with severe MS urodynamic and clinical symptoms may not correlate. The treatment and intensity of follow-up depends on the underlying neurological disease and the associated bladder pathology.

A thorough urological assessment of patients with neurological disease includes S2–S4 neurological assessment (sensations, anal tone and bulbocavernosus reflex), full UDS, video UDS, electromyography and imaging, e.g. renal ultrasonography, to check for any upper tract damage caused by the high detrusor pressure. Treatment options are often limited as alpha-blockers and antimuscarinics have low efficacy and some patients may find it hard to perform ICSC due to their disability and many patients need to use incontinence products for life. Intravesical and urethral sphincter injection of Botox is particularly helpful in patients with high-pressure bladder conditions, and surgical procedures for sacral deafferentation and bladder neck incision are also used in suitable cases [48]. SNM may have a role in controlling DO and incomplete voiding before resorting to more invasive procedures such as bladder augmentation or urinary diversion. Patients with neurological disease often also suffer from bowel dysfunction, and SNM may benefit both conditions [49, 50].

In their early work, Tanagho and Schmidt [51] investigated sacral stimulation in patients with neurogenic bladder. Bosch and Groen reported the favourable impact of SNM on neurogenic bladder dysfunction in 1996 [52]. Since then many case series have been reported showing successful outcomes in patients with neurological disorders following SNM. A 2010 meta-analysis of 26 studies including 357 patients concluded that SNM is effective and safe for the treatment of neurogenic bladder dysfunction [53]. The authors concluded that after failed conservative treatments, SNM testing seems worthwhile as in 68% of patients a screening test was positive. Efficacy was comparable with the reported efficacy in patients with non-neurogenic bladder dysfunction at a mean follow-up

of 26 months. The adverse event rate was 24% and the explantation rate was 11%. Peters et al. [54] found that outcomes in patients with neurogenic bladder dysfunction were favourable and comparable to those in patients with non-neurogenic bladder dysfunction after a follow-up of 2 years. QoL measures were also included in the outcomes.

Chaabane et al. [55] evaluated clinical and urodynamic outcomes in 37 implanted patients out of 62 with neurogenic LUT dysfunction at a longer follow-up of 4.3 years. The efficacy of SNM was confirmed in 75.5% of the patients by urodynamics (maximum flow rate, residual volume, cystometric capacity, loss of DSD and increase in detrusor pressure) and frequency episodes. Efficacy varied according to the underlying disease and in particular whether it was a progressive disease such as MS. Overall, 75.5% of patients achieved more than 50% improvement, but in patients with Parkinson's disease the response rate was poor, while those with peripheral neuropathy with DO had better outcomes. DSD also disappeared with implantation in this study, but the authors suggest that urodynamic confirmation of improvement in DSD should be sought before permanent implantation. Additionally most patients with a loss of efficacy over time had a progressive disease such as MS.

In another recent study [56], of 50 patients with spinal cord injury, 35 had an IPG implanted, and excellent outcomes were achieved at 15 months in 11 patients with retention. all of whom were able to void after implantation, and 80% with DO achieved full continence. In patients with neurogenic overactivity following spinal cord injury in whom symptoms cannot be solely relied upon, the benefit of SNM should be confirmed with cystometric studies as detrusor pressures may not be normalized by SNM, despite symptomatic improvement (two of the 35 patients had the device removed). In all, 94% of the patients were either very satisfied or satisfied with SNM. Engeler et al. [57] investigated the use of SNM in 17 patients with MS with a follow-up of 3 years. A satisfaction rate of 80% and significant improvements in voided volume, residual volume and leakage frequency were noted. Lombardi and Del Popolo [58] evaluated 19 implanted patients with spinal cord injury. Patients with UR (detrusor underactivity and nonrelaxing sphincter) and patients with DO showed significant improvements in various objective parameters at a follow-up of 5.4 years. Loss of efficacy in 4 of the19 patients was successfully ameliorated with implantation on the contralateral side. A 10-year follow-up study in patients with spinal cord injury has also shown a success rate of 80% [59].

The 2013 International Consultation on Incontinence [60] includes SNM in the treatment algorithm of neurogenic LUT dysfunctions (level of evidence 3), acknowledging its limited role in neurogenic DO, although patients need to be carefully selected as the success rate may not be as high as in patients with non-neurogenic DO. Similarly the 2013 European Association of Urology guidelines on neurogenic LUT dysfunction state that SNM might be effective and safe for treating neurourological symptoms [47] acknowledging the lack of RCTs and a lack of clarity as to which neurological patients are suitable. Further research in this area is warranted.

Bladder pain syndrome

Bladder pain syndrome (BPS) is defined as a complaint of suprapubic pain, perceived to be related to the bladder often accompanied by other symptoms such as frequency and/or nocturia, in the absence of urinary infection or other bladder pathology [61]. BPS has replaced the terms interstitial cystitis and painful bladder syndrome [62]. BPS is often associated with negative cognitive, behavioural, sexual or emotional consequences.

Many patients with BPS exhibit features of pelvic floor dysfunction in addition to pain on bladder filling and a persistent urge to void. Whilst inflammation (Hunner's ulcers and glomerulations on cystoscopy) is not a universal feature of BPS, there may be specific types of inflammation as a feature in some patients. Cystoscopy with hydrodistension and biopsy is useful to define the phenotype and to exclude other pathology [63]. The cause of BPS is thought to be an initial insult that leads to urothelial damage and neurogenic inflammation resulting in pain sensation, which becomes self-perpetuating as a result of central nervous system modulation. The autonomic nervous system also plays a role in sensitization as there is evidence that damaged afferents may develop sensitivity to sympathetic stimulation [64]. There is wide variation in the prevalence of BPS (18–70/100,000) and a female predominance (10:1). The typical age of presentation is 42 years [65].

Treatment of BPS is multimodal. Behavioural, physical and psychological techniques should always be considered alongside oral or invasive treatments as BPS is often a difficult problem to treat. After life-style, oral and intravesical treatments and cystoscopy with hydrodistension, SNM is recommended as a fourth-line treatment for BPS by the European Association of Urology [64] and by the American Urological Association [66]. There are no RCTs evaluating SNM; the effectiveness data come from observational studies or case series. Several studies have indicated efficacy of SNM in the management of refractory BPS [67–72]. Reported outcomes include improvement in pain, increases in mean voided volume, reductions in mean frequency and nocturia, and increases in QoL measure scores.

Gajewski and Al-Zahrani [68] found good long-term efficacy (72%) at a mean follow-up of 61.5 months, but the explantation rate (28%) was also higher in their series. Another study from 2002 to 2004 in women with interstitial cystitis [69] showed excellent results with SNM at mean follow up of 86 ± 9.8 months: mean urgency and frequency scores were

significantly improved after the procedure (before 21.61 ± 8.6, after 9.22 ± 6.6), as were mean visual analogue pain scale (VAPS) scores (before 6.5 ± 2.9, after 2.4 ± 1.1). The authors concluded that SNM was associated with significant symptomatic improvement with a low reoperation rate (25%); most revisions were due to trauma causing wire displacement or device malfunction. Concomitant UI was found to be a positive predictor of success of SNM in BPS patients [71]. Although the available case series point towards the efficacy of SNM for BPS, there is a real lack of good quality studies in this area and further research with RCTs is warranted.

Chronic pelvic pain

CPP is nonmalignant pain perceived in the pelvis, present for at least 6 months not exclusively associated with pregnancy, menstruation or sexual intercourse. CPP is a prevalent condition (about 4–14%) [73], has a female preponderance, and can greatly affect QoL and sexual function [74]. Many of the pelvic floor disorders including cystitis, urgency and frequency, UI, UR, and constipation, may be associated with pelvic pain.

The pelvis has a complex neuroanatomy, comprising both visceral and somatic structures, all of which receive innervation from the sympathetic, parasympathetic, and somatic nervous systems. Pain within the pelvis is triggered by a nociceptive stimulus such as infection, surgery, neuropathic conditions, voluntary retention and chronic straining, that over time can mediate sensory stimuli with excessive discharge, C-fibres remain in a partially depolarized state leading to enhanced afferent signalling, resulting in chronic pain sensation. The increased perception of stimuli in the viscera is known as visceral hyperalgesia, and the underlying mechanisms are thought to be responsible for CPP in inflammatory bowel syndrome, BPS and dysmenorrhoea. The pelvic viscera share their nerve supply leading to viscerovisceral hyperalgesia, due to converging sensory projections, for example overlap of bladder and uterine afferents or uterine and colon afferents [64].

It is well established that peripheral nerve stimulation may interrupt pain pathways at the spinal cord level and this technique is established in the treatment of chronic regional pain syndromes and occipital neuralgia. SCS exerts a similar effect that reflexly inhibits somatic afferent processing in the spinal cord. However, if nerves in the sacral region of the spinal cord are stimulated, the visceral pain in the pelvis that is transmitted partly through the sympathetic fibres of the autonomic nervous system via the lumbar splanchnic nerves may not be effectively blocked. The autonomic innervation in the pelvis originates at L1–L2 and travels directly between the sympathetic trunk and the pelvic viscera via local ganglia. Although SCS is a well described intervention for CPP [75], there is as yet no consensus on the optimal location for placement of the lead. Concerning SNM, an improvement in concomitant pelvic pain was noted when the IPG was implanted for a primary indication of bladder dysfunction. There are also many small case series reporting the success of SNM in treating CPP [76–79], but its role is not established due to a lack of consistency in reported success. SNM may be effective in carefully selected patients with global pelvic floor dysfunction. The cost and adverse events profile of SNM need to be considered before it is offered to patients with CPP as some referred pain may remain refractory. Less invasive nerve stimulation techniques, for example transcutaneous tibial or sacral nerve stimulation, or injection blocks, for example pudendal, hypogastric plexus block or ganglion impar block, may be considered to better select patients for SCS techniques [64].

Sexual dysfunction

Female sexual dysfunction is a prevalent disorder that can greatly affect QoL. Several studies have shown that SNM improves sexual function [80–84]. Direct stimulation of the pudendal nerve through the S2–S4 nerve roots is thought to be the underlying mechanism. The pudendal nerve provides motor and sensory innervation to the pelvic floor and its stimulation could improve all aspects of sexual response, including desire, arousal, lubrication, orgasm, and even satisfaction [81]. Gill et al. [80] found that 6 weeks after SNM sexual function and sexual desire in sexually active women had improved based on PISQ-12 and FSFI scores, respectively. Parnell et al. [81], using FSFI scores and pudendal nerve terminal motor latencies, also found improvement in sexual function after SNM. Although the literature on the subject is scanty and most reported studies include small numbers of patients, a trend for improvement has been found using objective measures (via use of validated questionnaires) and patient satisfaction scores.

Much data regarding sexual function comes from studies of SNM for primary urinary dysfunction in which improvements in sexual function have also been noted [28]. Lombardi et al. [84] found significant improvements in sexuality and total FSFI scores in women with idiopathic OAB undergoing SNM. Interestingly, using a different implantation technique and location for placement of the lead, Zabihi et al. [77] found significant improvements in all domains and total FSFI scores (average total FSFI 9.2). Taking these data together, it appears that SNM may improve sexual function when implanted for other pelvic dysfunctions.

Combined faecal and urinary incontinence

Faecal incontinence refers to uncontrolled loss of stools, either liquid or solid. It affects approximately 8% of the adult

population, and the rate increases with age [85]. Nearly 25% of patients with urinary incontinence also have faecal incontinence [86] and this may indicate a shared motor disorder in these patients [87]. The effectiveness of SNM for faecal incontinence was discovered incidentally in patients treated for urinary incontinence [88]. However, it is now a recognized treatment for faecal incontinence in selected patients who do not have an organic disease as a cause of incontinence, and who have failed conservative measures and medical treatment [89, 90].

A few studies have investigated outcomes in patients with UUI and faecal incontinence. In a systematic review [49] a wide variation in results was noted from one series to another. Improved faecal incontinence was observed in 44–100% of patients, while an improvement in urinary incontinence was observed in 20–100% of patients. Faucheron et al. [50] investigated outcomes in 57 patients, the largest series so far at a median follow-up of 62 months. Using the Cleveland Clinic incontinence score (*0* normal continence, *20* complete faecal incontinence), faecal incontinence improved from 14.1 to 7.2 at 6 months and to 6.9 at the end of follow-up, and 73% of patients were highly satisfied. UI was also significantly improved. Most other series have consisted of small numbers of patients (4–18) making it difficult to draw conclusions. A systematic review commissioned by NICE on faecal incontinence [91] found that following permanent implantation, 41–75% of patients achieved complete faecal continence and 75–100% showed an improvement of 50% or more in the number of incontinence episodes.

The literature on the role of SNM in double incontinence is scanty. However, carefully selected patients are likely to benefit. In a recently published consensus statement from the Italian Sacro-neuromodulation Expert Group on management of double incontinence, the role of SNM was recognized [92]. Prospective trials would be useful to determine which disease parameters are likely to affect prognosis and how best to select patients.

Complications

Initial studies of SNM [23, 24] showed a relatively high complication rate: pain at the implant or lead site (6%), lead-related problems (15%; migration, breakage, loosened connection, insulation defects), replacement and repositioning of the IPG (15%), wound problems and infection (7%), adverse effects on bowel function (6%), new-onset pain 5% (leg, perineal, buttock), and the need for revision surgery (33–40%). Permanent removal of the device was reported in 9–10% of patients due to side effects or lack of benefit. Studies with longer follow up periods have shown higher revision surgery rates. Common reasons for revision surgery were adjustment or modification of the lead system, relocation/repositioning of the IPG because of pain at the implant site or mechanical failure. Pain at the IPG site is often treated by adjustment of the current amplitude and frequency or by relocation of the IPG. Aversion (psychological rejection) leading to explantation has also been reported. Device malfunction may also occur as a result of trauma. However, technical improvements over time have been associated with reduced rates of complications. A newer tined lead is associated with lower loss of efficacy and revision surgery rates. A recent study showed a reoperation rate of 13% and an infection rate of 4% at 12 months [28]. SNM has not been associated with major irreversible complications or permanent nerve damage. Most adverse events, such as leg pain, perineal pain of altered physiology of the bowel, resolve with time or can be managed by reprogramming or removal of the IPG.

Chughtai et al. [93] investigated the safety of SNM in a large random (5%) sample of Medicare claims from 2001 to 2011. Of patients followed for at least 5 years, 17.3% had the device removed and 11.3% had the device replaced. SNM is a relatively expensive treatment: as well as the initial equipment and theatre costs, there are additional costs for revision procedures and planned periodic replacements every 5–7 years. However, the cost effectiveness might be increased if more stringent criteria are used for patient selection. Treatment costs must also be balanced against the burden to the patient and his/her family of an otherwise untreatable condition and considering potential savings to the healthcare system and the benefit to the patients' QoL. The reported efficacy of SNM for various indications is 50–75%. Only one third of patients may report a 'cure' and two thirds experience improvement. Efficacy may not be maintained in the long term. SNM is a form of maintenance therapy with frequent change in programming or revision surgery required during follow-up. Patients must also have the cognitive capacity to use the remote control to optimize device function.

Conclusions

SNM offers promise in the therapy of many pelvic floor disorders and its use is increasing. It is a minimally invasive, completely reversible safe procedure with good long-term outcomes. However, the treatment is costly, the revision rate is high and patients require life-long follow-up. SNM should always be considered before offering bladder augmentation procedures or urinary diversion for intractable UUI or permanent catheterization. Given the potential of this therapy, it is recommended that all urogynaecology training programmes include SNM in the curriculum. Further research is needed on how best to select appropriate patient groups to further improve the success rate and also to find the best stimulation parameters [94] and schedule, e.g. selective or event-driven stimulation for urinary, bowel or sexual function for an effective and lasting implant. Appropriate patient selection may

be optimized if care of patients with pelvic dysfunction involving urinary, vaginal and bowel symptoms is discussed in a multidisciplinary team comprising gynaecology, urology and bowel surgeons.

Compliance with ethical standards

Conflicts of interest None.

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