Sacral neuromodulation in patients with faecal incontinence

SACRAL NEUROMODULATION IN PATIENTS WITH FAECAL INCONTINENCE

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'We don't always have a choice how we get to know one another. Sometimes, people fall into our lives cleanly - as if out of the sky, or as if there were a direct flight from Heaven to Earth - the same sudden way we lose people, who once seemed they would always be part of our lives.'

John Irving

CHAPTER 1

Faecal Incontinence

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Submitted

Introduction

Faecal incontinence is a common disorder with a broad variety of causes. It is a complex problem that can have profound effects on patient well being as it is a psychologically devastating and socially incapacitating condition. Faecal incontinence imposes a high cost on the patient and the community, both in terms of direct medical costs and indirect costs including utilization of health resources, loss of employment and referral to a nursing home. A thorough work-up for assessing the cause and degree of the incontinence is imperative and should include adequate clinical, physiological and structural assessment. Advances in imaging have made these assessments an important step in the evaluation of patients with faecal incontinence. Therapeutic strategies vary from conservative management (medicinal therapy, biofeedback training and colonic irrigation) to surgical interventions (sphincter repair, neosphincter formation, artificial bowel sphincter, sacral modulation or formation of a stoma) and are dependent on available knowledge and existing facilities. Treatment strategies have changed over time, as, especially with the emerging of biofeedback, (reconstructive) surgery is now viewed as a last resort. [1-5]

Epidemiology and aetiology

The most commonly used definition for faecal incontinence is involuntary loss of faecal material for a period of at least three months. Faecal material embraces solid or liquid faeces or mucus. Flatus incontinence alone should be excluded, partly because it is too complex to define when passage of flatus is abnormal. The diagnosis should not be made in children under the age of four. [6-8]

Due to the impact on the patient' s life, caused by embarrassment or insufficient knowledge concerning the availability of treatment, patients are reluctant to seek medical advice and thus spontaneous reporting of this problem is rare. [2,9-11] A systemic underestimation of the incidence and prevalence is therefore to be expected, as recent studies on the rate of faecal incontinence in the general population reported prevalence for solid or liquid faecal incontinence ranging from approximately 2 to 9%. [2,8,12,13] Whitehead at al reported that, in their cohort of 4773 patients, 8.3% of non-institutionalized adults were incontinent for faeces once monthly. [8] Moreover, they noted that faecal incontinence occurred at least weekly in 2.7% of the population, whereas daily faecal incontinence occurred in 0.9%. The most common type of faecal material lost was liquid stools, followed by loss of mucus. These findings are consistent with other, survey-based studies. [2,14,15] Furthermore, faecal incontinence is more common among elderly, as its prevalence is higher in people over the age of 60. [2,16] Among inhabitants of long-term care facilities of 60 years of age and older, faecal incontinence was reported in approximately 20%; risk factors in this group included a history of urine incontinence, neurological disease, impairment of activities of daily living, severe cognitive decline and age over 70 years. [17,18]

While some studies noted a higher prevalence in women, [19-21] which is attributed to the most common aetiological factors as injury to the pudendal nerve or sphincter muscle due to obstetric perineal trauma and less commonly irritable bowel syndrome, [22-25] the vast majority of population based surveys display a relatively high incidence in males as well. [2,8,15,21,26] This proposes other causative factors outside those related to childbirth, although pregnancy has a prominent association with faecal incontinence. A summary of causes of faecal incontinence is shown in table 1. Emphasis should be put on the fact that in the majority of cases faecal incontinence is a multi-factorial disorder.

Assessment

Although faecal incontinence has been proven to have a devastating impact on the patient's quality of life, astonishingly only a minority of patients spontaneously report this condition to their healthcare workers and additionally many healthcare workers are equally reticent or ignorant. [8,11,27,28] Adequate clinical, physiological and structural assessment is therefore imperative in the work up of patients with faecal incontinence.

Clinical assessment

Taking a patient's history is a crucial step in determining management strategies. Consequently a direct but sensitive way of questioning is essential. As the type of faecal incontinence may suggest the cause and sometimes degree of the disorder, differentiating true faecal incontinence from perineal soiling due to lack of hygiene or prolapsing haemorrhoids is crucial. Risk factors for developing faecal incontinence should be evaluated and information concerning preceding anorectal surgery and obstetric history should be obtained. [7,11,29]

Trauma		
	Obstetric*	
	Iatrogenic*	(anal stretch, haemorrhoidectomy, sphincterotomy, fistula surgery, colectomy, pouch procedures, radical prostatectomy)
	Accidental injury	(motorcycle accidents, impalement)
	Anal intercourse	(non-consensual > consensual)
Pudendal Neuropathy		
	Idiopathic*	(childbirth, chronic straining)
	Neurological disorders	
Degenerative		
	Internal anal sphincter degeneration*	
	Radiation damage to internal sphincter	
Prolapse		
	Rectal prolapse*	
	Pelvic organ prolapse*	
Small rectal compliance		
	Inflammatory bowel disease	
	Radiation proctitis	
	Pouch	
Congenital		
	Imperforate anus	
	Anal agenesis	
	Hirschsprung's disease	
Medical cause		
	Inflammatory bowel disease	(diarrhoea or perianal disease)
	Irritable bowel syndrome	(diarrhoea)
	Celiac disease	
	Diabetes mellitus	(diarrhoea or neuropathy)
	Multiple sclerosis	
	Psychiatric illness	(behavioural)
	High BMI	(poor toilet hygiene)
	Debility	
Gastrointestinal stimulants		
	Drugs	
	Foods	(caffeine, alcohol, aspartamine)
	Osmotically active foods	(lactose, sorbitol, fat substitute)
Neurological		
	Spinal cord trauma	
	Meningocele/myelomeningocele	
	Spina bifida*	
Impaired mental status		
	Dementia	
	Stroke	
	Learning disability	

Table 1 Causes of Faecal Incontinence * Most common Causes

The commencement of faecal incontinence, occurrence of episodes of stool loss, and consistency and volume of faecal material lost should be analyzed to assess severity. Patients can be classified as having either passive faecal incontinence (i.e. without the patient's knowledge) or urge incontinence (i.e. occurring due to lack of voluntary control). [30] It is assumed that, because of the characteristic function of the anal canal, continence of solid faeces is easier maintained. Therefore leakage of solid stool is generally seen as a sign of a more profound physiological impairment. Conversely, incontinence of liquid stool is perceived by patients to be more influential on quality of life than occasional loss of solid stool. [29,31] The severity of faecal incontinence can be derived from the protection methods used, for instance protective pads, or from the extent of lifestyle changes. However, these measures may be more elicited by patient's anxiety due to the unpredictability of the disorder than by the actual degree of the incontinence. [7,11,29] Social, occupational or sexual dysfunction may also arise due to loss of confidence. Moreover, even though severity of the disorder and the impact on the patient's life are undoubtedly intertwined, disease-specific questionnaires to assess the degree of incontinence show only moderate correlation to disease-specific measurements of quality of life. It is therefore essential to evaluate both variables to quantify the true impact of the disorder, as an emphasis on only the frequency and type of episodes will result in underestimation of the impact. [32,33]

Clinical examination can reveal the cause and severity of anal incontinence in many cases. Features indicative of either sphincter weakness or chronic skin irritation should be assessed by the examiner, as they can provide clues regarding the underlying aetiology. Preceding obstetric or surgical trauma is suggested by perineal scarring, small perineal body size and a wide genital hiatus. Gaping of the anus is suggestive of rectal prolaps, which can usually be demonstrated with Valsalva's manoeuvre. Digital rectal examination can be used to asses both the resting sphincter tone and its increase with voluntary squeeze. Moreover, digital rectal examination has particular importance in elderly patients in whom the cause of stool loss is often simply overflow incontinence due to faecal impaction. Vaginal examination may show evidence of a rectocele, cystocele or uterine prolaps or a combination of these. [7,11,29,34,35]

Furthermore, a detailed physical and neurological examination should be performed to exclude the possibility of a systemic or neurological disorder. Therefore, perianal sensation should also be assessed while impaired or absent anocutaneous reflex could be a sign of afferent or efferent neuronal damage. [34,36]

Physiological assessment

Assessment of the physiological function of the anorectum by performing various key investigations is an important step in determining both the cause and degree of the faecal incontinence, especially in those cases in which no abnormalities were found on physical examination. Physiological assessment should be tailored to specific patient characteristics, degree of the disorder, impact on patient's quality of life and, if applicable, response to commenced treatment.

Anorectal manometry evaluates sphincter physiology by determining the resting sphincter pressure (internal anal sphincter function), squeeze sphincter pressure and the duration of the sustained squeeze(s) (maximum anal squeeze pressure), recto-anal inhibitory reflex, threshold volume of rectal distension required for first sensation and for desire to defecate as well as the maximum tolerable volume and recto-anal pressure changes during attempted defecation. [6,37] While both longitudinal and radial variations exist between the normal pressures within the population, implications of this diagnostic tool can be difficult to assess. Furthermore, after successful treatment for faecal incontinence the majority of patients show no improvement in manometric abnormalities. [11,29]

Electromyography may be performed with a surface electrode or with a concentric needle. [38] Currently, it is seldom used to assess sphincter function. It is proposed that electromyography can identify both myogenic and neurogenic damage of the external sphincter after obstetric, surgical, or traumatic sphincter injury. [6,38] Pudendal nerve terminal motor latencies are of limited use in evaluating patients with faecal incontinence, therefore it is recommended not to use this controversial technique in the evaluation of patients with faecal incontinence. [6,39] Moreover, presence of prolonged latencies does not seem to correlate with outcomes of therapy. [7,40]

Structural assessment

Imaging has become increasingly important in the evaluation of patients with faecal incontinence. Therefore, structural assessment and physiological assessment should be viewed as complimentary investigations to achieve the most thorough evaluation of sphincter function.

Defaecography demonstrates the anorectal anatomy and pelvic floor motion at rest and during pressure-inducing action (coughing, squeezing, and straining). [6] By opacifying the rectum through instillation of barium and obtaining images by lateral fluoroscopy during attempted defecation, a wide range of pathologies associated with incontinence can be diagnosed. [41]

Anal endosonography has proven to be invaluable in the work-up of patients with faecal incontinence, [42] as it enables clear imaging of both the internal and external sphincter muscles and thereby facilitates visualization of the presence or absence of defects to the sphincters with a high sensitivity and specificity.[43,44] Moreover, it is a simple and rapid diagnostic test with very good intraobserver and interobserver reliability. [45]

Another approach for imaging of the pelvic floor is endoanal magnetic resonance imaging (MRI). Endoanal MRI has been proven to provide an accurate description of the anatomy of the anal canal and perianal structures, which is thought to be due to its capacity to differentiate between fat and muscle. [46]

Whereas endoanal ultrasonography is more sensitive for displaying the internal anal sphincter, endoanal MRI is more accurate in diagnosing injuries of the external anal sphincter. [7,11,47] However, in the pre-operative evaluation for identifying those patients suitable for surgical management, endoanal ultrasonography and endoanal MRI have both proven to be sensitive diagnostic tools that have comparable characteristics in the depiction of clinically relevant anal sphincter defects. [48,49]

Treatment

The treatment of faecal incontinence should be causal if possible, therefore a key step in the management of patients with faecal incontinence should be to identify and possibly eliminate exacerbating or contributing factors. Additionally, advice on hygiene, on protective measures, such as absorptive pads, and on prevention of skin irritation is particularly important. The different treatment strategies can be subdivided in conservative therapy and surgical interventions.

Conservative therapy

The first step in the management of patients with faecal incontinence should be to offer conservative therapy. Most patients benefit from simple dietary changes, supplementary intake of fibre and possibly bowel habit training. [50-53] Therefore, all patients should be counselled on fluid and fibre intake. It is assumed that because fibre increases the weight and improves the consistency of the faeces, intake of fibre improves anal incontinence. [54]

As diarrhoea is an important cause of faecal incontinence, anti-diarrhoeal medications may help when stool is loose. [54,55] Loperamide, a synthetic opioid, does not only cause formation of a firmer stool and reduction in frequency of defecation, but also has direct effects on the anal sphincter by reducing the rectoanal inhibitory reflex and increasing the maximum basal sphincter pressure. [56,57] Diphenoxylate, a natural opioid, combined with atropine has been shown to reduce the average frequency of defecation and the average weight of faeces produced daily, without influencing the rectal or anal sphincter pressure. [58] In a double-blind cross-over study set up comparing loperamide and diphenoxylate, the former was found to be more effective than the latter in treating chronic diarrhoea. [59]

It has been reported that topical application of phenylephrine gel results in altered neural sphincter control thereby increasing the resting tone of the internal anal sphincter. After augmenting the doses, the pressure was in fact noted to approximate the normal range, with minimal toxicity. [60,61]

Santoro et al. [62] found that amitriptyline, a tricyclic antidepressant, improved symptoms of faecal incontinence in a considerable number of patients. This drug was noted to influence rectal motor complexes, thereby causing a decrease in amplitude and frequency. Secondly, it was reported that amitriptyline prolonged colonic transit time and improved stool consistency while reducing frequency of passage. The newer antidepressants do not posses this characteristic, conversely these drugs may in fact predispose to incontinence of faeces. [7]

Biofeedback, usually the first line of treatment if medical therapy fails, uses operant conditioning to improve voluntary control over sphincter function. The aim of this treatment is to improve contraction of the external anal sphincter in response to rectal distension by giving instant feedback on subconscious body processes. [29,63] It is a simple and cheap therapy that does not have adverse effects. Equipment is used to detect and intensify a physiological response. [64] Different protocols and equipment for providing biofeedback have been described in the literature, such as electromyography based treatment [65,66] and systems that use intrarectal balloon placement. [67,68] In nonrandomized trials and systematic reviews of the literature, success rates of biofeedback therapy for faecal incontinence are reported to be over 70%. [69-72] This therapy has proven to increase maximum squeeze pressure and saline retention capacity irrespective of surgical repair of sphincter damage. Secondly, it has shown to improve patient's quality of life. [72,73] Patient selection is of utmost importance for achieving success after biofeedback therapy, as it is essential for patients to not only have insight into their problem but also to possess the motivation to complete the training. [7]

Anal plugs are disposable devices consisting of compressed foam. Soaked in faecal content the plug self-expands blocking the passage of stool resulting in pseudo-continence. [74,75] A present pelvic floor function is needed to support the plug and furthermore the device is not well tolerated by many patients. When tolerated well plugs can be helpful in preventing incontinence in a selected group of patients. [76]

Pseudocontinence can also be reached by retrograde colonic irrigation using 1-2 litres of water that can be introduced by using a pump (Fig. 1) or irrigation bag (Fig. 2). The pump works on a storage battery and the speed of water ejection can be regulated while the water ejection with the irrigation bag is induced by gravity and therefore may take more time. Retrograde colonic irrigation is an often forgotten and undervalued treatment option. Success rates of 38-75% have been reported with a significant improvement in quality of life. [77-79]

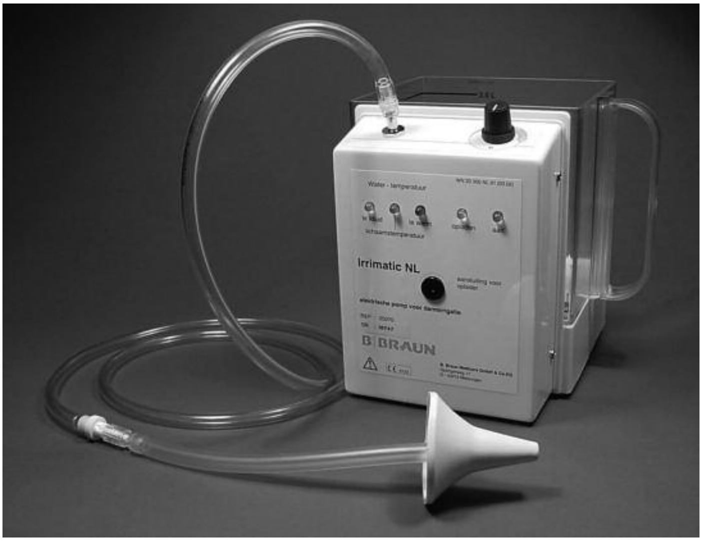

Figure 1 The Irrimatic bowel irrigation pump (B.Braun®)

Figure 2 Irrigation bag (B.Braun®)

Surgical interventions

Surgical intervention is indicated when conservative treatment fails. While most surgical interventions are aimed at correcting the underlying mechanism of the incontinence, some intend to reduce the symptoms and thereby the impact the disorder has on the patient's life. [80]

As stated previously, one of the main causes of faecal incontinence is obstetric trauma to the anal sphincter, as up to 25% of primiparous and approximately 30% of multiparous present with an anal sphincter laceration after vaginal delivery. [81,82] Symptoms of faecal incontinence occur in about one third of these patients. [81] This type of damage to the sphincter is usually corrected immediately after birth, resulting in regaining of continence in the majority of patients irrespective of the technique used (overlapping or end-to-end). [83,84] However, long-term results are far less positive, as recent studies have shown that continence after sphincter repair deteriorates over time. [85,86] In these cases, post-operative biofeedback therapy has been noted to improve quality of life and maintain functional outcome. [87]

Post-anal repair, developed by Sir Alan Parks [88] to treat idiopathic faecal incontinence, is intended to increase the length of the anal canal, to restore the anorectal angle and to recreate a flap valve mechanism by posterior plication of the levator, puborectalis and external anal sphincter to regain continence. [7,89,90] Although data on the short-term outcomes seemed promising, post-anal repair has now fallen into disgrace as reports of its long-term outcome showed that only a minority of patients remained continent. [90,91]

Dynamic graciloplasty (DGP), developed in the late eighties as a derivative of conventional graciloplasty, [92] is based on the observation that electrical stimuli cause fibre type transformation of the muscle fibres from the gracilis muscle from type 2 into type 1, [93,94] resulting in formation of a slow-twitch non-fatigable muscle from which a neosphincter can be created. [95] This neosphincter is formed by mobilization of the gracilis muscle towards its insertion while preserving the neurovascular bundle and thereby leaving the native innervation intact. The muscle is wrapped around the anus and anchored to the contralateral ischial tuberosity (Fig. 3.) The second part of the procedure, performed simultaneously or in a staged fashion, consists of implantation of the intramuscular electrodes in close proximity to the nerve and placement of the pulse generator beneath the rectus fascia in the lower abdomen.

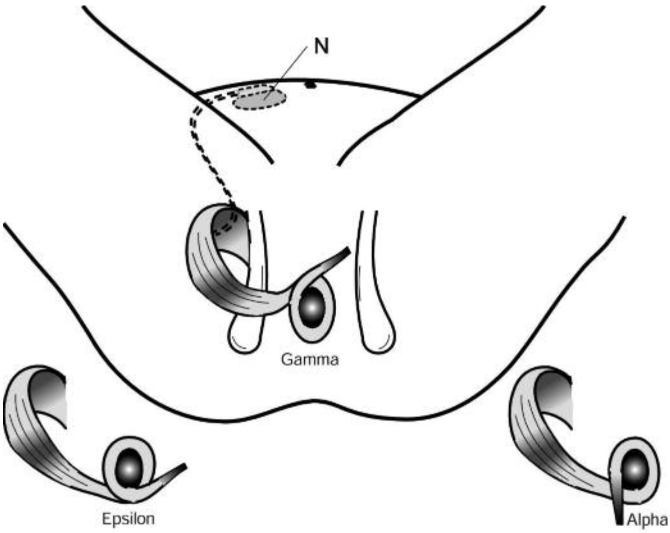

Figure 3 Dynamic graciloplasty

The electrodes are tunnelled subcutaneously and connected to this pulse generator. The pulse generator can be controlled by using a magnet or a hand held programmer. [96] Conflicting data on safety and efficacy of this procedure are available. [92,96-100] However, it is presumed that outcome after therapy correlates with surgical experience, as a learning curve has been noted. [96,98] Quality of life has been reported to improve significantly after DGP. [100] The reported surgery associated morbidity ranges from infections or wound healing-related problems to erosion or pain at the cuff site to functional problems like constipation. [101-104] Obstructed defecation due to a wrap that is too tight can be resolved by revision of the DGP and other causes of constipation may be treated with conservative therapy (dietary measures, medical therapy or biofeedback). If these options provide unsatisfactory results, retrograde colonic irrigation has been put forward as an effective alternative.[79]

For patients in whom anal repair is not warranted, for instance in case of absence of a vital gracilis muscle or after unsatisfactory results from DGP, creation of an artificial bowel sphincter (ABS) by means of an inflatable cuff (Fig. 4) may help improve continence. [105,106] This technique consists of three interconnected components: a perianally placed fluid-filled inflatable cuff, a pressure-regulating balloon in the retroperitoneum or cavum Retzii and a control pump situated in the scrotum or labia. [107] When defecation is desired, the fluid is pumped from the inflatable cuff into the pressure-regulating balloon. After approximately 5 minutes the fluid will automatically return to the cuff due to overpressure in the balloon. [105] Multiple studies [107-113] have shown that placement of an ABS can dramatically improve faecal incontinence, with success rates up to 88%, simultaneously improving quality of life in these patients. However there is a high rate of morbidity requiring reintervention or even explantation. The most important complication reported is infection, probably largely attributable to implantation of a foreign object; but erosion of the device has also been noted to occur frequently, making careful placement of the cuff essential. [114,115]

Figure 4 Acticon® neosphincter (American Medical Systems®)

A completely different option in the management of faecal incontinence is appliance of sacral neuromodulation (SNM). This technique, derived from electrical stimulation techniques used in the treatment of neurogenic bladder, [116] was first described as a treatment option for patients with faecal incontinence by Matzel *et al*. [117] In contrast to the other surgical interventions for faecal incontinence, SNM has the advantage of the possibility to predict outcome of treatment before permanent implantation (Fig. 5) of the device, by applying a test stimulation (peripheral nerve evaluation). [105] However, the exact mechanism of action remains poorly understood. As some studies showed enhancement of resting and/or squeeze pressures after applying SNM, [118-123] suggesting direct sphincter stimulation analogue to the effect of DGP, others reported no such alterations in either pressure. [1,124-126] It is therefore proposed that there is not only a motor effect, due to stimulation of the efferent nerves leading towards the sphincters, but also a sensory effect of SNM, by modulation of the afferent fibres of the sacral nerve. [123,127] Moreover, it is hypothesized that SNM might modulate higher cortical functions by causing reduction in cortico-anal excitability, in this manner influencing anal continence due to dynamic brain changes. [128]

Figure 5 X-ray of an implanted electrode and neurostimulator

Another new promising technique is percutaneous/peripheral tibial nerve stimulation (PTNS), a less invasive and simpler technique in comparison to SNM. Through the posterior tibial nerve, which originates from the sacral plexus, the same nerves are stimulated as in SNM. This stimulation can be achieved by using a percutaneous needle electrode (Fig. 6) or through the use of adhesive surface electrodes for transcutaneous stimulation. Several studies have been published on the subject showing an improvement of 60-78% on the short term. [129-131] Further research is necessary to determine long-term outcome. Moreover, a randomized controlled study comparing PTNS with SNM seems unavoidable.

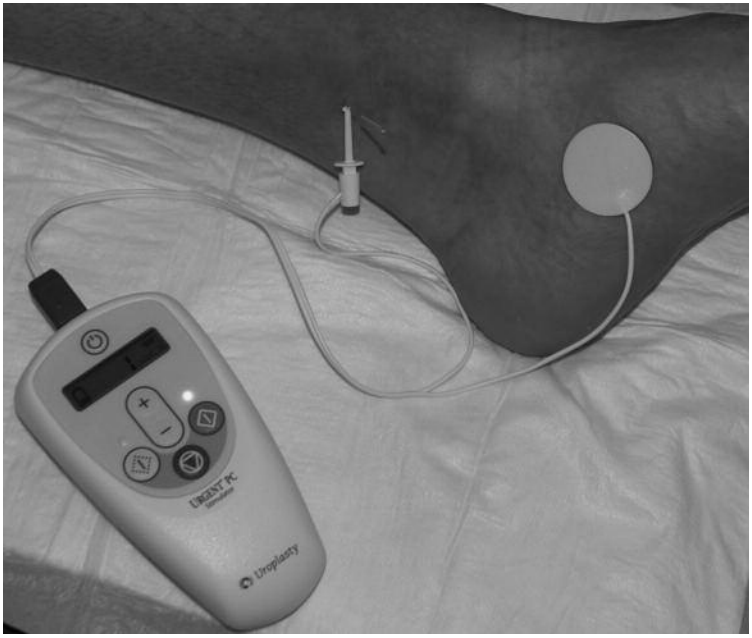

Figure 6 Percutaneous tibial nerve stimulation

The last resort treatment for patients with faecal incontinence is formation of a colostomy or ileostomy. Although the aim of formation of a permanent stoma is not to regain continence, it does restore control of bowel evacuation and is therefore an option to manage faecal incontinence in a hygienic manner permitting a normal social life. Preoperative stoma siting and counselling are extremely important. [132]

While many patients initially reject this treatment option, studies to assess quality of life of patients that received a permanent stoma for faecal incontinence show that the majority is satisfied with their surgery. [133,134] Although a number of patients severely disliked their stoma, these results do imply that healthcare workers should at least present the choice of stoma formation to those patients whose lives are severely restricted by their faecal incontinence, as it is a viable option to regain control of their lives.

Aims and outline of this thesis

The aim of this thesis is to evaluate the feasibility, outcome, safety and the possible working mechanism of SNM in patients with faecal incontinence. All studies described were performed in the period 2000-2009 and exclusively based on the data from the department of general surgery of the Maastricht University Medical Centre ($MUMC^+$).

In **chapter 2** the outcome of the first seventy five patients with faecal incontinence treated with SNM in the MUMC are presented.

Chapter 3 focuses on the mechanism of action and describes the effects of SNM on the rectum in patients with faecal incontinence who qualified for SNM.

In **chapter 4** the question if SNM affects rectoanal angle in patients with faecal incontinence is answered through defaecography studies performed prior to and during SNM.

Chapter 5 evaluates the effect of SNM on bowel frequency and (segmental) colonic transit time.

In **chapter 6** the long-term outcome and quality of life in our first fifty patients with faecal incontinence treated with permanent SNM are presented.

Chapter 7 summarizes this thesis.

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CHAPTER 2

Sacral Neuromodulation in Patients with Faecal Incontinence:
A Single Centre Study

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Abstract

Purpose

Faecal incontinence is a psychologically devastating and socially incapacitating condition. Conventional treatment is likely to improve continence in many patients, however there remains a group with persisting symptoms who are not amenable for a simple surgical repair. We evaluated the effect of sacral neuromodulation in patients with structurally intact sphincters after failure of conventional treatment.

Methods

Patients between the ages of 18-75 were evaluated. Incontinence was defined as involuntary loss of stool at least once a week, which was objectified by completion of a 3-weeks bowel habits diary. During ambulatory electrode stimulation at the S3 or S4 foramen patients completed a 3-weeks bowel habits diary. Patients were qualified for permanent stimulation when showing a reduction of at least 50 percent in incontinence episodes or days.

Results

Seventy five patients (66 women) were treated with an average age of 52 (26-75) years. Three patients had partial spinal cord injury, two patients a previous low-anterior resection and nine patients had a sphincter repair previously. Evaluation after trial screening showed that 62 patients (83%) had improved continence. Median incontinence episodes per week decreased from 7.5 to 0.67 ($P < 0.01$), median incontinence days per week from 4.0 to 0.5 ($P < 0.01$). The symptomatic response stayed unchanged after implantation of a permanent electrode and pacemaker in 50 patients. After a median follow-up of 12 months this effect could be sustained in 48 patients. Anal manometry during stimulation showed no increase of sphincter pressures.

Conclusion

Sacral neuromodulation is a feasible treatment option for faecal incontinence in patients with structurally intact sphincters.

Introduction

Faecal incontinence (FI) is a complex problem with various causes. It mainly affects women as a result of direct damage to the anal sphincter(s) or indirect damage due to stretching of the pudendal nerve during childbirth. Although FI is a psychologically devastating and socially incapacitating condition, only 5 percent of patients report this problem spontaneously. Thus, prevalence and incidence estimations based on medical chart studies give an underestimation of the problem. [1] Studies based on anonymous questionnaires show a prevalence between 2.2 and 19.6 percent for any form of FI (gas, liquid, solid) in the adult population. [2-5] When conventional treatments like dietary changes, antidiarrhoeal agents and biofeedback therapy does not improve continence surgery is an option. Patients with a sphincter defect are amenable for anal repair with an initial success rate varying from 47 to 100 percent. [6] In patients with no structural defect of the anal sphincters with primary degeneration and weakness of the anal sphincters and the pelvic floor success rates are considerably lower (10-63 percent). [6] Other forms of "repair" like the postanal repair and total pelvic repair give high initial success rates, however results on the longer run are disappointing. [6-8] Neosphincters like the gluteoplasty, graciloplasty and artificial bowel sphincter are accepted alternatives with success rates of respectively 60, 56-100 and 77-88 percent. [6,9] Neosphincter procedures however are invasive, technically demanding, require a considerable learning curve and are associated with morbidity.

Sacral neuromodulation (SNM) is a well established treatment in patients with urinary voiding disorders especially in patients with structurally intact urinary tracts. [10-14] During sacral neuromodulation both the efferent fibres as well as the afferent fibres in the sacral nerve are stimulated/modulated. How this process affects urinary incontinence is still unclear. When modifying the sacral nervous system can positively influence the micturition process, the same could possibly be achieved in FI. This idea led to the application of SNM in patients with FI. Matzel *et al* were the first to publish their successful experience in three patients. [15] Since then more reports have followed on the subject with varying numbers of patients (2-28). [16-31]

We report the results of our own experience with SNM in patients with FI in a prospective study performed in one institution.

Patients and Methods

Included were patients between the ages of 18-75 who were seen in our out-patient clinic for assessment of FI. All patients had persisting symptoms despite conventional treatment and had a structurally intact external sphincter which was confirmed by endoluminal ultrasound (EUS). In patients who underwent an anal repair previously the external sphincter had to be circumferentially intact over more then half of the length of the anal canal, this also was confirmed by endoluminal ultrasound. Exclusion criteria were a history of congenital anorectal malformations, previous rectal surgery within the last 12 months, presence of a rectal prolaps or a stoma, neurological diseases such as diabetic neuropathy and multiple sclerosis, inflammatory bowel disease, chronic diarrhoea and skin and tissue diseases resulting in an increased risk of infection. Patients completed a 3-weeks bowel habits diary. Incontinence was defined as involuntary loss of stool at least once a week.

Anal manometry was performed using a Konigsberg® catheter (Konigsberg Instrument Inc., Pasadena, Ca., USA) that was connected to a computer-assisted polygraph (Synectics Medical, Stockholm, Sweden), resting and squeeze pressures were measured before SNM and during SNM. Pudendal nerve terminal motor latency (PNTML) was recorded with the St. Marks's glove electrode, a PNTML > 2.4 msec on either side was considered to be pudendopathy. Also a defaecography was performed in all patients to exclude patients with an intussusception or a rectocele.

Previous reports have extensively described the surgical technique and equipment for SNM. [10,16,29] Electrodes were placed at the S3 or S4 foramen based on the best motor or sensory response during peripheral neural evaluation. After every surgical procedure an X-ray of the sacrum was performed to confirm the position of the electrode.

During ambulatory electrode stimulation for three weeks at the S3 or S4 foramen patients also completed a bowel habits diary. Patients were qualified for permanent stimulation when showing a reduction of at least 50% in incontinence episodes or days.

Statistical analysis was performed with the Wilcoxon's signed-rank test, data are given by their median values and range.

Results

75 patients (66 women) with a mean age of 52 (26-75) years underwent peripheral neural evaluation (PNE). All patients were initially treated with dietary changes, antidiarrhoeal agents and biofeedback therapy by their physician or surgeon before referral to our out-patient clinic. 55 patients had idiopathic incontinence, 3 patients had partial spinal cord injury, 2 patients had a previous lowanterior resection (LAR), 9 patients had a sphincter repair previously and 6 patients had a spine operation for a slipped disc. The median preoperative duration of FI was 5 (1.0-66) years, one patient had never been continent in his life. Unilateral prolonged PNTML was found in 36 patients, median PNTML values were 2.3(1.3-5.9) msec. on the right side and 2.2(1.6-8.3) msec. on the left.

Screening electrodes were placed operatively in 6 patients and with Percutaneous Nerve Evaluation in 69. During acute needle testing two patients showed no typical visual motor (contraction of the pelvic floor and the external sphincter) or subjective (vaginal/scrotal or rectal paresthesia) response. Therefore the temporary stimulation electrode was not inserted in these two patients. After X-ray of the sacrum 54 of the 73 electrodes proved to be in the foramen of S3 (19 on the left and 35 on the right side) and in 19 cases they were localised in the foramen of S4 (9 on the left and 10 on the right side).

	≥50% improvement	No improvement	Total
Idiopathic	47 (85%)	8 (15%)	55
Anal Repair	8 (89%)	1 (11%)	9
Spinal operation	6 (100%)	0 (0%)	6
Partial spinal cord injury	1 (33%)	2 (67%)	3
Low anterior resection	0 (0%)	2 (100%)	2
Total	62 (**83%**)	13 (17%)	75
Pudendopathy	29 (81%)	7 (19%)	36

Figure 1 Distribution of patients and respective success/failure rates.

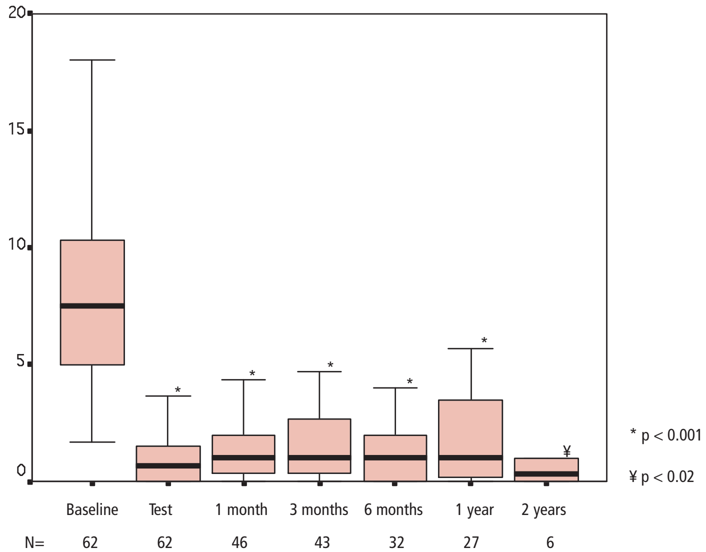

Figure 2 Median incontinent episodes per week.
(N=number of patients)

Evaluation after a 3-week trial screening period showed that 62 patients (83 percent, 95% confidence interval (95%CI) 74-91%) had improved continence (Fig. 1). Median incontinence episodes a week decreased from 7.5 to 0.67 ($P < 0.001$), median incontinence days a week from 4.0 to 0.5 ($P < 0.001$) (Figs. 2 and 3). Median improvement in continence for days and episodes were respectively 90% (36-100%) and 92% (50-100%) (Fig. 4). The symptomatic response was reproduced after implantation of a permanent electrode and neurostimulator in 50 patients (Fig. 5). For permanent implantation the same foramen was used as in the trial screening period and all patients were admitted for 3 days. After a median follow-up of 12 months improvement of continence could be sustained in 48 patients (Figs. 2-4). In two patients the symptomatic response slowly deteriorated to baseline after a follow-up of 1 year. Altering Stimulation parameters in these patients did not have any effect on their incontinence and eventually the neurostimulator and electrode were removed. So the success rate after a median follow up of 1 year, excluding the 12 patients awaiting implantation, is 76% (95%CI 66-87%). The implantation success rate, after a 50% or more improvement during trial screening, is much higher namely 96 % (95%CI 91-100%).

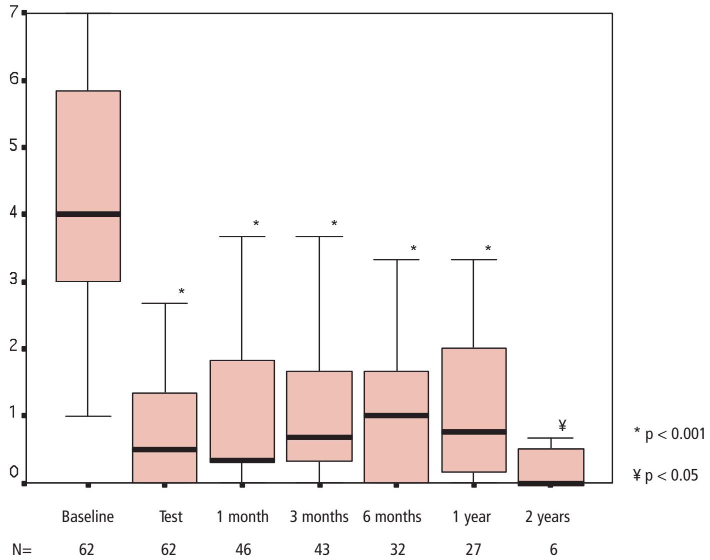

Figure 3 Median incontinent episodes per week.
(N=number of patients)

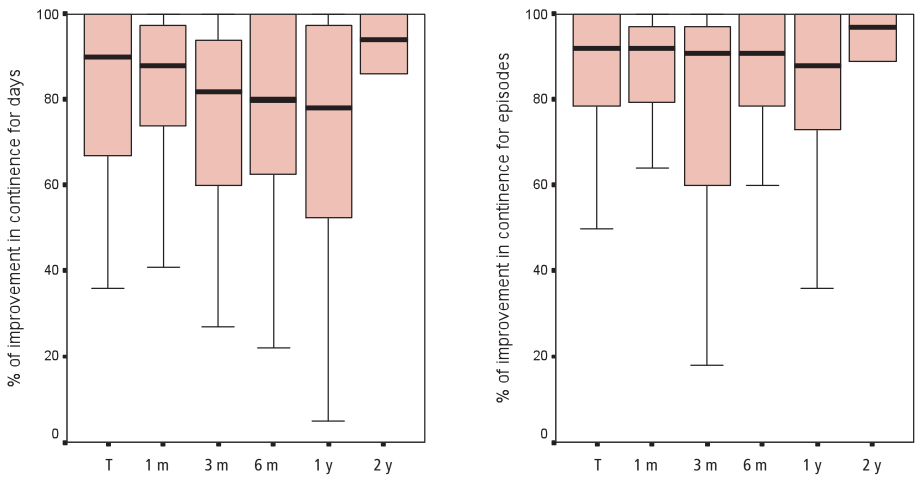

Figure 4 Percentage of improvement in continence during trial screening and follow-up.
(T=trial screening, m=months, y=years)

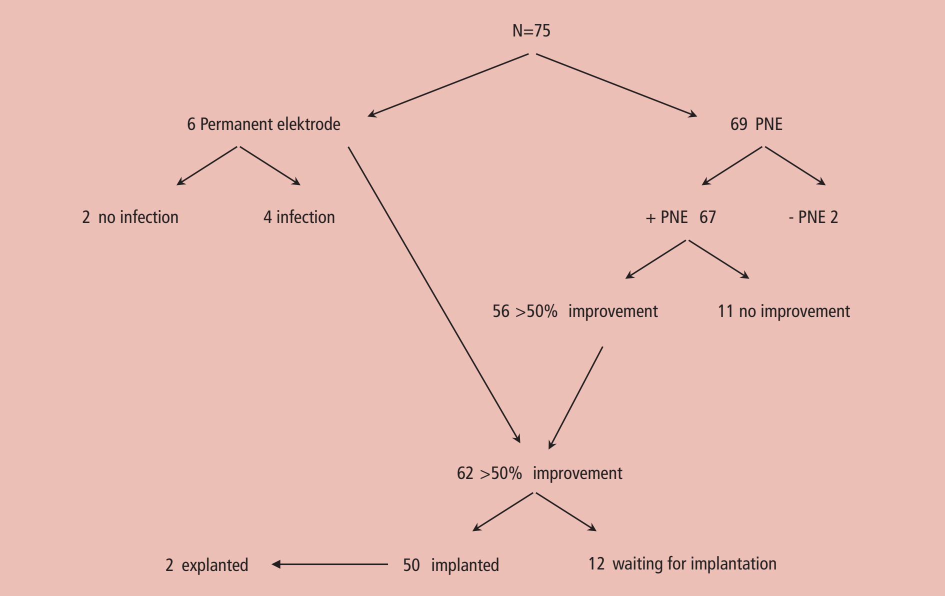

Figure 5 PNE = peripheral neural evaluation.

Urinary incontinence was present in 18 patients, 9 of these patients noticed improvement of urinary symptoms, however urodynamic studies were not performed and urinary symptoms were not objectified by urinary voiding diaries. Subjective improvement of urinary symptoms stayed unchanged during follow-up.

Continuous stimulation parameters were set at a pulse width of 210 μs, frequency of 16 Hz and at the lowest sensible amplitude possible. Except for minor changes in amplitude and polarity stimulation parameters did not change during permanent stimulation, the median stimulation amplitude at 1 month follow-up was 1.7(0.1-3.9) V (Fig. 6).

	1 month	3 months	6 months	1 year	2 years
Amplitude	1.7 (0.1-3.9) V	1.7(0.1-4.3) V	1.8(0,1-5.3) V	1.8(0.6-5.3) V	2.7(1.0-5.0) V

Figure 6 Median stimulation amplitude at follow-up.

Anal manometry during stimulation showed no significant change in both resting and squeeze pressures (Fig. 7). There was no correlation between clinical

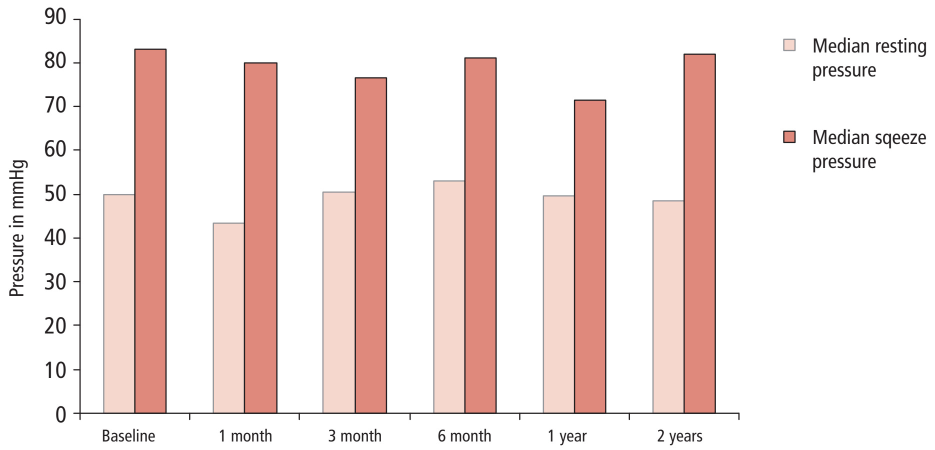

Figure 7 Median resting and squeeze pressures during permanent stimulation.

outcome and PNTML values, 81% of patients with pudendopathy had improved continence versus 85% of patients with no pudendopathy (Fig. 1).

The first 6 patients underwent the trial screening with a permanent electrode and an external stimulation cable, 4 of these patients developed a wound infection which led to the removal of the permanent electrode in 3 patients and in 1 patient also the neurostimulator was removed because the operation for permanent stimulation had already taken place. All of the remaining patients were tested with a temporary electrode, in 8 patients the temporary electrode dislodged and in 2 cases a lead breakage occurred during trial screening. In 4 patients a new PNE was performed because dislodgement/breakage occurred in the first week of trial screening. After permanent implant 2 patients developed a wound infection, the system was removed in both, 8 patients developed wound seroma which was successfully treated with antibiotics. No wound infection occurred in these 8 patients. In total 4 re-interventions took place due to technical failure after permanent implant.

Discussion

Traditionally the pathophysiology of faecal incontinence has been and still remains focussed on anal sphincter dysfunction. [32-35] Continence is not only determined by anal sphincter function but also affected by rectal sensation and compliance, pelvic floor function, colonic activity and consistency of stool. The nervous control of continence and evacuation mechanisms is mediated by a close interaction between the autonomic and somatic system. A perfect balance between them is needed for continence and normal evacuation. During sacral neuromodulation both the efferent fibres as well as the afferent fibres in the sacral nerve are stimulated. It is still unclear by which mechanism sacral neuromodulation affects urinary incontinence. The discussion is ongoing on whether this positive effect is through the activation of the pelvic floor and subsequent amplified and more physiologic afferent impulses or the direct stimulation of the afferents. [36] The effects on both the internal and external sphincter are inconsistent as uncertain. Thus, 6 studies [16-19,37,38] show an increase in both resting and squeeze pressures, whereas in 8 studies [15,20,23,25,26,28,30,31] only an increase in squeeze pressure is observed. Finally in one study [21] there is no significant change in either of the two, in accordance with our own observations. These inconsistencies can probably be explained by the level of stimulation amplitude used during stimulation. Continence is probably not just restored by a simple direct effect on the efferent motor supply to the sphincter raising anal sphincter pressures but via a more complex mechanism. Neuromodulation might also have an effect on rectal sensitivity, wall tension and compliance through modulation of the sacral reflex arcs. This might play a more important role than the stimulation of efferent motor nerves to the anal sphincters. Alteration in sacral reflexes results in stabilisation and inhibition of smooth muscle contractile activity in neuromodulation of the bladder. The same may be true for the bowel since Vaizey *et al.* observed a stabilisation of rectal contractile activity. [31]

Several studies have shown that patients with neurogenic incontinence have impaired rectal sensation to distension and to electrical stimulation. [39-43] Delay in rectal sensation may cause a delay in external anal sphincter activity leading to faecal incontinence when internal sphincter relaxation occurs before the sensation is perceived. [44] Sphincter relaxation occurs early in the defaecation process which is thought to be mediated by the intrinsic nervous system which consists of intracolonic and intrarectal nerves and a number of interconnecting plexuses. [45,46] In neurogenic incontinence this intrinsic innervation of the internal anal sphincter is normal and the visceral sensory abnormality is more likely to involve the extrinsic nerve supply which not only affects the sphincter mechanism but also the afferent pathways from the rectum. [41] It is known that in patients with bilateral loss of sacral nerves there is a serious impairment of rectal filling sensations in contrast to patients with unilateral loss of the sacral nerves who have no significant impairment of rectal filling sensations. [47,48]

The continence and evacuation mechanisms are probably, like urine storage and voiding, regulated at different levels of the nervous system. In the anterior side of the pons cerebri the micturition centre is located which mediates the micturition reflex. [49] It is thought that the micturition reflex has a threshold and that this is influenced by many afferent nerves from the conscious and unconscious cortical levels, the limbic system, the peripheral organs in the pelvis like the bladder sphincter and pelvic floor. [36,50] The same kind of regulation is also believed to exist in faecal continence and evacuation mechanisms; neurons in the reticular area of the pons respond to stimulation of parasympathetic afferent nerves that run from the rectum and it is known that patients with a vascular lesion of the pons do not have any sensation during rectal balloon distension. [51,52] Although it is difficult to explain how SNM works, this study shows it improves symptoms in a large group of patients with therapy resistant FI of varying aetiologies. The success rates in the different groups are comparable, except for the patients after LAR (0 percent) and the patients with a partial spinal cord injury (33 percent). This might have been expected because the damage to the nerve supply innervating the rectum and pelvic floor can be extensive in these patients. The medium term efficacy of SNM is promising, in several urological studies the symptomatic improvement was sustained on the long-term, if this will be the case in FI is yet to be seen. [14,53] One of the major advantages of this treatment is the fact that trial screening is predictive for symptomatic improvement after permanent implantation. The surgical procedure is relatively easy to learn and associated morbidity is low especially in comparison with other surgical options. Except for the two patients who returned to baseline 1 year after implant, almost all patients maintained initial improvement after implantation and follow-up. Some patients needed minor changes in amplitude and polarity during follow-up. Deterioration or non-reproducibility of symptomatic improvement after permanent implant could suggest a placebo effect. However Vaizey *et al.* published a double-blind cross-over study in two patients, with and without stimulation, which contradicts this suggestion. [30] A similar study with more patients would be desirable. In case of deterioration or non-reproducibility of symptomatic improvement the neurostimulator can be used in other surgical procedures like the dynamic graciloplasty. Before SNM became available in our hospital for patients with faecal incontinence, dynamic graciloplasty was advised as a surgical option to patients with persisting symptoms despite conventional treatment. Nowadays, because of our own positive experiences, our protocol has changed and SNM is the first choice of treatment in patients with failure of conventional treatment.

The present study provides data supporting a role for SNM in patients with persisting symptoms of FI after failure of conventional treatment. Further research is necessary to develop a better understanding of the working mechanism and the long term efficacy of SNM.

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Chapter 3

The Effect of Sacral Neuromodulation on the Rectum

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Br J Surg 2005 Aug;92(8):1017-23

Abstract

Background

Sacral neuromodulation is a new treatment modality for faecal incontinence. At present the exact working mechanism is still unclear. Modulation of the sacral reflex arcs might have an effect on rectal sensitivity, wall tension and compliance.

Methods

15 consecutive patients with faecal incontinence who qualified for sacral neuromodulation were asked to undergo a barostat measurement before and during sacral neuromodulation. An "infinitely" compliant plastic bag with a volume of 600 ml was placed into the rectum and connected to a computer-controlled barostat system. An isobaric phasic distension protocol was used. Patients were asked to report rectal filling sensations: first sensation (FS), earliest urge to defaecate (EUD) and an irresistible, painful urge to defaecate (maximum tolerable volume (MTV)). With these recordings rectal wall tension and compliance were calculated. Statistical analysis was performed with the Wilcoxon's rank-sum test.

Results

During isobaric phasic distension all patients experienced all rectal filling sensations at time of stimulation. Median volume thresholds decreased significantly ($P < 0.01$) for FS: 98.1 vs. 44.2 ml, EUD: 132.3 vs. 82.8 ml and MTV: 205.8 vs. 162.8 ml during stimulation. Pressure thresholds tended to be lower for all filling sensations, but the only significant reduction was in the pressure threshold to evoke MTV: 37.3 vs. 30.3 mmHg. Median rectal wall tensions decreased significantly ($P < 0.01$) for all filling sensations. There was no significant difference in compliance before and during stimulation.

Conclusion

Sacral neuromodulation affects rectal sensory perception. Further research is necessary to understand this mechanism.

Introduction

Sacral neuromodulation (SNM) is a new treatment form for faecal incontinence, especially in patients with structurally intact external sphincters who are not amenable for surgical repair. Since Matzel *et al.* published their first results in 1995, [1] several studies have been published on the subject with varying numbers of patients (n=1-37). [2-20] The exact working mechanism is still unclear. How and if the internal and external sphincter are affected by SNM are both inconsistent as uncertain. Nine studies [1,3-6,9,16,19,20] show an increase in squeeze pressure only, whereas in 6 studies [10-14,17] an increase in both resting and squeeze pressures are observed. In accordance with our own observations, [18] in 1 study [8] there is no significant change in either of the two. The working mechanism of SNM is probably more complex then just the simple stimulation of efferent motor nerves to the anal sphincters, resulting in an increase of anal pressures. Modulation of the sacral reflex arcs affecting rectal sensitivity, wall tension and compliance might play a more important role. Vaizey *et al.* using 24h ambulatory recordings during neuromodulation observed a stabilisation of rectal contractile activity. [20] In the same study rectal sensory response to balloon distension were also altered, as evidenced by increased initial sensation, urge and maximum tolerated volume. However other studies show a decrease in these measurements. [9,12-14] Although there is no simple explanation for these observations an effect of sacral neuromodulation on the rectum through sacral pathways seems highly likely.

The aim of this present study is to evaluate the effect of sacral neuromodulation on rectal sensitivity, rectal wall tension and rectal compliance.

Patients and Methods

15 consecutive patients with faecal incontinence who qualified for sacral neuromodulation were asked to undergo a barostat measurement before and during neurostimulation at the end of the peripheral neural evaluation period of three weeks. All patients had structurally intact external sphincter which was confirmed by endoluminal ultrasound. Both conservative (drug) treatment and biofeedback therapy had not improved continence. Faecal incontinence was defined as involuntary loss of stool at least once a week, which was objectified by completion of a 3-weeks bowel habit diary. During ambulatory electrode stimulation patients also completed a 3-weeks bowel habits diary. A unipolar monophase impulse was used with a pulse width of 210 and a frequency of 15 Hz at the maximum comfortably tolerated amplitude by the patient.

Patients were excluded from participation in the study if they had a history of congenital anorectal malformations, previous rectal surgery within the last 12 months, presence of rectal prolaps or stoma, neurological diseases such as diabetic neuropathy and multiple sclerosis, inflammatory bowel disease, chronic diarrhoea and skin and tissue diseases resulting in an increased risk of infection.

Anal manometry was performed with a Konigsberg® catheter (Konigsberg Instrument Inc., Pasadena, Ca., USA) that was connected to computer-assisted polygraph (Synectics Medical, Stockholm, Sweden). Pudendal nerve terminal motor latency (PNTML) was recorded with the St. Marks's glove electrode (PNTML < 2.4 msec on both sides was considered normal).

Patients were placed in the left lateral position. No bowel preparation was used. An "infinitely" compliant plastic bag with a volume of 600 ml was secured air-tight to the tip of a polyvinyl catheter. Before placement in the anorectum the bag was distended and checked for leakage. The lower border of the plastic bag to the anal verge was 5 cm. The catheter was then connected to a computer-controlled barostat system (G&J Electronics Inc., Ontario, Canada). An isobaric phasic distension protocol (fig. 1) was used starting with a baseline pressure of 0.5 mmHg. To unfold the rectal balloon and for reassurance of the patient the pressure in the rectal balloon was first raised up to 10 mmHg for 5 minutes and then lowered to baseline for 30

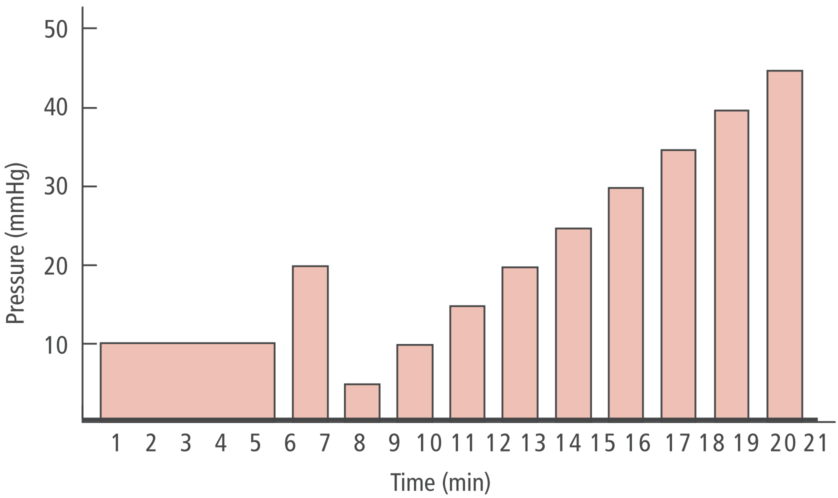

Figure 1 Representation of the isobaric phasic distension protocol.

sec. Subsequently, pressure was raised again to 20 mmHg for 1 minute and then again lowered to baseline. Next the pressure within the bag was raised in steps of 5 mmHg for 1 minute and lowered in between to baseline pressure for 30 sec., starting with 5 mmHg up to a maximum of 45 mmHg. Patients were asked to report rectal filling sensations: first sensation of content in rectum (FS), earliest urge to defecate (EUD) and an irresistible, painful urge to defecate (maximum tolerable volume (MTV)). Patients were asked to neglect sensations felt during the first 15 sec. of each distension step, only sensations lasting more then 15 sec., were registered as thresholds for the various sensations. Distension was stopped after MTV was reported by the patient.

We assumed, based on previous studies, that the distended bag within the rectum had a cylindrical shape. [21,22] Although the rectum as other biologic tissues reacts actively to distension, it is not a perfect cylinder and the balloon probably does not attain a simple geometric shape, no techniques are available to obtain a more precise indication of the form of the balloon. [23] Rectal wall tension was calculated using Laplace's law applied to a cylinder, where Tension equals pressure x radius(r). To calculate the radius the law for a cylinder was used where Volume=height (12.5 cm in this bag) x r^2 x π.

Several techniques have been described to calculate rectal compliance (the capacity to stretch to an imposed force). [23] We chose to calculate rectal compliance as follows:

$\Delta V / \Delta P$ = volume at MTV - volume at FS / pressure at MTV - pressure at FS As FS and MTV are the most parted subjective sensations which are important in relevance to incontinence. Statistical analysis was performed with the Wilcoxon's signed-rank test. Data are given as median (range).

Results

15 patients (13 women) with a mean age of 57 (35-73) years underwent a barostat measurement before and during sacral neuromodulation. Patients were incontinent for an average of 8.8 (1.0-39) years. One patient had a partial spinal cord injury and 2 patients had a sphincter repair previously. PNTML was prolonged in all patients. Screening electrodes were placed operatively in 3 patients and with Peripheral Neural Evaluation (PNE) in 12. Evaluation after trial screening showed an incontinence reduction (episodes or days, ≥ 50%) in all 15 patients. Incontinence episodes per week decreased from 10.4 (26.3-2.0) to 1.9 (5.0-0.0) ($P = 0.01$),

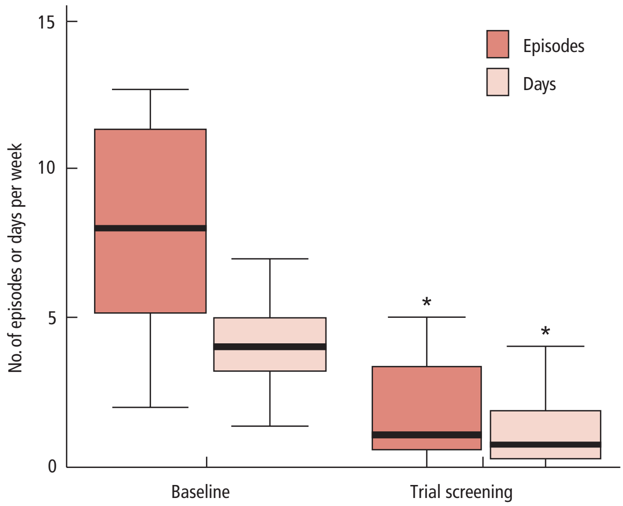

Figure 2 Number of incontinent episodes and number of days affected by incontinence per week before and during stimulation. *$P < 0.001$ versus baseline

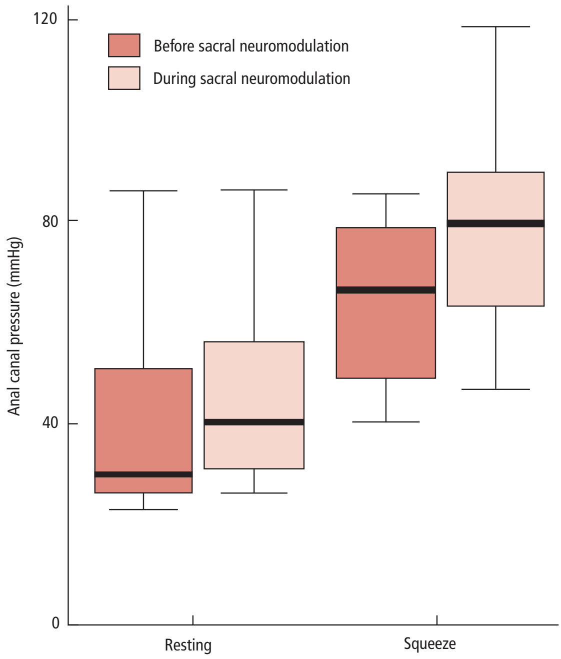

Figure 3 Anal resting and squeeze pressures before and during sacral neuromodulation.

incontinence days per week from 4.2 (7.0-1.4) to 0.7 (4.0-0.0) (*P* = 0.01) (Fig. 2). Incontinence episodes decreased with a mean of 82.4% (50-100%)(95% confidence interval(CI) 73,9-90,8%) and incontinence days decreased with a mean of 76,4%(20-100%)(95% CI 63,9-88,9%).

Anal manometry during stimulation showed no significant increase of sphincter pressures (Fig. 3). During isobaric phasic distension all rectal filling sensations were experienced by all patients except for one who experienced no sensation at all before stimulation but did experience all filling sensations during stimulation, so the data of this one patient could not be used for statistical analysis. Median volume thresholds for FS, EUD and MTV decreased significantly during stimulation (Fig. 4). Median pressure thresholds also tended to be for all filling sensations during stimulation but the only significant reduction was in the pressure threshold to evoke MTV (Fig. 5). Median rectal wall tensions decreased significantly for all filling sensations (Fig. 6). There was no significant difference in compliance before and during stimulation (Table 1).

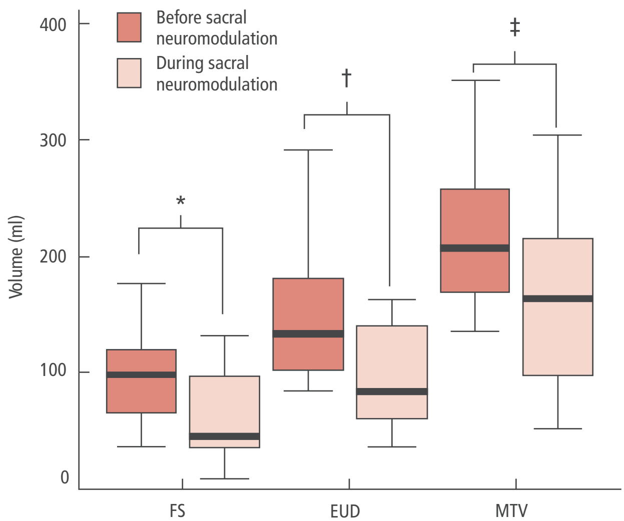

Figure 4 Volume thresholds for rectal filling sensations during isobaric phasic distension. FS = first sensation, EUD = earliest urge to defaecate, MTV = maximum tolerated volume. * *P* = 0.003, † *P* = 0.001, ‡ *P* = 0.002

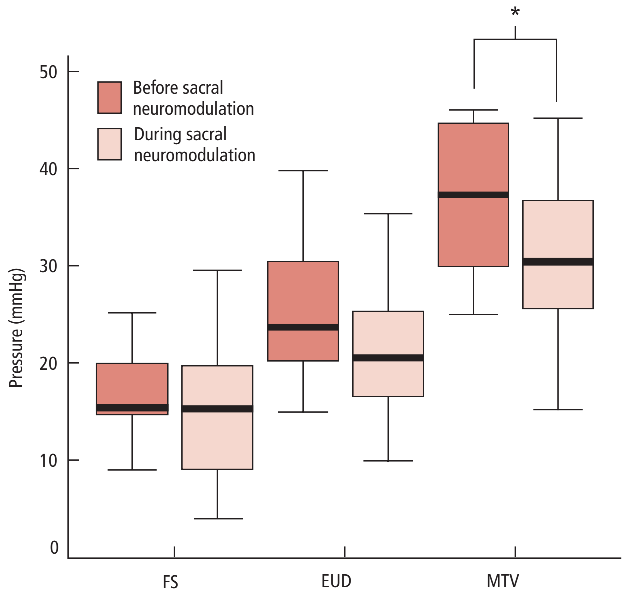

Figure 5 Pressure thresholds for rectal filling sensations during isobaric phasic distension. FS = first sensation, EUD = earliest urge to defaecate, MTV = maximum tolerated volume. * *P* = 0.005

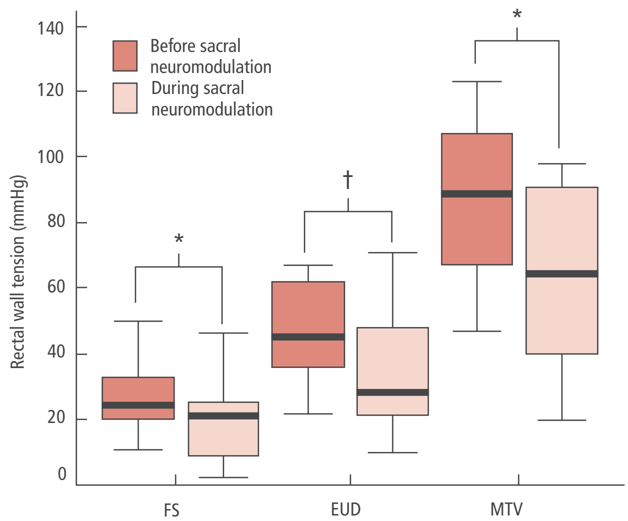

Figure 6 Rectal wall tensions for rectal filling sensations during isobaric phasic distension. FS = first sensation, EUD = earliest urge to defaecate, MTV = maximum tolerated volume. * *P* = 0.002, † *P* = 0.011

	Before Sacral Neuromodulation	During Sacral Neuromodulation	P value
Compliance (ml/mmHg)	5.8 (3.3-12.6)	4.7 (0.7-14.6)	0.9

Table 1 Compliance before and during Sacral Neuromodulation. Values are median (range).

Discussion

Although the pathophysiology of faecal incontinence has traditionally been and still remains focussed on anal sphincter dysfunction, [24-27] altered rectal sensation and adaptation are probably also major contributing factors. [28-30] Speakman *et al.* showed that patients with neurogenic incontinence have impaired rectal sensation to distension and to electrical stimulation. [31] Others have also shown impaired rectal sensation in faecal incontinence [28,32-37] contrary to studies reporting either no abnormalities or enhanced perception. [30,38-41] These conflicting data are probably due to both variation in patient population and variation in type of stimulus.

In the present study all patients had neurogenic incontinence including the two patients who had an anal sphincter repair previously. The main goal of this study was to evaluate the effect of sacral neuromodulation on rectal sensation, compliance and rectal wall tension, therefore no control group was needed to compare baseline values. Although ascending method of limits, as we decided to use, is believed to be vulnerable to response bias there are significant practical and ethical problems in using random order phasic distensions. Pain thresholds vary across subjects which may lead to presenting distensions that are well above pain threshold and the sequence for each subject has to be modified. [42] One study even concluded that the simplest and fastest method (ascending methods of limits) could be used seeing that no differences in rectal sensitivity thresholds were found in comparing different distension protocols. [43] It is believed that sensations in distension are reproducible on a day to day basis so we chose not to repeat the protocol after turning the screener off. [21,23,44,45] In addition it is unclear how long the effect of sacral neuromodulation is sustained after stopping stimulation.

The data suggest that these patients have an impaired rectal sensation considering that volume thresholds for FS, EUD and MTV during neuromodulation show a significant decrease. Pressure thresholds also show a slight decrease although the only significant decrease was seen in the threshold for MTV. Although we don't have a control group of continent subjects to prove this, these findings are in accordance with the findings of Speakman et al. Who also found a significantly higher threshold for both FS en EUD in patients with neurogenic incontinence without a significant difference in pressure thresholds and rectal compliance. Rectal compliance also showed a wide variation in this study no significant change was measured before and during neuromodulation. Although small number of subjects may also account for this finding, it suggests that sensory abnormalities in these patients were not caused by altered rectal compliance. The improvement of rectal sensation without significant change in compliance suggests normal viscoelastic properties of the rectal wall in these patients with neurogenic incontinence. These findings confirm the findings of others who found normal rectal compliance in patients with faecal incontinence. [40,41,46-48] Improvement of rectal sensation probably leads to an increased awareness of rectal content which leads to continence. When internal sphincter relaxation occurs before rectal sensation is perceived it may lead to faecal incontinence because the delay in rectal sensation may cause a delay in external anal sphincter activity. [34] The intrinsic nervous system which consists of intracolonic and intrarectal nerves and a number of interconnecting plexuses mediates sphincter relaxation which occurs early on in the defecation process. [49,50] This intrinsic innervation of the internal anal sphincter is normal in neurogenic incontinence, the abnormality in visceral sensory function is more likely to involve the extrinsic nerve supply than the intrinsic nerves. Extrinsic denervation not only affects the sphincter mechanism but also the afferent pathways from the rectum.[31] The activity in the intrinsic system is not only altered by local factors but also by the extrinsic nervous system. The extrinsic system is mainly sympathetic and parasympathetic. Both parasympathetic and sympathetic nerves are involved in transporting sensory signals from the rectum. [51] The parasympathetic nerve fibres to the rectum and descending colon are distributed by the sacral nerves S2-S4 via the inferior hypogastric (pelvic) plexus branching out in an extensive network of nerve fibres that are situated on both sides of the rectum, around the cervix uteri, both lateral vaginal surfaces and base of the bladder. [52-54] Rectal filling sensations are thought to be mediated by these parasympathetic afferent fibres. [55-57] A serious impairment of rectal filling sensations is seen in patients with bilateral loss of sacral nerves in contrast to patients with unilateral loss of sacral nerves. [58,59] From the rectum together with the parasympathetic afferent nerve fibres, the sympathetic afferent nerves run through the superior hypogastric plexus, crossing the inferior hypogastric plexus, to the spinal cord to enter between the third thoracic and third lumbar segments. Some branches run directly to the sympathetic trunk enter at the sacral portion and run upwards to also enter the spinal cord at the third thoracic and third lumbar segments. [52-54] The true physiologic role of these afferent sympathetic fibres in visceral sensation is unclear. [56,60] Both defecation pattern and rectal filling sensations are not affected by destruction of these nerves. [56,61] However, in patients with thoracic spinal cord lesions, in whom the parasympathetic nerves are completely blocked and the sympathetic nerves are partially intact, these nerves seem to mediate non-specific sensations in the pelvis or lower abdomen. [62-64]

The nervous control of continence and evacuation mechanisms are probably mediated and regulated at different levels of the nervous system. During rectal balloon distension patients with a vascular lesion of the pons do not have any sensation, furthermore it has been reported that neurons in the reticular area of the pons cerebri respond to the stimulation of parasympathetic afferent nerves from the rectum. [65,66]

There is ongoing debate on how SNM affects urinary incontinence; is it through the activation of the pelvic floor and subsequent amplified and more physiologic afferent impulses or the direct stimulation of the afferents? [67] Sacral nerves are mixed nerves containing autonomic and somatic fibres, both the efferent fibres as well as the afferent fibres are stimulated during SNM. The myelinated somatic afferents will be activated by electrostimulation before the thinner parasympathetic afferents. The IA sensory fibres which respond to phasic muscle stretch are the largest fibres with the lowest threshold, followed by the alpha motor neurones [68]. The level of stimulation needed to activate the afferent A fibres is 1.5 times that necessary to activate the alpha motor neurones. Efferent autonomic fibres have a threshold three to five times higher and the C fibres, responsible for pain, show an even higher threshold. [69] Obviously a chronic low grade stimulation is insufficient to raise sphincter pressure however the stimulus may be enough to affect the A fibres and modulate sacral reflexes. [12,20]

Whether neuromodulation gives a normalization of rectal sensory perception remains unanswered. However the provided data support a role for SNM in rectal sensory perception. The underlying mechanism unfortunately remains unclear. Future studies will have to address these issues.

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Chapter 4

Sacral Neuromodulation: Does it Affect the Rectoanal Angle in Patients with Faecal Incontinence

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Abstract

Background

In the past decade numerous studies have been published on the successful treatment of faecal incontinence with sacral neuromodulation (SNM). The underlying mechanism of action for lower bowel motility disorders remains hitherto unclear. In this study, the effect of SNM on the rectoanal angle in patients with faecal incontinence was investigated.

Patients and Methods

In twelve consecutive patients who qualified for SNM a X-defaecography study was performed before SNM and at six months after permanent implant. Three single lateral rectal views were taken: one during rest, one during squeeze and one during Valsalva's manoeuvre after which the patient was asked to evacuate as rapidly and completely as possible during lateral fluoroscopy. At six months two further defaecography studies were performed, one during stimulation on and one with the pacemaker off.

Results

The defaecography studies showed that the rectoanal angle decreased during rest, squeeze and Valsalva's manoeuvre. A slight increase in rectoanal angle was seen during defaecation. However, the differences did not reach statistical significance. SNM improved faecal continence significantly in all patients at six months. Median incontinence episodes per week decreased from 6.2 to 1.0 (P = 0.001) and incontinent days per week from 3.7 to 1.0 (P = 0.001) with SNM. There were no significant changes in the median resting and squeeze anal canal pressures, 46.5 vs. 49.7 mmHg and 67.1 vs. 72.3 mmHg respectively. Median stimulation amplitude at follow-up was 2.7(0.9-5.3) V.

Conclusion

Rectoanal angle did not decrease significantly in patients with faecal incontinence during SNM.

Introduction

Sacral neuromodulation (SNM) has emerged as a successful treatment for urinary voiding disorders and lower bowel motility disorders in recent years. [1,2] However understanding and knowledge about the underlying mechanism of action for urological disorders as well as lower bowel motility disorders remains limited. Since 1995, numerous studies have been published on SNM as a potential treatment for faecal incontinence. Some authors demonstrated a significant increase in both the maximum resting and squeeze anal canal pressures, while others did not. [3,4] Consequently a simple direct effect on the efferent motor nerve supply of the anal sphincters resulting in increased pressures is not likely to be the underlying mechanism of action. Several other hypotheses on the mechanism of action have been suggested. Altered rectal sensation and motility, effects on the sensory and autonomic function, modulation of anorectal reflexes and cortico-spinal pathways and a central modulation effect have all been proposed to be involved. [5-8] The observed clinical effect of SNM is probably caused by a combination of all these mechanisms. Through stimulation or modulation of the sacral nerve plexus all structures and pathways involved in continence and defecation are likely to be affected and altered.

Matzel *et al*. performed a cadaveric dissection study of the neuroanatomy of the striated musculature of the anal continence mechanism. [9] They found that the neural supply of the pelvic floor and external anal sphincter derives from S2-S4. However direct branches emerging proximal to the sacral plexus supply the levator ani and puborectal muscles. The remaining fibres of the sacral nerves form the sacral plexus from which the pudendal nerve originates supplying the external anal sphincter. The functional relevance of these findings was also investigated in five patients with lower urinary tract dysfunction in whom pudendal nerve stimulation resulted in a maximal rise in anal canal pressure. Stimulation of the root of S2 also increased anal canal pressure probably through the pudendal nerve, its contribution of motor fibres deriving mostly from S2. Stimulation of S3 caused a contraction of the pelvic floor musculature with a slight increase in anal canal pressure, but primarily and maybe more importantly decreasing the rectoanal angle.

An analysis by our own group, of all studies published, showed that in those studies reporting an increase in anal canal pressures the maximum stimulation amplitude comfortable to the patient was used. In those studies using voltages just above sensory threshold for stimulation no increases in anal canal pressures were found. The same publication showed that a therapeutic effect is obtainable with stimulation below the sensory threshold while the resting and squeeze anal canal pressures remained unaffected during stimulation. [10] As expected the motor threshold was significantly higher than the sensory threshold. Thus a chronic low-grade stimulation at sensory or therapeutic (lower) threshold is insufficient to raise anal canal pressures, providing evidence against a role for increased resting and squeeze anal canal pressures as the mechanism of action of SNM in faecal incontinence. Against this background and with the notion that the neural supply of the pelvic floor musculature is distinct from that of the external anal sphincter, we hypothesized that the mechanism of action of SNM might involve an effect on the rectoanal angle in patients with faecal incontinence.

The aim of this study was to analyze the effect of SNM on the rectoanal angle in patients with faecal incontinence. To that purpose data were obtained before and during SNM in patients with faecal incontinence.

Patients and methods

Twelve consecutive patients with faecal incontinence who qualified for permanent SNM were asked to undergo a defaecography study before and six months after permanent neurostimulator implantation. Patients completed a three-week bowel habits diary before and during SNM, objectifying incontinence episodes and incontinent days. Faecal incontinence was defined as involuntary loss of stool at least once a week. Conventional treatment consisting of both conservative (drug) and biofeedback therapy had failed in all patients. Exclusion criteria were a history of anorectal malformation, rectal surgery within the past 12 months, presence of a rectal prolaps, rectocele or intussusception, inflammatory bowel disease and chronic diarrhoea.

Resting and squeeze anal canal pressures were recorded with a Konigsberg® catheter (Konigsberg Instrument Inc., Pasadena, Ca., USA) that was connected to a computer-assisted polygraph (Synectics Medical, Stockholm, Sweden). Pudendal nerve terminal motor latency (PNTML) was measured with a St. Marks's glove electrode (PNTML < 2.4 msec on both sides was considered normal). Endoluminal ultrasound (SDD 2000, Multiview, Aloka, Japan, 7.5 MHz endo-anal transducer) was used to assess the external anal sphincter.

The pre-operative defaecography study was part of the pre-operative work-up to exclude intussusception or a rectocele. To perform the X-defaecography study the rectum was filled with approximately 250 ml of barium sulphate gel, the patient was then seated on a special commode. Three single lateral rectal views were taken, one during rest, one during squeeze and one during Valsalva's manoeuvre after which the patient was asked to evacuate as rapidly and completely as possible during lateral fluoroscopy. Oral barium solution was given as part of the standard examination. At six months two defaecography studies were performed, one with the neurostimulator on and one with the neurostimulator off. Both the same radiologist and the same surgeon evaluated the defaecography studies independently from each other. The rectoanal angle was measured by drawing two straight lines, one at the level of the posterior rectal wall and one at the central longitudinal axis of the anal canal.

The surgical procedure and equipment for SNM were performed and used as described extensively in previous reports. [11] To confirm electrode position an X-ray was taken on the day of surgery.

Data were analyzed using the Wilcoxon's signed-rank test in SPSS 16.0 (SPSS, Chicago, Illinois, USA). Results are given by their median values and range unless stated otherwise, $P < 0.05$ was considered significant.

Results

Twelve patients (11 women) were included with a mean age of 51.2 (26.1- 68.4) years. Patients had been incontinent for faeces for an average of 6.7 (1.5-20) years. All patients had idiopathic incontinence and additionally one patient also had a mild form of multiple sclerosis. All patients had structurally intact external sphincters on endoluminal ultrasound (two after an anal repair). Six patients also suffered urinary incontinence. Prolonged PNTML was found in ten patients, nine had bilateral pudendopathy; median PNTML values were 2.4(2-5.4) msec. on the right and 2.2(2-2.8) msec. on the left side. Ten permanent electrodes were placed in the foramen of S3 (six on the right and four on the left side) and two in the foramen of S4 (one on each side). There were only minor complications, two patients experienced wound leakage that was managed conservatively with antibiotics and in two patients the neurostimulator was re-implanted in the abdominal wall because of pain at the site of implantation in the buttock.

Defaecography showed no significant change in rectoanal angle during stimulation at six months. However, a clear tendency was observed towards a decreased or sharpened rectoanal angle during rest, squeeze and Valsalva's manoeuvre and an increased or blunted rectoanal angle during defaecation with the SNM on (Fig. 1 and 2). The interobserver agreement was assessed by the Bland-

Altman plot; 98% of the rectoanal angle measurements of both raters lie within the ± 2sd of the mean difference (Fig. 3).

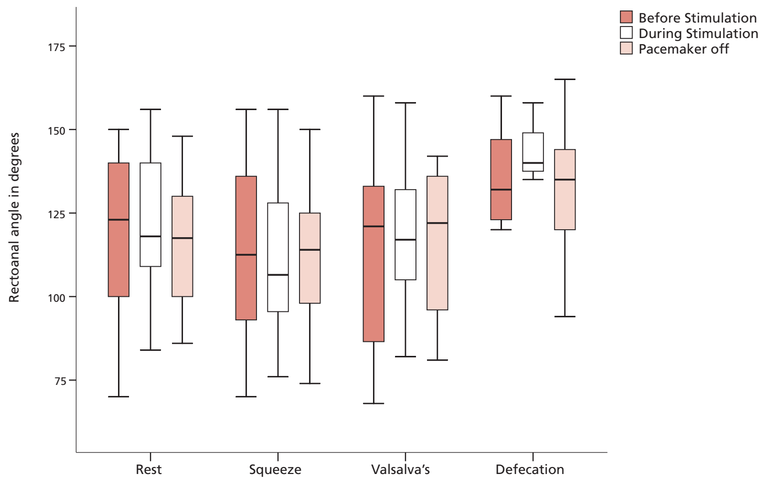

Figure 1 Median rectoanal angles measured by Radiologist during rest, squeeze, Valsalva's manoeuvre and defaecation.

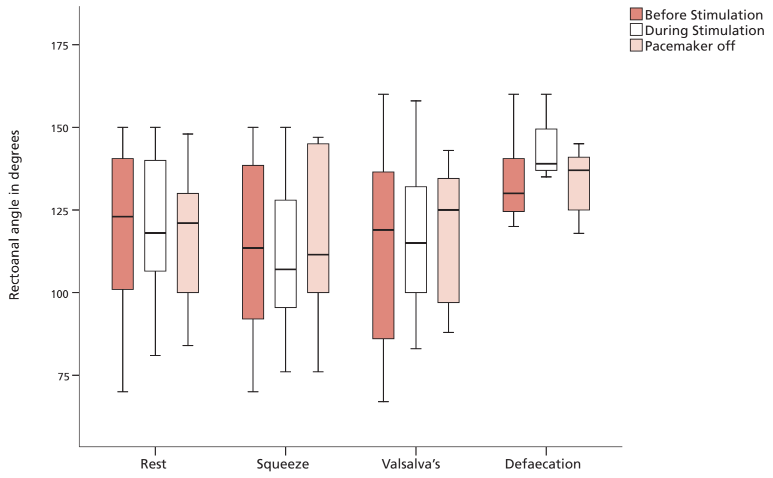

Figure 2 Median rectoanal angles measured by Surgeon during rest, squeeze, Valsalva's manoeuvre and defaecation.

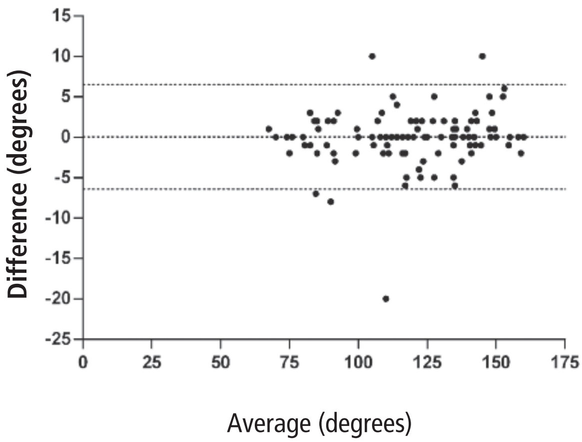

Figure 3 Bland-Altman plot; comparison of the rectoanal angles measured by a Radiologist and a Surgeon.

In all 12 patients the initial significant continence reduction of more than 50% during trial screening was reproduced after permanent implant (Fig. 4). The mean improvement six months after implantation of continence for episodes and days was respectively 86%(60-100%)(95% confidence interval (CI) 78-95%) and 77%(43-100%)(95% CI 63-90%). Anal manometry showed no significant difference in mean anal canal resting pressures (baseline: 46.5 vs. six months: 49.7 mmHg) and squeeze

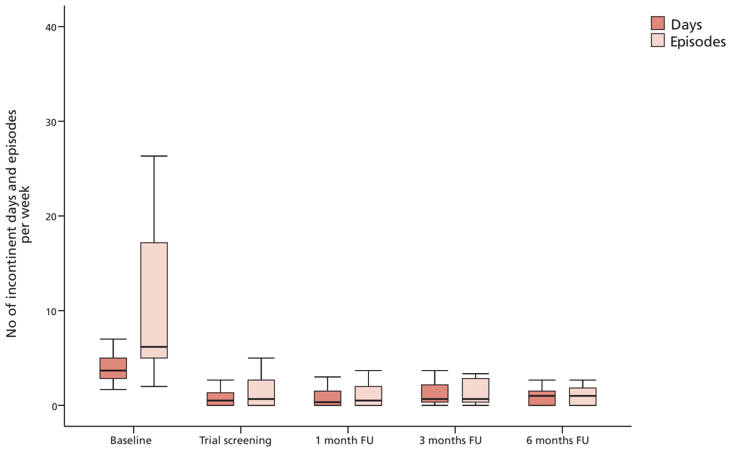

Figure 4 Box-and-whisker plot with results of median incontinent days and episodes per week. ★ $P = 0.002$ ‡ $P = 0.003$.

pressures (baseline: 67.1 vs. six months: 72.3 mmHg) before and during stimulation (Fig. 5). Median stimulation amplitude at six months follow-up was 2.7(0.9-5.3) V (Fig. 6). Three out of six patients with urinary incontinence also noticed a subjective improvement in urine continence.

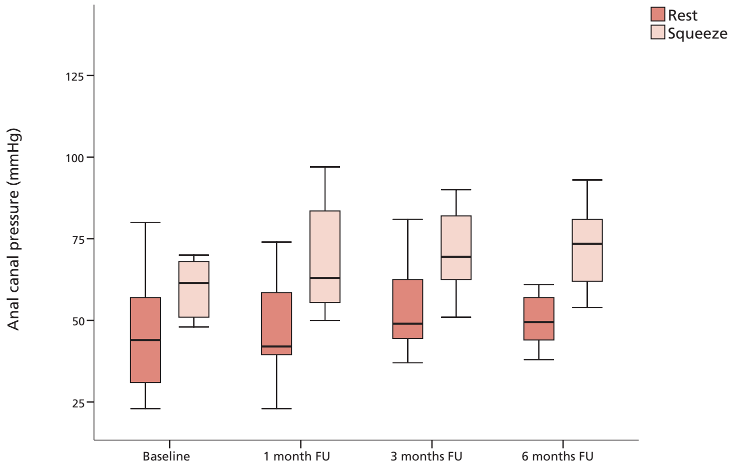

Figure 5 Box-and-whisker plot with results of median anal canal resting and squeeze pressures.

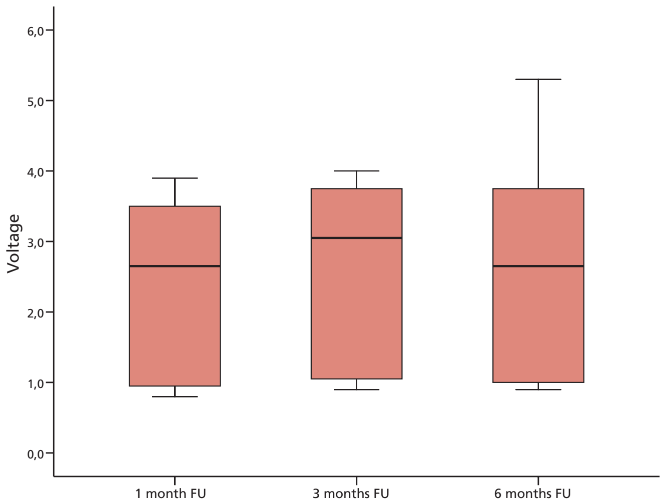

Figure 6 Box-and-whisker plot with results of median stimulation voltages after permanent implant.

Discussion

In this study the aim was to evaluate the effect of SNM on the rectoanal angle as the neural supply of the pelvic floor musculature being different of that of the external anal sphincter. A clear tendency was observed towards a decreased or sharpened rectoanal angle during rest, squeeze and Valsalva's manoeuvre and an increased or blunted rectoanal angle during defaecation when the SNM was activated. Although, this would be a logical action of SNM, which could at least partly explain the therapeutic effects, the differences were not statistically significant. This can be explained by the small population size.

The solution for faecal incontinence is probably as multifactorial as the aetiology of the problem. Since the introduction of SNM the traditional focus on anal sphincter dysfunction [12-14] is shifting towards a more complex approach. As stated by Melenhorst *et al*. the anal sphincter injury itself is an indication of existing damage and not the sole cause of faecal incontinence. [15] Altered rectal sensation and adaptation, traction and damage to the pudendal nerve and pelvic floor are also major contributing factors. [16,17] This is supported by the observation that both biofeedback therapy and SNM can improve faecal incontinence in patients with sonographic evidence of sphincter disruption. [15,18] This provides additional evidence that integrity of the sphincter is not the most important factor. Equally the working mechanisms of treatment options like biofeedback therapy and SNM targeting multiple contributing factors for fecal incontinence are completely different and therefore the positive effects difficult to explain. Although biofeedback therapy has been commonly used as the next step in conservative treatment with an overall success rate of 72% (range from 29 to 92%), [19] quantification in physiologic parameters of this improvement has been difficult. Some studies have shown improvements in rectal filling sensations and anal canal pressures, while other studies did not confirm this. Moreover there is a lack of correlation between symptomatic improvement and manometric parameters, [19,22] which is also true for SNM.

A similar study comparing rectoanal angle before and after biofeedback therapy we could not find. A comparison between both therapies concerning the rectoanal angle would be interesting and might give more insight in the mechanism of action.

Pudendal nerve dysfunction is found in 38% of women with fecal incontinence after childbirth. [23] Less is known about the damage to the pelvic splanchnic nerves (S2-S4) during childbirth and the subsequent dysfunction of these nerves. The neural control of continence and evacuation mechanisms is likely to be mediated at different levels of the nervous system as combined sensory and motor dysfunctions are found in patients with faecal incontinence. [24,25] Disruption at any level as a result of stroke, multiple sclerosis and spinal or peripheral nerve injury can give rise to incontinence due to abnormalities in visceral afferent nerve sensitivity, motor efferent nerve activity and/or central processing.

Despite these advances in our knowledge of the pathophysiology of incontinence, it is still largely unclear at what level SNM has an effect in regaining continence. The effect is probably not a simple direct efferent stimulation as the anal sphincter contractions seen at the trial screening stage for SNM during peripheral neural evaluation are mediated by afferent input. [26] Data from biofeedback therapy suggest that both an enhanced use of the residual functional capacity and cortical awareness may be involved. [27] The latter also seems to be true for SNM as patients treated with SNM not only show an improvement in rectal sensation [6] but also attribute their improvement to an increased awareness to evacuate. In urological studies it is shown that SNM modulates sensorimotor learning areas in the brain during the acute phase and brain areas implicated in the awareness of bladder filling, the urge to void and timing of micturition during the chronic phase. [7] This suggests that areas involved in alertness and awareness may play a role. The effect on the cortical sensory area in urological patients was also seen through somatosensory evoked potentials (SEPs) of the pudendal nerve, which showed a significant decrease in threshold voltage and SEP latency during SNM. [28] In patients with faecal incontinence SNM reduces cortico-anal excitability, which is reversible as a rebound effect is seen after termination of SNM. [5] Whether these dynamic brain changes directly influence the functional improvement in continence or whether they are a reactive result of the patient being continent again remains to be elucidated.

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CHAPTER 5

Sacral Neuromodulation; Does it Affect Colonic Transit Time in Patients with Faecal Incontinence

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Abstract

Objective

Sacral neuromodulation (SNM) has been a successful treatment in urinary voiding disorders for years. A concomitant effect on bowel function was observed leading to the treatment of faecal incontinence with SNM. In this study we describe the effect of SNM on bowel frequency and (segmental) colonic transit time.

Patients and Methods

Fourteen patients with faecal incontinence who qualified for permanent SNM underwent a colon transit study before and one month after permanent implant. Patients completed a three-week bowel habits diary before and during stimulation.

Results

Median incontinence episodes and days per week before SNM were respectively 8.7 and 4.2, both decreased significantly to 0.67 (P = 0.001) and 0.5 (P = 0.001) during trial screening and to 0.33 (P = 0.001) and 0.33 (P = 0.001) after permanent implant. The median number of bowel movements per week decreased from 14.7(6.7-41.7) to 10.0(3.7-22.7) (P = 0.005) during trial screening and to 10.0(6.0-24.3) (P =0.008) during permanent stimulation. Resting and squeeze pressures did not change significantly during stimulation. Segmental colonic transit time before and during stimulation for right colon, left colon and recto sigmoid were respectively 6(0-25) vs. 5(0-16) hours, 2(0-29) vs. 4(0-45) hours and 7(28) vs. 8(0-23) hours. No significant changes were found in both segmental and total colonic transit time; 17(1-65) vs. 25(0-67) hours.

Conclusion

SNM in patients with faecal incontinence led to a significant decrease of bowel movements however (segmental) colonic transit time was not influenced.

INTRODUCTION

For several years now sacral neuromodulation (SNM) has been successfully used in the treatment of urinary voiding disorders, in both detrusor instability and urinary retention. Chronic neuromodulation did not only have a positive effect on the urological disorders of patients. Patients and researchers also noticed a concomitant effect on bowel function. Decrease of coexisting symptoms of faecal incontinence, an increase or decrease in bowel frequencies and even change in stool consistency were reported by patients. Following these experiences SNM has also been used in the treatment of faecal incontinence. In 1995 Matzel *et al.* were the first to report the successful treatment in three patients with faecal incontinence. [1] Since then more reports have followed. [2-12]

The working mechanisms in both urological disorders and in faecal incontinence are still unclear. Some studies in patients with faecal incontinence show an increase in both resting and squeeze pressures, which might suggest a simple direct effect on the efferent motor nerve supply of the sphincters resulting in increased pressures. [3-5,10] Our own observations did not provide evidence of significant changes in either of the two and subsequent barostat studies in some of our patients suggested an increase in rectal sensitivity to distension. [12] It is more likely that chronic stimulation of sacral nerves not only influences pelvic organs directly but probably and more importantly through modulation of sacral reflexes influencing distal colon, rectum and pelvic floor function. Direct short stimulation at high voltage through anterior sacral nerve root electrodes has been applied therapeutically in patients with spinal cord injury to induce high-pressure peristaltic waves resulting in bowel evacuation. [13,14] A similar approach would be impossible in patients with normal sensation, because it would be too painful. However it is possible to apply continuous low grade stimulation through foramen electrodes as used with SNM in patients with urinary voiding disorders and faecal incontinence. So far four reports have been published on the effect of SNM in patients with idiopathic constipation. [5,15-17] The first two studies report the effect of temporary stimulation. In the first report on ten patients who experienced difficulty with rectal emptying, the number of bowel movements decreased as did the difficulty in emptying the rectum, number of unsuccessful attempts and time necessary to evacuate. If and how colonic transit time was influenced was not clear. In the second report two out of eight patients with slow transit constipation proved to have marked clinical benefit (increase in bowel movements) with temporary stimulation, but none of the eight patients had improved colonic transit time. The two patients were included in another study from the same group applying permanent stimulation in four patients with chronic idiopathic constipation. [16] All patients had initially shown marked improvement with temporary stimulation. In three patients this symptomatic improvement could be reproduced after permanent implant and sustained after a median follow-up of eight months. Colonic transit time was delayed in two out of four patients, in one patient colonic transit time normalized during permanent stimulation.

In this study we evaluated the possible concomitant effect of permanent SNM on bowel frequency and (segmental) colonic transit time in patients with faecal incontinence.

Patients and Methods

Fourteen consecutive patients with faecal incontinence who qualified for permanent SNM were asked to undergo a colon transit study before permanent implant and one month after permanent neurostimulator implant. All patients had involuntary loss of stool at least once a week prior to stimulation, which was objectified by a three-week bowel habits diary. Conventional treatment including biofeedback therapy had failed in all patients. None of the patients had a history of anorectal malformations, rectal surgery within the last 12 months, neurological diseases such as multiple scleroses, chronic diarrhoea, or the presence of a rectal prolaps.

To determine maximum resting and squeeze pressures a Konigsberg® catheter (Konigsberg Instrument Inc., Pasadena, Ca., USA) connected to computer-assisted polygraph (Synectics Medical, Stockholm, Sweden) was used. A St. Marks's glove electrode was used to record pudendal nerve terminal motor latency (PNTML). PNTML > 2.4 msec on either side was considered to be pudendopathy. All patients underwent defaecography to exclude intussusception or a rectocele.

Patients completed a three-week bowel habits diary before and during sacral neuromodulation, clinical parameters that were objectified were frequency of stool, incontinence episodes and incontinent days.

Colonic transit time was measured using the segmental Sitzmarks method using 3 Sitzmarks® capsules (Konsyl Pharmaceuticals, Fort Worth, Texas, USA), each capsule containing 24 radiopaque markers with three different shapes. The patients ingested one Sitzmarks capsule daily for three consecutive days, on day five a flat plate abdominal X-ray was taken to determine the location and amount of the radiopaque markers. If at day five more than a total of fifty markers were present a second x-ray was taken on day eight. The amount of markers present in each segment was equivalent to the transit time in hours.

The surgical technique and equipment for SNM have been described extensively in previous reports. [10,18] Under general anaesthesia, a permanent electrode (Medtronic 3080; Medtronic, Minneapolis, Minnesota) was surgically positioned into one of the sacral foramina S2-S4 and sutured to the periost of the sacrum. A pocket in the ipsilateral buttock was created to place the impulse pulse generator (Medtronic 3023) after connecting it to the permanent electrode. On the first postoperative day the stimulation parameters were set at a pulse width of 210 μs, frequency of 16 Hz and at the lowest amplitude that was still noticeable by the patient. On the same day an X-ray was taken to confirm the position of the electrode.

Data were analyzed using the Wilcoxon's signed-rank test. Data are given by their median values and range unless stated otherwise, $p<0.05$ was considered significant.

Results

Fourteen females with a mean age of 51.2 (26.1-64.1) years were included. Patients were incontinent for a median of 5.0 (1.5-39.0) years. Eleven patients had idiopathic incontinence and three patients had an anal repair previously. Six patients had pudendopathy; bilateral prolonged PNTML was found in five. Median PNTML values were 2.4(1.7-5.4) msec. on the right and 2.1(1.7-3.0) msec. on the left side. None of the patients had a history of constipation or evacuation problems. In all fourteen patients the initial continence improvement during trial screening was reproduced after permanent implant. An X-ray of the sacrum post implant showed that nine permanent electrodes were placed in the foramen of S3 (six on the right and three on the left side) and five in the foramen of S4 (four on the right and one on the left side). During permanent implant, it was attempted to place the electrodes in the same foramen as during trial screening. However, X-rays showed that in three cases the electrodes were placed in S4 instead of S3. This had no effect on clinical outcome after permanent implant. Median incontinence episodes and incontinent days per week before SNM were respectively 8.7 and 4.2, both decreased significantly to 0.67 ($P = 0.001$) and 0.5 ($P = 0.001$) during trial screening and to 0.33 ($P = 0.001$) and 0.33 ($P = 0.001$) after permanent implant (Fig. 1). The improvement in continence for episodes and days, one month after implantation, were respectively

93.1%(50.0-100%)(95% confidence interval(CI) 86.1-100%) and 90.8%(47.6-100%)(95% CI 83.1-98.6%). Median resting (39.5 vs. 48.5 mmHg) and squeeze pressures (66.5 vs. 71.5) did not change significantly during stimulation. Median stimulation amplitude at one month follow-up was 1.6(0.1-3.6) V.

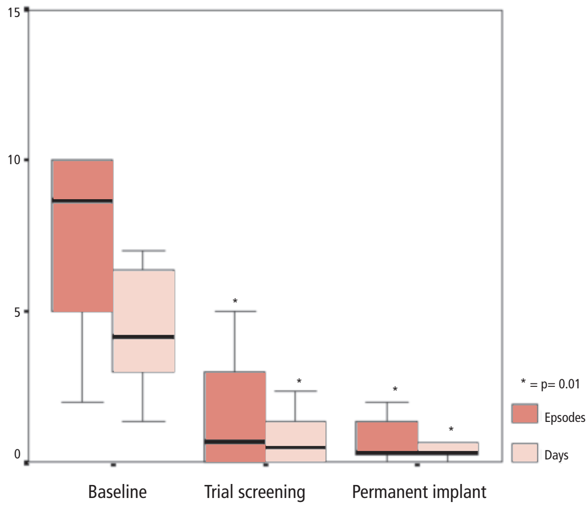

Figure 1 Median incontinence episodes and days per week.

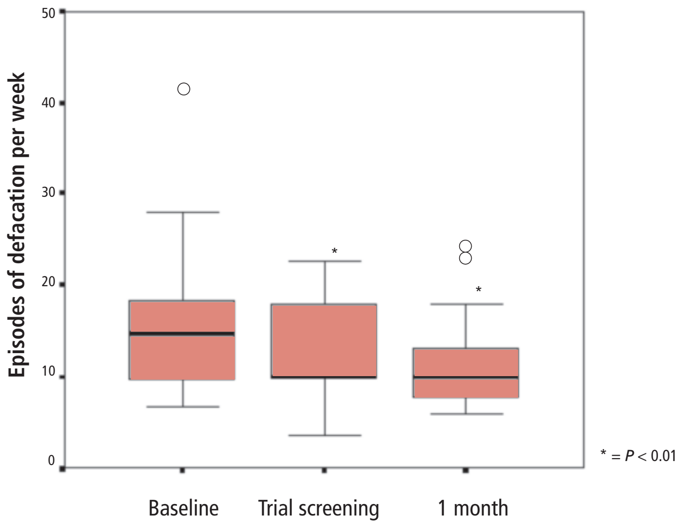

Figure 2 Median episodes of defecation per week.

The median number of bowel movements per week decreased from 14.7(6.7-41.7) to 10.0(3.7-22.7; P = 0.005) during trial screening. This decrease was also seen one month after implantation 10.0(6.0-24.3; P = 0.008)(Fig. 2). All fourteen patients underwent a colonic transit study before implantation, but a successful second colonic transit study was only obtained in thirteen patients. One patient had started to ingest the capsules one day too early and as a consequence her data could not be used in the statistical analysis. In two patients a second abdominal X-ray had to be taken on day eight. One patient had a total of 65 markers before stimulation and another patient 67 during stimulation. The second abdominal X-ray showed no markers in both patients. Segmental colonic transit time before and during stimulation for right colon, left colon and recto sigmoid were 6(0-25) vs. 5(0-16) hours, 2(0-29) vs. 4(0-45) hours and 7(28) vs. 8(0-23) hours respectively. No statistical significance was found in both segmental and total colonic transit time; 17(1-65) vs. 25(0-67) hours (Fig. 3).

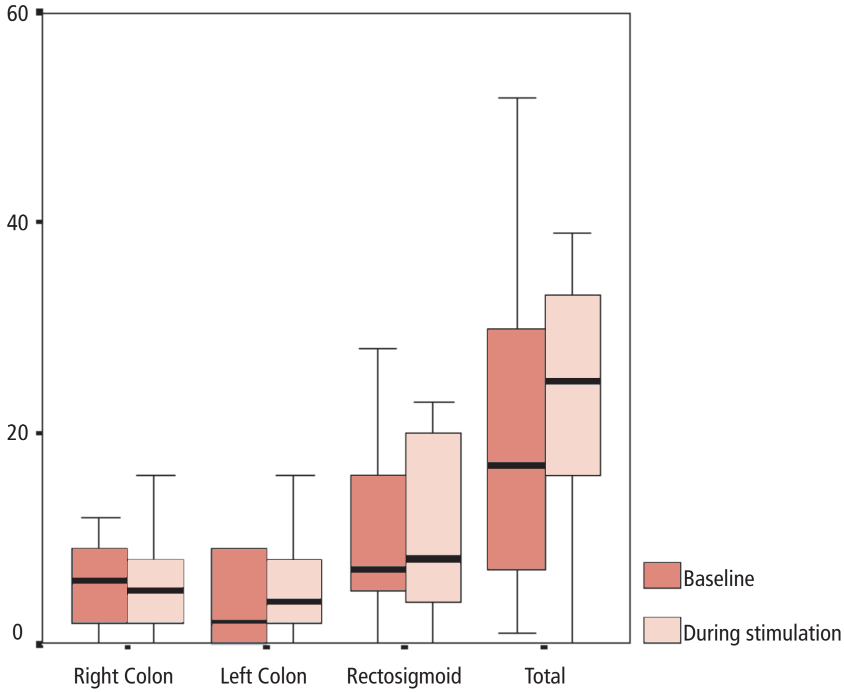

Figure 3 Median segmental and total colonic transit time

Discussion

Constipation is a complex condition defined by an international workshop on management of constipation as two or fewer bowel movements per week or the presence of two or more of the following symptoms; straining, hard stool consistency or incomplete evacuation for at least a quarter of the time. [19] Several different causes can lead to constipation but the majority of patients have idiopathic constipation. [20,21] Treatment of idiopathic constipation is difficult, although dietary changes and exercise do occasionally help most patients rely on pharmaceutical agents, which are unfortunately associated with side-effects and unsatisfactory results. Biofeedback therapy has been used successfully in some patients, with overall success rates of 68.5% for constipation due to paradoxical puborectalis contraction. [22] In the remaining substantial group of patients, in whom conservative treatment has no effect on symptoms, surgery is an option. Although sub-total colectomy leads to good results in about half of the patients, it is associated with considerable morbidity and eventually leads to permanent ileostomy in up to 23% of patients. [23,24]

In this study, we tried to quantify subjective changes in bowel frequency in patients during SNM. The number of bowel movements decreased significantly in our study both during trial screening and after permanent implant. These findings are similar to the findings of Ganio et al. but differ from three other reports from St Mark's Hospital which showing an increase in bowel frequency in patients with constipation who have a marked clinical benefit of SNM. [5, 15-17] Despite this difference in changes in bowel frequency, all four studies show an improvement in bowel symptoms using a bowel symptoms diary. All diaries differed and the most complete in our view was the one assessing the number of bowel movements, the difficulty of emptying/evacuation, the number of unsuccessful attempts, the time to evacuate and the use of laxatives. [5] However this diary did not include the percentage of time with abdominal pain and bloating nor the consistency of stool which are, in our view, important factors in patient's perception of constipation. The three other studies did include the percentage of time with abdominal pain and bloating as well as a visual analogue score for bowel symptoms. [15-17] The two latter studies also included the Wexner constipation score and the Short Form (SF) 36 health status survey giving a more broad insight in bowel function and the impact on mental an physical well-being. [25,26]

As mentioned before, two studies have already reported colonic transit time studies during SNM in patients with idiopathic constipation. One showed prolonged colonic transit time in two out of four patients, in one patient colonic transit time normalized during permanent stimulation. The other showed no improvement of colonic transit time at all, despite symptomatic improvement in two out of eight patients. We also saw no significant change in segmental and total colonic transit time, whereas bowel frequency did change significantly. Although the present study did not include patients with constipation, some effect on (segmental) colonic transit time through modulation of the extrinsic autonomic nervous system, which comprises both sympathetic and parasympathetic fibres, was anticipated. The parasympathetic nerve fibres to the rectum and descending colon, which predominantly stimulate colonic motility, are distributed by the sacral nerves S2-S4 via the inferior hypogastric (pelvic) plexus. Sacral neuromodulation might have a similar effect on the extrinsic autonomic nervous system as it does in the treatment of faecal incontinence, changing rectal sensitivity and contractile activity. Colonic transit study however failed to show any effect on colonic motility in our patients. Furthermore, it is well known that colonic transit time has no significant correlation with the presence of bowel symptoms and bowel frequency and is hampered by a large variation. [27-30] A colonic transit study might not be the correct method to evaluate the effect of sacral neuromodulation in patients with constipation.

A more correct way to evaluate the effect of sacral neuromodulation in patients with constipation would in our view be a complete bowel symptoms diary. Such a diary should asses the number of bowel movements, number of unsuccessful attempts and painful evacuations, difficulty of emptying/evacuation, time to evacuate, abdominal pain and bloating, consistency of stool, use of laxatives and assistance for evacuation. In addition, overall severity of patient symptoms, severity of constipation symptoms and the quality of life should be assessed using a visual analogue score for bowel symptoms, the Wexner constipation score and the SF 36 health status survey questionnaire. If and when these measurements are used in studies including more patients and with longer follow-up we might not only learn more about success rates but also develop a better understanding of the working mechanism in patients with idiopathic constipation.

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Chapter 6

Sacral Neuromodulation: Long-term Outcome and Quality of Life in Patients with Faecal Incontinence

Ö. Uludağ, J. Melenhorst, S.M.P. Koch, W.G. van Gemert, C.H.C. Dejong, C.G.M.I. Baeten

Accepted Colorectal Disease

Abstract

Background

Since 1994 sacral neuromodulation (SNM) has gradually and increasingly been applied in the treatment of faecal incontinence, but so far no long-term data in a substantial group of patients have been published. We evaluated the long-term outcome and quality of life in the first fifty patients with faecal incontinence treated with permanent SNM in our institution.

Patients and Methods

In our hospital the treatment with SNM was started in 2000. Data from the first fifty patients with faecal incontinence who qualified for permanent SNM have been included in the present study. Using a three-week bowel habits diary, efficacy was assessed and the Quality of Life scores were obtained by the Faecal Incontinence Quality of Life questionnaire (FIQOL) and the standard Short Form Health Survey questionnaire (SF-36).

Results

During a median follow-up of 7.1 (5.6- 8.7) years continence improvement of 50% or more was sustained in forty-two (84%) patients. Median incontinent episodes and days of incontinence per week decreased significantly during trial screening and follow-up ($P < 0.002$). The FIQOL scale showed a significant improvement in all four categories, and improvements were also found in some subscales of the SF-36 QOL questionnaire. There were no clinical significant changes in the median resting and squeeze anal canal pressures.

Conclusion

Initial improvement in continence with SNM was sustained in the majority of patients. With an overall success rate of 80% after permanent implant, SNM is a safe and effective long-term treatment in patients with faecal incontinence.

Introduction

Faecal incontinence (FI) is an underestimated debilitating disorder with marked social and psychological impediment. Although the condition has a major impact on life style, the majority of patients is reluctant to present their problem spontaneously to a doctor due to both embarrassment and insufficient knowledge of available treatment. [1] Reported community based prevalence of FI ranges between 0.4 up to 18%. [2] Studies performed in nursing homes report an even higher prevalence from 10 to 47% [3,4] with an annual incidence of 20%. [5] The prevalence of FI rises with age, suggesting degenerative changes, 63% of affected elderly are women which is related to another common cause, obstetric trauma. [6] Not only sphincter defects during childbirth are related to FI. [7] Also traction and damage to the pudendal nerve [8] and rectal sensory and motor dysfunction contribute to FI. [9] This socially incapacitating condition has a significant negative impact on both social and work-related quality of life due to anxiety, embarrassment and inability to travel.

Conventional treatments like dietary changes, antidiarrhoeal agents and biofeedback therapy are initial therapy options. If continence does not improve with conservative therapies surgery is the subsequent therapeutic option. Although restoring anatomy by anal, postanal and total pelvic repair in case of sphincter defect provides reasonable initial success rates varying from 47 to 100 percent, results decline in the longer run. [10-13] Neosphincters like the gluteoplasty, graciloplasty and artificial bowel sphincter are established alternatives. [10,14] However they are invasive, technically demanding, require a considerable learning curve and are associated with morbidity, in particular obstructed defecation in 25% of treated patients.

The first report on successful treatment of faecal incontinence with sacral neuromodulation (SNM) was published in 1995. [15] Since then, many reports on this technique have followed. [16,17] In our clinic we started with SNM for faecal incontinence in 2000. About 75% of our patients qualify for permanent implant after a positive test stimulation. [18] In this study we evaluated the long-term outcome of SNM and the quality of life in patients who qualified for permanent implant.

Patients and Methods

SNM as treatment for FI was started in our institution in 2000. Prospective data from our first fifty patients with faecal incontinence who qualified for permanent SNM have been included in this study (2000-2009). Faecal incontinence was defined as involuntary loss of stool at least once a week, which was objectified by a three-week bowel habits diary. Patients qualified for SNM when a decrease of at least 50 % in incontinence episodes or days was seen during trial screening. Conventional treatments (drug and biofeedback therapy) had failed in all patients. A history of anorectal malformation, rectal surgery within the past 12 months, presence of a rectal prolaps, rectocele or intussusception, inflammatory bowel disease and chronic diarrhoea were exclusion criteria. Patients were followed up at 1 month, 3 months, 6 months and then yearly. Quality of life was assessed with the disease-specific Faecal Incontinence Quality of Life scale (FIQOL) on a scale from 1 to 5 with 1 indicating a lower functional status [19] and the non disease-specific standard Short Form Health Survey quality of life questionnaire (SF-36 QOL) on a scale from 1 to 100. [20] All patients filled in both the FIQL and SF-36 QOL questionnaires at each follow-up.

A Konigsberg® catheter (Konigsberg Instrument Inc., Pasadena, Ca., USA) connected to a computer-assisted polygraph (Synectics Medical, Stockholm, Sweden) was used to record resting and squeeze anal canal pressures. Pudendal nerve terminal motor latency (PNTML) was measured with a St. Marks's glove electrode and PNTML < 2.4 msec on both sides was considered normal.

The used equipment for trial screening and definitive implant and the performed surgical procedures have been described extensively in previous reports. [21]

Statistical analysis was performed using SPSS version 16.0 (SPSS, Chicago, Illinois, USA). The Wilcoxon's signed-rank test or paired t-test was used for baseline and follow-up data comparison. $P < 0.05$ was considered significant, adjustments were made for multiple comparisons by using $P < 0.0125$ (0.05/4) for the FIQOL questionnaire and $P < 0.006$ (0.05/8) for the SF-36 QOL components. Results are given by their median values and range unless stated otherwise.

Results

Forty-five women and five men with a median age of 54.3 (26.1- 74.1) years were included; patients were suffering from faecal incontinence for an average of 11.5 (1-60) years. The group of women counted 93 vaginal deliveries. Previous medical history of patients is shown in Table 1. Urinary incontinence was also present in sixteen patients. All patients had structurally intact external sphincters on endoluminal ultrasound; eight patients had undergone an anal repair in the past. In twenty patients prolonged PNTML was found and fourteen had bilateral pudendopathy. The median PNTML values were 2.3(1.3-5.9) msec. on the right and 2.1(1.0-8.3) msec. on the left side. Twenty-five electrodes were placed in the foramen of S3 on the right and thirteen on the left side, in total twelve were placed in the foramen of S4 (seven on the right and five on the left side).

	Number of patients
Vaginal delivery	36
Hysterectomy	19
Recto(vagino)pexy	16
Anal repair	8
Hemorhoidectomy	4

Table 1 History of included patients

Median follow-up was 7.1(5.6- 8.7) years, eight (16%) patients showed deterioration of continence during follow-up. Currently three of these patients have a colostomy (one after dynamic graciloplasty which also failed to improve continence) and another three patients use colonic irrigation. In seven patients the neurostimulators and electrodes were removed, one patient still uses sacral neuromodulation in combination with colonic irrigation.

In four patients infection of the device occurred and both the neurostimulator and the electrode had to be removed. In two patients the infection occurred after a re-intervention, in one after repositioning of the electrode and the other after implanting a second electrode. All patients were re-implanted.

Two patients stopped with sacral neuromodulation because of radiating pain towards the leg. One of these patients was treated with a dynamic graciloplasty and one with colonic irrigation, both with satisfying results. Wound leakage because of seroma occurred in six patients, which was managed conservatively with antibiotics. In one patient the neurostimulator was re-implanted in the abdominal wall due to pain at the site of implantation in the buttock. In total eleven re-interventions were performed because of electrode dislocation (7), electrode breakage (2), implantation of a second electrode and revision of a neurostimulator pocket.

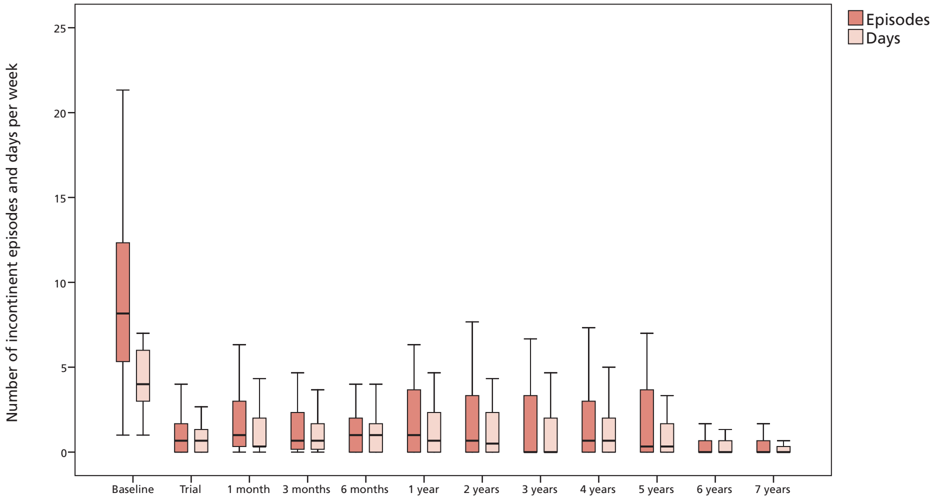

Figure 1 Box-and-whisker plot with results of median incontinence days and episodes per week, P for all values during follow-up is < 0.002 compared to baseline. (Data of all patients included up to explantation in case of deterioration)

The improvement of continence of 50% or more, observed during trial screening was sustained in forty-two (84%) patients until last follow-up visit. Median incontinent episodes and days of incontinence per week decreased significantly during trial screening and follow-up ($P < 0.002$) (Fig. 1). The improvement of continence remained stable at a low level over time in those who retained the stimulator. The FIQOL scores showed a significant improvement in all four categories ($P < 0.0125$) (Fig. 2). Analysis of the SF-36 QOL questionnaire showed improvement in some subscales (Fig. 3). Significant improvement was seen in the social functioning, role emotional and mental health subscales ($P < 0.006$). No clinically significant change was found in median anal canal resting pressures and squeeze pressures before and during stimulation (Fig. 4). Median stimulation amplitude at follow-up is shown in

Figure 5. Of the sixteen patients with urinary incontinence, five also noticed a subjective improvement in urine continence.

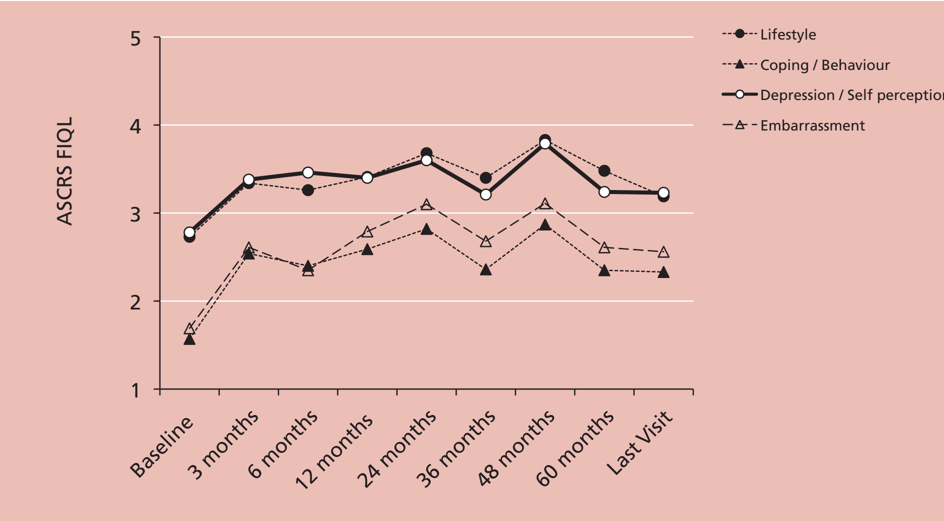

Figure 2 Mean Fecal Incontinence Quality of Life Scores, $P < 0.0125$ comparing all follow-up scores with baseline.

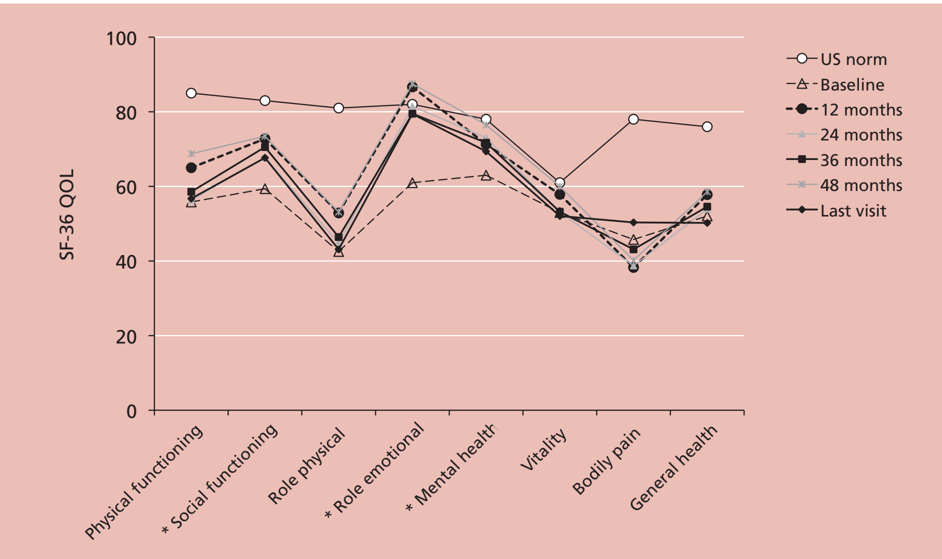

Figure 3 Mean SF-36 Quality of Life Scores Compared to US Norm, * $P < 0.006$ compared to baseline.

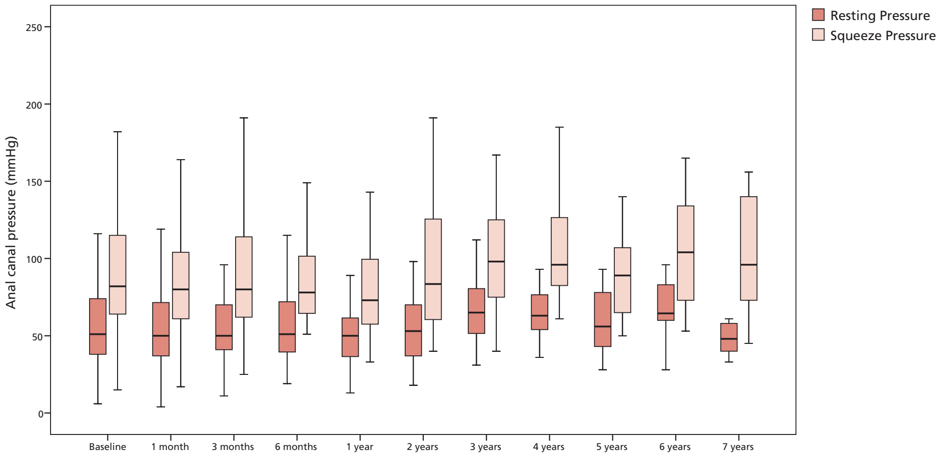

Figure 4 Box-and-whisker plot with results of median anal canal resting and squeeze pressures.

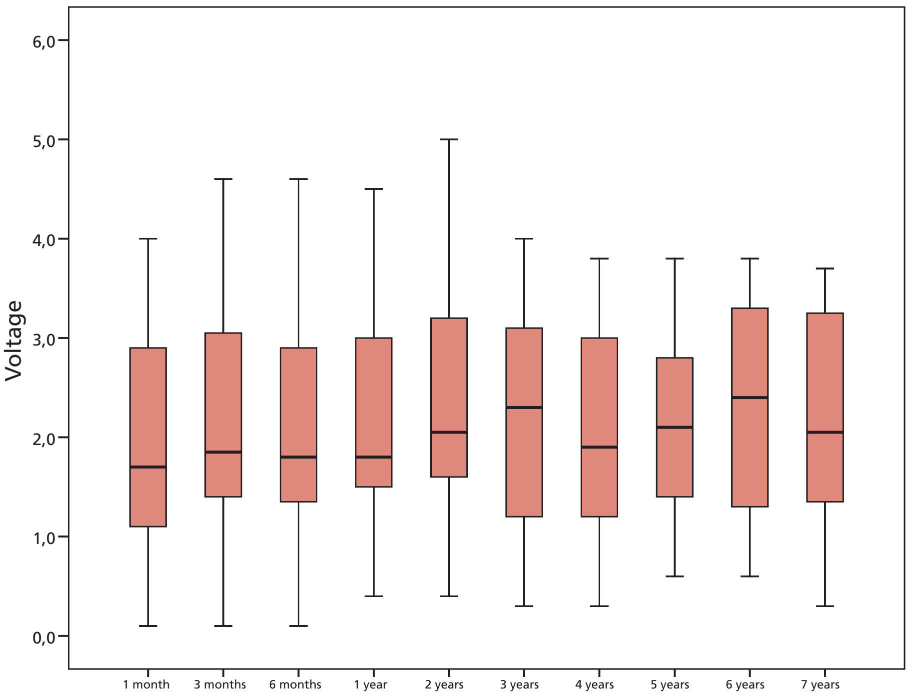

Figure 5 Box-and-whisker plot with results of median stimulation voltages after permanent implant.

Discussion

In this study we have shown that SNM is an effective method for the long-term treatment of faecal incontinence in patients who qualify for permanent implant. SNM is not only effective in functional improvement in patients with faecal incontinence, whatever its cause, but also in improving quality of life. This is not unexpected since FI is a socially debilitating disorder. [22] During follow-up the FIQOL scores improved significantly in all four categories in contrast to the SF-36 QOL scores, which only showed significant improvements in the social functioning, role emotional and mental health subscales. These findings can probably be attributed to the fact that the SF-36 QOL scale is a generic measure and therefore not as sensitive as the FIQOL scale, which is a condition-specific QOL scale designed to address the specific elements that will affect the lives of patients with FI. [19]

Our findings are in accordance with previous reports, [17,21,23] although these were limited by a short follow-up. Up till now only one report with a mean follow-up of 9.8 years has been published but this was a very small series of patients. Only nine patients had a long-term follow-up and a pre- and post-SNM quality of life analysis was performed in only four patients. [24]

In the present study initial improvement of continence could not be maintained in eight patients during follow-up and in addition two patients stopped SNM because of radiating pain towards the leg resulting in an overall long-term success rate of 80%. Since 75% of the screened patients in our institution qualify for permanent implant the overall long-term success rate in patients who qualify for trial screening would be 60%. The reason for secondary loss of the therapeutic effect after permanent implant is not clear. Thus far no predictive variables could be associated with therapeutic success after permanent implant although one study has shown that patients who have a neurologic cause of incontinence are more likely to achieve therapeutic effect after permanent implant. [25] It may well be as suggested earlier that the mechanisms of action are not completely identical. Chronic stimulation may induce persistent changes through plasticity in the neuronal control mechanism of the central nervous system. [26] This may not be the case in temporary or acute stimulation, which modulates predominantly areas involved in sensorimotor learning that might become less active during the course of chronic SNM. [27]

Only four (8%) patients had a serious infection that led to the removal of both the neurostimulator and the electrode, all infections occurred after re-intervention. Wound seroma occurred in 6 (12%) patients and all were treated conservatively.

Sacral neuromodulation for faecal incontinence seems to be a relatively safe procedure with minimal risk of serious complications in accordance with findings concerning its long-term use in urologic disorders. [28,29] Alternative procedures like dynamic graciloplasty and artificial bowel sphincter are known to be more invasive and are associated with a higher complication and morbidity rate. [30]

The initial costs of the device are high and thus far our hospital is the only hospital in the Netherlands where it is permitted by the healthcare providers to perform this procedure in patients with faecal incontinence. However, recent cost analysis studies of sacral neuromodulation for faecal incontinence have shown it to be highly cost effective. [31,32] The 5-year cumulative costs for sacral neuromodulation are lower than the costs of a colostomy. Furthermore, progressive introduction of sacral neuromodulation in 75 to 100 patients/year would lead to an estimated incremental budget impact of merely 0.1% in the total costs of patients with faecal incontinence.

In our opinion SNM, with its excellent short and long-term outcome with respect to FI and its beneficial effect on quality of life in relation with the safety of this procedure, should be considered as first choice in the surgical treatment of faecal incontinence when conservative management is unsuccessful.

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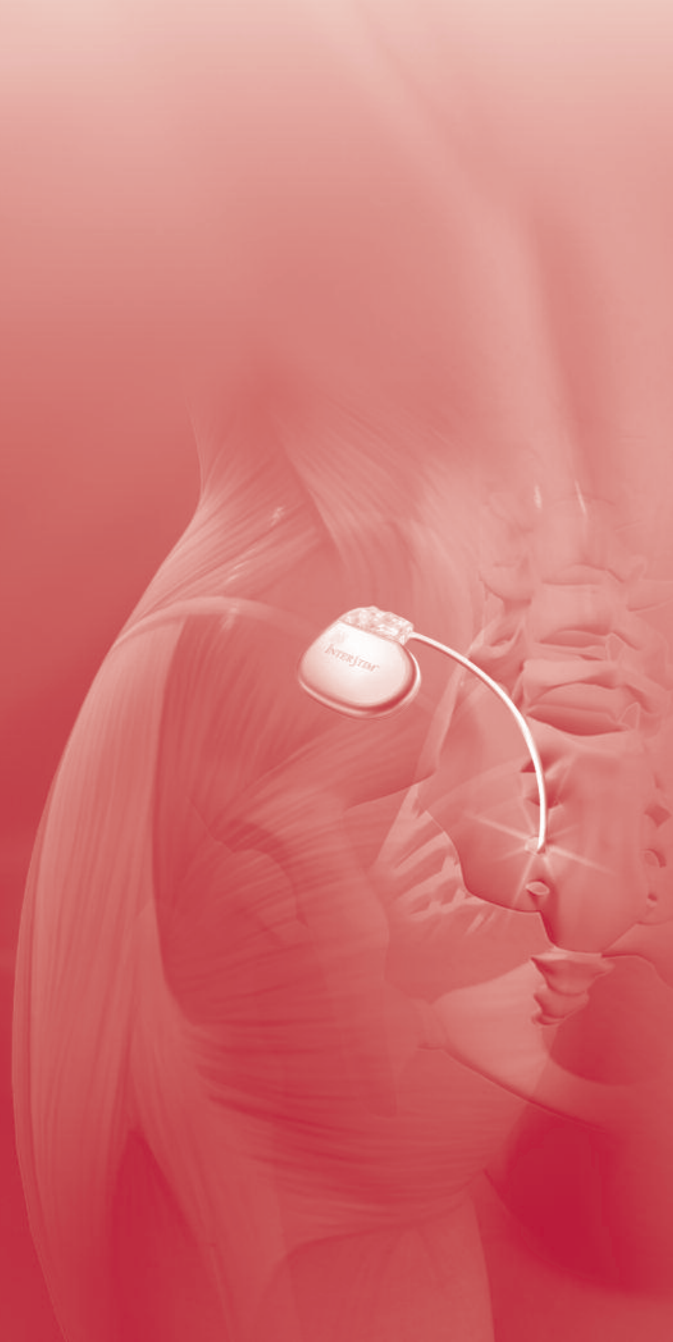
CHAPTER 7

Summary and General Discussion



In the present thesis, the applicability, safety and feasibility of sacral neuromodulation (SNM) as a treatment for faecal incontinence is summarized. After a decade of experience with SNM in our hospital we can conclude that SNM is an effective and in the meanwhile well-established treatment for functional bowel disorders, especially in patients with faecal incontinence. [1-3] The numerous international publications on the subject not only support our findings in patients with faecal incontinence but have also paved the way for SNM in the surgical treatment of faecal incontinence. [4-6] The traditional treatment of faecal incontinence solely focusing on anal sphincter dysfunction has been abandoned and the focus has shifted towards a more complex approach.

Chapter 1 provides an overview of the literature on faecal incontinence and its treatment options. Faecal incontinence is a common but complex problem with high costs for the patient and the community. It is a psychologically devastating and socially incapacitating condition that can have profound effects on patient well being.

Adequate clinical, physiological and structural assessment through advanced imaging techniques is fundamental for assessing the cause and degree of the incontinence. Both conservative therapies (medicinal therapy, biofeedback training and colonic irrigation) and surgical interventions (sphincter repair, neosphincter formation, artificial bowel sphincter, sacral neuromodulation or formation of a stoma) are therapeutic options. However, the choice of treatment is mostly dependent on available knowledge and existing facilities.

In **Chapter 2** the outcome of our first seventy five patients treated with SNM are presented. Incontinence was objectified by completion of a 3-weeks bowel habits diary that patients also completed during ambulatory electrode stimulation at the S3 or S4 foramen. Reduction of at least 50% in incontinent episodes or days per week qualified patients for permanent implantation. Sixty six female and nine male patients were treated; the average age was 52 years (26-75). Sixty two patients (83%) had improved continence during trial screening. Median incontinence episodes per week decreased from 7.5 to 0.7 ($P < 0.01$), median incontinence days per week from 4.0 to 0.5 ($P < 0.01$). The symptomatic response remained unchanged in the fifty patients who received an implantation of a permanent electrode and neurostimulator. However, after a median follow-up of 12 months this effect could only be sustained in forty eight patients. SNM proved to be a feasible treatment option for faecal incontinence in patients with structurally intact sphincters.

In **Chapter 3** the effect of SNM on the rectum was evaluated by barostat measurements in patients with faecal incontinence who qualified for SNM. Fifteen consecutive patients were asked to undergo barostat measurements before and during sacral neuromodulation. An isobaric phasic distension protocol was used and patients were asked to report rectal filling sensations: first sensation (FS), earliest urge to defaecate (EUD) and irresistible, painful urge to defaecate (maximum tolerable volume (MTV)). Rectal wall tension and compliance could be calculated from these recordings. During stimulation median volume thresholds decreased significantly ($P < 0.01$) for FS: 98.1 vs. 44.2 ml, EUD: 132.3 vs. 82.8 ml and MTV: 205.8 vs. 162.8 ml. Pressure thresholds tended to be lower for all filling sensations and median rectal wall tensions decreased significantly ($P < 0.01$) for all filling sensations. There was no significant difference in compliance before and during stimulation. Sacral neuromodulation does affect rectal sensory perception, but it remains unclear if the success of SNM is explained solely by its effect on the rectum.

Chapter 4 describes the effect of SNM on the rectoanal angle in patients with faecal incontinence. In twelve consecutive patients who qualified for SNM a defaecography study was performed before SNM and two further studies at six months after permanent implant, one during stimulation and one with the neurostimulator off. The rectoanal angle decreased during rest, squeeze and Valsalva's manoeuvre and a slight increase in rectoanal angle was seen during defaecation. However, the differences did not reach statistical significance.

In **Chapter 5** the effect of SNM on bowel frequency and (segmental) colonic transit time is described. Fourteen consecutive patients with faecal incontinence who qualified for permanent SNM underwent a colon transit study before and one month after permanent implant. The median number of bowel movements per week decreased from 14.7(6.7-41.7) to 10.0(3.7-22.7) ($P = 0.005$) during trial screening and to 10.0(6.0-24.3) ($P = 0.008$) during permanent stimulation. No significant changes were found before and during stimulation in both segmental (right colon 6(0-25) vs. 5(0-16) hours, left colon 2(0-29) vs. 4(0-45) hours and recto sigmoid 7(28) vs. 8(0-23) hours) and total colonic transit time (17(1-65) vs. 25(0-67) hours). Although no significant change occurred in (segmental) colonic transit times a significant decrease of bowel movements was seen in patients with faecal incontinence during SNM.

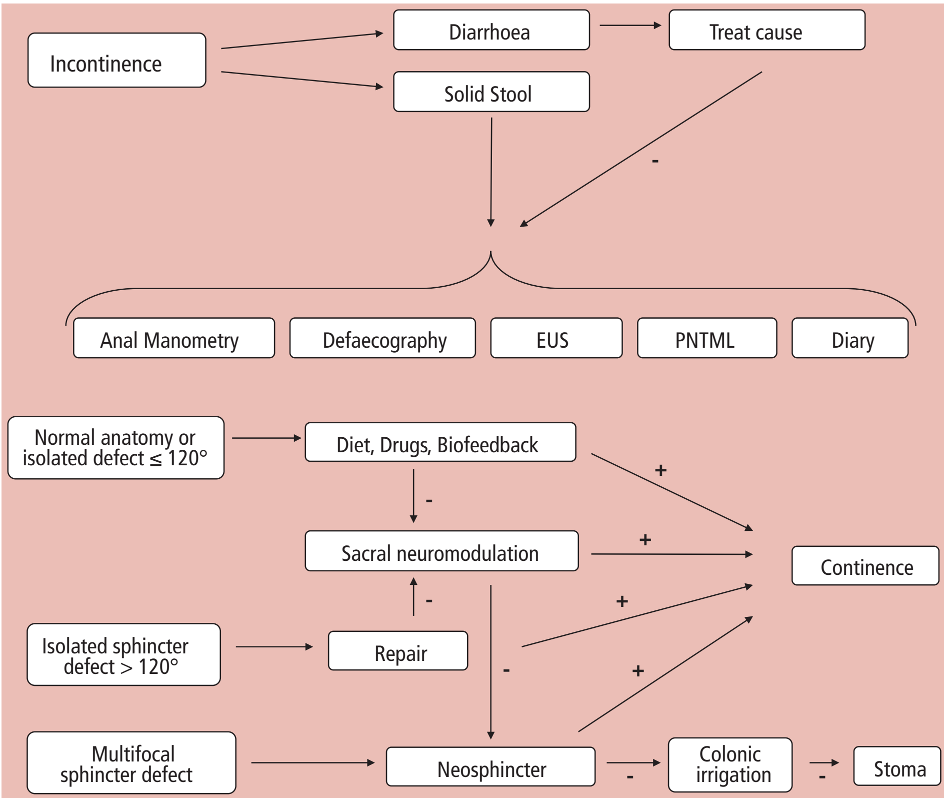
Chapter 6 evaluates the long-term outcome and quality of life in patients with faecal incontinence treated with permanent SNM. Data from our first fifty patients who qualified for permanent SNM were included in this study. A three-week bowel habits diary assessed efficacy, and the quality of life scores were obtained by the Faecal Incontinence Quality Of Life questionnaire (FIQOL) and the standard Short Form Health Survey questionnaire (SF-36). With a median follow-up of 7.1 years this is the longest reported follow-up in a substantial group of patients treated by SNM hitherto. Continence improvement of 50% or more was maintained during follow-up in forty two (84%) patients. A significant decrease in median incontinent episodes and days per week was seen during trial screening and follow-up ($P < 0.002$). Quality of life improved significantly in all four categories of the FIQOL scale and in some subscales of the SF-36 QOL questionnaire. Differences in median resting and squeeze anal canal pressures did not reach clinical significance. Although initial improvement in continence with SNM could not be maintained in all patients, with an overall success rate of 80% after permanent implant, SNM proves to be a safe and effective long-term treatment in patients with faecal incontinence.

Future perspectives and research should focus on the physiological mechanism of action and the cost effectiveness of SNM in patients with faecal incontinence. A better understanding of the physiological mechanism might not only lead to a better patient selection, but may well make the test stimulation, which currently is the only predictor available, eventually obsolete. With better understanding the application of SNM could also be broadened to other groups of patients with conditions other than FI. [7] SNM has already been successfully used in the treatment of patients with 'late-onset' constipation. [8-10] Patients suffering from constipation since childhood have not been studied yet. In our institution, we started a study to treat adolescent constipation patients with SNM with very good results. These results will be published in the near future. Studies reporting the effect of SNM on peri-anal pain, clitoral/pelvic pain and erectile/sexual dysfunction have been published but need further investigation. [11-14] Furthermore, a significant reduction in diarrhea-predominant irritable bowel symptoms and improvement of quality of life was seen with percutaneous sacral nerve evaluation in patients with irritable bowel syndrome. [15] These applications of SNM for various conditions solely suggest a complex mechanism of action affecting sensory and possibly autonomic function.

The availability of functional brain imaging such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) are intriguing possibilities. [16, 17] Future research using PET and fMRI should give us a better insight in both the pathophysiology of FI as well as the working mechanism of SNM.

Costs of SNM are a main concern. Although the exact costs associated with faecal incontinence are unknown the indirect or non-medical costs, such as loss of productivity, are more than half of total costs of FI. [18] Several studies have already shown SNM to be cost effective in the treatment of faecal incontinence. [19-21] Cost effectiveness studies will probably have to be performed in each country separately to convince local healthcare providers of the beneficial effect of SNM in patients with FI on both healthcare and society reducing the macro-economic burden. Further technical developments can also affect costs of SNM by reducing post-operative adverse events, such as infection, pain and lead migration. Stimulators with a longer life span or even rechargeable devices should lower costs further since the number of patients needing a replacement of the stimulator will grow in the future.

Clinical Pathway at the MUMC+ for Patients Presenting with Faecal Incontinence



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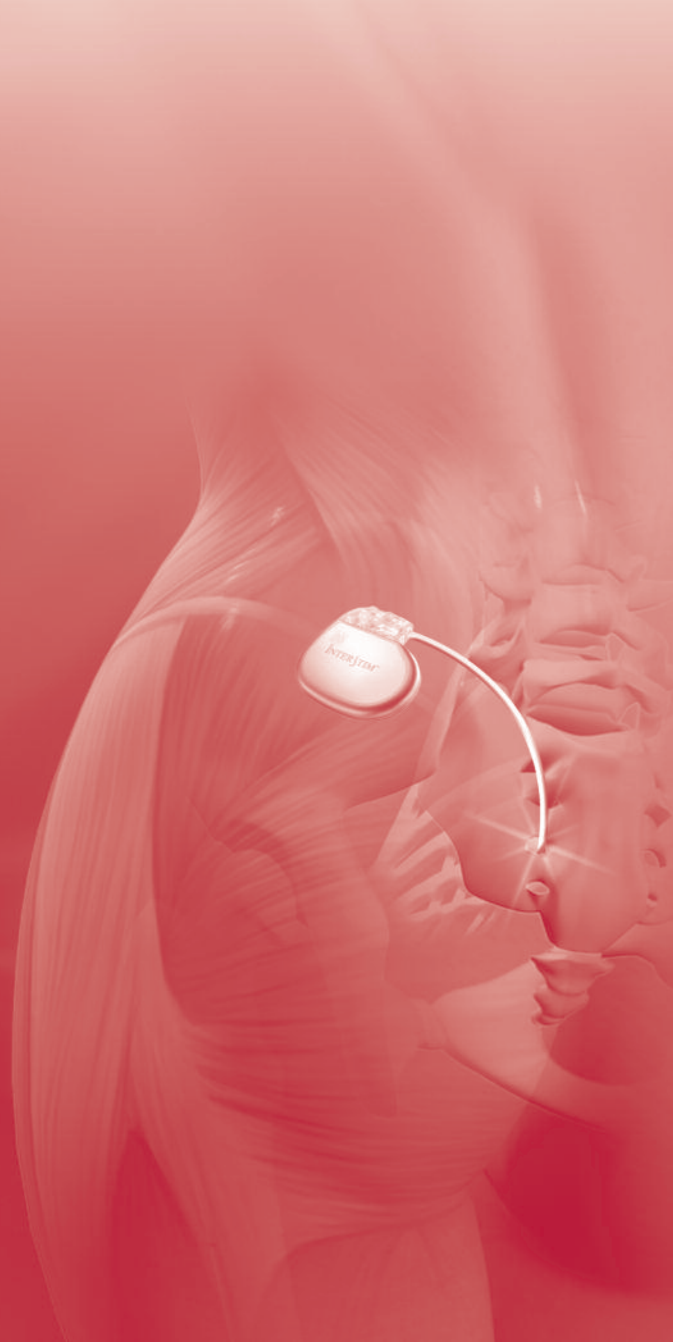
CHAPTER 8

Samenvatting en Discussie



In dit proefschrift wordt de toepasbaarheid, veiligheid en de haalbaarheid van sacrale neuromodulatie (SNM) als behandeling voor faecale incontinentie (FI) beschreven. Na 10 jaar klinische ervaring met SNM in ons ziekenhuis kunnen we concluderen dat SNM een effectieve en in de tussentijd ook erkende behandeling is voor functionele dikkedarm klachten, met name bij patiënten met faecale incontinentie. [1-3] De talloze internationale publicaties bevestigen niet alleen onze bevindingen maar hebben tegelijkertijd ook de weg vrij gemaakt voor SNM in de chirurgische behandeling van patiënten met FI. [4-6] De traditionele behandeling van FI welke zich met name concentreerde op de anale disfunctie is verlaten en is de aandacht nu verschoven naar een meer complexe benadering.

Hoofdstuk 1 geeft een overzicht van de literatuur met betrekking tot faecale incontinentie en de verschillende behandelmogelijkheden. FI is een veel voorkomende en complexe aandoening met hoge kosten voor de patiënt en de gemeenschap. Naast een grote psychische belasting heeft het een enorm sociaal invaliderend aspect dat diepgaande gevolgen heeft voor het welzijn van de patiënt. Adequate klinische, fysiologische en anatomische evaluatie door middel van onder andere geavanceerde beeldvorming is fundamenteel om de oorzaak en de mate van de incontinentie vast te stellen. Zowel conservatieve behandelingen (medicamenteus, biofeedback training en darmspoeling) als chirurgische ingrepen (sfincter herstel, neo-sfincter formatie, artificiële anale sfincter, sacrale neuromodulatie en aanleggen van een stoma) zijn therapeutische opties. De keuze voor behandeling wordt echter met name bepaald door de aanwezige kennis bij de behandelaars en de beschikbare faciliteiten.

In **Hoofdstuk 2** worden de resultaten van onze eerste vijfenzeventig patiënten die behandeld werden met SNM beschreven. Incontinentie werd geobjectiveerd door het invullen van een dagboek gedurende drie weken. Hetzelfde werd gedaan tijdens de drie weken durende proefstimulatie periode, waarbij ter hoogte van het foramen van S3 of S4 elektrisch werd gestimuleerd middels een externe stimulator. Een verbetering van de continentie van 50% of meer kwalificeerde patiënten voor een permanente implantatie. Zesenzestig vrouwelijke en negen mannelijke patiënten werden behandeld; de gemiddelde leeftijd was 52 jaar (26-75). Tweeënzestig patiënten (83%) hadden een verbeterde continentie tijdens de proefstimulatie. Het aantal incontinente episoden per week daalde van mediaan 7.5 naar 0.7 ($P < 0.01$), en het aantal incontinente dagen per week van mediaan 4.0 naar 0.5 ($P < 0.01$). De symptomatische verbetering bleek reproduceerbaar in de vijftig patiënten bij wie een permanente elektrode en neurostimulator geïmplanteerd werd. Na een mediane follow-up van 12 maanden bleef dit effect slechts gehandhaafd in achtenveertig patiënten. SNM bleek een toepasbare behandeling voor faecale incontinentie bij patiënten met een intacte sfincter.

In **Hoofdstuk 3** wordt het effect van SNM op het rectum geëvalueerd door middel van barostat metingen bij patiënten met faecale incontinentie die werden behandeld middels SNM. Bij vijftien achtereenvolgende patiënten werden barostat metingen verricht vóór en tijdens permanente SNM. Een isobaar fasisch distensie protocol werd gebruikt en aan de patiënten werd gevraagd rectale vulling sensaties aan te geven: eerste sensatie (ES), eerste aandrang tot defaecatie (EAD) en onweerstaanbare/pijnlijke aandrang tot defaecatie (maximum tolereerbaar volume (MTV)). De rectale wandspanning en compliantie konden met deze metingen worden berekend. Tijdens stimulatie daalden de mediane volumes significant ($P < 0.01$) voor ES: 98.1 vs. 44.2 ml, EAD: 132.3 vs. 82.8 ml and MTV: 205.8 vs. 162.8 ml. De druk metingen neigden lager uit te vallen voor alle vullingsensaties en de rectale wandspanning daalde significant ($P < 0.01$) bij alle vullingsensaties. Er was geen significant verschil in compliantie voor en tijdens SNM. Sacrale neuromodulatie beïnvloedt dus de rectale viscerale sensitiviteit maar het blijft onduidelijk of dit effect alléén het succes van SNM kan verklaren.

Hoofdstuk 4 beschrijft het effect van SNM op de anorectale hoek bij patiënten met faecale incontinentie. Bij twaalf achtereenvolgende patiënten die in aanmerking kwamen voor SNM werden een defaecografie studie vóór SNM en twee defaecografie studies 6 maanden na implantatie vericht, één tijdens stimulatie en de ander met de neurostimulator uit. De anorectale hoek werd kleiner tijdens rust, knijpen en Valsalva's manoeuvre en er werd een lichte toename van de anorectale hoek gezien tijdens defaecatie. De verschillen bereikten echter geen statistische significantie.

In **Hoofdstuk 5** wordt het effect van SNM op de defaecatiefrequentie en (segmentele) colon transittijd onderzocht. Veertien achtereenvolgende patiënten met faecale incontinentie die behandeld werden middels SNM ondergingen een colontransit studie vóór de SNM behandeling en één maand na permanente neurostimulator implantatie. Het aantal defaecatiemomenten per week daalde van mediaan 14.7(6.7-41.7) naar 10.0(3.7-22.7) ($P = 0.005$) tijdens proefstimulatie en naar mediaan 10.0(6.0-24.3) ($P = 0.008$) tijdens permanente stimulatie. Er werden geen significante verschillen gevonden vóór en tijdens stimulatie in zowel segmentele (rechter colon 6(0-25) vs. 5(0-16) uren, linker colon 2(0-29) vs. 4(0-45) uren en rectosigmoïd 7(28) vs. 8(0-23) uren) als totale colon transittijd (17(1-65) vs. 25(0-67) uren). Alhoewel er geen significante verschillen werden gevonden in (segmentele) colon transittijd werd er wel een significante vermindering gezien in het aantal defaecatie momenten bij patiënten met faecale incontinentie tijdens SNM.

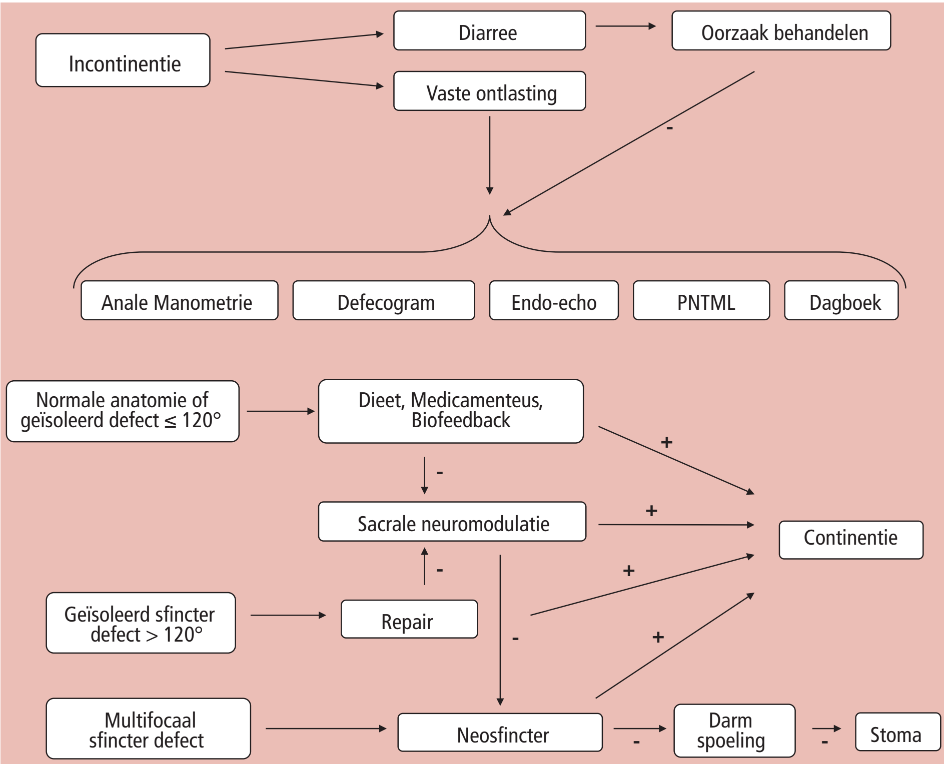
Hoofdstuk 6 evalueert de lange termijn resultaten en kwaliteit van leven bij patiënten met faecale incontinentie die behandeld werden met permanente SNM. De data van onze eerste vijftig patiënten die in aanmerking kwamen voor een permanente stimulatie werden gebruikt in deze studie. Patiënten hielden een defaecatiedagboek bij en de kwaliteit van leven scores werden verkregen middels de Faecal Incontinence Quality of Life vragenlijst (FIQOL) en de standard Short Form Health Survey vragenlijst (SF-36). Met een mediane follow-up van 7.1 jaar is dit de langste follow-up tot nu toe beschreven in een aanzienlijke groep patiënten die behandeld zijn met SNM. Tijdens follow-up kon in 42 (84%) patiënten de continentie verbetering van 50% of meer worden gehandhaafd. Er werd een significante afname van incontinente episoden en dagen per week gezien tijdens proefstimulatie en follow-up na permanente stimulatie ($P < 0.002$). Kwaliteit van leven verbeterde significant in alle vier categorieën van de FIQOL schaal en in enkele categorieën van de SF-36 vragenlijst. Verschillen in mediane anale rust- en knijpdrukken bereikten geen klinische significantie. Alhoewel het initiële succes niet gehandhaafd kon blijven in alle patiënten, blijkt permanente SNM met een overall succespercentage van 80% een veilige en effectieve lange termijn behandeling voor patiënten met faecale incontinentie.

Toekomstige perspectieven. Verder onderzoek zal zich moeten richten op het fysiologisch werkingsmechanisme en de kosteneffectiviteit van SNM bij patiënten met faecale incontinentie. Een beter begrip van het fysiologisch mechanisme zou kunnen leiden tot een betere patiëntenselectie en zou eventueel zelfs de proefstimulatie, welke op het moment de enige voorspellende factor is, uiteindelijk overbodig kunnen maken. Met een beter begrip zou ook de toepassing van SNM verbreed kunnen worden naar groepen patiënten met een andere aandoening dan faecale incontinentie. [7] SNM is al succesvol gebruikt in de behandeling van patiënten met therapie resistente obstipatie die op latere leeftijd is ontstaan. [8-10] Patiënten met obstipatie klachten sinds de kinderleeftijd zijn nog niet onderzocht. In ons ziekenhuis zij we gestart met een studie waarbij adolescenten met obstipatie worden behandeld middels SNM. De eerste resultaten lijken veelbelovend en zullen binnenkort worden gepubliceerd. Effecten van SNM op peri-anale pijn, clitorale/bekken pijn en erectiele/sexuele disfunctie zijn reeds beschreven maar moeten nader onderzocht worden. [11-14] Een significante reductie van symptomen en verbetering van kwaliteit van leven werd gezien tijdens proefstimulatie bij een subgroep patiënten met prikkelbare darm syndroom bij wie diarree het belangrijkste symptoom was.[15] Deze verschillende toepassingen van SNM alléén al suggereren een complex mechanisme waarbij sensorische en mogelijk autonome functies beïnvloed worden.

De beschikbaarheid van functionele beeldvorming van de hersenen zoals positron emissie tomografie (PET) en functionele magnetische resonantie imaging (fMRI) zijn interessante mogelijkheden. [16, 17] Toekomstig onderzoek met PET en fMRI kunnen ons een beter inzicht geven in zowel de pathofysiologie van faecale incontinentie als het werkingsmechanisme van SNM.

De kosten van SNM zijn een grote zorg. Alhoewel de exacte kosten geassocieerd met faecale incontinentie onbekend zijn blijken de indirecte non-medische kosten, zoals verminderde productiviteit van de patiënt op de arbeidsmarkt, meer dan de helft te zijn van de totale kosten van FI. [18] Meerdere studies hebben reeds de kosten effectiviteit van SNM bij de behandeling van faecale incontinentie aangetoond. [19-21] Kosteneffectiviteit studies zullen hoogstwaarschijnlijk in elk land apart uitgevoerd moeten worden om lokale zorgverleners te overtuigen van het positieve effect van SNM bij patiënten met FI op zowel de gezondheidszorg als de gemeenschap door het reduceren van de macro-economische last. Toekomstige technische ontwikkelingen kunnen de kosten van SNM beïnvloeden door bijvoorbeeld het verminderen van postoperatieve complicaties zoals infecties, pijn en elektrodemigratie. Door de ontwikkeling van neurostimulatoren die langer meegaan of zelfs opgeladen kunnen worden zullen kosten verder moeten dalen aangezien het aantal patiënten dat toekomt aan een vervanging van de neurostimulator in de toekomst alleen maar zal toenemen.

Behandel Stroomdiagram in het MUMC+ voor Patiënten met Faecale Incontinentie



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CHAPTER 9

Sonuçlar ve Tartışma

Sonuçlar ve Tartışma

Bu tezde, fekal inkontinans tedavisi için sakral nöromodülasyon (SNM) uygulamasının fizibilitesi, uygulanabilirliği ve güvenirliği özetlenmiştir. Hastanemizde SNM ile 10 yıllık klinik deneyim sonrasında sonuçlarımız SNM in fonksiyonel bağırsak şikayetlerinde, özellikle fekal inkontinans hastalarında, etkin ve bu arada kanıtlanmış bir yöntem olmasıdır. [1-3] Konuyla ilgili çok sayıdaki uluslararası yayınlar sadece bulguları doğrulamakla değil aynı zamanda fekal inkontinans hastalarının cerrahi tedavisinde SNM'in uygulanabilir olması yolunu açtı. [4-6] Geleneksel fekal inkontinans tedavisinde özellikle anal disfonksiyonu üzerine odaklanılması terkedildi ve ilgi daha kompleks bir yakla ıma yöneltildi.

Bölüm 1 fekal inkontinans ile ilgili edebiyat özetini ve farklı tedavi seçeneklerini gösterir. Fekal inkontinans yaygın ve kompleks bir hastalık olmasının yanı sıra hastalar ve toplum için yüksek maliyeti olan bir hastalıktır. Büyük psikolojik stresin yanısıra hastanın sosyal hayatına derin negatif etkileri vardır. Inkontinans derecesini ve sebebini belirlemek için uygun klinik, fizyolojik ve anatomik değerlendirme önemlidir. Hem konservatif (ilaç, biofeedback terapisi ve kolon irrigationu) hem de cerrahi tedaviler (sfinkter onarımı, neo-sfinkter oluşumu, yapay anal sfinkter, sakral nöromodülasyon ve stoma oluşturma) terapötik seçeneklerdir. Tedavi seçimi ancak mevcut olan bilgi ve imkanlar sonucunda belirlenir.

Bölüm 2'de SNM ile tedavi edilen ilk yetmiş beş hastanın sonuçları açıklanmaktadır. Inkontinans üç hafta boyunca bir günlük tutularak somutlaştırıldı. Stimülasyon testi döneminde, aynı şekildi üç haftalık günlük tutulmuştur. Inkontinansta %50 veya daha fazla bir gelişme hastaya kalıcı implantasyon uygulanması için kriter kabul edildi. Altmış altı kadın ve dokuz erkek hasta tedavi edildi; yaş ortalaması 52 (dağılım 26-75). Altmış iki hastada (%83) test stimülasyonu sırasında kontinansın iyileştiği tespit edildi. Haftalık inkontinans dönemleri ortalama olarak 7.5 tan 0.7'e düşmüştür ($P < 0.01$), inkontinans gün sayısı ortalama 4.0 dan 0.5'e düşmüştür ($P < 0.01$). Semptomatik yanıt kalıcı bir elektrot ve pacemaker implante edilen elli hastada değişmedi. Bu etki 12 aylık medyan takip sonrası sadece kırk sekiz hastada muhafaza edilebildi. SNM bozulmamış sfinkter hastalarında fekal inkontinans için uygulanabilir bir tedavi olarak kanıtlandı.

Bölüm 3 te SNM'in, fekal inkontinans için SNM ile tedavisi kabul edilen hastalarda, barostat ölçümleri vasıtasıyla rektuma olan etkisi değerlendirildi. On beş ardışık hasta üzerinde SNM öncesi ve sonrası barostat ölçümleri yapıldı. Izobarik fazik distansiyon protokolü kullanıldı ve hastalara rektal dolum hislerini belirtmeleri istendi: birinci his (BH), ilk dışkılama dürtüsü (IDD) ve dayanılmaz/ağrılı dışkılama dürtüsü (maksimum tolere hacmi (MTH)). Rektal duvar gerilimi ve rektal komplians bu ölçümlerle hesaplandı. Stimülasyon esnasında ortalama hacim ölçümleri anlamlı ölçüde azaldı ($P < 0.01$); BH: 98.1 vs 44.2 ml, IDD: 132.3 vs 82.8 ml, MTH: 205.8 vs 162.8 ml. Basınç ölçümlerinde tüm rektal dolum duyumlarında azalma görüldü. Rektal duvar geriliminde, tüm dolum duyumlarında, anlamlı ölçüde ($P < 0.01$) azalma tespit edilmiştir. SNM öncesi ve sonrası rektal komplians anlamlı ölçüde bir değişiklik tespit edilmemiştir. SNM rektal visseral duyarlılığı etkiler ama bu etkinin tek başına SNM başarısını açıklayabileceği belirsizdir.

Bölüm 4 te fekal inkontinansı olan hastalarda SNM'in anorektal açıya olan etkisi açıklanmaktadır. SNM ile tedavi için nitelendirilmiş oniki ardışık hasta üzerinde defecografi çalışması yapılmıştır. SNM öncesi bir çalışma ve 6 ay SNM sonrası, biri stimülasyon sırasında ve diğeri neurostimülatör kapalı iken, iki çalışma düzenlenmiştir. Anorektal açı istirahat, sıkma ve Valsalva's manevrası esnasında küçüldü ve dışkılama sırasında anorektal açı hafif bir artış gösterdi. Ancak farklılıklar istatistiksel olarak anlamlı ölçüde bir değişiklik göstermedi.

Bölüm 5'te SNM'in dışkılama sıklığı ve segmental kolonik transit zamanına etkisi araştırılmıştır. SNM ile tedavi gören ondört ardışık fekal inkontinans hastalarında, SNM öncesi ve kalıcı implantasyondan bir ay sonra, kolon transit çalışması yapıldı. Haftalık dışkılama sayısında, stimülasyon testi esnasında ortalama 14.7'den (6.7-41.7) 10.0'a (3.7-22.7) ($P = 0.005$), kalıcı stimülasyon esnasında ortalama 10.0'a kadar (6.0-24.3) ($P = 0.008$) azalma görüldü. Stimülasyon öncesi ve sonrası her ikisindede, segmental (sağ kolon 6 (0-25) vs 5. (0-16) saat, sol kolon 2 (0-29) vs. 4 (0-45) saat ve rektosigmoid 7(28) 8 (0-23) saat) ve total kolonik transit zamanında (vs 17 (1-65) vs. 25 (0-67) saat), anlamlı ölçüde değişiklikler bulunmadı. Segmental kolonik transit zamanında anlamlı ölçüde farklılık bulunmamısına rağmen, SNM esnasında fekal inkontinans hastalarında defekasyon sayısında anlamlı ölçüde azalma tespit edilmiştir.

Bölüm 6 uzun vadeli sonuçları ve kalıcı SNM ile tedavi edilen fekal inkontinans hastalarının yaşam kalitesini değerlendirir. Kalıcı stimülasyon için tedavi gören ilk elli hastanın verileri bu çalışmada kullanıldı. Hastalar defekasyon günlüğü tuttular ve yaşam kalitesi skoru Faecal Incontinence Quality Of Life anketi (FIQOL) ve standart Short Form Health Survey anketi (SF-36) ile elde edildi. Ortalama 7.1 yıllık izlem ile bu araştırma, şimdiye kadar SNM ile tedavi edilen büyük bir grup hastada, yapılan en uzun izlem çalışmaşıdır. Izlem esnasında 42 (%84) hastada %50 veya daha fazla kontinans iyileşmesi elde edilmiştir. Stimülasyon esnasında ve kalıcı stimülasyon sonrası izleminde inkontinans dönemlerinde ve günlerinde anlamlı ölçüde azalma tespit edilmiştir ($P < 0.002$). Yaşam kalitesi, FIQOL ölçeğinin dört kategorisinde ve SF-36 anketinin bir kaç kategorisinde, anlamlı ölçüde iyileşme göstermiştir. Ortalama anal istirahat ve sıkma basınçları arasındaki farkta anlamlı ölçüde bir değişiklik tespit edilmedi. İlk başarı tüm hastalarda muhafaza olmamasına rağmen, kalıcı SNM'in fekal inkontinans hastalarında %80 genel bir başarı oranı ile güvenli ve etkili uzun süreli bir tedavi şekli olduğu kanıtlanmıştır.

Gelecek perspektifler ve araştırmalar, fizyolojik mekanizma ve fekal inkontinansı olan hastalarda SNM'in maliyet etkinliği üzerinde odaklanmalıdır. Fizyolojik mekanizmaların daha iyi anlaşılması doğru hasta seçimine neden olabilir ve hatta test stimülasyonunu neticede gereksiz kılar. Aynı zamanda daha iyi bir anlayış ile SNM tedavisi sadece fekal inkontinansı olan hastalarda değil diğer rahatsızlıkları olan hastalardada uygulanabilir. [7] SNM tedavisi zaten, ileri yaşlarda ilaç dirençli kabızlık rahatsızlığı gören hastalarda, başarıyla uygulanmıştır. [8-10] Çocukluk döneminden itibaren kabızlık rahatsızlığı olan hastalar henüz araştırılmamıştır. Biz kabızlık rahatsızlığı gören ergenlere SNM tedavisi uygulamaya başladık ve iyi sonuçlar elde ettik. Sonuçlar kısa sürede yayınlanacaktır. SNM'in peri anal ağrıya, klitoral/pelvik ağrıya ve erektiel/cinsel işlev bozukluğuna etkileri zaten tarif edilmiştir ancak daha fazla araştırılması gerekmektedir. [11-14] Stimülasyon testi sırasında, ishal baskın irritabıl barsak sendromu hastalarında, belirtilerde ve yasam kalitesi iyilesmesinde anlamlı ölçüde azalma tespit edilmiştir. [15] Sadece bu farklı kullanımlar bile SNM in duyusal ve otonomik fonksiyonları içeren karmaşık bir mekanizmayı etkiledigini düşündürmektedir.

Beynin fonksiyonel görüntüleme durumunu gösteren cihazlar, pozitron emisyon tomografisi (PET) ve fonksiyonel manyetik rezonans görüntüleme (fMRI), ilginç olanaklardır. [16, 17] PET ve fMRI ile ileri çalışmalar SNM'in etki mekanizmasını ve fekal inkontinansın patofizyolojisi hakkında daha iyi bir fikir verebilir.

SNM'in maliyeti büyük bir endişedir. Fekal inkontinans ile ilgili maliyet kesin olmasada, dolaylı tıbbi olmayan maliyetler (verimlilik gibi) toplam maliyetin yarısından fazlasını kapsamaktadır. [18] Çeşitli çalışmalar SNM'in fekal inkontinans tedavisinin maliyetini ve etkinliğini zaten belirtmiştir. [19-21] Yerel sağlık hizmetlerini SNM'in fekal inkontinans hastalarında olumlu etkilerini (sağlık hizmetleri vede toplum için makro-ekonomik yükü azaltarak) inandirmak için muhtemelen ayrı ayrı ülkelerde maliyet çalışmaları yapılmalıdır. Gelecek teknik gelişmeler örneğin ameliyat sonrası komplikasyonlarını (enfeksiyon, ağrı ve elektrot göçü) etkileyebilir ve bu yüzden SNM'in toplam maliyetini azaltabilir. Gelecekte neurostimülatörü değiştirilmesi gereken hasta sayısı artacaktır. Bunu göz önüne alırsak daha uzun ömürlü ve hatta şarj edilebilir neurostimülatörlerin geliştirilmesi ile SNM'in maliyeti düşmeye devam etmesi gerekir.

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List of Abbreviations

Artificial bowel sphincter	**ABS**	Artificiële anale sfincter
Dynamic graciloplasty	**DGP**	Dynamische gracilisplastiek
Earliest urge to defaecate	**EUD/EAD**	Eerste aandrang tot defaecatie
Endoluminal ultrasound, also my nickname	**EUS**	Endo-echo, tevens mijn roepnaam
Faecal incontinence	**FI**	Faecale incontinentie
Faecal incontinence quality of life scale	**FIQOL**	
First Sensation	**FS/ES**	Eerste sensatie
Maximum Tolerable Volume	**MTV**	Maximum tolereerbaar Volume
Peripheral neural evaluation	**PNE**	Perifere zenuw teststimulatie
Pudendal nerve terminal motor latency	**PNTML**	Pudendus latentietijd
Percutaneous/peripheral tibial nerve stimulation	**PTNS**	Percutane/perifere nervus tibialis stimulatie
Somatosensory evoked potentials	**SEP**	Somatosensorisch opgewekte potentialen
Short form health survey quality of life scale	**SF-36 QOL**	
Sacral neuromodulation	**SNM**	Sacrale neuromodulatie

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