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URODYNAMIC ASSESSMENT OF SACRAL ROOT NEUROMODULATION IN PATIENTS WITH INTRACTABLE STORAGE AND VOIDING DYSFUNCTIONS

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Objective Sacral root neuromodulation is becoming one of the standard options for the treatment of intractable voiding dysfunction. The current report presents the urodynamic changes supporting the subjective improvement achieved by sacral root neuromodulation in patients with both voiding and storage problems.

Patients and Methods Out of 50 patients being candidates for peripheral nerve evaluation (PNE) for various voiding and storage problems, 38 patients agreed to be subjected to urodynamics before, during and after subchronic PNE. Seventeen patients presented with an urgency-frequency syndrome, 9 with urge incontinence and 12 with chronic idiopathic urinary retention. All patients had previously failed to respond to various oral and intravesical treatments. The protocol included a four-day voiding diary and urodynamics before, during and after subchronic PNE.

Results Significant changes in the urodynamic results of the patients during PNE were noted. Urodynamics of the urge incontinence and urgency-frequency patients showed an increased volume compared to the first urge cystometric bladder capacity after sacral root neuromodulation. The cystometrograms of patients with chronic idiopathic urinary retention did not show any difference during PNE when compared to the pre-PNE tests. Pressure-flow studies that were not possible before PNE became normalized during PNE. The urodynamics of all patients one week after PNE showed variable degrees of deterioration. The urodynamic findings of 7 patients who had an implantation of permanent programmers still showed the same results as after PNE testing.

Conclusion There is a definite correlation between both subjective and objective improvement of patients on neuromodulation proved by urodynamic studies. However, this needs to be further evaluated as a predictor for success.

Key Words voiding dysfunction, urodynamics, detrusor instability, chronic retention

INTRODUCTION

The physiology and the neuroanatomy of the pelvic floor and detrusor mechanisms are complex and incompletely understood[1].

While the precise mechanism of how electrotherapy might inhibit detrusor overactivity is not clear, it is known that current may affect the integration of stimuli between the cerebral cortex and sacral nerve outflow and, thus, reorganize the neural control of the bladder[2]. Most authors have used vaginal or anal plug electrodes when delivering neuromodulation to patients with urgency. However, in 1992, Webb and Powell reported encouraging results when they applied current across the skin of the S3 dermatome (peri-anus) using a transcutaneous electrical nerve stimulation machine[3]. This technique was tested during cystometry in 24 patients with intractable detrusor instability, of whom 45% became stable while the remaining patients demonstrated a larger volume at first detrusor contraction. Later studies indicated a significant change in urodynamic parameters after a 3-week clinical trial in similar patients[4]. At the same time, others refined direct electrical stimulation using surgically implanted electrodes at the S3 sacral segmental nerve roots in patients with refractory detrusor instability[5].

Apparently, cystometry was not performed during the initial percutaneous nerve evaluation phase of this procedure.

Over the past few years, sacral neuromodulation has gained wide acceptance as an alternative new, minimally invasive therapeutic tool for the treatment of lower urinary tract dysfunction. It bridges the gap between conservative treatment options and highly invasive surgical procedures. Several reports have demonstrated the effectiveness of this modality, unfortunately without correlating it with urodynamic data[6,7,8].

Peripheral nerve evaluation (PNE) is a temporary screening test that identifies patients who respond to complete implantation. The current report was a trial to assess the patients with intractable voiding or storage problems both subjectively and objectively, and to reflect the picture of detrusor activity changes due to neuromodulation during PNE.

PATIENTS AND METHODS

In total, 50 patients with chronic intractable voiding dysfunction were enrolled in this study during a 20-month period. All patients gave a complete history and underwent full physical and neurological examination. All of them had failed to have significant improvement on conservative treatment (pharmacotherapy) as well as on various oral and intravesical treatments. Oral treatments included anticholinergics, imipramine hydrochloride, calcium channel blockers and alpha adrenergic blockers. Failed intravesical treatments included bladder distension, anticholinergics and local anaesthetics.

The standard evaluation of the patients included urine analysis and blood chemistry, together with radiological examination in the form of KUB, abdomino-pelvic ultrasonography with or without urethrocystography in suspected urethral stricture, bladder diverticulum or vesico-ureteral reflux. A preliminary multichannel urodynamic assessment was done for all the patients.

Exclusion criteria included an active urinary tract infection, pregnancy, a cardiac pacemaker, a structural abnormality or urodynamically proved instability or acontractility secondary to a known neurological condition, i.e. neurogenic bladder. Percutaneous nerve evaluation (PNE) was performed for those who met the selection criteria and accepted the program of extensive voiding diaries with repeated urodynamic studies. A standardized explanation was given and informed consent was obtained.

Of the 50 patients evaluated, only 38 were included as they accepted the program of extensive voiding diaries with repeated urodynamic studies. The patients were 27 females and 11 males with a mean age of 36.5 years (range 21-48 years). There was a storage problem in 26 patients (Group I) either in the form of urgency-frequency syndrome in 17 patients (12 females and 5 males), or urge incontinence in 9 patients (7 females and 2 males). Voiding problems in the form of chronic idiopathic urinary retention (Group II) was encountered in 12 patients (8 females and 4 males).

The patients were instructed to complete a 4-day voiding diary and voiding questionnaire once prior to PNE, during PNE and a week after PNE each. The diary included the measurement of: frequency and voided volume, grading of leakage (none, mild, moderate and severe), whether they felt empty after voiding or not, and the degree of urgency felt prior to voiding (none, mild, moderate and severe).

Patients with chronic retention were also asked to write the timing of catheterization and to measure the volume drained by the catheter before PNE. During and after PNE they additionally had to use the catheter to measure the residual urine after micturition.

Urodynamic assessment was performed prior to PNE, during PNE (on the day following the insertion of the temporary electrodes) and one week after PNE. It included simple uroflowmetry with residual urine determination and water cystometry with pressure flow studies according to the International Continence Society (ICS) guidelines. The volume at the first desire to void, the maximum cystometric capacity, the subtracted detrusor pressure at the first desire to void and at maximum capacity, the filling volume at which the first unstable contraction occurred (threshold volume) and the maximum detrusor pressure during the filling phase of cystometry were noted. When leakage occurred during an unstable contraction, the amplitude of the detrusor contraction and concurrent volume were recorded (detrusor pressure and volume at leakage).

Table 1: Cystometric Results in Group I (Urgency-Frequency Syndrome and Urge Incontinence)

Water Cystometry	Pre-PNE	PNE
Mean voiding volume	114 ml	217 ml
Volume at first sensation	115 ml	170 ml
Volume at mild urgency	131 ml	192 ml
Volume at moderate urgency	187 ml	214 ml
Volume at severe urgency	250 ml	295 ml
Volume at 1st unstable contraction	135 ml	195 ml
Amplitude at unstable contraction	86 cm H2O	41 cm H2O
Cystometric capacity	271 ml	335 ml

Peripheral nerve evaluation (PNE) was performed with the patient in the prone position. The evaluation usually started by mapping of the sacral foramina in order to locate the S3 foramen. The S3 sacral root was identified according to bony landmarks. The S4 nerve root foramen is at the level of the sciatic notch one finger breadth lateral to the midline. The S2 sacral root corresponds to the level of the posterior superior iliac spine one finger breadth lateral to the midline. The S3 sacral root is at the midline of the two points. Local anaesthesia was applied to the overlying tissues, after which insertion of an insulated needle gently took place through the S3 foramen at an angle of 30 degrees.

Correct needle placement was achieved when a pelvic floor "belows" contraction, perianal sensations or plantar flexion of the big toe were noted. This was followed by passing a temporary pacing wire (lead) to which a portable external stimulator (screener) was connected. All the patients were left with continuous stimulation for 4-5 days adjusting the parameters to be unipolar, monophasic, square pulse. The pulse width was 210 ms, the frequency 10 Hz and the maximum voltage 10 volts. A pulse amplitude of 0 to 10 V was adjusted by the patient to the highest level of sensory awareness without discomfort.

Successful neuromodulation was achieved when there was a subjective improvement in the urgency-frequency group or spontaneous voiding in the chronic retention group. Those patients were scheduled for a permanent neuromodulation implant.

RESULTS

The voiding diaries of both groups (Group I: urgency-frequency and urge incontinence / Group II: chronic idiopathic urinary retention) showed a significant improvement. In Group I, 21 patients (80.7%) showed an improvement that involved the mean voided volume together with much less urgency and urinary leakage. In Group II, 8 patients (66.6 %) showed improvement in the form of spontaneous voiding with a regular decrease of the post-void residual urine.

Uroflowmetry of the patients with pure urge incontinence (Group I) showed a significant improvement. The voided volumes during uroflowmetry increased up to 2-fold when comparing the baseline to the post-PNE follow-up. The peak and mean flow rates stayed within the pre-PNE normal range.

Cystometrography showed the disappearance of bladder instability in only 9 out of 26 patients (34.6%) of Group I. However in 12 patients (46%) the bladder volume at which the first unstable contractions occurred increased from a mean of 135 to 195 ml. Also the maximum amplitude of the unstable contractions was lower (86 cm H_2O pre-PNE compared to 41 cm H_2O during PNE). In the remaining 5 patients of this group who had sustained symptoms, the cystometrograms did not show any significant changes except that the unstable contractions became less frequent than before the PNE.

In all the responders of this group, the bladder volume at first sensation increased by

Table 2: Results of Pressure-Flow Study in Group II (Chronic Idiopathic Urinary Retention)

Pressure-Flow Study	Pre-PNE	PNE
Peak flow (ml/sec)	-	13.6
Mean flow (ml/sec)	-	5.8
Opening pressure (cm H2O)	-	32.4
Pdet max. flow (cm H2O)	-	37.5

50% (115.17 ± 25.31 ml pre-PNE to 169.75 ± 42.29 ml during PNE). Also higher filling volumes were recorded for mild, moderate and severe urgency, increasing from 131.34, 187.56 and 250.17ml pre-PNE to 192.22, 214.14 and 295.48 during PNE, respectively. The cystometric bladder capacity increased by 25% (271.93 ± 48.32 pre-PNE to 335.83 ± 51.05 ml during PNE). Pressure-flow studies of the patients with pure urge incontinence did not demonstrate any difference (Table 1).

Eight patients (66.6%) with idiopathic non-obstructive chronic urinary retention (Group II) showed a highly statistically significant increase in the amount of voided urine, and mean and peak flow rates. The uroflowmetry results of this group were impressive, reflecting the tremendous improvement in symptomatology, because most patients had not been able to void in the uroflowmetry device at baseline. They had at least a 50% improvement in voided and post-void residual volumes on PNE screening.

The remaining 4 patients of this group did not show any significant response to the PNE test, but 2 of them reported that they experienced a better sense of desire to void and a better bowel evacuation than before the PNE.

Cystometry of the responders of this group showed no significant changes in the filling phase. There was a normalized pressure flow study. Nomograms were shifted to the non-obstructive zone. The mean peak and average flow rates were 13.6 and 5.8 ml/sec, respectively. The opening pressure was 32.4 cm H_2O and the detrusor pressure at maximum flow was 37.5 cm H_2O (Table 2).

The patients of both groups who were proven to benefit from sacral nerve neuromodulation were scheduled for implantation of a permanent stimulator.

A urodynamic evaluation one week after PNE showed the recurrence of the bad results for both groups with a rapid recurrence of the symptoms, especially in the group with urinary retention. The 21 responders of Group I regained their symptoms within 1-6 weeks after the end of PNE, while all the patients of Group II went into retention within 1-2 weeks.

No complications or morbidity were encountered throughout the whole study except for some mild pain that occurred within the gluteal region on the side of stimulation. This pain occurred in 7 patients (18.4%) and it either resolved spontaneously or after using ordinary analgesics.

DISCUSSION

Until recently urge incontinence was difficult to treat. It has been estimated that pharmacotherapy and other types of conservative management of urge incontinence provide only a 44% subjective improvement with no significant objective improvement[9,10]. Patients who do not achieve a satisfactory response to these treatments are left with more drastic options such as urinary diversion.

On the other hand, patients with chronic idiopathic urinary retention only have one possibility to evacuate their bladders, which is clean intermittent catheterization (CIC) for a lifetime.

In the past, patients refractory to behavioural and pharmacological therapy had the option of either living with their old symptoms or proceeding with augmentation cystoplasty, an effective but morbid operation. Neuromodulation through sacral nerve stimulation appears to be replacing augmentation in many centers as a logical next step in the treatment of patients refractory to conservative measures.

The patients most likely to benefit from this treatment are those with detrusor hyperactivity or hypo-activity. Those with pain syndromes are less likely to respond and to benefit from treatment. All patients regardless of the indication must undergo a percutaneous test stimulation (acute and subchronic stimulation) before they can be offered chronic neuromodulation with an implanted system[8].

Percutaneous nerve evaluation represents a milestone in the application of the concept of neuromodulation and provides to both physician and patient evidence of what to expect from the permanent implant.

Neuromodulation for voiding dysfunction was introduced to modern urology practice after the pioneering work of Tanagho et al[6]. The rationale behind this concept of treatment is to restore the spinal reflexes controlling storage and evacuation.

The mechanism by which sacral nerve stimulation affects dysfunctional bladder behaviour is not fully understood and controversial. The activation of spinal inhibitory pathways through stimulation of the afferent input in the S3 nerve can provide a partial explanation in patients with urgency and incontinence[11]. Many researchers suggest blocking c-afferent fiber activity as one of the primary mechanisms of action of sacral neuromodulation[7,12].

However, stimulation of large sensory afferents running from the pelvic floor may also produce inhibition of the detrusor motor neurons, either directly at a spinal level or via other neural pathways[13]. Sacral nerve stimulation is believed to have a conditioning effect on neural excitability and can restore the neural equilibrium[14].

Sacral root neural stimulation is also becoming a recognized concept of therapy to restore bladder function in patients with idiopathic, non-obstructive chronic urinary retention[15]. The mechanism by which neuromodulation restores bladder function in chronic nonvoiders is also not clearly understood. Schmidt believed that neuromodulation might function through directing the patient to re-localize the pelvic floor and, hence, regain the capability of relaxing it and initiating voiding[16].

In consideration of these theories, sacral nerve stimulation has been demonstrated to treat effectively severe symptoms of urgency-frequency and urinary urge incontinence, and now provides clinicians with an important new option for treating patients with chronic idiopathic urinary retention.

Urodynamic improvement occurs as a result of sacral neuromodulation but not in well-designed drug trials[9,10]. These groups of patients usually receive extensive pharmacologic therapy for a prolonged time before any attempts at neuromodulation. Urodynamic evaluation of these patients rarely shows any objective improvement even though there may be good subjective improvement.

The current study assessed the functional changes in the micturition pattern (urodynamically) in response to neuromodulation in patients with urgency-frequency and urge incontinence refractory to conservative management, as well as in patients with idiopathic chronic urinary retention.

All the patients of Group I who were still receiving their anticholinergic therapy had different degrees of detrusor instability though some of them had a variable subjective improvement. During the preliminary percutaneous neuromodulation, all the patients who experienced improved symptoms showed this objectively on urodynamic evaluation in the form of a decrease or absence of the instability and an increase in the voided volumes plus reporting better results in the voiding diaries. The urodynamic studies showed an increase in volume at first sensation and cystometric capacity, and the disappearance of bladder instability in only 9 of 26 patients. Nevertheless, 12 of the remaining 17 patients demonstrated an increased volume at the first uninhibited contraction and a marked clinical improvement.

In the patients of Group II the urodynamic difference was obvious between a silent and a reactive bladder, best shown in the voiding pressure studies in the form of a normalized pressure during micturition.

In conclusion, increasing evidence shows an objective response to neuromodulation. There are definite urodynamic changes that support the subjective and clinical improvement in patients who respond to neuromodulation. However, no urodynamic data are available to predict a response.

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RESUME

Evaluation Urodynamique de la Neuromodulation des Racines Sacrées chez les Patients Présentant des Dysfonctions Rebelles de la Collection et de l'Evacuation des Urines

Objectifs : La neuro-modulation des racines sacrées devient une option de choix dans le traitement des dysfonctions rebelles de l'évacuation des urines. Cette étude présente les innovations urodynamiques ayant permis de mettre en évidence les améliorations subjectives réalisées par neuromodulation des racines sacrées chez des patients présentant à la fois des dysfonctions dans la collection et l'évacuation des urines. **Patients et Méthodes:** Des 50 patients candidats à une évaluation des nerfs périphériques (ENP), 38 ont accepté une exploration urodynamique avant, pendant et après cette évaluation. Dix sept patients avaient présenté une pollakiurie avec impériosité, 9 avaient présenté une incontinence et 12 avaient présenté une rétention chronique idiopathique. Tous les patients avaient bénéficié de divers traitements par voie orale ou intra-vésicale sans succès. Le protocole avait inclus un calendrier mictionnel de 4 jours et des examens urodynamiques avant, pendant et après l'ENP. **Résultats:** Des changements significatifs sur les résultats urodynamiques des patients ont été notés durant l'ENP. L'étude urodynamique des patients présentant une incontinence et une pollakiurie et impériosité avait montré une augmentation de volume comparativement à la capacité vésicale estimée par la cystométrie après neuromodulation des racines sacrées. Les cystomanogrammes des patients présentant une rétention chronique idiopathique n'avaient pas montré de différence entre la période d'ENP et avant celle-ci. L'étude de la pression d'écoulement des urines qui n'était pas possible avant l'ENP a donné des résultats normaux durant celle-ci. Les résultats de l'urodynamique de tous les patients une semaine après l'ENP ont montré des perturbations de degré variable. Les résultats urodynamiques de 7 patients porteurs d'un programmeur permanent sont identiques à ceux trouvés après l'ENP. **Conclusion :** Il existe une corrélation nette entre l'amélioration objective et subjective des patients sous neuromodulation à l'étude urodynamique. Toutefois cela nécessite d'autre études pour conforter l'intérêt de ce procédé.

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