SIX-YEAR FOLLOW-UP OF INTRADETRUSORIAL INJECTIONS OF BOTULINUM TOXIN TYPE A IN PATIENTS WITH REFRACTORY NEUROGENIC DETRUSOR OVERACTIVITY: CLINICAL AND URODYNAMIC RESULTS

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INTRODUCTION AND AIM OF THE STUDY

Neurogenic detrusor overactivity (NDO) is a condition that causes urinary incontinence, high intravesical pressure, reduced capacity, low compliance of the bladder and can lead to upper urinary tract damage. Current therapeutic options mainly rely on clean intermittent catheterization to drain the bladder, and oral anticholinergics to block the efferent parasympathetic innervation of the detrusor muscle and inhibit involuntary detrusor contractions. However, about 60% of patients cannot tolerate these drugs because of severe side effects, and the majority of them stop assuming anticholinergics within a few months of therapy. Other therapeutic options may be represented by intravesical application of vanilloid-antagonists, but the efficiency of this intervention is still controversial. Bladder auto-augmentation, enterocystoplasty and ileal conduit are weighty surgical options which are to be considered as last alternative. Recent studies have reported successful treatment of patients with spinal cord injury (SCI) and detrusor overactivity using intravesical botulinum A toxin (BoNT/A), but in a short term follow-up.
Aim of this study was to investigate the effectiveness and safety of BoNT/A injections into the detrusor muscle in a group of spinal cord-injured patients with NDO unresponsive to conventional anticholinergic therapy, who were followed-up for more than 6 years.

MATERIALS AND METHODS

Since October 2000, our Institution has been using intravesical BoNT/A to treat more than 90 patients with refractory NDO non NDO, bladder hypersensitive disorders and BPH. Among them, 17 SCI patients were followed-up for more than 6 years and received multiple treatments over time. We reviewed clinical evaluations, voiding charts, records of local and/or systemic side effects, frequency of urinary tract infections (UTI), imaging of

the upper urinary tract (UUT) and urodynamic examinations. We also considered patient dropout and satisfaction over the course of their long-term follow-up.

RESULTS

Seventeen patients were included in this study. During the first two years, clinical evaluation, urodynamics and UUT imaging were repeated every 4 months; subsequently they were performed in the event of a decline in both clinical and urodynamic data. A total of 119 injections were given. Mean number of injections was 7±1.3 for each patient, and mean interval between 2 consecutive injections was 11.0 ± 2.4 mos. At the six-year follow-up, we observed a significant decrease in the frequency of daily incontinence episodes ($p < 0.01$) and maximum pressure of uninhibited detrusor contractions (UDC, $p < 0.01$), and a significant increase in first UDC ($p < 0.001$) and maximum bladder capacity ($p < 0.001$), compared to baseline. No patients showed any impairment of UUT function. Improvements were remarkable in 15 patients (88.2%) after the second treatment, probably due to the surgeon's inevitable learning curve. At the two-year follow-up, 15 patients achieved complete urinary continence that was maintained over time. At the six-year follow-up the frequency of UTI was significantly reduced compared to baseline. No local or systemic side effects were recorded. Patient satisfaction was very high after just the first intravesical injection.

DISCUSSION

First line treatment for detrusor overactivity is the use of antimuscarinic medications. However, these medications can have unwanted side effects and often are not effective enough to decrease incontinence in cases of severe detrusor overactivity. Recently, data have been accumulating on the clinical application of BoNT/A to detrusor muscle in hyperactive bladders of neurogenic detrusor overactivity. Nevertheless, no consistent data exist on the results of long-term follow up of intradetrusorial injections of BoNT/A in SCI patients.

CONCLUSION

The present study shows that repeated intradetrusorial treatments with BoNT/A are effective in improving clinical and urodynamic conditions, as they allow a large percentage of patients to achieve complete urinary continence and a remarkable control of UTI. In addition, no local or systemic unwanted side effects have been recorded during the whole follow-up. Detailed cost-benefit and cost-utility analyses over time should be performed to provide a definitive assessment of the role of BoNT/A in treating neurogenic bladder.

BOTULINUM A TOXIN INTRAVESICAL INJECTIONS IN THE TREATMENT OF REFRACTORY DETRUSOR OVERACTIVITY DUE TO PARKINSON'S DISEASE AND MULTIPLE SYSTEMIC ATROPHY: PRELIMINARY RESULTS

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INTRODUCTION AND AIM OF THE STUDY

Bladder control can be a major clinical problem in patients with Parkinson's disease (PD) and Multiple Systemic Atrophy (MSA). Previous studies demonstrated a correlation between bladder dysfunction, PD stage and neurological disability, suggesting a relationship between dopaminergic degeneration and bladder dysfunction. The depletion of dopaminergic neurons in the substantia nigra and the subsequent loss of striatal dopamine concentration could induce detrusor overactivity through an inability to activate the D1-mediated tonic inhibition. In MSA, urinary dysfunction is common and appears earlier; the progressive course of bladder and sphincter dysfunction differentiates MSA from other degenerative parkinsonisms. While in PD patients detrusor overactivity is the main urodynamic dysfunction, in MSA patients detrusor overactivity is frequently associated with impaired detrusor contractility and external urethral sphincter dyssynergia, and patients complain of urgency/urge incontinence and incomplete or complete urinary retention. In PD and MSA bladder symptoms are usually treated with anticholinergics, but no placebo-controlled, double-blind or randomized studies have been performed so far. In these patients the use of anticholinergics is usually limited by adverse effects, generally present in more than 60% of cases, which induce the majority of patients to discontinue the above pharmacological therapy within few months. Aim of the present study was to investigate the efficacy and safety of Botulinum A toxin intravesical injections in patients affected by refractory neurogenic detrusor overactivity due to PD and MSA.

MATERIALS AND METHODS

Five female patients (4 with PD and 1 with MSA) have been selected and included in this prospective study. Mean age was 62.25 ± 17 yrs and mean disease duration was 10.5 ± 10.4 yrs. Patients underwent a baseline evaluation including history, physical examination,

urinalyses and culture, voiding diary with the recording of daytime and night-time urinary frequency, Visual Analog Scale for subjective degree of treatment efficacy, and urodynamics. From a neurological point of view, patients underwent clinical evaluation according to the Unified Parkinson's disease Rating Scale (UPDRS). *Treatment:* patients underwent intravesical injections of BoNT/A, 200 U diluted in 20 ml of normal saline, under cystoscopic control. The floor and the lateral walls of the bladder have been injected, together with the trigone. Clinical and urodynamic evaluations have been repeated 1 and 3 months afterwards.

RESULTS

Baseline evaluation. Mean daytime and night-time urinary frequency were 7.8 ± 4.2 and 2.7 ± 0.9, respectively. All patients complained of refractory urge urinary incontinence, and mean VAS score was 2 ± 0.8. On urodynamics, mean uninhibited detrusor contractions threshold was 175.2 ± 166. 4 ml, and mean maximum pressure of these contractions was 26.2 ± 20.6 cm H_20. Mean maximum bladder capacity was 322.5 ± 181.3 ml. On pressure-flow studies all patients but 1 completely emptied the bladder. At 1 and 3 months follow up respectively, no patients complained of urge urinary incontinence, and there was a reduction in mean daytime and night-time urinary frequency (at 3 months: 4.5 ± 0.5 and 0.5 ± 0.5, respectively). One patient with MSA went on self-intermittent catheterizations. On urodynamics, there was a significant amelioration of all the considered parameters at the same time points, but all patients presented with postvoid residual volume higher than 100 ml (at 3 months: 173.3 ± 72.9 ml). However, at 3 months mean VAS score was significantly increased to 8.5 ± 0.5. No systemic side effects were noted. No urinary tract infections have been detected at 1 and 3 months follow-up.

DISCUSSION AND CONCLUSIONS

To our knowledge this is the first demonstration of the effects of BoNT/A intravesical injections in the treatment of neurogenic bladder due to PD and MSA. These data show that the neurotoxin can be used to control urge urinary incontinence and OAB symptoms of different neurogenic origins, and also in patients with PD and MSA it can lead to high treatment satisfaction. Worthy of noting, one adverse side effect is due to the presence of large post-void residual volume, particularly important in old and disable patients who may not be able to perform intermittent catheterizations. Thus, BoNT/A doses and techniques need to be accurately investigated in these cases. However, patients in this study could be adequately treated with oral alpha-blockers. Obviously, we are conscious that these are

preliminary data which need to be confirmed in prospective studies with a larger number of patients.

OBSERVATIONAL STUDY ON BOWEL DYSFUNCTION IN MULTIPLE SCLEROSIS PATIENTS

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INTRODUCTION AND AIM OF THE STUDY

Bowel problems are frequent in Multiple Sclerosis (MS), although not as typical and investigated as bladder dysfunction. Aim of our study was to assess the frequency and the form of bowel dysfunctions (BD) in MS patients through a cross-sectional survey.

MATERIALS AND METHODS

Fifty-one outpatients with moderate/medium MS, recruited during 2006 (13 males and 38 females, aged 21-76 years), were interviewed about bowel function with a questionnaire with simple multiple answers. Faecal continence was estimated through the AMS score: with a score between 1 and 120 the faecal incontinence (FI) has been quantified. For constipation (C) we have used the Constipation Scoring System (CSS), which weighs the degree of C through a score between 0 and 30. Clinical disability was measured by the Expanded Disability Status Scale (EDSS). The statistic analysis has been performed with the Chi Square Test.

RESULTS

Mean disease duration was 9.6 years (range 1-38), and EDSS score 2.8 (range 1-7). Forty-one MS patients (80.4%) had relapsing/remitting (RR) and 10 (19.6%) secondary progressive (SP) form; 19 (37%) had paraparesis, 3 showed unilateral leg paresis. Thirty-four subjects (67%) showed bladder symptoms: irritative in 59%, obstructive in 12% and a combination of both in 29%.

BD were found in 12 cases (23%), more precisely C, with CSS score>8 (range 8-15) and a mean disease duration of 16.6 years. Nine patients (17.6%) usually used aperient or purge, 2 (4.1%) enema or micro-enema; in such subgroup mean EDSS score was higher (4.2); 2 of them reported also FI due to urgency, with high AMS scores. Seven cases (14%) had faecal urgency, but none of them made use of pads. All patients interviewed

perceived stool transit, but 3 (5.9%) did not distinguish gas from stool. Eleven out of 12 subjects (91.6%) with C had associated urinary disturbances, while 56% reported isolated bladder symptoms. The coexistence of bladder and bowel dysfunction appeared statistically significant in comparison with patients with regular belly (Chi square 10.12, $p<0.005$). Moreover, there was a strong correlation between MS duration and BD (16.6 versus 7.5 years, $p<0.0005$), while EDSS score significantly correlated both with bladder symptoms and BD ($p<0.005$). Sphincteric disturbances (SD) and form of MS were not correlated, contrary to bladder and bowel urgency. Faecal urgency was associated with bladder urgency in 6 out of 7 cases, and it was emphasized in 26% out of 23 subjects with bladder urgency (Chi square 4.06, $p<0.05$).

DISCUSSION

BD etiopathogenesis in MS is multifactorial. C has a prevalence of 35-54%, against 2-20% found in the healthy population, and the prevalence of BD reaches 39-73% if we consider also FI. In the available studies, SD appears to correlate with the degree of disability, but our study emphasizes the important presence of BD (23%) also in subjects with moderate MS.

BD correlated strongly with MS duration: in symptomatic patients mean MS duration was 16.6 years, while in asymptomatic ones it was 7.5 years. We haven't found the same correlation for bladder symptoms, probably for the reason that bladder dysfunctions appear more prematurely than BD. 92% of subjects with BD reported bladder symptoms, while 59% of those with regular belly showed isolated bladder symptoms ($p<0.005$). Therefore, we assume that BD is retarded and expression of a more compromised neurological condition. Despite the limited sample size, our data show a correlation between urinary and faecal urgency: Six out of 23 cases with urinary urgency showed also faecal urgency ($p<0.05$).

CONCLUSION

Our study confirms the correlation between SD, MS duration and degree of disability, but demonstrates that BD, essentially C, are present in a considerable percentage (23%) of subjects with moderate MS and are associated with bladder symptoms in 92% of cases. In our opinion a careful clinical evaluation and a minimalist approach are fundamental in BD management in MS, but in selected cases we think that sacral nerve modulation would have to be considered as a therapeutic option.

PERMANENT URETHRAL CATHETER AND COMMUNICATION IMPAIRMENT IN STROKE PATIENTS.

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INTRODUCTION AND AIM OF THE STUDY

It is well known that permanent indwelling urethral catheter correlates with worse functional performance in stroke patients. We would like to assess if there is an independent effect due to communication impairment.

MATERIALS AND METHODS

We enrolled 701 consecutive patients affected by stroke who were admitted to our rehabilitation unit between 2000 and 2007. All of them underwent a complete clinical and functional evaluation within 24 hours after admission.

We considered urethral catheter at admission, motor sub scale of FIM (Functional Independence Measure), comprehension, expression and the sum of the remaining three items of non motor sub scale of FIM (we will name it “FIM3”).

For statistical analysis we used non parametric Spearman rank correlation both general and partial.

RESULTS

Permanent indwelling catheter showed a strong negative correlation with motor sub scale of FIM, comprehension, expression and FIM3. It was not a big surprise. Worse functional conditions associate with permanent urethral catheter. But also partial correlation, when effects of other functional conditions were ruled out, shows a strong correlation between urethral catheter and comprehension (ρ = -0.36, $P<0.0001$) and catheter with expression (ρ = -0.14, $P=0.0002$).

DISCUSSION

Independent correlation between urethral catheter and communication items of functional scores suggests that communication plays an independent role in explaining why a stroke patient needs a urethral catheter.

CONCLUSION

Evidence reported above shows that rehabilitation team – as well as every team involved in stroke patients' care – has to pay particular attention to communication tasks, as in some cases this will lead to an earlier removal of permanent urethral catheter.

REFERENCES

1. Macciocchi S, Diamond PT, Alves WM, Mertz T.Ischemic stroke: relation of age, lesion location, and initial neurologic deficit to functional outcome. *Arch Phys Med Rehabil* 1998;79:1255–7

2. Liu M, Tesuji T, Tsuyuchi K, Chino N. Comorbidities in stroke patients as assessed with a newly developed comorbidity scale*. Am J Phys Med Rehabil* 1999; 78:416-24.

3. Weimar C, Ziegler A, Konig IR, Diener HC. Predicting functional outcome and survival after acute ischemic stroke. *J Neurol* 2002;249:888–95

INTEGRATED TREATMENT FOR URGENCY/FREQUENCY AND PAINFUL BLADDER SYNDROME

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INTRODUCTION AND AIM OF THE STUDY

Painful bladder syndrome is the complaint of suprapubic or retropubic pain related to bladder filling, accompanied by other symptoms such as urgency/frequency in the absence of proven urinary infection or other obvious pathologies. The syndrome is a constellation of at least 2 symptoms that are functional abnormalities for which a precise cause has not been defined. Treatment is frequently only temporarily successful or even unsuccessful and, therefore, different opportunities should be offered. When improvement is obtained, continuous treatment should be maintained for many years in order to stabilize the results.
Here we present our results with integrated different treatments and after prolonged follow-up.

MATERIALS AND METHODS

Fifty-five patients were treated and followed from 2000 to 2007 for urgency/frequency and painful bladder syndrome. Forty-six were females aged between 25 and 80 yrs (average age 54) and 9 were males between 21 and 79 yrs (average age 52). They were all affected by frequency/urgency symptoms reported in the bladder diary with suprapubic or retropubic pain at bladder filling that was mild in 14 (30%) women and 2 (22%) men and from severe to strong in
the remaining cases. Among the women 4 had associated Systemic Erithematosus Lupus (SEL), 3 pelvic endometriosis and 2 fibromialgia.
Functional bladder capacity was recorded with at least 4 day diary and results are shown for women in Fig. 1 and for men in Fig. 2.
Urine cytology and search for Mycobacterium, Chlamydiae and Mycoplasma were always negative.
Urodynamics performed in 1 man and 29 women showed bladder stability and reduced cystometric capacity (only in 3 cases it reached 300 mls).

Cystoscopies with hydrodistention and bladder biopsies under anesthesia were performed in 8 men and 42 women. Bladder mucosa appeared normal in 3 men and 35 women, red and with glomerulations after hydrodistention in 5 men and 9 women and with Hunner ulcers in 2 women. Bladder capacity reached during hydrodistention at 80 cmH2O is shown in Fig. 1 and 2. Pathological findings recognized inflammation in all the cases which was mild in 5 men and 19 women, heavy in the remaining ones and with Mast cells count over 50 mmsq in 1 man and 18 women.

Treatment modalities have been changed during the years.

Initial treatment consisted in administering urine alkalinizers (sodium or potassium cytrate or sodium bicarbonate) and antidepressants and in suggesting change in life style, such as a proper diet and possibly to quit smoking.

Bladder hydrodistention under general or local anesthesia was always performed in order to allow increase of bladder capacity and sometimes repeated always under local anesthesia. Subsequent vesical instillations with a cocktail of heparin 25.000 IU and desamethasone 32 mg and sodium hyaluronate 40 mg were administered weekly for 2 months and then gradually reduced but continued with only heparin at home after proper training for at least 1 year.

Dimethyl sulphoxide bladder irrigations were better tolerated by older patients and allowed to maintain longer the benefits both on pain and urinary symptoms and to reduce the frequency of instillations.

Three men and eighteen women followed this regimen; however the drug should be administered in Hospital due to the fact that is not yet on the market in Italy.

Electrical stimulation of posterior tibial nerve has been more recently associated to therapy in 26 patients with 30 minute sessions each week for 3 months and then monthly for at least 1 year, obtaining good results on frequency and urgency symptoms but less on pain.

RESULTS

Follow-up varies from at least 6 months to 7 years (mean 3.5 years).

Functional bladder capacity increased and was maintained after at least 6 months follow-up, as shown in Fig. 1 and 2.

Only 1 man and 28 women healed and did not need further treatment. The remaining cases continue to be treated either with heparin (self administered) or dimethyl sulphoxide instillations and/or with posterior tibial nerve stimulation.

Among the 28 healed females 16 (out of 18) were treated with dymethyl sulphoxide and 12 (out of 28) with sodium hyaluronate.

Two females became pregnant and continued bladder instillations with sodium hyaluronate during the first 3 months of pregnancy and then after delivery.

DISCUSSION AND CONCLUSION

Urgency/frequency and painful bladder syndrome requires an integrated different modality of treatment in order to obtain improvement and then maintain good results. Rapid improvement is only reached with bladder hydrodistention under general or local anesthesia. Healing is not often obtained but it is more frequent in older female patients, especially when treatment can be shifted to bladder

irrigations with dimethyl sulphoxide that can give more prolonged benefits, but is not well tolerated in younger patients. Due to the prolonged time of treatment this should be simplified and, if possible, self administered. Follow-up must be long enough before drawing conclusions on the efficacy of different treatments.

fig.1. Bladder capacity variations in women during hydrodistention and follow up.

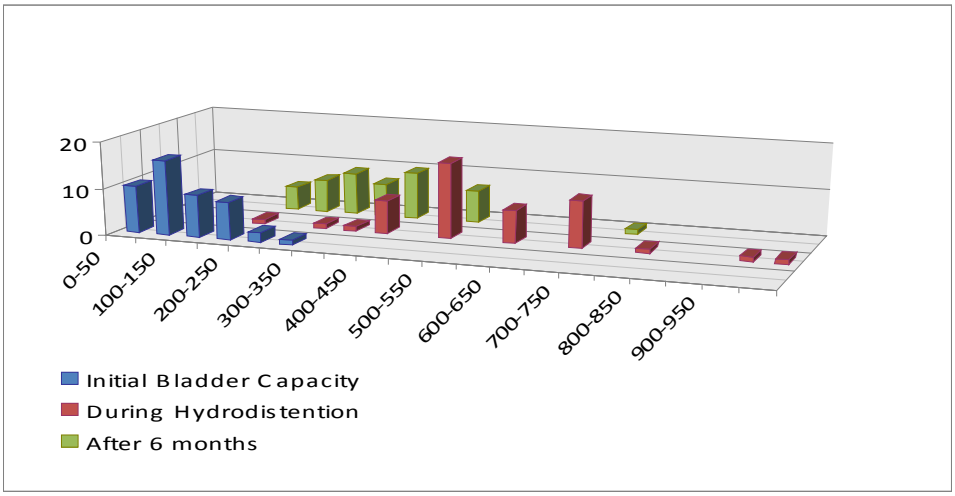
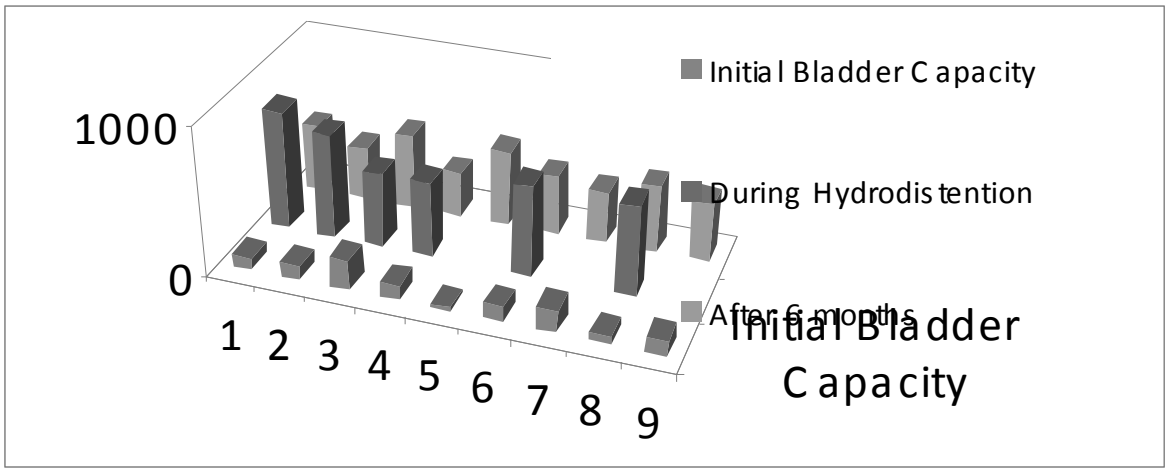


fig.2. Individual bladder capacity variations in men during hydrodistension and follow up


1000
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1 2 3 4 5 6 7 8 9
Initial Bladder Capacity
During Hydrodistention
After 6 months
Initial Bladder Capacity

PERIPHERAL NEUROMODULATION OF THE S3 IMPROVES BLADDER CAPACITY AND REDUCES PERCEPTION OF URGENCY IN PATIENTS WITH OVERACTIVE BLADDER: A LONG TERM FOLLOW-UP

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INTRODUCTION AND AIM OF THE STUDY

The prevalence of urinary incontinence (UI) and overactive bladder rises with age, and elderly people are the fastest-growing segment of the population. Many elderly people assume that UI is a normal part of the aging process and do not report it to their doctors, who must therefore make the effort to elicit the information from them. Coexisting medical problems in older patients and the multiple medications that many of them assume make diagnosis and treatment more complex in this population. Just as the aetiology of incontinence is often multifactorial, the treatment approach may need to be integrated, with behavioural, environmental and medical components; in any case, it must be targeted to the individual patient. New, less-invasive surgical techniques and devices are available if the conservative therapy fails. The percentage of population over 65 years of age has increased dramatically over the past 100 years and is expected to continue to increase well into the 21th century. Furthermore, the segment of this population with the greatest need for health care, those aged 85 and older is predicted to undergo a rapid expansion, from 10 to 19% by the year 2040.

The lower urinary tract consists in a group of interrelated structures that function in the adult to bring about efficient and low-pressure bladder filling and low-pressure urine storage with perfect continence.

An urgency and frequency syndrome due to an overactive bladder can successfully be treated by efferent nerve stimulation of the S3 spinal regions that affect bladder control, with a minimal invasive transcutaneous access to the posterior tibial nerves. This technique, called SANS (Stoller Afferent Nerve Stimulation) is named after its inventor, the urologist Marshall Stoller, born in Canada in 1989. SANS is used by urologists and gynaecologists to treat urinary urge incontinence, urgency, frequency, and pelvic pain.

The SANS device works by sending a mild electrical current through a very fine needle inserted near a nerve bundle in the ankle (posterior tibial nerve). The stimulation is carried up the nerve bundle to the sacral region of the spine that controls the bladder function. Stimulating this region reconditions the nervous pathways and restores normal bladder control. This technique has the advantage, versus traditional sacral root neuromodulation, to be less invasive and better accepted by the patients. Patients normally receive one 30 minute nerve stimulation session weekly for 10 to 12 weeks.

Aim of this study was to investigate SANS efficacy in a group of patients affected by frequency- urgency syndrome due to an overactive bladder, no responders to conservative treatment.

MATERIALS AND METHODS

Thirty-six patients (24 women and 12 men), mean age 54 years (range 34-70) suffering from urgency-frequency syndrome, as documented by a voiding chart, were diagnosed with overactive bladder. An urodynamic study was performed, according the ICS recommendations, before and after peripheral stimulations with SANS utilising a minimal invasive transcutaneous access to the posterior tibial

nerves. The patients, before and after the treatment, filled a voiding diary, VAS, SF36 questionnaire, subject's perception of bladder condition, subject's perception

of urgency and at the end of the treatment the subject's perception of treatment benefit. The mean follow-up was of 18 months post treatment.

RESULTS

One patient discontinued the treatment for leg pain. No other complications were observed. Twelve patients (33,3%) had a complete response and were considered healed; six (16,7%) showed significant improvement; and 18 (50%) were classified as non-responders, according to the subject's perception of treatment benefit. Urodynamic evidence of bladder overactivity, evident in all patients prior to treatment, was eliminated in 55% of patients. In all patients, mean (SD) total bladder capacity increased significantly from 155 (50-259) to 230 (85-400) ml ($p<0.001$).

In 75% of patients the treatment reduced the perception of urgency.

We also obtained a decrease in the number of pads per day.

DISCUSSION AND CONCLUSION

Considering the long term follow-up, our experience with SANS in treating urgency-frequency syndrome is satisfactory. According to the data reported in literature, the use of SANS in the treatment of overactive bladder is efficacious, safe, little expensive, increases

significantly the bladder capacity and reduces the perception of urgency. Therefore, we consider this as a first line treatment after a medical therapy failure.

REFERENCES

1) Finazzi Agrò E, et al: Use of Stoller Afferent Nerve Stimulation (SANS) in the treatment of detrusor hyperactivity: preliminary data. Urodinamica 10;153-154, 2000.

2) Klingler HC, et al. Use of peripheral neuromodulation of the S3 region for treatment of detrusor overactivity: A urodynamic-based study. Urology, 1;766-71, 2000.

LOW FREQUENCY REPETITIVE TRANS-CRANIAL MAGNETIC STIMULATION PRODUCES INHIBITION OF DETRUSOR OVERACTIVITY IN PATIENTS WITH PARKINSON'S DISEASE

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INTRODUCTION AND AIM OF THE STUDY

Transcranial magnetic stimulation (TMS) is a non invasive method of brain stimulation frequently used as diagnostic and research tool since its introduction in 1985 (1). TMS uses magnetic fields to induce electric currents that cross the nervous tissue, producing neuronal depolarization. It is performed by positioning an electromagnetic coil on the skull over the cerebral motor area (motor hot spot). The evoked motor responses are recorded as electromyographic potentials from the muscles. The repetitive transcranial magnetic stimulation (rTMS) is the application of magnetic stimuli at frequencies of 1 Hz (low frequency) or higher (high frequency). When applied over the motor cortex, high frequency rTMS is able to induce facilitatory effects on cortico-spinal excitability, while low frequency stimulation rather induces inhibitory effects (2). High frequency rTMS has been found to improve the voiding phase parameters in multiple sclerosis patients, with detrusor underactivity (3). Low frequency rTMS could theoretically produce opposite effects (e.g. improvement of detrusor overactivity). Aim of this study was to analyse effects of low frequency rTMS on lower urinary tract activity in Parkinson's disease (PD) patients.

MATERIALS AND METHODS

Ten patients (6 females and 4 males) affected by mild-moderate (Hoehn Yahr scale □3) PD were included in this study, after signing an informed consent. Mean age was 63 (58-70) years. All patients had overactive bladder (OAB) syndrome. No patients had any obvious lower urinary tract pathology or abnormality. None of them were using drugs conditioning the lower urinary tract, except those with PD; PD therapy remained unchanged during the entire study period. Each patient was submitted to 10 inhibitory (1 Hz) rTMS sessions in two consecutive weeks. rTMS was applied over the primary motor cortex (pelvic floor hot spot) of the dominant hemisphere at 100% resting motor threshold intensity. Every session was composed of 20 trains of 10 seconds (50 stimuli each train)

with intervals of 30 seconds. One to 5 days before, and 1 to 3 days after rTMS treatment, a urodynamic evaluation was performed; an IPSS symptom score was also fulfilled by all patients before and after treatment. Results obtained were statistically compared.

RESULTS

Results are reported in the table.

N. Pts.10	Before rTMS (mean)	After rTMS (mean)	p
IPSS (total)	12,5	8,7	0.01
IPSS (filling phase symptoms)	10,3	6,5	0.004
IPSS (QoL)	3,8	2,4	0.01
First desire (ml)	125	184	0,01
Bladder capacity (ml)	324	386	0.01
Detr. Involuntary contractions volume (ml)	286	311	0.01
Detr. involuntary contractions amplitude (cmH2O)	34	26	0.12

The remaining urodynamic parameters analysed during the filling and the voiding phase did not significantly change after rTMS.

DISCUSSION

While high frequency rTMS has been shown to produce effects on voiding phase of the micturition cycle, inhibitory low frequency rTMS seems to produce effects on the filling phase. In our series, PD patients with OAB syndrome showed a symptomatic and urodynamic improvement of their condition after inhibitory rTMS. In particular, a reduction of IPSS symptom score was noticed: this reduction was produced by a significant decrease of the scores of the three questions on filling phase symptoms (frequency, urgency, nocturia); on the other hand, no difference was noticed between scores of the remaining questions (voiding phase symptoms). It is worthy noting that the score of IPSS final question on quality of life was reduced significantly as well, thus demonstrating that this treatment could produce a good clinical improvement of PD patients with OAB. Urodynamic parameters showed an improvement of detrusor overactivity, with significant increase of first desire, volume at detrusor involuntary contractions appearance and bladder capacity.

CONCLUSION

Inhibitory rTMS seems to be an effective, non invasive treatment for mild-moderate PD patients with OAB. Further studies on the long-term effects of this treatment are needed.

REFERENCES

1) Electroencephalogr. Clin. Neurophysiol. 1994; 91: 79-82.

2) Exp Brain Res. 2003;148: 1-16.

3) Mult Scler. 2007 Mar;13(2):269-71.

Abstract 21

Experimental sacral roots thermoablation. A new tool in refractory neurogenic overactive bladder?

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INTRODUCTION AND AIM OF THE STUDY

In case of neurogenic bladder due to upper motor neurolesion, mixed symptoms in storage and voiding phase are present. Under an urodynamic point of view, it is common to find an overactive neurogenic bladder with detrusor sphincter dyssynergia.

According to ICI the first line treatment in neurogenic bladder is, when it's possible, to achieve a low pressure filling phase, using antimuscarinic drugs and intermittent catheterization for voiding phase.

When this approach fails, the use of neurostimulation or botulinum toxin injection in detrusor muscle is actually the common options.

Few patients are resistant to these procedures and the choice of treatment is generally difficult.

Sacral posterior rhizotomy (SDAF) represents a choice in complete lesions but it is always refused by patients because too invasive and irreversible.

Recently, a series of SCI patients treated by means of radiofrequency were reported by D'Ancona et al, but no further studies were published.

We report a preliminary experience with Rf in 5 patients using intraoperative monitoring.

MATERIALS AND METHODS

Five spinal cord injured patients, 3 males, 2 females, aged between 19 and 50 years (mean age 28), 4 dorsal and 1 cervical complete lesion (mean time from lesion 4.5 years), resistant to antimuscarinics and with low success rate with intradetrusor botulinum toxin, and in 2 cases non responder to bilateral chronic pudendal nerve stimulation, gave their consent to be submitted to radiofrequency sacral rhizotomy. All patients were submitted to a previous anaesthetic block of sacral roots under urodynamic monitoring to check acute response.

In prone position a 12 gauge needle was used under neurophysiological and fluoroscopic monitoring, to identify bilaterally S2 and S3 roots. Pulsed thermocoagulation was subsequently applied to obtain the disappearance of neurophysiological responses to electrical stimulation. Bursts of energy used for every root started from 120 to 240 seconds at a temperature of 60°C.

The procedure was applied without anaesthesia and no autonomic dysreflexia was registered.

RESULTS

After 24 hours 4 patients were completely continent while one patient became continent after 20 days.

At one month urodynamics demonstrated a medium increase of bladder capacity of 160 ml with residual low pressure overactivity. After 3 months all patients returned to baseline parameters.

DISCUSSION

The research of a reversible approach to neurogenic detrusor overactivity is one of the goals of modern neuro-urology.

In the last ten years, sacral area neuromodulation and botulinum toxin represent an impressive help in treating neurogenic overactive bladder.

On the other side, the research of a reversible treatment directly on sacral roots seems to be a good approach.

CONCLUSION

In our preliminary experience radiofrequency seems to be a safe, less invasive and promising approach.

Short term results are related to the attempt to define the right “dose” of treatment and, after this experience, a protocol with urological and neurophysiological functional monitoring has been defined for the future.

REFERENCES

Neurourol, Urodyn, Proceedings 2003, abst.562

Pudendal nerve block under neurophysiologic guidance for the treatment of chronic pelvic pain (CPP): technical notes and clinical results

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INTRODUCTION AND AIM OF THE STUDY

Chronic pelvic pain is a non-malignant pain perceived in structures related to the pelvis of either men or women. In the case of documented nociceptive pain that becomes chronic, the pain must have been continuous or recurrent for at least 6 months. In all cases, negative cognitive, behavioural and social consequences (ICS statement) may be associated. Guided pudendal nerve blocks, the first line of conservative treatment of pudendal nerve entrapment (PNE), have been attempted in different ways by fluoroscopy with or without nerve stimulation, CT, US or with the "low tech" finger, using only anatomic landmarks. Until today nobody has tried to reach the nerve under neurophysiologic guidance to deliver drugs in close proximity to the nerve -as blocks can fail if drugs are not placed near the nerve.

MATERIALS AND METHODS

From March 2006 to December 2007, 32 patients (8 males, 24 females) mean age 46 years, underwent a therapeutic pudendal nerve block under neurophysiologic guidance using nerve C-MAP derived from the anal sphincter. They were suffering from CPP since at least 6 months (6 months to 15 years) with no response to all other conservative treatments (nerve mobilization with manual therapy, oral drugs,
neuromodulation. All other possible causes and other underlying conditions for symptoms referred by the patients were excluded before concluding that the patient was suffering from pudendal neuralgia. All of them underwent a comprehensive neurological and neurophysiologic evaluation. Pain intensity was assessed at the time of the first visit and then 15 days after each procedure using a Visual Analogue pain Score (VAS). The first step of the procedure is to find the ischial spine as the pudendal nerve is formed just proximal to it. We find it with a dorsal approach, under fluoroscopy, at the intersecting point of two lines: 1 horizontal from the great trochanter, 1 vertical from the ischial tuberosity tip.

A filter setting of 100 Hz - 1 KHz, gain of 500 mV/div and sweep speed of 50 ms (5 ms/div) are used during registration of C-MAP to find the nerve, delivering rectangular pulses of 50 μsec duration as a repeated single stimulus. The lower is the intensity to evoke a repeatable C-MAP, the nearer is the nerve and at 2-4 mA we are sure to be in close proximity of the nerve. We ask the patient if he/she feels the stimulation in the painful area, we check the C-MAP that is repeatable and aspirate before injecting a mixture of 6 cc of Ropivacain HCl and 1 cc/4 mg of desametasone in small boluses. If the nerve is blocked, immediately the C-MAP is abolished using a stimulating current up to 20 - 25 mA .

RESULTS

Twenty-five patients out of thirty-two were evaluated at a median follow-up of 11.5 months. Seven of them were lost at follow-up after the first treatment, unwilling to repeat the procedure. The mean VAS before the procedure was 7.8 (10-2) with a mean duration of the pain of 36.8 months (6-180). The mean number of infiltration procedures was 2.12 (1-6). The mean VAS at follow-up time was 3.48 (0-9). We considered a successful result a decrease in VAS more than 50% and an intermediate result a decrease of at least 2 points in VAS score with a reduction in the use of painkiller drugs, lasting at least 3 months. Fifteen patients out of 25 (60%) had a successful result, 6 out of 25 (24%) an intermediate one and only 4 (16%) no result. Responders had a complete relief of pain for about 36-48 hours, a mild flare up of pain for 3 to 4 days and then a relief up to complete wellness for about 15-20 days. The subsequent blocks were made at 2 to 3 week interval, after a clinical reassessment of the patient and an evaluation of the VAS, until a complete recovery or stabilization of the pain at an acceptable level was obtained.

DISCUSSION

The use of pudendal nerve blocks for treating pudendal neuralgia was popularized by Maurice Bensignor in Nantes: he used a series of 3 injections around the pudendal nerve reporting an “optimistic” 70% improvement in his patients with no mention about length of time the symptoms improved. Amarenco reported a 15% of success using CT guided blocks, Robert indicated very inconsistent and divergent results in 2 papers published in 1998 with success rates ranging from 2 to 65-70%. Labat reported 60% of success with a “very poor” follow-up of 3 months. Recent papers suggested new techniques for approaching the pudendal nerve: transperineal, transvaginal, sono – guided or TC guided. However, they have some limitations, such as high cost, difficulty to perform in practice, inaccurate and unreliable results. Furthermore, as reported by Antolak, block can fail if drugs are not placed near the nerve and, in his opinion, complete accuracy is not possible

with any injection technique available. To overcome these limitations, we tried neurophysiologic pudendal block with posterior approach with the aim to do better in terms of results and costs. Accuracy in detecting nerve position and drugs mixture delivery is higher than all other techniques available: a “functional approach for a functional disease”.
Despite the numbers of our series, results are very interesting in terms of success (60%), follow-up (11.5 months) and procedure costs.

CONCLUSION

Guided pudendal nerve blocks are the first line of conservative treatment for pudendal neuralgia, usually associated with oral drugs and physical therapy.
They are performed to make a diagnosis of pudendal neuralgia, for its prognostic value (the longer the pain relief after a block, the better the surgical results) and mainly for the therapeutic effect. Our technique allows an accurate delivery of the mixture of drugs as near as possible to the affected nerve using a very easy neurophysiologic approach with good results and low costs, avoiding more invasive surgical therapies. New drugs are going to be introduced to improve results in the treatment of pudendal neuralgia: the important issue is to deliver these very close to the nerve!

REFERENCES

R.A. Schmidt. Technique of pudendal nerve localization for block or stimulation. J. Urol.,142:1528-31, 1989.

Robert R, Prat-Pradal D, Labat JJ, Bensignor M, Raoul S, Rebai R, Leborgne J. Anatomic basis of chronic perineal pain: role of the pudendal nerve. Surg Radiol Anat 1998; 20:93-8.

S-S Choi, P-B Lee, Y-C Kim, H-J Kim, S-C Lee. C-arm guided pudendal nerve block: a new technique. Int J Clin Pract 2006;60(5): 553-556