

POSTERIOR TIBIAL NERVE STIMULATION AS NEUROMODULATIVE TREATMENT OF LOWER URINARY TRACT DYSFUNCTION

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ABSTRACT

Purpose: Recently, intermittent percutaneous posterior tibial nerve stimulation was introduced as a treatment modality filling the gap between conservative and surgical therapies in patients with certain types of lower urinary tract dysfunction.

Materials and Methods: In a prospective multicenter trial posterior tibial nerve stimulation was evaluated in 37 patients who presented with symptoms of bladder overactivity, that is the urgency and frequency syndrome and/or urge incontinence, and 12 with nonobstructive urinary retention. Results were recorded in voiding diaries and on quality of life questionnaires before and after treatment. Patients were classified as responders, including those in whom therapy was successful and chose to continue treatment after the initial 12 weeks, and nonresponders, those who chose to stop treatment.

Results: Overall, a positive response was seen in 60% of all patients. In patients with bladder overactivity a statistically significant decrease was observed in leakage episodes, number of pads used, voiding frequency and nocturia, and an equal increase in mean and smallest volume voided. Improvements were also seen in nonobstructive urinary retention, including number of catheterizations, total and mean volume catheterized, and total and mean volume voided. Disease specific quality of life and some domains of general quality of life improved, especially of bladder overactivity. Only mild side effects were observed.

Conclusions: Posterior tibial nerve stimulation is a minimally invasive and successful treatment option for patients with certain types of lower urinary tract dysfunction.

KEY WORDS: bladder, neurotransmitters, transcutaneous electric nerve stimulation, tibial nerve

Non-neurogenic lower urinary tract dysfunction is a common urological problem that strongly affects quality of life. Patients can complain of urgency and frequency, urge incontinence or present with urinary retention. In most patients the etiology of these symptoms remains unclear.¹ Conservative treatment options for bladder overactivity, that is the urgency and frequency syndrome and/or urge incontinence, consist of behavioral techniques with and without biofeedback, bladder reeducation, pelvic muscle exercise or pharmacotherapy involving anticholinergics, antispasmodics and tricyclic antidepressants. Patients with nonobstructive urinary retention can be treated with clean intermittent or permanent catheterization. For refractory cases more aggressive surgical procedures, including bladder distension, ileocystoplasty or urinary diversion have been advocated. However, a high recurrence and complication rate limits the widespread application of these treatments.

Recently, continuous sacral root stimulation (Medtronic, Inc., Minneapolis, Minnesota) has been proposed as an alternative, less invasive therapeutic option for patients with non-neurogenic lower urinary tract dysfunction not responding to conservative treatment.² Although highly effective in select patients, this technique is expensive and requires explicit surgical skill. Posterior tibial nerve stimulation is technically less demanding and probably more cost-effective for management of lower urinary tract dysfunction. We present our initial experience with this new neuromodulation technique in a prospective clinical trial.

PATIENTS AND METHODS

Between November 1999 and March 2000, 15 male and 34 female patients were enrolled in a prospective clinical multicenter trial that received approval by the institutional review board. All patients were evaluated for urgency and frequency, urge incontinence and nonobstructive retention by history, voiding diaries consisting of frequency volume charts, and physical as well as urological examination, including urodynamics. Urgency and frequency was defined as greater than 8 voids per 24 hours and the sudden urge to void could hardly be suppressed. Urge incontinence was characterized by urgency leading to urinary leakage occurring at least 3 times weekly and/or phasic involuntary bladder contractions with concomitant incontinence on cystometry. Nonobstructive retention was distinguished by urinary retention necessitating intermittent catheterization at least 4 times daily without urodynamic signs of outflow obstruction, as defined on the Abrams-Griffiths nomogram.³ The use of parasympatholytic medication or other pharmaceuticals influencing bladder function, including antidepressant agents, should have been stopped 2 weeks or longer before posterior tibial nerve stimulation or continued without dose changes during the entire study. Specific exclusion criteria for our study are given in the Appendix.

Patients. A total of 10 men and 27 women with a mean age of 52.5 years (range 23 to 74) were treated for bladder overactivity. These patients lived with symptoms for a median of 4 years (range 1 to 30). The symptoms were said to be induced by childbirth in 3, pelvic surgery in 9, including 7 hysterectomies, 1 anterior prolapse correction and 1 Burch colposuspension, and other events in 3 patients, including

fracture of the coccygeal bone, urinary tract infection and bowel infection. The remaining patients had no history of any pelvic event before the onset of symptoms. Of the 37 patients 32 (91.4%) received unsuccessful prior medical therapy, including anticholinergics, with a mean number of 1.9 (range 1 to 5) drugs used. Almost half of all (48.6%) patients underwent up to 3 surgical procedures, most frequently colposuspension, for symptoms. Other unsuccessful therapies included physiotherapy and/or biofeedback in 22 (59.4%), electrical stimulation, including transcutaneous electrical nerve stimulation or peripheral nerve evaluation, in 5 (13.5%) and alternative therapies, such as Chinese herbs in 5 (13.5%) patients. Physical examination did not show overt or neuro-urological abnormalities in any patients.

There were 5 men and 7 women with a mean age of 50.8 years (range 36 to 64) treated for nonobstructive retention. These patients had symptoms for a median of 3.5 years (range 1 to 36). Initiation of symptoms was related to childbirth in 1, pelvic surgery, including Wertheim's-Meigs operation in 1 and Burch colposuspension in 1, other surgery, including hip replacement in 1 and inguinal hernia repair in 1, and benign prostatic hyperplasia without any effect of transurethral prostatic resection in 1 patient. The remaining 6 patients had no history of any pelvic event before the onset of symptoms. Of the 12 patients 11 (92%) received unsuccessful medical therapy previously, including α -blockers or sympathomimetics. Almost half the patients (5 of 12) had undergone lower urinary tract surgery, mostly urethral dilatation or urethrotomy, for symptoms previously. Other unsuccessful therapies included physiotherapy and/or biofeedback in 3 (25%) and electrical stimulation in 1 patient. All patients had clean intermittent catheterization. In addition, physical examination did not show overt or neuro-urological abnormalities in these patients. Urodynamic investigations revealed hypo-contractile detrusors in all patients.

Treatment method. Posterior tibial nerve stimulation was applied according to Stoller.⁴ Patients are in the supine position with the soles of the feet together, and knees abducted and flexed ("frog-position"). A 34 gauge stainless steel needle is inserted approximately 3 to 4 cm., about 3 fingerbreadths cephalad to the medial malleolus, between the posterior margin of the tibia and soleus muscle. A stick on electrode is placed on the same leg near the arch of the foot. The needle and electrode are connected to a low voltage (9 volts) Uro-surge stimulator (Uro-surge, Coralville, Iowa) with an adjustable pulse intensity of 0 to 10 mA., a fixed pulse width of 200 microseconds and a frequency of 20 Hz. The amplitude is slowly increased until the large toe starts to curl or toes start to fan. If the large toe does not curl or pain occurs near the insertion site the stimulation device is switched off and the procedure is repeated. If the large toe curls or toes start to fan stimulation is applied at an intensity well tolerated by the patient. If necessary the amplitude can be increased during the session. Patients underwent 12 weekly outpatient treatment sessions, each lasting for 30 minutes. If a good response occurred the patient was offered chronic treatment.

Evaluation of results. After providing informed consent all patients completed a voiding diary, as well as general and disease specific quality of life questionnaires at study entry and completion of the 12-week treatment. In the 24-hour voiding diary frequency and voided volumes, number and volume of catheterizations, number of leakage periods, leakage severity as well as the number of pads or diapers used were recorded. The leakage severity was scored on a scale of 0 to 3 and included 0—no leakage, 1—leakage of some drops, 2—loss of a small amount and 3—loss of a massive amount, that is change of clothes. General and disease specific quality of life questionnaires were evaluated with the 36-item short-form health survey (SF-36) and the adjusted quality of life questionnaire, respectively.^{5,6} The SF-36 consists of 36 items regarding 8 distinct health status concepts and 1 item measuring self-reported health transition, including physical function, role physical, pain, general health, emotional well-being, role emotional, social functioning, energy and fatigue and change in general health. The maximum score for each domain is 100, and a higher score relates to better quality of life. The quality of life questionnaire consists of 22 items, each with a 5 point response scale. As with the SF-36, a high score means good quality of life.

Success was defined as the patient request for continued chronic treatment for maintenance. Analysis was done on an intention-to-treat basis. Within group comparisons of parametric results at baseline and 12-week treatment were conducted with the paired sample t-test. Statistical analysis was performed with commercial software.

RESULTS

Bladder overactivity. Of the 444 treatment sessions stimulation was performed on the right posterior tibial nerve with a mean pulse intensity of 3.7 mA. (range 1.4 to 6.8) per session in 265 (60%). Complications, including minor bleeding or a temporary painful feeling at the insertion site, were seen only rarely. Of the 37 patients posterior tibial nerve stimulation in 7 men and 15 women (59.4%) was considered successful because they requested continuation of therapy after completion of the 12-week treatment (group 1, responders). In 3 male and 12 female patients treatment was unsuccessful since they did not choose maintenance therapy (group 2, nonresponders).

At completion of the 12-week treatment all 33 patients with urgency and frequency had significant improvement of voiding frequency during the day and night (table 1 and fig. 1, A). When discriminating group 1 (21 responders) from group 2 (12 nonresponders), these improvements appeared to be significant only in group 1. The smallest mean values and mean volumes voided also improved, whereas the largest volumes voided did not change in this group.

A statistically significant overall decrease in incontinence was seen in the 30 patients who were urge incontinent (table 2 and fig. 1, B). When comparing group 1 (18 responders) with group 2 (12 nonresponders), improvements found in

TABLE 1. Voiding parameters in 33 patients with urgency and frequency

	Frequency	Nocturia	Vol. Voided		
			Smallest	Largest	Mean
All pts:					
Mean $\pm$ SD (0 wks.)	16.5 $\pm$ 6.8	2.6 $\pm$ 2.3	65 $\pm$ 49.3	289.8 $\pm$ 161	140 $\pm$ 82.2
Mean change (95% CI)	-2.8 (-0.8, -4.9)	-1 (-0.2, -1.8)	14.2 (32.8, -4.5)	13.9 (48.7, -20.9)	19.3 (40.3, -1.7)
p Value	<0.05	<0.05			
Group 1:					
Mean $\pm$ SD (0 wks.)	16.1 $\pm$ 6.1	2.5 $\pm$ 2.7	62.6 $\pm$ 52.1	268.8 $\pm$ 146.4	133 $\pm$ 82.8
Mean change (95% CI)	-4.8 (-2.7, 6.8)	-1.4 (-0.4, 2.3)	29.8 (49.2, 10.3)	9.5 (50.6, -31.6)	35.1 (62.6, 7.7)
p Value	<0.0005	<0.05	<0.005		<0.05
Group 2:					
Mean $\pm$ SD (0 wks.)	17.1 $\pm$ 8.3	2.7 $\pm$ 1.6	71 $\pm$ 44.8	334 $\pm$ 188.5	153.6 $\pm$ 83.7
Mean change (95% CI)	0.8 (5, -3.3)	-0.2 (1.3, -1.6)	-18.5 (19.4, -56.4)	23 (100.6, -54.6)	-14 (8.5, -36.5)

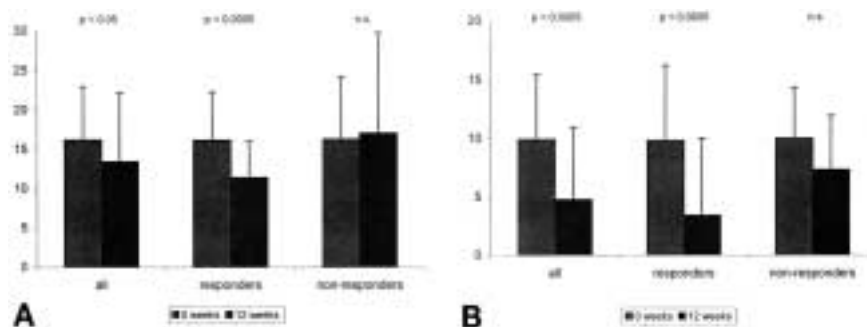


FIG. 1. Before and after posterior tibial nerve stimulation for responders, nonresponders and both combined. A, voiding frequency. B, number of leakage episodes. Error bar represents SD. ns, not significant.

TABLE 2. Voiding parameters in 30 patients with urge incontinence

	Leakage Episodes	Pads Used	Leakage Severity
All pts:			
Mean $\pm$ SD (0 wks.)	9.8 $\pm$ 5.6	6.3 $\pm$ 3.2	1.7 $\pm$ 0.5
Mean change (95% CI)	-4.8 (-2.2, -7.5)	-2.5 (-1.2, -3.9)	-0.7 (-0.4, -1.0)
p Value	<0.005	<0.005	<0.005
Group 1:			
Mean $\pm$ SD (0 wks.)	9.8 $\pm$ 6.4	5.8 $\pm$ 2.6	1.6 $\pm$ 0.5
Mean change (95% CI)	-6.2 (-2.9, -9.5)	-3.3 (-1.5, -5.1)	-0.8 (-0.3, -1.3)
p Value	<0.005	<0.005	<0.005
Group 2:			
Mean $\pm$ SD (0 wks.)	9.8 $\pm$ 4.4	7.1 $\pm$ 3.9	1.9 $\pm$ 0.5
Mean change (95% CI)	-2.4 (2.4, -7.3)	-1.3 (0.9, -3.4)	-0.5 (-0.2, -0.8)
p Value			<0.05

leakage episodes and number of pads used appeared to be greater in group 1. Leakage severity scores showed improvement in all patients who were urge incontinent, and groups 1 and 2. General quality of life improved in regard to physical and social functioning in all patients with bladder overactivity. Mean physical functioning plus or minus standard deviation (SD) was 53.7 ± 27.9 (mean change +9.1, 95% confidence interval [CI] +14.1, +4, $p < 0.005$) and social functioning 64.7 ± 31.2 (mean change +10.3, +16.5, +4.1, respectively, $p < 0.005$) at 0 weeks. In group 1 both scores also increased. Mean physical functioning plus or minus SD was 61.6 ± 26.3 (mean change +11.2, 95% CI +18.8, +3.5, $p < 0.05$) and social functioning 70.6 ± 26.7 (mean change +11.6, +20.9, +2.3, respectively, $p < 0.05$) at 0 weeks. Only social functioning improved (55.9 ± 35.9 , mean change +8.4, 95% CI +16.6, +0.2, respectively, $p < 0.05$) at 0 weeks in group 2. Disease specific quality of life showed improvement in all patients (60.3 ± 19.3 , mean change +12.3, 95% CI +17.3, +6.8, $p = 0.00004$), as well as in group 1 (60.6 ± 18.2 , mean change +14.4, +22.3, +6.6, $p < 0.005$) and group 2 (59.9 ± 21.5 , mean change +8.5, +15.1, +2, respectively, $p < 0.05$) at 0 weeks (fig. 2, A).

Nonobstructive retention. Of the 144 treatment sessions stimulation was performed on the right posterior tibial nerve with a mean pulse intensity of 4 mA. (range 2.5 to 7) per session in 87 (60%). As seen in patients treated for urgency and frequency and/or urge incontinence, complications were rarely noted. Of the 12 patients posterior tibial nerve stimulation was considered successful in 1 man and 6 women (58.3%) because they requested continuation of therapy after completion of the 12-week treatment (group 3, responders). Treatment was unsuccessful in 4 men and 1 woman since they did not choose maintenance therapy (group 4, nonresponders).

At completion of the 12-week treatment all patients clearly had a decrease in the number of catheterizations, and mean and total volumes catheterized, and an increase in mean and total volumes voided. However, statistical significance could not be obtained (table 3). When discriminating group 3 (7 responders) from group 4 (5 nonresponders) these changes could also be observed in group 3 but not in group 4. In regard to quality of life hardly any significant improvement could be found in the adjusted disease specific (fig. 2, B) or general quality of life questionnaire. The only exceptions appeared to

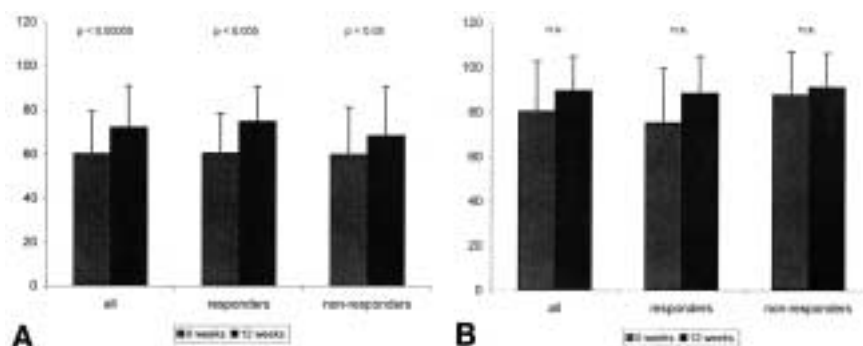


FIG. 2. Before and after posterior tibial nerve stimulation for responders, nonresponders and both combined. A, disease specific quality of life scores for patients with bladder overactivity. B, nonobstructive retention. Maximum disease specific quality of life score was 110. Error bar represents SD. ns, not significant.

TABLE 3. *Voiding parameters in 12 patients with nonobstructive retention*

	All Pts.		Group 3		Group 4	
	Mean $\pm$ SD (0 wks.)	Mean Change (95% CI)	Mean $\pm$ SD (0 wks.)	Mean Change (95% CI)	Mean $\pm$ SD (0 wks.)	Mean Change (95% CI)
No. catheterizations	5.3 $\pm$ 2.4	-0.8 (-0.6, -2.3)	5.9 $\pm$ 2.6	-1.4 (1.2, -4.1)	4.4 $\pm$ 2	0 (0.9, -0.9)
Mean vol. catheterized	336 $\pm$ 171	-83.3 (27.4, -194)	325 $\pm$ 181	-131.9 (63.2, -326.9)	351 $\pm$ 176	-15.4 (87.5, -118.4)
Total vol. catheterized	1,552 $\pm$ 776	-537 (175, -1249)	1,707 $\pm$ 915	-921.4 (284.5, -2127.4)	1,335 $\pm$ 547	1 (659.7, -657.7)
Mean vol. voided	206 $\pm$ 192	5.9 (113.2, -101.4)	141 $\pm$ 107	94.3 (233.3, -44.7)	297 $\pm$ 258	-117.8 (16.5, 252.1)
Total vol. voided	919 $\pm$ 658	173.8 (639.2, -291.7)	758 $\pm$ 567	482.1 (1164.7, -200.4)	1,145 $\pm$ 774	-258 (374.6, -890.6)

be the SF-36 score for emotional well-being, which increased (58.3 ± 12.2 , mean change $+14.3$, 95% CI $+20.6$, $+7.9$, $p < 0.005$) in patients who thought treatment was successful (group 3), and the score for change of health, which significantly increased in all (45.8 ± 27.9 , mean change $+22.9$, $+44.9$, $+1$, $p < 0.05$) but not in group 3 or 4 at 0 week, respectively.

DISCUSSION

For treatment of refractory urinary tract dysfunction various methods of intermittent neuromodulation have been advocated, including intravesical, anal, vaginal, penile and perineal stimulation, and transcutaneous electrical stimulation of the suprapubic or sacral region and posterior tibial nerve.⁷⁻¹⁵ Because of poor results or uncomfortable stimulation sites, most of the aforementioned treatment modalities did not gain widespread acceptance. In the 1980s implantable neurostimulation electrodes became available for modulation of the sacral spinal nerves, especially S3.¹⁶ Stimulation could be performed continuously, leading to better results but drawbacks included invasiveness of the procedure, the high costs involved and limited service life of the stimulation device, which was 7 to 10 years. In addition, symptoms appear to recur almost immediately after discontinuation of stimulation.² Therefore, the development of an easily applicable, noninvasive or minimally invasive, cost-effective neuromodulation device with good treatment outcome was anticipated. The recent advent of posterior tibial nerve stimulation may offer urologists a treatment modality that meets the aforementioned criteria.^{4,17}

Stimulation of the tibial nerve was first described by McGuire et al in 1983.¹⁵ In studies of nonhuman primates with spinal cord injury bipolar anal sphincter stimulation resulted in the inhibition of detrusor activity. Similar results could be obtained by applying current through a transcutaneous electrode over the common peroneal or posterior tibial nerve, with a ground electrode being contralaterally placed over the same nerves. The idea of stimulating these nerves was based on the traditional Chinese practice of using acupuncture points over the common peroneal or posterior tibial nerves to affect bladder activity.¹⁵ Electrical stimulation of the tibial nerve was subsequently performed in 22 patients with detrusor instability, interstitial or radiation cystitis or neurological disease with promising results, including continence in 12 and urodynamics improvement in 7. However, in a prospective study by Geirsson et al in patients with interstitial cystitis, transcutaneous tibial nerve stimulation or traditional Chinese acupuncture revealed no difference in voiding frequency, mean and maximal voided volumes and visual analog symptom scores before or after either treatment modality.¹⁸

In our study percutaneous stimulation resulted in a success rate of about 60% of 49 patients with bladder overactivity or nonobstructive urinary retention. Although our definition of success was a subjective one, responders differed significantly from nonresponders in almost every semi-objective parameter. The same result was observed in disease specific and several domains of general quality of life scores.

Because our study was not placebo controlled, the observed

improvements might theoretically be the result of regression to the mean, synchronous other treatment or placebo effect rather than a positive response to posterior tibial nerve stimulation. Regression to the mean is not likely as all patients included had to present with symptoms for at least 6 months (median 4 years). To prevent interference of other treatment modalities, concomitant physiotherapy during posterior tibial nerve stimulation was not permitted, as was the case with starting parasympatholytic medication or other pharmaceuticals influencing bladder function, including antidepressant agents, within 2 weeks before treatment. In patients who were already using any of the aforementioned drugs medication had to be stopped 2 weeks before beginning posterior tibial nerve stimulation or continued without dose changes during the entire 12 weeks. In placebo controlled studies success rates in the placebo group are usually much lower than the response rate of about 60% in our study. Because most patients had symptoms for a long period and undergone various treatments before trying neuromodulation, it is not likely that they were highly susceptible to the placebo effect of this treatment modality. Nevertheless, to validate these data a properly designed placebo controlled study is warranted. However, it can be anticipated that the feasibility of such studies will be difficult.

Notwithstanding the promising results and only mild complications of this neuromodulation technique found in our study, this therapy also has some disadvantages, including percutaneous insertion of the stimulation electrode, necessity of regular visits to the outpatient clinic and, thus far, unknown results of chronic treatment of initially successful cases. In the near future most of the aforementioned problems may be solved with an implantable subcutaneous electrode, which can be radiographically stimulated by the patients at home and on a regular basis. Studies regarding long-term effects are ongoing but results are not yet available. In conclusion, although thorough research is anticipated to improve patient selection criteria, optimize the technique and help learn more about the precise mode of action, posterior tibial nerve stimulation is a promising, cost-effective and easily applicable treatment option for patients with lower urinary tract dysfunction.

APPENDIX: EXCLUSION CRITERIA

- Younger than 18 years
- Symptoms existing for less than 6 months
- Pregnancy or intention to become pregnant during the course of study
- Active urinary tract or recurrent urinary tract infection (5 or greater recurrent infections during the last 12 months), carcinoma in situ, bladder malignancy, interstitial cystitis
- Bladder or kidney stone
- Severe cardiopulmonary disease
- Use of pentosan polysulfate sodium or bladder installations, including dimethyl sulfoxide, bacillus Calmette-Guerin, Chloropectin or heparin
- Uncontrolled diabetes
- Diabetes with peripheral nerve involvement

Petitioner - Avation Medical, Inc.

Neurological disease like multiple sclerosis, Parkinson's disease, cerebrovascular accident, bifid spine or spinal cord lesion

Change in parasympatholytic medication or other pharmaceuticals influencing bladder function, including antidepressant agents, within 2 weeks before or during the study

Physiotherapy during the study

Bladder outlet obstruction (Abrams-Griffiths nomogram)

Transurethral instrumentation 4 weeks or less before or during the study

REFERENCES

1. Hasan, S. T., Robson, W. A., Pridie, A. K. et al: Transcutaneous electrical nerve stimulation and temporary S3 neuromodulation in idiopathic detrusor instability. *J Urol*, **155**: 2005, 1996
2. Bemelmans, B. L., Mundy, A. R. and Craggs, M. D.: Neuromodulation by implant for treating lower urinary tract symptoms and dysfunction. *Eur Urol*, **36**: 81, 1999
3. Abrams, P. H. and Griffiths, D. J.: The assessment of prostatic obstruction from urodynamic measurements and from residual urine. *Br J Urol*, **51**: 129, 1979
4. Stoller, M. L.: Afferent nerve stimulation for pelvic floor dysfunction. *Eur Urol*, suppl., **35**: 16, 1999
5. Ware, J. E. and Sherbourne, C. D.: The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*, **30**: 473, 1992
6. Wagner, T. H., Patrick, D. L., Bavendam, T. G. et al: Quality of life of persons with urinary incontinence: development of a new measure. *Urology*, **47**: 67, 1996
7. Madersbacher, H.: Intravesical electrical stimulation for the rehabilitation of the neuropathic bladder. *Paraplegia*, **28**: 349, 1990
8. Merrill, D. C.: The treatment of detrusor incontinence by electrical stimulation. *J Urol*, **122**: 515, 1979
9. Janez, J., Plevnik, S. and Suhel, P.: Urethral and bladder responses to anal electrical stimulation. *J Urol*, **122**: 192, 1979
10. Lindström, S., Fall, M., Carlsson, C. A. et al: The neurophysiological basis of bladder inhibition in response to intravaginal electrical stimulation. *J Urol*, **129**: 405, 1983
11. Nakamura, M. and Sakurai, T.: Bladder inhibition by penile electrical stimulation. *Br J Urol*, **56**: 413, 1984
12. Vodusek, D. B., Light, J. K. and Libby, J. M.: Detrusor inhibition induced by stimulation of pudendal nerve afferents. *Neurourol Urodyn*, **5**: 381, 1986
13. Fall, M. and Lindström, S.: Transcutaneous electrical nerve stimulation in classic and nonulcer interstitial cystitis. *Urol Clin North Am*, **21**: 131, 1994
14. Walsh, I. K., Johnston, R. S. and Keane, P. F.: Transcutaneous sacral neurostimulation for irritative voiding dysfunction. *Eur Urol*, **35**: 192, 1999
15. McGuire, E. J., Zhang, S. C., Horwinski, E. R. et al: Treatment of motor and sensory detrusor instability by electrical stimulation. *J Urol*, **129**: 78, 1983
16. Schmidt, R. A.: Applications of neurostimulation in urology. *Neurourol Urodyn*, **7**: 585, 1988
17. Klingler, H. C., Pycha, A., Schmidbauer, J. et al: Use of peripheral neuromodulation of the S3 region for treatment of detrusor overactivity: a urodynamic-based study. *Urology*, **56**: 766, 2000
18. Geirsson, G., Wang, Y. H., Lindström, S. et al: Traditional acupuncture and electrical stimulation of the posterior tibial nerve. A trial in chronic interstitial cystitis. *Scand J Urol Nephrol*, **27**: 67, 1993