Percutaneous Nerve Evaluation (PNE) for Treatment of Non-Obstructive Urinary Retention: Urodynamic Changes, Placebo Effects, and Response Rates

Farzaneh Sharifiaghdas, Mahboubeh Mirzaei, Babak Ahadi

Department of Urology, Shaheed Labbafinejad Medical Center, Urology and Nephrology Research Center, Shaheed Beheshti University of Medical Sciences Tehran, Iran.

Corresponding Author:

Mahboubeh Mirzaee, MD
Department of Urology, Urology and Nephrology Research Center, Shaheed Labbafinejad Medical Center, Shaheed Beheshti University of Medical Sciences, Tehran , Iran.

Tel: +98 21 22567222
Fax: +98 21 22567282
Email: mirzaeimahboubeh@yahoo.com

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Purpose: To evaluate the results of percutaneous nerve evaluation (PNE) implantation in the treatment of non-obstructive urinary retention and report the changes in the urodynamic parameters.

Materials and Methods: Patients with non-obstructive urinary retention or incomplete bladder emptying were included. All patients filled a 7 days voiding diary chart and underwent PNE for one week, and the patient was asked to record the second voiding diary chart and repeat urodynamic study in this period. Then the PNE lead was removed from the S3 foramen, but the connections remained fixed in place for another 3 days to exclude the placebo effects and the third voiding diary chart was completed by the patient. The patient wasn't aware of lead removal. Success was defined as, more than 50% improvement in at least one of the urinary tract symptoms.

Results: Forty five patients with a mean age of 37.1 years (ranged 9-83 years) were treated with PNE for refractory, non-obstructive urinary retention. Of study subjects 28 complained from complete urinary retention, and 17 had incomplete emptying. Of participants, 28 (62.2%) demonstrated greater than 50% improvement in the urinary symptoms. Urodynamic data, showed a statistically significant increase in maximum flow rate (8 ± 2.2 mL/sec to 16 ± 3.6 mL/sec, $P = .06$) and voided volume (35 mL to 187 mL, $P = .032$) in the responders. Any placebo effects in PNE have not been seen.

Conclusion: Patients with complete non obstructive urinary retention were good responders to PNE. The placebo effect in sacral nerve stimulation was negligible.

Keywords: electric stimulation therapy; humans; urinary incontinence; urination disorders; therapy.

INTRODUCTION

Non obstructive urinary retention is one of the most difficult diseases to manage. These patients not only have some degrees of urinary incontinence but also they suffer from recurrent (urinary tract infection UTI) and decrease of renal function.[1,2,3] Medical treatment and urethral dilation are usually unsuccessful and patients ultimately have to do intermittent catheterization or to use permanent catheter.[4] Neuromodulation has been approved by the US Food and Drug Administration (FDA) since 1997 to treat idiopathic overactive bladder (I-OAB) and non-obstructive urinary retention.[5-10] The relative ease of the technique, hopeful results and low complication rate make this therapy a superior alternative to the standard treatment of idiopathic non obstructive urinary retention. Candidates for neuromodulation first should undergo a trial known as the percutaneous nerve evaluation (PNE). More than 50% improvement in at least one of the urinary tract symptoms is considered success; this is currently the only proven predictive factor in determining long-term prognosis.[6,7] If the patient is considered a suitable candidate for sacral nerve modulation (SNM), an implantable nerve stimulator (INS) is inserted at the second stage. In this study we assess efficacy and complications of temporary simple lead PNE in non-obstructive urinary retention.

MATERIALS AND METHODS

Patients with complete or incomplete urinary retention who were refractory to medical treatment (full dose of bethanechol and baclofen and α-blocker administration) were included. All of the participants underwent physical examination and filled a 7 days voiding diary chart. Urine analysis and culture, ultrasound imaging, urodynamic study including filling cystometry with electromyography (EMG) patch and cystoscopy was performed to rule out obstruction, infection and malignancy. Residual urine was measured by ultrasound, urodynamic study and cystoscopy. Medical and surgical history were recorded.

Exclusion criteria were, morbid obesity (body mass index > 40, for high risk of lead displacement), active urinary tract infection, urinary tract obstruction, and uncorrected coagulation disorders. Patients who might need to be evaluated by magnetic resonance imaging in the future or to be treated by radiation therapy or high-frequency diathermy and pregnancy were also excluded.

PNE lead (conventional PNE-test with thin wire electrodes) was implanted under fluoroscopic guide with local anesthesia in the left or right S3 foramen, on an outpatient basis. The nerve was tested for the appropriate motor responses, plantar flexion of the great toe and anal sphincter contraction (bellows reflex) which represented the contraction of the levator muscles. Simultaneous sensory responses at the time of lead placement helped to optimize positioning. The lead was connected to an external pulse generator and fixed with adhesive dressings. The patient and his/her caregiver were taught how to replace the battery and regulate voltage. Test period was 1-week, and the patient was being asked to record another 7 days voiding diary chart and urodynamic study was repeated at this period.

The PNE lead was removed from the S3 foramen, but the connections and external pulse generator remained fixed in place for another 3 days and the third voiding diary chart was completed by the patient. The patient wasn't aware of lead removal. More than 50% improvement in at least one of the following parameters was considered positive response: reduction in the number of catheterization times, increase in the voided volume and the number of voids per day, and decrease in postvoid residual urine volume.

Multichannel urodynamic study was performed in all patients with medium-fill water cystometry (50 mL per minute) and dual-lumen 6 French catheter. The patients were allowed to void in the sitting position and all the events of filling and voiding phases were recorded. The study was approved by the local research Ethics Committee (Urology and Nephrology Research Center) and the trial was independent of any industry support and involvement.

Statistical Analysis

Data were analyzed using paired-samples *t* test with the statistical package for the social science (SPSS Inc, Chicago, Illinois, USA) version 19.0. A *P* value of < .05 was considered statistically significant, confidence interval was set at 95%.

RESULTS

The study results are summarized in Tables 1-4. Of study

Table 1. Response rate in different study groups with percutaneous nerve evaluation.

Variables		Patients (no.)	Responder (no.)	Rate (%)	*P*
	Total patients	45	28	62.2	
Retention	Complete	28	21	75.0	.023
	Incomplete	17	7	41.1	
Gender	Male	14	7	50.0	.256
	Female	31	21	67.7	
Type	Secondary	18	9	50	.167
	Idiopathic	27	19	70.3	
Age range (year)	1-18	7	4	57	.076
	19-50	27	20	74	
	51-70	7	4	57	
	> 70	5	0	0	

subjects 31 (68.9%) were female, 28 had complete urinary retention and were dependent on clean intermittent catheterization or permanent catheter, and 17 had incomplete bladder emptying (evaluated by post void residual urine volume). The mean duration of emptying disorders was three years. Twenty seven patients had idiopathic urinary retention (60%), and 18 patients (40%) had the past history of spinal cord trauma or tumor, previous pelvic surgery and neurogenic disease.

Of the 45 patients, 28 (62.2%) demonstrated greater than 50% improvement in urinary symptoms. Response rate was higher in the complete urinary retention group versus incomplete emptying (75% vs. 41.1%, $P = .023$). The details are summarized in Table 1.

Patient with idiopathic urinary retention demonstrated better response rate compared to those with a history of neurogenic disease (70.3% vs. 50%, $P = .167$). The patients were divided into four groups according to their age range: 1-18 years, 19-50 years, 51-70 years and > 70 years. The response rate in female and male was 67.7% and 50%, respectively ($P = .256$). The mean age of men who responded to the test was 30.8 years (41.7 years in non-responders) and 57% of them were neurologic.

The patients were categorized into two subgroups groups, responders and non-responders.

Comparison between prestimulation and during stimulation data on uroflowmetry showed significant increase in the maximum flow rate in responders (from 6.1 mL/sec to 17.6 mL/sec, $P < .05$). Mean voided volume increase was significant in responders (from 35 mL to 187 mL, $P = .032$). Bladder contractibility index increased in the responders which was statistically significant (from 78.1 to 108.1). Post-void residual urine decreased from 125 mL to 17 mL in voiding diary and from 197.3 mL to 40.2 mL in urodynamic study that was not statistically significant. Mean maximum cystometric capacity on standard cystometry increased from 325 mL to 359 mL from the preoperational to post operation time. The post operation pattern of voiding was interrupted flow.

The complications were as follow, lead migration in 2 (4.4%), infection in 1 (2.2%), pain at lead site in 2 (4.4%), sensation of electrical shock in 1 (2.2%).

According to the permission of ethics committee, the PNE lead was removed from the S3 foramen, but the connections and external pulse generator remained fixed in place for another 3 days and the third voiding diary chart was completed by the patient. The patient was not aware of lead removal. None of the responders in the first 7 days observed greater than 50% improvement in the third voiding diary, so it seems that the placebo effect in sacral nerve stimulation is negli-

Table 2. Urodynamic parameters (pre- and postoperative) with percutaneous nerve evaluation.

	Baseline	Postoperative	*P*
Group 1*			
Pdet at maximum flow rate	19 (10-21)	31 (14-39)	.107
Bladder contractility index	78.1 (60-115)	108.1 (86-197)	.048
Bladder capacity (mL)	325 (226-450)	359 (317-524)	.165
Residual urine (mL)	197.3 (110-450)	40.2 (5-145)	.059
Maximum flow rate (mL/sec)	6.1 (0-12)	17.6 (15-22)	.018
Bladder outlet obstruction index	16.5 (-9-27)	-1.1 (-12-23)	.096
Time to maximum flow rate (sec)	10.7 (2.6-19.4)	7.7 (2.1-13.9)	.185
Voided volume (mL)	35 (0-150)	187 (90-340)	.032
Group 2**			
Pdet at maximum flow rate	18 (12-23)	21 (15-29)	.176
Bladder contractibility index	78.4 (61-105)	79.1 (76-98)	.436
Bladder capacity (mL)	315 (225-450)	335 (315-470)	.175
Residual urine (mL)	179 (120-446)	182 (103-435)	.269
Maximum flow rate (mL/sec)	9 (0-12)	9.6 (0-14)	.509
Bladder outlet obstruction index	16 (-5-29)	8 (-4-23)	.108
Time to maximum flow rate (sec)	10.8 (6-18)	10 (7-30)	.285
Voided volume (mL)	37 (0-140)	45 (0-120)	.845

Key: Pdet, detrusor pressure.
* Patients which responded > 50% to percutaneous nerve evaluation according to voiding diary.
** Patients which didn't response < 50% to percutaneous nerve evaluation according to voiding diary.
The numbers in the pirates are range.

gible .In both responder and non-responder groups voiding dairy chart returned to the base-line.

DISCUSSION

Neuromodulation was approved by the FDA since 1997 to I-OAB and non-obstructive urinary retention.[5-10] In patients with non-obstructive urinary retention, SNM offers a superior therapeutic alternative to intermittent self-catheterization or indwelling catheters, which significantly influences the quality of life.[11] Long-term results for SNM in patients with chronic urinary retention are better than overactive bladder.[12]

In reports, with at least 40 months follow up, success rate was between 55%-86%.[12-16] The best long-term results for SNM have been achieved in patients with non-obstructive urinary retention.[13,2] Side effects are low and/or uncommon. Infection, leg discomfort, pain at the lead site are the main complications, the less common adverse events are, bowel dysfunction, technical problems and nerve irritation.[14,17-19]

Although the mechanism of action of SNM is not clear, it is told that it affects brain networks, as well as modulation of spinal cord reflexes and afferent peripheral nerves. Candidates for neuromodulation must first undergo a screen test. There are two methods for screening, two-stage implantation technique with tined lead test, and the standard one-stage procedure following a positive PNE. The test duration is rather restricted in PNE due to the risk of lead migration, the success rate is between 33%-66% in different reports.[17,20-22] The risk with tined lead is lower, duration of the test is longer (about 4 weeks) and response rate is higher (about 60%-70%).[22-23] The cost of tined lead and the more difficult process of removal, compared to simple wire, are the drawbacks. Datta and colleagues reported equal results for both techniques in the women with urinary retention (one stage versus two stages) (about 70%).[14]

According to the literature, evaluation of the results in the test period is based on more than 50% improvement in subjective and objective measures reported by the voiding diary chart. This is currently the only proven predictive factor in determining long-term prognosis.[7] In this study we evaluated the

Table 3. Preoperative urodynamic parameters in responder and non-responder to percutaneous nerve evaluation.

Variables	Group 1 (Responders)	Group 2 (Non responders)	*P*
Pdet at maximum flow rate	19 (10-21)	18 (12-23)	.543
Bladder contractibility index	78.1 (60-115)	78.4 (61-105)	.508
Bladder capacity (mL)	325 (226-450)	315 (225-450)	.487
Residual urine (mL)	197.3 (110-450)	179 (120-446)	.309
Maximum flow rate (mL/sec)	6.1 (0-12)	9 (0-12)	.415
Bladder outlet obstruction index	16.5 (-9-27)	16 (-5-29)	.567
Time to maximum flow rate (sec)	10.7 (2.6-19.4)	10.8 (6-18)	.576
Voided volume (mL)	35 (0-150)	37 (0-140)	.498

Key: Pdet, detrusor pressure.
The numbers in the pirates are range.

pre and posttest urodynamic results, to look for another probable objective predictive factor.

There are few reports in the literature about urodynamic outcomes after neuromodulation. In 2004, Sgupta and colleagues reported changes in the urodynamic parameters in 30 women with urinary retention (fowler's syndrome) who were able to void following neuromodulation. Twenty one underwent a permanent implant and nine had PNE. The results of SNM in this study was attributed to the rise in the detrusor voiding pressure, they concluded that SNM does not relax the external sphincter directly.[24] In our study, 33.3% of patients which responded to PNE were male as detrusor voiding pressure is usually higher in men, although there was an increase in maximum detrusor pressure (from 19 cmH_2O to 31 cmH_2O), but it was not statistically significant (P = .107). The mechanism of action of SNM is unclear, although it seems both relaxant effect on the sphincter and increase in detrusor pressure are involved. Bannowsky and colleagues performed bilateral PNE in 42 patients (25 retention, 9 hypersensitive urinary bladder and 8 detrusor hyperactivity). The mean age of participants was 49.2 years (14 male, 28 female). Twenty (47.9%) had positive test results (9 with retention, 7 with overactive bladder and 4 with pelvic pain syndrome). They concluded that tined lead, leads to significantly higher response rate. The criticism over their conclusion is the rather low number of patients in the second group (11 patients).[25]

In our study with unilateral PNE in the retention group, response rate was higher (62.2%). In their study in the group with urinary retention the PNE led to an average increase of the maximum detrusor pressure from 19 cmH_2O (± 5 cmH_2O) to 32 cmH_2O (± 9.7 cmH_2O) and a mean reduction of residual urine by 71%; none of them was significant (P = .068). There were 9 patients with retention that had responded to PNE. In their study an average increase in maximum flow rate from 8 ± 2.2 mL/sec to 16 ± 3.6 mL/sec also was not statistically significant (P = .06). However, as they included three different groups (retention, overactive bladder and pelvic pain syndrome), the results have not been mentioned each group separately. Our study was focused on the retention group and according to results they were divided into two groups, responders and non-responders.

Jonas and colleagues reported the results of 68 patients with non-obstructive urinary retention which responded to PNE, 31 individuals were randomly assigned to a group with delayed implanted pulse generator implantation after 6 months, in this interval 9% of these patients (only 2 of 22) had more than 50% improvement in their symptoms, compared to the 83% in group with immediate implanted pulse generator implantation.[2] Demographic and clinical characteristics of these two patients were not mentioned in this study. A clinical trial in new onset (less than 2 years) idiopathic complete urinary retention with only percutaneous nerve evaluation may be useful.

CONCLUSION

Table 4. Findings demonstrating no placebo effect.

Responders (n = 28)	Pre-stimulation	PNE period*	Post PNE**
Mean Voided volume (mL)	35	187	39
CIC Time per day (mean)	8	1	8
Post void residual urine (mL)	125	17	127

Key: PEN, percutaneous nerve evaluation; CIC, clean intermittent catheterization.
*Seven days voiding diary
** The third voiding diary

In selected patients with non-obstructive urinary retention, SNM offers an effective, minimally invasive treatment option. Patients with complete non-obstructive retention are good responder to PNE. There was not any predictive parameter of failure of PNE according to urodynamic parameters. None of pre-operative urodynamic parameters could predict the success rate of PNE. Efforts should continue to further optimize patient selection and improvement of the testing technique. The placebo effect in sacral nerve stimulation is negligible.

CONFLICT OF INTEREST

None declared.

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