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Changes in Nocturia after Photoselective Vaporization of the Prostate for Patients with Benign Prostatic Hyperplasia

Chang Ju Lee, Min Chul Cho[1], Ja Hyeon Ku, Soo Woong Kim, Jae-Seung Paick

Department of Urology, Seoul National University College of Medicine, [1]Dongguk University, College of Medicine, Seoul, Korea

Purpose: To investigate changes in nocturia and predictive factors for improvement after photoselective vaporization of the prostate (PVP) for patients with benign prostatic hyperplasia (BPH).

Materials and Methods: A total of 103 patients who complained of nocturia of ≥2 times per night on baseline frequency-volume chart (FVC) and who underwent PVP were included in this retrospective study. All patients underwent a preoperative evaluation for BPH including multichannel video urodynamics. The efficacy of the PVP was evaluated at 1, 3, 6, and 12 months postoperatively by use of the International Prostate Symptom Score (IPSS) and FVC. Subjective and objective improvement of nocturia were defined as a reduction of ≥50% in nocturnal frequency compared with baseline on the IPSS and FVC, respectively.

Results: As shown by the IPSS and FVC, nocturia was significantly reduced starting from 1 month after PVP. The percentage of patients with improvement in nocturia was 20.0%, 20.7%, 36.2%, and 27.9% on the IPSS, and 30.1%, 48.6%, 52.2%, and 54.5% on the FVC at 1, 3, 6, and 12 months after PVP, respectively. None of the baseline parameters, including the presence or absence of nocturnal polyuria (NPU), reduced nocturnal bladder capacity (NBC), and detrusor overactivity (DO), were associated with improvement of nocturia.

Conclusions: Nocturnal frequency was significantly reduced from the early postoperative period after PVP. Improvement in nocturia after PVP was not affected by baseline nocturnal frequency, the presence or absence of preoperative NPU, or reduced NBC or DO on baseline urodynamics.

Key Words: *Laser therapy; Nocturia; Prostatic hyperplasia*

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Corresponding Author:
Jae-Seung Paick
Department of Urology, Seoul National University College of Medicine, 28, Yeongeon-dong, Jongno-gu, Seoul 110-744, Korea
TEL: +82-2-2072-2422
FAX: +82-2-742-4665
E-mail: jspaick@snu.ac.kr

INTRODUCTION

Nocturia, a common cause of interrupted sleep in the general adult population, is defined as waking at night one or more times to void [1]. Nocturia has adverse effects on quality of life (QoL), sleep patterns, daytime sleepiness, and even mortality associated with falls [2,3]. Nocturia is one of the major problems in older men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic obstruction [4]. Benign prostatic hyperplasia (BPH) can cause bladder outlet obstruction and induce secondary detrusor overactivity (DO) and reduction of functional bladder capacity, which may result in storage symptoms including nocturia [5]. Two or more episodes of nocturia were observed for more than 60% of patients with BPH in several studies [6,7]. Also, several other risk factors for nocturia have been reported, including nocturnal polyuria (NPU) and reduced nocturnal bladder capacity (NBC), which are generally known as the causal mechanisms of nocturia [5].

Several studies showed a reduction of 0.8 to 1.6 episodes of nocturia after surgical treatment such as transurethral resection of the prostate (TURP) in patients with BPH [5,8,9]. Although TURP has been the gold standard treatment of BPH, its complications, such as bleeding, transure-

thral resection (TUR) syndrome, incontinence, and erectile dysfunction, are significant problems. Recently, photoselective vaporization of the prostate (PVP) has shown clinical outcomes consistent with TURP but with improved morbidity in short- and long-term studies [10-13]. However, no research has been dedicated specifically to the effect of PVP for BPH on the reduction of nocturia or factors predictive of improvement in nocturia after PVP. In the present study, we investigated changes in nocturia and predictive factors for improvement after PVP in patients with BPH.

MATERIALS AND METHODS

1. Study design

This study was approved by the Institutional Review Board at the Seoul National University Hospital. Between January 2006 and April 2008, a total of 190 patients underwent PVP for BPH refractory to alpha-blocker medication. Among the patients, 103 patients who complained of 2 or more episodes of nocturia on a baseline frequency-volume chart (FVC) were included in this retrospective study. The exclusion criteria were as follows: previous prostate surgery, urethral stricture, prostate malignancy, and neurogenic bladder disease.

We used the 80 W potassium-titanyl-phosphate (KTP) laser for the PVP. The PVP was performed by a single surgeon (J.S.P) in a routine manner as reported previously [14]. All patients underwent a preoperative evaluation with transrectal ultrasound (TRUS) and multichannel video urodynamics (MMS UD-2000, Medical Measurement System, Ennschede, The Netherlands) in addition to a general standard evaluation for LUTS/BPH including a history, physical examination including digital rectal examination (DRE), International Prostate Symptom Score (IPSS), 3-day FVC, urinalysis, serum prostate-specific antigen (PSA), and TRUS. Patients with PSA levels exceeding 4.0 or DRE abnormalities underwent prostate biopsy and patients with prostate cancer were excluded from our study. Intraoperatively, we measured the operative time, lasing time, total laser energy used, and complications such as bleeding, injury of the ureteral orifice, or perforation of the prostatic capsule.

Changes in nocturia after PVP were assessed at 1, 3, 6, and 12 months postoperatively by use of the IPSS and 3-day FVC. Subjective and objective improvement in nocturia were defined as a reduction of $\geq 50\%$ in episodes of nocturia compared with baseline on the IPSS and FVC, respectively. We defined the nocturia index (NI), the nocturnal polyuria index (NPI), and the nocturnal bladder capacity index (NBCI) as follows. 1) NI was the nocturnal urine volume (NUV) divided by the maximum voided volume. An $NI > 1$ indicated that nocturnal urine production was greater than functional bladder capacity. 2) NPI was the NUV divided by the 24-h urine volume. An $NPI > 33\%$ implied nocturnal polyuria as opposed to diurnal polyuria. 3) The NBCI was the difference between the actual number of nocturnal voids (ANV) and the predicted number of nocturnal voids (PNV), where the PNV was the NI minus 1 [15]. Diminished nocturnal bladder capacity was defined as a $NBCI \geq 1$. From the urodynamic parameters, the bladder outlet obstruction index (BOOI) was defined as follows: detrusor pressure at maximum flow rate (PdetQmax) - 2Qmax [16]. BOO was defined as a BOOI greater than 40. DO was defined as a urodynamic finding characterized by involuntary detrusor contractions during the filling phase, either spontaneous or provoked [17]. All definitions corresponded to recommendations of the International Continence Society (ICS) [17].

2. Data analysis

All variables are reported as the mean±standard deviation or numbers of patients with the percentages in parentheses. The variables were evaluated for statistically significant differences between the baseline measures and the measures obtained after PVP by use of the paired t-test. A logistic

TABLE 1. Preoperative characteristics and perioperative data

Preoperative characteristics	
Mean±standard deviation or No. of patients (%)	
Demographic variables	
Age (years)	68.9±6.3
PSA (ng/ml)	3.0±3.7
Prostate volume (ml)	50.6±23.5
Transition zone volume (ml)	26.0±19.7
Uroflowmetry with PVR	
Qmax (ml/s)	10.2±6.0
PVR (ml)	67.5±68.2
IPSS	
Nocturia	3.0±1.0
Storage symptom	8.5±3.1
Total IPSS	20.9±6.9
QoL index	4.4±1.1
FVC	
Nocturia	2.5±0.8
NPI	0.40±0.10
NI	2.2±0.6
NBCI	0.8±0.8
$NPI > 0.33$	77/103 (74.8%)
$NBCI \geq 1$	63/103 (61.2%)
Urodynamics	
BOO	34/103 (33.0%)
DO	33/103 (32.0%)
MCC (ml)	368±102
Perioperative data	
Operative time (min)	53.0±25.9
Laser energy applied (kJ)	152.1±114.9
Catheter time (hr)	21.1±10.2

PSA: prostate-specific antigen, PVR: post-void residual urine volume, Qmax: maximum flow rate, IPSS: International Prostate Symptom Score, QoL: quality of life, FVC: frequency-volume chart, NPI: nocturnal polyuria index, NI: nocturia index, NBCI: nocturnal bladder capacity index, BOO: bladder outlet obstruction, DO: detrusor overactivity, MCC: maximum cystometric capacity

regression model and odds ratios (with 95% confidence intervals) were used to identify the factors influencing improvement in nocturnal frequency. The reported p-values are two-sided, and a p-value of 0.05 was considered statistically significant. The Statistical Package for the Social Sciences (SPSS for Windows, release 13.0, SPSS Inc., Chicago, IL, USA) was used for data analysis.

RESULTS

The preoperative characteristics and perioperative data are shown in Table 1. The mean age of the patients was 68.9±6.3 years. Mean prostate volume was 50.6±23.5 ml, mean operative time was 50.3±25.9 min, and mean laser energy was 152.1±114.9 kJ. The patients complained of a mean of 3.0±1.0 episodes of nocturia on the IPSS and recorded a mean of 2.5±0.8 episodes on the FVC. On the baseline FVC, 74.8% of the patients had nocturnal polyuria (NPI $>$ 0.33) and 61.2% of the patients had reduced NBC (NBCI $\geq$ 1). According to the baseline urodynamics, BOO and DO were diagnosed in 32.7% and 32.0% of the patients, respectively. The mean follow-up duration was 13.8±2.8 months.

Nocturnal frequency on the IPSS and FVC showed a statistically significant reduction starting from 1 month after PVP compared with baseline ($p < 0.05$) (Table 2). At 12 months postoperatively, nocturnal frequency had decreased from a baseline mean of 3.0±1.0 episodes to 2.1±1.0 episodes according to the IPSS and from 2.5±0.8 episodes to 1.5±0.8 episodes according to the FVC. Compared with the baseline data, the NBCI also decreased significantly by degrees.

Preoperatively, the number of patients who had taken an alpha-blocker, anticholinergics, and desmopressin was 85, 17, and 3, respectively. All patients were instructed to stop taking the medicine at the time of operation. Postoperatively, we prescribed an alpha-blocker to 5 patients with persistent voiding symptoms, anticholinergics to 11 patients with urgency or urge incontinence, and desmopressin to 3 patients with persistent nocturia. Excluding

TABLE 2. Baseline values and changes in PVP outcome parameters according to the IPSS and FVC (total patients)

	Baseline	1 month	3 months	6 months	12 months
No. of patients at follow-up	103	100	82	69	61
Mean±standard variation or percentage of patients					
IPSS					
Nocturia	3.0±1.0	2.4±1.2[a]	2.1±0.9[a]	2.0±0.9[a]	2.1±1.0[a]
Storage symptom	8.5±3.1	7.3±3.4[a]	5.7±2.7[a]	4.5±2.4[a]	5.1±3.2[a]
QoL index	4.4±1.1	2.7±1.4[a]	2.4±1.9[a]	2.0±1.3[a]	2.1±1.4[a]
FVC					
Nocturia	2.5±0.8	2.0±0.9[a]	1.7±0.8[a]	1.5±0.7[a]	1.5±0.8[a]
FBC	327±124	326±117	324±86	358±123[a]	359±123[a]
NBCI	0.83±0.82	0.54±0.65[a]	0.41±0.67[a]	0.34±0.50[a]	0.34±0.54[a]
NBCI $\geq$ 1	61.2	46.8	37.8	35.8	34.5

PVP: photoselective vaporization of the prostate, IPSS: International Prostate Symptom Score, FVC: frequency-volume chart, QoL: quality of life, FBC: functional bladder capacity, NBCI: nocturnal bladder capacity index, [a]$p < 0.05$: comparison between the baseline parameters and parameters obtained after PVP by use of the paired t-test

TABLE 3. Baseline values and changes in PVP outcome parameters according to the IPSS and FVC (patients who did not take medication postoperatively)

	Baseline	1 month	3 months	6 months	12 months
No. of patients at follow-up	84	83	68	62	54
Mean±standard variation or percentage of patients					
IPSS					
Nocturia	3.0±0.9	2.5±1.3[a]	2.0±0.9[a]	2.0±0.9[a]	2.2±1.0[a]
Storage symptom	8.6±3.0	7.5±3.6[a]	5.9±2.7[a]	4.6±2.5[a]	4.9±3.1[a]
QoL index	4.4±1.1	2.7±1.3[a]	2.4±1.9[a]	2.1±1.4[a]	2.1±1.4[a]
FVC					
Nocturia	2.5±0.7	1.9±0.9[a]	1.8±0.8[a]	1.6±0.8[a]	1.6±0.8[a]
FBC	330±120	328±110	330±95	352±120[a]	355±118[a]
NBCI	0.83±0.80	0.52±0.60[a]	0.41±0.69[a]	0.35±0.48[a]	0.36±0.50[a]
NBCI $\geq$ 1	60.7	50.6	38.2	38.7	37.0

PVP: photoselective vaporization of the prostate, IPSS: International Prostate Symptom Score, FVC: frequency-volume chart, QoL: quality of life, FBC: functional bladder capacity, NBCI: nocturnal bladder capacity index, [a]$p < 0.05$: comparison between the baseline parameters and parameters obtained after PVP by use of the paired t-test

TABLE 4. Patients with improvement of nocturia postoperatively according to the IPSS or FVC

	1 month	3 months	6 months	12 months
Patients				
by IPSS	20/100	17/82	25/69	17/61
(%)	(20.0)	(20.7)	(36.2)	(27.9)
by FVC	29/94	36/74	35/67	30/55
(%)	(30.1)	(48.6)	(52.2)	(54.5)

IPSS: International Prostate Symptom Score, FVC: frequency-volume chart

the 19 patients who took medicines such as an alpha-blocker, anticholinergics, and desmopressin postoperatively, the outcome parameters of the 84 patients who did not take medication were not significantly different from those of the total group of patients (Table 3).

Table 4 shows the patients (%) with improvement of nocturia when subjective and objective improvement was defined as a reduction of ≥50% in episodes of nocturia compared with baseline on the IPSS and FVC, respectively. The patients with subjective improvement of nocturia on the IPSS increased from 20.0% at 1 month postoperatively to 36.2% at 6 months postoperatively, then decreased to 27.9% at 12 months postoperatively. The patients with objective improvement of nocturia on the FVC increased continuously from 30.1% at 1 month postoperatively to 54.5% at 12 months postoperatively. At 12 months postoperatively, 27.9% and 54.5% of the patients reported subjective and objective improvement of nocturia on the IPSS and FVC, respectively. Also, the NBCI decreased significantly starting from 1 month after PVP compared with baseline ($p < 0.05$) (Table 2).

There were no serious intraoperative complications, such as bleeding or TUR syndrome. Delayed bleeding was reported in 12 cases out of 103 (11.7%). However, no transurethral coagulation was needed, and delayed bleeding was resolved spontaneously. Postoperative complications were 1 case of urethral stricture (1.0%), 1 of bladder neck contracture (1.0%), 8 of urge incontinence (7.8%), and 30 of retrograde ejaculation (29.1%). There was no de novo erectile dysfunction.

A logistic regression analysis was performed to identify the factors influencing improvement in nocturia. However, none of the factors, including NPU, reduced NBC, and the presence of DO at baseline, were associated with subjective or objective improvement in nocturia (Table 5). In addition, postoperative parameters, including maximum flow rate (Qmax), post-void residual urine, functional bladder capacity, NBCI, and the presence of de novo urgency, were not associated with improvement of nocturia.

DISCUSSION

Nocturia is a major cause of disturbed sleep onset and sleep maintenance in the general elderly population [18].

TABLE 5. Predictive factors of improvement in nocturia

Variables	OR (95% CI)	
	Nocturia on IPSS	Nocturia on FVC
Age (years)	0.986 (0.876-1.110)	0.915 (0.810-1.033)
BMI (kg/m^2)	1.133 (0.826-1.554)	0.967 (0.709-1.320)
Hypertension	1.091 (0.747-1.595)	1.033 (0.934-1.142)
Diabetes	1.167 (0.853-1.462)	1.017 (0.874-1.185)
PSA (ng/ml)	1.132 (0.973-1.318)	1.029 (0.879-1.204)
Prostate volume (ml)	1.104 (0.985-1.044)	1.001 (0.976-1.026)
Qmax (ml/s)	0.971 (0.849-1.110)	0.981 (0.893-1.079)
PVR (ml)	0.997 (0.986-1.009)	1.001 (0.992-1.010)
IPSS		
Nocturia	1.396 (0.621-3.134)	1.369 (0.626-2.995)
Urgency	1.383 (0.511-3.744)	1.199 (0.451-3.192)
Voiding symptoms	1.088 (0.877-1.349)	1.206 (0.998-1.458)
Storage symptoms	1.111 (0.781-1.580)	1.434 (0.967-2.127)
Total IPSS	1.064 (0.911-1.244)	1.176 (0.999-1.376)
FVC		
ANV	1.386 (0.367-5.238)	0.975 (0.295-3.224)
NPI		
≤0.33	1.000	1.000
>0.33	1.111 (0.177-6.990)	0.234 (0.039-1.416)
NI		
≤1.5	1.000	1.000
>1.5	1.281 (0.899-1.962)	1.361 (0.787-2.110)
NBCI		
<1	1.000	1.000
≥1	1.328 (0.831-2.261)	1.569 (0.720-3.472)
UDS		
First sense to void (ml)	1.007 (0.993-1.020)	1.005 (0.994-1.017)
MCC (ml)	1.004 (0.993-1.015)	1.002 (0.994-1.012)
Compliance		
Normal	1.000	1.000
Low	1.278 (0.112-9.587)	0.786 (0.095-6.501)
DO		
Absence	1.000	1.000
Presence	3.150 (0.528-9.803)	0.750 (0.146-3.841)

TABLE 5. Continued

Variables	OR (95% CI)	
	Nocturia on IPSS	Nocturia on FVC
BOO		
Absence	1.000	1.000
Presence	3.182 (0.516-9.639)	1.143 (0.250-5.224)
PdetQmax (cmH_2O)	0.991 (0.958-1.025)	0.989 (0.950-1.029)
Postoperative parameters		
Qmax	1.017 (0.927-1.116)	1.031 (0.937-1.133)
PVR	1.003 (0.992-1.010)	0.996 (0.986-1.009)
FBC	1.101 (0.910-1.318)	1.203 (0.956-1.576)
NBCI	1.567 (0.789-2.486)	1.638 (0.799-0.978)
De novo urgency	2.089 (1.150-3.795)	1.649 (0.635-4.277)

OR: odds ratio, CI: confidence interval, IPSS: International Prostate Symptom Score, FVC: frequency-volume chart, BMI: body mass index, PSA: prostate-specific antigen, Qmax: maximum flow rate, PVR: post-void residual urine volume, ANV: actual number of nocturnal voids, NPI: nocturnal polyuria index, NI: nocturia index, NBCI: nocturnal bladder capacity index, UDS: urodynamics, MCC: maximum cystometric capacity, DO: detrusor overactivity, BOO: bladder outlet obstruction, PdetQmax: detrusor pressure at maximum flow rate, FBC: functional bladder capacity

Nocturia has adverse effects on QoL, sleep patterns, daytime sleepiness, and even mortality associated with falls. Elderly people who need to void three or more times per night had a greater mortality rate over a 54-month observation period than did those voiding less often [2,3]. Nocturia of 2 or more times is present in 30% of men aged 50 to 54 years and in 60% of those aged 70 to 78 years old [19]. Two or more episodes of nocturia were observed for more than 60% of patients with BPH [6,7]. In this study, two or more episodes of nocturia were observed for 54.2% (103/190) of patients who underwent PVP due to BPH.

The causal mechanisms of nocturia fall into four categories: diurnal polyuria, NPU, reduced NBC, and mixed nocturia, which is a combination of NPU and reduced NBC [4]. BPH is likely associated with reduced NBC. BOO caused by BPH results in detrusor instability, neural degeneration, and decreases in bladder compliance, and then nocturnal bladder capacity is decreased [20]. In our study, 27.9% and 54.5% of the patients reported subjective and objective improvement in nocturia on the IPSS and FVC at 12 months postoperatively. The reduced episodes of nocturia were 0.9 and 1.0 on the IPSS and FVC, respectively.

A plausible explanation for the improvement in nocturia after PVP is thought to be similar to that after TURP. After prostatectomy, reinnervation of the bladder and recovery of detrusor stability occur as a result of relief from the obstruction [21-23]. The relief from obstruction may be associated with a reduction of urinary frequency and reversal of neural changes [24]. Furthermore, TURP effectively destroys the entire urothelium and submucosal tissue of the prostatic urethra and the bladder neck region, as well as resecting prostatic tissues [25]. Although side-fire laser is not as effective in reducing mechanical obstruction, it is probably as effective at destroying the prostatic and bladder neck urothelium and suburothelial structures [25]. Hence, both laser and TURP may be effective by producing a "deafferentation" of the afferent neurons responsible for initiating the involuntary detrusor contractions characteristic of DO and causing symptoms of overactive bladder [25]. Therefore, the denervation effects of prostatectomy on the bladder neck and prostatic urethra, or the relief from obstruction by the prostatectomy, may also apply to the improvement of nocturia after PVP. Also, there is another explanation for the improvement of nocturia after PVP. The decreases in post-void residual urine volume, and subsequently the time for bladder filling increases, which leads to a reduction of frequency and nocturia; these features might be secondary to the relief from obstruction [9].

In the present study, NBC increased significantly starting from the early postoperative period; therefore, the improvement in nocturia might be partially attributed to the increase in NBC. However, some patients did not respond to the treatment and complained of persistent nocturia. In clinical practice, nocturia might be a symptom of not only LUTS/BPH but also of other associated medical conditions such as natriuresis, congestive heart failure, diabetes, and peripheral edema. Nocturia is influenced by various factors other than BPH.

In the present study, the IPSS tended to indicate a higher prevalence of nocturia than did the FVC. Consistent with the present results, McCormack et al reported poor agreement between the FVC and questionnaire results [26]. In addition, patients with subjective improvement of nocturia on the IPSS decreased from 36.2% at the 6-month visit to 27.9% at the 12-month visit after the surgery, although those increased by 6 months postoperatively. However, this could have been due to the relatively high rate of loss to follow-up at 12 months postoperatively, resulting in selection bias.

The limitations of this study include the following. First, because the present study was retrospective, it might be limited by a possible selection bias. Second, the degree of irritation and effects on the disease-specific QoL were assessed only by the IPSS QoL index. Validated questionnaires are necessary to evaluate the clinical significance of nocturia. Third, our study did not include a large cohort and the follow-up period was only short-term. Fourth, our study was not randomized or controlled by the reference standard, TURP. Accordingly, we could not exclude a placebo effect or bias affecting the results of this study. Finally, in the present study, the relatively high dropout rate of 40.8% 12 months after the PVP may have

inadvertently created a selection bias.

CONCLUSIONS

The results of this study suggest that nocturia can improve significantly starting from the early postoperative period after PVP for symptomatic BPH. However, we found no factors influencing improvement in nocturia. The improvement in nocturia after PVP was not affected by baseline nocturnal frequency, the presence or absence of preoperative NPU, or reduced NBC and DO on baseline urodynamics. However, longer follow-up studies with a larger cohort are needed to confirm these findings.

Conflicts of Interest

The authors have nothing to disclose.

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