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A prospective, randomized trial comparing the use of KTP (GreenLight) laser *versus* electroresection-supplemented laser in the treatment of benign prostatic hyperplasia

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Introduction Photoselective laser vaporization of the prostate (PVP) is one of the most popular techniques of treatment of benign prostatic hyperplasia (BPH). The aim of this study was to assess the risk of thermal damage to the external urethral sphincter during PVP at distal part of prostatic urethra.

Material and methods 66 men submitted to PVP with 80-W Green Light Laser were randomly assigned to receive standard PVP only (group A) or PVP in proximal part followed by transurethral resection in distal part of prostatic urethra (group B). Primary end-points of the study assessed at baseline, 24 hours and 8 weeks after the surgery were: urinary continence, urinary flow (Qmax), post void urine retention (PVR), international prostate symptom score (IPSS), quality of life (QoL).

Results Per protocol analysis was eventually performed in 60 patients. Study groups did not differ in age, preoperative continence, values of Qmax, PVR, IPSS, QoL, or the rate of complete urinary retention ($p > 0.05$). During the 8-week follow-up no patient reported urinary incontinence, while decrease in IPSS (16.3 *vs.* 14.9, $p > 0.05$), QoL improvement (4.7 *vs.* 4.7, $p > 0.05$), increase in Qmax (18.2 *vs.* 17.4, $p > 0.05$) were similar in both study groups. Patients assigned to group B were more likely to have bleeding complications (85.2% *vs.* 18.2%), including patients requiring transfusion (14.8% *vs.* 0%). Moreover, postoperative catheterization time was shorter in group A (29.1 hrs *vs.* 37.2 hrs, $p = 0.04$).

Conclusions Laser vaporization for treatment of BPH is safe and effective, with no significant effect on the risk of urinary incontinence in comparison to traditional methods.

Key Words: BPH ‹› benign prostatic hyperplasia ‹› laser therapy ‹› vaporization of the prostate ‹› GreenLight laser

INTRODUCTION

Benign prostatic hyperplasia (BPH) is the most common disorder originating in the lower urinary tract in men over the age of 50. In the last 20 years a number of modern methods of surgical treatment have been developed to treat this common condition. For years the gold standard procedure for treatment of BPH has been the transurethral resection of the prostate (TURP). However, this method is associated with a variety of complications affecting >18% of patients [1]. Bleeding during and after the procedure, post-TURP syndrome, secondary urethral strictures and repeated reoperations resulting from urinary incontinence are a select few, which, along with its steep learning curve, have necessitated the search for and development of alternative methods of therapy. Laser therapy is decidedly considered one such alternative.

The application of laser for the treatment of BPH was first attempted in the 1980s. Since then the popularity of this method has grown continuously, along with the advancement of associated interventional devices (from coagulation to cutting and vaporization methods). Currently, two different laser systems have come to dominate urological surgery: holmium laser – Holmium-Yttrium-Aluminium-Garnet (Ho:YAG)

– applied primarily in ablation, enucleation and resection of prostatic tissue (including the breakdown of deposits in the urinary tract) and Green Laser – potassium-titanyl-phosphate (KTP) – serving exclusively the vaporization of prostate adenoma.

The treatment of BPH using the 80-W potassium-titanyl-phosphate laser (KTP) was first reported in 1997 [2]. The first procedure in Poland was carried out in 2013 by professor Jeromin in Łódź [3].

In comparison to previous technology (Nd:YAG laser), the wavelength of the KTP laser (532 nm) has been halved, placing it in the green electromagnetic spectrum (Greenlight-laser). The result is a completely different optical and energetic interaction in contrast to other laser types [4]. Combing the high average power of a quasi-continuous wave laser (80 W) with the high peak power delivery within each micro-pulse (up to 280 W) offers efficient vaporization of prostate tissue. The short duration of each laser beam pulse (0.25 s) limits the thermal effect on deeper-lying tissue. KTP laser energy is selectively absorbed by hemoglobin (and not by water), which, at this wavelength, has a very high absorption coefficient and therefore penetrates prostate tissue to a maximal depth of 0.7 mm. This leads to immediate vaporization of prostatic tissue [4, 5, 6, 7].

Though the laser energy penetrates to a tissue depth of only 0.8 mm, the thermal effect spreads within a 5–10 mm radius from the point of vaporization. Thermal damage of the external sphincter is a distinct risk, especially when the prostate adenoma is considerably enlarged beyond the verumontanum, approaching the above-mentioned sphincter. Numerous authors have suggested that the degree and frequency of postoperative urinary incontinence is strongly dependent on the age of the patient, but also, and perhaps more significantly, on prostate size, forcing the operator to intervene in the proximity of the external sphincter muscle [8].

The goal of this study was to assess the risk of thermal damage to the external sphincter of the urethra in men undergoing GreenLight laser vaporization of BPH.

MATERIAL AND METHODS

98 consecutive men with lower urinary tract symptoms due to BPH were qualified for photoselective KTP laser vaporization of the prostate (PVP). Mean age of the cohort was 68.3 years. All patients gave written consent to participate in the study.

Inclusion criteria were as follows: clinical symptoms of BOO progressing or refractory to conservative treatment, international prostate symptom score (IPSS) of >10 or urinary retention, prostate volume of 40–80 ml measured by transabdominal ultrasound, the presence of enlarged prostate adenoma at the level of verumontanum confirmed at urethroscopy directly before PVP. Exclusion criteria were as follows: active urinary tract infection, suspicion of prostate cancer, urethral stricture, previous urethral surgery, neurological disorders, lack of informed consent to participate in the study. Local review board approved study protocol.

Among 98 initially screened men, inclusion criterion of enlarged prostate adenoma at the level of verumontanum was not met in 32 patients; hence they were excluded from the study. Eventually 66 consecutive patients were assigned into two study groups, based on consecutive patient numbers. Patients with even and odd numbers were assigned to the study group A and the study group B, respectively. In the group A, patients underwent vaporization prostatectomy, seemingly incomplete, with the termination of the procedure at the level of the verumontanum. The remaining fragments of the lateral lobes extending in various degrees beyond the seminal colliculus/veromontanum were left intact. In the group B, the vaporization procedure was also discontinued at the level of the verumontanum, however, the remaining fragments of the lateral lobes of the adenoma were resected by means of the standard TURP method (of course after changing endoscopic equipment).

All procedures were performed by the same surgeon, using a single 80-W Green Light Laser fiber (American Medical Systems), water-cooled, emitting a monochromatic light source, operating at a 532 nm wavelength. The laser fibers were introduced using a laser cytoscope (Storz).

All patients undergone full urological evaluation before treatment, including transabdominal ultrasound (TRUS) measurement of prostate volume performed by the same radiologist, accounting for median (III) prostate lobe and retention, determination of prostate-specific antigen (PSA), measurement of maximum flow rate Qmax (except in patients with complete urinary retention) and digital rectal examination (DRE). All patients were also asked to complete the IPSS and QL questionnaire, and gave their informed consent to participate in the study.

Patients were followed-up for 8 weeks postoperatively. Primary end-points of the study were change in continence status, urinary flow (Qmax), post void urine retention (PVR), international prostate symptom score (IPSS), including 7-scale (0-delighted, 6-terrible) quality of life assessment (QoL). Secondary study end-points were surgery time, bleeding rate, catheterization time, storage symptoms in postoperative course and surgical complications.

The data, obtained during the course of the study, were analyzed using Statistica 10.0. Normal distribution of all quantitative variables was confirmed with the use of the Shapiro-Wilk test, while homogeneity of variance was tested according to Levene's formula. The student's t-test was used to compare the results between the groups, when achieving a positive outcome of both afore-mentioned tests. In case of a negative outcome, U-Mann-Whitney test was considered. The Chi-square test was implemented for nonparametric variables. Statistical significance was defined as $p < 0.05$.

RESULTS

Per protocol analysis was eventually performed in 60 patients, including 32 and 28 patients in group A and B, respectively. From the group of 66 randomized men 5 patients were lost in follow-up (1 patient from group A and 4 patients from group B) and one patient from group B died from cardiac insufficiency not related to urological procedure. The general characteristics of patients in study groups are presented in Table 1. Urinary tract infection was excluded in all patients before inclusion into the study. Mean PSA was 2.47 ng/ml and 2.68 ng/ml in group A and B, respectively. In the single case of elevated PSA (25 ng/ml), two series of TRUS-guided prostate biopsies were performed to rule out prostate cancer. Prior to the procedure, attention was paid to the presence of an median (III) lobe protruding into the bladder, posing further difficulties in performing vaporization and thus prolonging the operation time. This was observed in a total of 18 patients (29%) across both groups. Statistical analysis failed to yield significant differences between the two groups of patients.

During the 8-week follow-up no patient reported urinary incontinence. Results in primary end-points of the study are presented in Table 2. In postoperative studies of both 24 hours and 6–8 weeks after treatment, there was a significant symptomatic decline in accordance to the questionnaire results, and a significant increase in urinary flow.

Surgery time was 80.3 min (60–120) in group A and 101.3 min (85–150) in group B. The difference in operation times was observable both clinically and statistically ($p = 0.00$), attributable to the necessary variation of technique in group B (apparatus and irrigation fluid change). The majority of the procedures were carried out under spinal anesthesia. Only a few patients required general anesthesia, as a result of the presence of concurrent illness.

Assessment of bleeding during the procedure was carried out by the operator, according to a self-devised scale: 0 – represented no bleeding, 1 – bleeding requiring coagulation during the procedure (without the need for blood transfusion, with no drop in hemoglobin), 2 – persistent bleeding despite coagulation postoperatively (without the need for blood transfusion, but with a 1–2 unit drop in hemoglobin) and 3 – bleeding requiring either plasma extract or re-coagulation and blood transfusion (where the drop in the hemoglobin exceeds 2 units). The evaluation is presented in Table 2. In group A, no bleeding (0 on the bleeding scale) was clearly encountered more frequently, whereas group B was evidently more frequently characterized by persistent bleeding despite coagulation attempts, but without the need for further intervention ($p = 0.00$).

After surgery, an 18 Ch Foley catheter was inserted and left for 24 hours. In 4 patients from group B, a three-way Dufour 20 Ch catheter was left due to bleeding. One of these patients required extraction for a few hours. The average holding time, of the catheter after surgery, in group A was

Table 1. *General characteristics of patients in groups A and B*

	Group A	Group B	P value
Number of patients	32	28	–
Age	67.2 ±8.4 years	69.5 ±9.0 years	0.29
Rate of patients with complete urinary retention	21.9% (n = 7)	35.7% (n = 10)	0.24
Prostate volume	53.7 ±8.3 ml	52.3 ±8.7 ml	0.55
PSA	2.51 ±4.3 ng/ml	2.65 ±1.8 ng/ml	0.87
IPSS	22.3 ±3.5	20.8 ±2.9	0.16
IPSS quality of life score	5.1 ±0.8	5.2 ±0.7	0.55
Qmax	6.7 ±4.1 ml/sec	5.0 ±4.0 ml/sec	0.14
Presence of third lobe	(n = 12)	(n = 6)	0.17

PSA – prostate specific antigen; IPSS – international prostate symptom score; QoL – quality of life; Qmax – maximal urinary flow rate

Table 2. *Postoperative results*

	Group A	Group B	p	Postoperative correction		p
				A	B	
IPSS 6-8 weeks postop.	6.0 ±3.4	5.9 ±2.6	0.73	-16.3	-14.9	0.58
IPSS quality of life score 6–8 weeks postop.	0.4 ±0.9	0.5 ±0.6	0.42	-4.7	-4.7	0.89
Q max 24h postop.	15.4 ±4.1 ml/sec	14.0 ±3.7 ml/sec	0.25	230%	280%	0.26
Q max 6-8 weeks postop.	24.9 ±10.3 ml/sec	22.4 ±6.8 ml/sec	0.29	370%	450%	0.99

IPSS – international prostate symptom score; QoL – quality of life; Qmax – maximal urinary flow rate

Table 3. *Assessment of bleeding in operated patients*

Bleeding Scale	0	1	2	3	Number of bleeding patients
Group A	27	6	0	0	6
Group B	4	7	12	4	23

significantly shorter in comparison to group B (29.1 hours *vs.* 37.2 hours, p = 0.04).

All patients in group A had their catheters removed 24 hours after treatment. However, 4 men required reinsertion of a catheter for another 24 hours due to urine retention. Two patients, although urinating independently, required catheter reinsertion due to significant urine retention. A catheter was maintained maximally for 72 hours.

2 patients from group B required re-coagulation due to bleeding within the first 24 hours after surgery. 16 patients had a catheter maintained for a longer period: due to bleeding – 9 patients, repeated/significant urine retention – 7 patients.

All patients who underwent surgery, had urinary flow and retention tests performed before leaving the hospital. All patients were asked to return to the clinic 6–8 weeks after surgery. Maximal urinary flow and retention tests were performed once again, and patients were asked to complete an IPSS and QL questionnaire. Table 3 depicts these results.

The major patient complaints encountered at follow-up (in some even earlier voluntarily) were sudden urge to urinate, groin and urethral pain. 12 patients from group A (36%) and 9 (31%) from group B reported the above-mentioned complaints. Urine cultures were negative for infection. Patients were prescribed alpha-blockers with or without anti-inflammatory medication, as well as cholinolytics. The medications were discontinued after approximately 6 weeks. 4 patients (6.5%) (both groups – under further observation) were re-admitted to the ward due to urinary bladder neck and/or urethra narrowing. One patient (from group A) was reoperated after 14 months, performing TURP. None of the patients, from either of the groups, complained of problems with urinary incontinence. The frequency of reporting any of these symptoms did not differ between groups (p> 0.05).

DISCUSSION

We performed a prospective randomized trial assessing the risk of functional complications related to PVP in the region of urethral external sphincter. This issue was never addressed before, despite clinical relevance. The depth of tissue injury is proven to be much deeper than visible during endoscopy, what makes injury to the urethral external sphincter possible [6, 7].

The early results of prostate vaporization in our group of patients are very promising. Vaporization of prostatic adenoma is characterized foremost by its efficacy and safety. The main problem considered by our study, urinary incontinence, following 80W KTP laser vaporization of the prostate, was not observed in any patient. Overall, 100% patients were found to be continent postoperatively, regardless of the methodology used. We are aware that our patients were selected on the basis of prostate volume, though all satisfied the criteria of our trial – prostate adenoma reaching or slightly exceeding the level of the verumontanum. Some authors highlight the fact that a significantly enlarged prostate, along with the patient's advanced age, are predisposing factors for developing postoperative complications, such as urinary incontinence [8], associated with the 'thermal margins' accompanying laser vaporization.

In group B patients, the significantly prolonged operation time is attributable to the necessary endoscopic apparatus and irrigation fluid change. Following classic TURP, even partial, problems with hemostasis are more frequently observed. The average holding time of the catheter after surgery in this group was consequently longer. The supplementary electroresection had no impact on either urinary flow (though worse 24 hours postoperatively than in group A, these may be due to greater tissue swelling) or IPSS and QoL parameters.

Approximately 30% of patients had various types of complaints after surgery – urgency, groin and urethral pain. Nearly all authors of similar publications refer to such transient symptoms in their patients. These are most likely associated with tissue reactions after laser light exposure and a significant degree of neurological receptor irritation [9, 10].

Late complications occurred in 5 patients (8%), resulting in further surgical intervention. Similar results were presented in patients after classic surgery – TURP [1, 9]. In other trials, this percentage was slightly higher, reaching even 14%, but it should be noted that we are well aware of the number and specificity of our patients [10].

CONCLUSIONS

Where the prostate lobes of a large BPH extend beyond the verumontanum, the procedure may be interrupted at the level of the verumontanum without compromising urodynamic parameters or patient's well being. Additional resection of the lateral lobes

of the prostatic hyperplasia using traditional methods is only associated with an elevated risk of bleeding during and after the procedure, prolongation of operation time, increased urinary catheterization times postoperatively, without affecting patients' urodynamic and IPPS and QL parameters. Laser vaporization for treatment of BPH is safe and effective, with no significant effect on the risk of urinary incontinence in comparison to traditional methods.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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