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New Advances in Benign Prostatic Hyperplasia: Laser Therapy

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Abstract Throughout the past decade, numerous techniques for the treatment of benign prostatic hyperplasia have emerged. Laser therapy, in particular, has gained widespread popularity among urologists. Since its inception in 1996, holmium laser enucleation of the prostate (HoLEP) has been evaluated rigorously in the treatment of glands of all sizes. HoLEP has produced superior relief of bladder outlet obstruction as compared to transurethral resection of the prostate based on urodynamics, and has proved equally as effective as open prostatectomy, for the management of very large glands (>100 cc), with lower morbidity. In addition to HoLEP, several newer but less well-studied laser techniques currently are available. These include photoselective laser vaporization utilizing the potassium-titanyl-phosphate (KTP or "green light") laser, thulium laser enucleation, and high-power diode laser vaporization. This report reviews the most current literature on laser therapies utilized in the treatment of benign prostatic hyperplasia with regards to safety, outcome, efficiency, and long-term durability.

Keywords Prostate · Prostatic hyperplasia · Bladder outlet obstruction · Laser therapy · Holmium · Potassium-titanyl-phosphate · Laser vaporization · Prostate-specific antigen

Introduction

Electrosurgical transurethral resection of the prostate (TURP) long has been considered the gold standard for the treatment of bladder outlet obstruction (BOO) related to benign prostatic hyperplasia (BPH) in small to moderate-sized prostate glands, while open simple prostatectomy (OP) has served as the standard surgical approach for treating larger glands. Although these techniques have demonstrated long-term, durable results in the treatment of prostatic hypertrophy, they are not without complications, which include bleeding and transfusion requirements, fluid absorption and associated transurethral resection (TUR) syndrome (monopolar resection with hypotonic irrigation), prolonged catheterization, urethral stricture, and bladder neck contracture. While bipolar electrocautery systems allow for normal saline irrigation and a reduction in the incidence of TUR syndrome, the remaining aforementioned complications remain a concern for all urologists performing these procedures [1••].

The first reports of prostate laser therapy date back to 1992, when Costello and associates [2] described the use of a neodymium:yttrium-aluminum-garnet (Nd:YAG) laser in the treatment of BPH. In 1994, Gilling et al. [3] was the first to describe the use of a holmium:YAG (Ho:YAG) laser in combination with the Nd:YAG laser for prostatic coagulation. Subsequently, holmium laser ablation (HoLAP), and ultimately enucleation (HoLEP), procedures were developed. Since it was first described in 1996, HoLEP has gained worldwide attention and has been rigorously assessed and compared to TURP and OP with regards to efficacy, efficiency, safety, cost, and durability. HoLEP has yet to become widely used secondary to a perceived steep learning curve and the costs associated with obtaining high power 100 W holmium laser systems [4••].

More recently, photoselective vaporization (PVP) techniques have achieved popularity among practicing urologists. These techniques generally involve the use of 532 nm wavelength potassium-titanyl-phosphate (KTP or "green light") technology. Initial vaporization procedures were performed using 60 W KTP lasers, but due to the

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slow vaporization times associated with the 60 W laser, higher-powered 80 W KTP and 120 W lithium triborate laser systems have been developed. These high-powered lasers have allowed for increased ablative efficiency and, in the short term, appear to generate outcomes similar to TURP with regards to improvement in American Urologic Association Symptom Score (AUASS), maximum flow rate (Q_{max}), and quality-of-life (QOL) scores when used to treat smaller glands [5]. However, little robust data on the long-term outcomes and reoperation rates associated with these procedures exist at this time [1••].

Newer techniques such as diode laser vaporization and thulium laser enucleation (ThuLEP) are in their infancy, but their development clearly demonstrates the continued growing interest in the use of lasers for the treatment of BPH/BOO. This report reviews the currently available laser technologies being utilized for the endoscopic management of BPH.

Holmium Laser: Physics

The Ho:YAG laser is a pulsed, solid-state laser that emits a wavelength of 2,140 nm (infrared). It is highly absorbed by water, has a penetration depth of 0.5 mm, and is used with saline irrigation. Given the high water content of the prostate, the holmium wavelength is well absorbed, allowing for either laser ablation or resection/enucleation of prostatic tissue [2].

Holmium Laser Ablation of the Prostate

HoLAP procedures initially were performed using 60 W systems and side-firing 550 μm laser fibers. Slow ablation times and the development of more efficient tissue removal techniques such as HoLEP ultimately led to diminished utility of HoLAP for the treatment of BPH. However, with the introduction of high-powered, 100 W Ho:Yag laser systems, interest in HoLAP for the treatment of small to moderate-sized prostates has resurfaced because this technique is simpler to perform [6].

In 2007, Kumar [7] evaluated high power HoLAP for the treatment of prostates larger than 80 cc in a small cohort of patients. The mean preoperative prostate volume as determined by transrectal ultrasound (TRUS) was 122 cc. They reported a mean postoperative TRUS volume of 55 cc, accounting for a 67% reduction in tissue volume. Mean laser time was 77 min, yielding a tissue removal rate of 0.87 g/min, comparable to rates reported in the literature for TURP and HoLEP. The mean preoperative AUASS was 20.4, and at a mean postoperative follow-up of 3.3 months, it was 5.7. Mean preoperative Q_{max} (mL/s) was 6.9 and improved to 15.06 postoperatively. They did not experience any significant perioperative complications [7]. While this study shows promise for the use of HoLAP for the treatment of larger glands, long-term follow-up and a larger cohort of patients are necessary to determine its utility.

HoLAP has not been well studied in terms of its efficacy for the treatment of BPH compared to other laser technologies. A recent 2009 study by Elzayat et al. [8] compared HoLAP (80 W system) to PVP (80 W system) for the treatment of glands 60 cc or smaller. They reported a statistically significant increased operative time for HoLAP (69.8 min) as compared to PVP (55.5 min). Both forms of treatment led to similar improvements in International Prostate Symptom Score (IPSS) and Q_{max} (comparable to TURP) at 1 year. The incidence of hematuria, postoperative irritative symptoms, need for recatheterization, and postoperative incontinence (stress or urge) were similar in both groups. Reoperation rates at 1 year were 3.5% and 1.9% for the HoLAP and PVP groups, respectively. Bladder neck contracture (BNC) rates of 3.5% and 7.7% for the HoLAP and PVP groups, respectively, were noted and attributed to the authors' early phase of the learning curve and smaller size of the glands being treated [8].

Holmium Laser Enucleation of the Prostate

The HoLEP technique has been described in great detail [9]. Throughout the past decade, HoLEP has emerged as the most rigorously studied, minimally invasive technique for the treatment of BPH. Numerous level 1 studies have confirmed the efficacy of HoLEP as compared to TURP and OP, and the results of medium-term and long-term follow-up have demonstrated excellent durability of this procedure [3, 4••, 10, 11].

In 2007, Ahyai et al. [11] reported 3-year follow-up results of a randomized clinical trial comparing HoLEP and TURP for the treatment of glands smaller than 100 cc (mean size 51.7 cc). In this study, both procedures resulted in statistically significant improvements in AUASS, Q_{max}, and PVR. AUASS was significantly better at 2 years of follow-up in the HoLEP group (1.7 vs 3.9; $P<0.0001$) and similar at 3 years of follow-up (2.7 vs 3.3; $P=0.17$). Q_{max} was similar in the HoLEP and TURP groups at all points of follow-up (29.0 vs 27.5 mL/s at 3 years). At all points, PVR volume was significantly better in the HoLEP group. Perioperative results heavily favored HoLEP, because patients in this group had significantly less blood loss and no transfusion requirement. Additionally, patients in the HoLEP group experienced a significantly shorter median length of catheterization (LOC) than patients in the TURP group (1 day vs 2 days) as well as a shorter median hospital stay (2 days vs 3 days). Rates of urethral stricture and BNC were the same for both groups, as were reoperation rates (7.2% and 6.6% for HoLEP and TURP, respectively). An accurate comparison of operative times for these procedures cannot be made from this study because the authors did not have access to a tissue morcellator at the time of the study and required an electrocautery loop to resect the enucleated prostate lobes, which is more time consuming than morcellation [11].

In 2008, Kuntz and associates [12] published 5-year follow-up results of a randomized clinical trial comparing HoLEP to OP for the treatment of glands larger than 100 g. There was no statistically significant difference between the HoLEP and OP groups with regard to AUASS (3.0 vs. 3.0), Qmax (24.3 mL/s vs 24.4 mL/s) and PVR volume (10.6 mL vs 5.3 mL) 5 years postoperatively (and at all earlier points of follow-up),. The perioperative outcomes in this study clearly favored HoLEP, as demonstrated by a significantly lower transfusion rate (0% vs 13.3%), shorter LOC (30 h vs 194 h) and shorter hospital stay (70 h vs 250 h). The rates of urethral stricture or BNC requiring intervention were similar in both groups (5% HoLEP and 6.7% OP). No patients developed reobstruction related to BPH recurrence. While operative time was significantly longer for HoLEP (136 min vs 91 min), the authors attribute this to an initial lack of availability of a morcellating device, as they reported a significant decrease in operative time when performing HoLEP with morcellation (Kuntz et al., unpublished data) [12]. The authors concluded that HoLEP is a viable alternative to OP with regards to safety profile, efficacy, and long-term durability, and suggest that HoLEP may be regarded as the new gold standard for the treatment of large glands.

Even longer–term data on the durability of HoLEP has been reported. Gilling et al. [3] published results at a mean of 6 years follow-up. In this cohort of 38 patients, the mean IPSS, QOL score, and Q_{max} 6 years postoperatively were 8.5, 1.8, and 19 mL/s, respectively (preoperative means were 25.7, 4.9, and 8.1 mL/s, respectively). No significant differences in these postoperative values were identified at any time point of follow-up, aside from Q_{max} at 6 months and 6 years, further demonstrating the durability of this procedure. One patient in this group (1.4%) required reintervention (HoLEP) 5 years postoperatively.

More recently, Krambeck et al. [4] reported on experience with over 1,000 HoLEP procedures with results at short-term, intermediate-term, long-term, and greater-than–5 year follow-up. In this large series of patients, the mean preoperative prostate volume was 99.3 mL (9–391 mL), mean AUASS was 20.3, mean Q_{max} was 8.4 mL/s, mean prostate-specific antigen (PSA) was 7.2 mg/dL (0.47–26.8 mg/dL), and 38.7% of patients were in urinary retention. Postoperatively, 99.7% of patients voided spontaneously. For the cohort of patients followed for 5 years or longer (n=83; mean follow-up: 7 years), mean AUASS was 5.1. Q_{max} was not routinely followed after 1 year. Only 1 patient (0.1%) in this group required repeat HoLEP (6 years after initial treatment) for regrowth. This group reported a low urethral stricture/BNC rate compatible with rates reported in the literature (< 2%) and noted a correlation between postoperative BNC and gland size smaller than 40 g. The authors now routinely perform an incision of the bladder neck for patients with glands smaller than 40 g. An additional finding in this study was the stable, low postoperative PSA noted in the group followed for over 5 years (0.95 mg/dL), another indicator of the durability of HoLEP in the treatment of BPH (see below).

Holmium Laser Enucleation of the Prostate and Postoperative Prostate-Specific Antigen Stability

HoLEP produces a significant reduction in PSA (81–86%), which is correlated with the amount of tissue resected, and is similar to that achieved with open prostatectomy. After HoLEP, the new "reset" PSA level should be sustained, as the transition zone is the major source of PSA production. Elmansy and associates [13•] have evaluated PSA velocity (PSAV) to assess for treatment durability after HoLEP and for the detection of malignancy. A cohort of 335 patients was followed for 7 years after HoLEP. Nine patients developed adenocarcinoma of the prostate over the course of the study. All patients had significant and durable improvements in IPSS, Q_{max}, and PVR comparable to results previously described in this review. There was no significant difference with regard to preoperative prostate volume in the patients with and without progression to adenocarcinoma of the prostate (75.33 g and 73.95 g, respectively), nor with regard to the amount of tissue resected (51.4 g and 44.46 g, respectively). However, a significant difference was noted in terms of preoperative PSA (5.44 benign group, 9.46 malignant group), postoperative PSA nadir (0.91 benign group, 5.83 malignant group), and percent PSA reduction (75.39% benign group, 47.49% malignant group). The mean PSAV for the benign group at 1 and 3 years were 0.13 and 0.09 ng/mL/year, respectively. For the malignant group, the PSAV were 1.28 and 2.4 ng/mL/year, respectively. In this large cohort of patients undergoing HoLEP without evidence of malignancy, the extremely low values of PSAV confirm the durability of HoLEP with regards to permanent tissue removal [13•]. In patients without significant reductions in PSA postoperatively or in those with elevated PSAV after HoLEP, a diagnosis of adenocarcinoma of the prostate must be considered and appropriate actions for diagnosis, when indicated, should be pursued.

Holmium Laser Enucleation of the Prostate in Anticoagulated Patients

While most urologists prefer stopping anticoagulants before HoLEP, the procedure can be performed safely in the setting of active anticoagulation. In 2006, Elzayat et al. [14] reported their results after performing HoLEP in 14 patients with therapeutic international normalized ratios (INR; mean 2.0) and in 34 patients transitioned to low molecular weight heparin (LMWH). They reported a 14.2% transfusion rate in the full anticoagulation group and a 14.7% transfusion rate in the LMWH group, both rates being lower than those reported for patients undergoing standard TURP while anticoagulated. In 2009, Tyson and Lerner [15] published the results of a series in which they performed HoLEP in 13 patients on warfarin (mean INR 1.5) and in 25 patients on aspirin. Two patients (8%) in the aspirin group and five patients (14%) in the control (no anticoagulation) group required termination of the procedure secondary to hematuria-induced intraoperative visual obstruction. No blood transfusions were required in any patients regardless of anticoagulation status. Length of catheterization and hospitalization were not different among the groups. While interruption of anticoagulation always should be considered before performing any form of resection, in those patients in whom cessation of anticoagulation is deemed too risky, HoLEP still can be performed safely, albeit with slightly higher transfusion rates than for nonanticoagulated patients undergoing the same procedure.

Photoselective Vaporization of the Prostate: Physics

PVP is performed with a nonreusable 532 nm laser. This technology first was developed by doubling the frequency of a pulsed Nd:YAG laser with a KTP crystal, thus generating a visible green wavelength (532 nm) [5, 16]. This “green light” wavelength is selectively absorbed by hemoglobin within prostatic tissue, allowing for photoselective vaporization secondary to rapid photothermal vaporization of heated intracellular water. The penetration depth is 0.8 mm and allows for a more precise coagulation zone of 1–2 mm when compared to Nd:YAG (4–7 mm coagulation zone). This improved precision decreases the severe dysuria, sloughing, and prolonged obstruction associated with Nd:YAG laser treatment [16]. Initial PVP procedures were performed using 60 W laser systems. Due to the slow vaporization times achieved with 60 W systems, higher power lasers were developed. Currently, 80 W KTP lasers and 120 W lithium triborate lasers are available for the treatment of BPH [5].

High Power Photoselective Vaporization of the Prostate: 80 W and 120 W Laser Systems

Most contemporary studies on the use of PVP technology have been conducted using 80 W KTP laser systems. Control trials comparing PVP to other accepted surgical procedures have been published only recently. Additionally, intermediate and long-term data on the efficacy and durability of this treatment modality now are becoming available.

Bouchier-Hayes and colleagues [17] recently reported their 1-year results comparing 109 patients randomized to PVP or TURP for the treatment of symptomatic BPH. Operative times for TURP and PVP were not statistically different (34.3 min and 30.13 min, respectively). At 12 months, both groups demonstrated equivalent, significant improvements in Q_{max} and IPSS. Mean improvements in Q_{max} at 12 months for the TURP and PVP groups were 154% and 136%, respectively. Mean decreases in IPSS for these groups were 53% and 61%. Both procedures resulted in equal reductions of detrusor pressure at Q_{max} when reassessed at 6 months (88–51.5 cm H_2O for TURP patients and 85–46.7 cm H_2O for PVP patients). Modest reductions in postoperative TRUS volumes (8.7 g TURP, 6.3 g PVP) were noted. Greater than 50% reduction in preoperative PSA was reported for patients undergoing TURP, while PSA reduction in PVP patients was not statistically significant. LOC (44.2 h vs 13.8 h), and length of stay (3.28 days vs 1.1 days) were significantly longer in the TURP group. Two patients (4%) in the TURP group and 6 (10.2%) in the PVP group required reintervention for persistent obstruction. The authors concluded that PVP appears to be a safe procedure with comparable results to TURP for the treatment of small glands, with the caveat that decreased transition zone removal (as indicated by minimal reduction in PSA) may contribute to a higher rate of reintervention [17].

In a 2010 report, Goh et al. [18] performed a cost analysis comparing PVP (high power, 120 W) to TURP. In this study, 95% of PVP and 78% of TURP procedures were performed on an outpatient basis (<23 h of hospitalization). Outpatient and inpatient costs for each procedure were not significantly different; however, when comparing overall cost among the entire cohorts, PVP was statistically less expensive than TURP. Unfortunately, the authors did not comment on the efficacy or the reintervention rate associated with each procedure, both factors that could contribute to increased future costs [18].

PVP has been compared to OP for the treatment of larger glands. In 2008, Skolarikos and associates [19] published 18-month results evaluating PVP with an 80 W system and OP for the treatment of glands larger than 80 cc. Operative time was significantly longer in the PVP cohort (80 min vs 50 min). As expected, LOC and length of hospitalization were significantly shorter in the PVP group (24 h vs 120 h and 48 h vs 144 h respectively). At all points of follow-up, patients in both groups had statistically significant improvements in IPSS, Q_{max}, and PVR volumes. Notably, postoperative prostate volume was significantly lower in the OP group, and at 18 months, PSA was significantly lower in the OP group as well. While the transfusion rate was higher in the OP group (13% vs 0%), rates of other minor and major perioperative complications were comparable. Reoperation rates were 4.62% in the PVP group and 5% in the OP group, with one patient in the PVP group requiring apical tissue resection for persistent obstruction [19]. While this study shows promise for the use of PVP for treating larger glands, studies with longer-term follow-up are necessary to assess the durability of PVP, especially given the significantly lower volume of tissue that can be removed with this procedure.

Few reports exist regarding the long-term durability of PVP. Hai [20•] has retrospectively reported his 5-year experience with PVP in a cohort 246 men with a mean preoperative TRUS prostate volume of 55 cc. At 5 years, patients experienced a stable 78.7% reduction in AUASS and a 171.8% improvement in Q_{max}. Mean TRUS prostate volume at 5 years was 42.7 cc, which represented only a 17% reduction in prostate volume. Mean PSA reduction was 10.2%. A total of 19 patients (7.7%) required retreatment for recurrent or persistent obstruction. These results seem to indicate that PVP provides durable results in patients with moderate-sized prostates, albeit with less robust tissue removal and PSA reduction and a higher rate of reintervention than that reported for HoLEP.

Thulium Laser Procedures

The Thulium:YAG laser (continuous wave) emits a 2,013 μm wavelength. It is highly absorbed by water and has a penetration depth of about 1 mm. This laser recently has been introduced into the armamentarium available for the treatment of BPH and techniques involving vasoresection and vapoenucleation (ThuLEP) have been described [21, 22]. Szlauer et al. [21] recently have published results on their first 56 patients with a mean prostate volume of 50 cc undergoing vaporesection. Average operative time was 60 min and mean resected tissue volume was 7 g. Mean PSA decreased from 5.7 ng/mL to 2.5 ng/mL at 9 months. LOC was 23 h and the transfusion rate was 3.6% (two patients with preoperative hemoglobin levels of<10 mg/dL). Mean preoperative IPSS was 19.8 and significantly improved to 8.6 at a median follow-up of 9 months. Q_{max} improved from a mean of 8.1 mL/s preoperatively to 19.3 mL/s. Four patients (7.1%) required repeat TURP for inadequate resection and urethral stricture and BNC each occurred in one patient. These results were comparable to those initially reported with the thulium laser [21, 23]. Herrmann and colleagues [22] have reported on the feasibility of ThuLEP, but studies evaluating the efficacy and durability of this technique are required.

Diode Lasers

The use of diode laser vaporization for the treatment of BPH now is being described in the literature. In animal models, high-powered diode lasers have allowed for rapid tissue ablation with excellent hemostasis. Recently, Erol and colleagues [24] have reported on their use of a continuous mode, 980 nm, high-power (80–132 W) diode laser for prostatic vaporization in humans. In this cohort of 47 patients, the mean preoperative TRUS prostate volume was 51 cc and the average operative time was 52.55 min. No patients required blood transfusion and mean LOC was 24 h. At 6 months, mean IPSS decreased from 21.93 to 9.87 and Q_{max} improved from 8.87 cc/s to 18.27 cc/s. Mean postoperative TRUS prostate volume decreased to 31.06 mL at 6 months and mean PSA decreased from 2.54 ng/mL to 1.77 ng/mL. Patients reported irritative voiding symptoms that appeared to resolve within 2 weeks. Additionally, 2 of 47 patients reported temporary urge and stress incontinence, which resolved within 2 weeks [24]. While these results seem promising, further studies comparing this technique to the currently accepted surgical treatment options for BPH with larger cohorts and longer follow-up will be required to truly determine its role.

Conclusions

Laser therapy has become widely accepted for the treatment of BPH and interest in this modality continues to grow, as evidenced by the rapidly expanding variety of lasers and techniques described in the literature. Based on this review, laser therapy in all forms appears to provide a better safety profile, lower rate of blood transfusion, and decreased LOC and length of hospitalization when compared to traditional TURP or OP. To date, HoLEP remains the most rigorously studied of all of these modalities. HoLEP is equivalent, if not superior to, TURP and OP in terms of efficacy and long-term durability, and in our experience with the treatment of over 1,000 patients, we have identified a reoperation rate for regrowth of only 0.1%. These results are due to the significant tissue debulking capability of this procedure, which is durable over the long term, as evidenced by persistent significant reductions in PSA. In our opinion, HoLEP should be considered the gold standard for the treatment of BPH, regardless of prostate size. While

PVP has proven to be effective with regards to improvements in Q_{max}, AUASS, and PVR volume, few control trials exist that assess its long-term durability or compare its effectiveness to other laser treatment modalities. It has been shown that significantly less tissue is removed with PVP as compared to HoLEP, leaving clinicians with valid concerns regarding durability and need for reintervention, especially in patients with larger glands. In a recent meta-analysis, Burke et al. [1••] identified only three randomized control trials comparing PVP to TURP. However, numerous abstracts regarding such trials without published data were identified, suggesting a possible publication bias. Publication of these results in the future certainly would be beneficial in assessing the utility of PVP. Thulium and diode laser techniques for the treatment of BPH show promise, but are still in their infancy. They will require rigorous comparison to TURP, OP, HoLEP, and PVP to determine their safety, efficacy, and durability.

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