PROTOCOL OF A THESIS FOR PARTIAL FULFILLMENT OF DOCTORATE DEGREE IN UROLOGY

Title of the Protocol*:*

Holmium laser enucleation of the prostate versus bipolar transurethral enucleation of the prostate in management of benign prostatic hyperplasia:

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What is already known on this subject? AND
What does this study add?

Benign prostatic hyperplasia (BPH) is one of the most common urinary disorders in elderly males. The symptoms of BPH include impaired physiological and functional well-being, which interferes with daily living.

At present, transurethral resection of the prostate (TURP) is the standard surgical treatment. However, the high rate of complications associated with TURP is a major drawback of this procedure.

Holmium laser enucleation of the prostate (HoLEP) was proven to be effective surgical treatment for BPH with no prostate size limitation with adequate haemostasis, bipolar enucleation of the prostate (BPEP) has been introduced as an alternative energy source with a promising outcome with equal safety and efficacy

1. INTRODUCTION/ REVIEW

Enlarged prostate represents the most common cause of lower urinary tract symptoms (LUTS) in elderly men including irritative, obstructive urinary symptoms or even urinary retention that significantly affects the quality life (QoL). (1)

Transurethral resection of the prostate (TURP) represents the standard surgical technique for the management of benign prostatic hyperplasia (BPH) with a prostate size less than 80 ml. However, considerable morbidities are associated with larger sizes. (1,2)

Endoscopic enucleation of the prostate (EEP) has been recognized as a treatment option for large prostatic adenomas, since first described by Hiraoka et.al, in 1986 (3), it started to gain popularity despite the long learning curve. Many studies have evaluated its efficacy against the gold standard open prostatectomy in large prostate size more than 80ml and showed its safety and efficacy. (2)

EEP represents an anatomical surgical technique resembling a surgeon's finger in open prostatectomy where any energy source that provides adequate haemostasis could be used (4). Many studies concluded that EEP relies on the surgeon's skills rather than the energy source itself (5,6). Holmium laser enucleation of the prostate (HoLEP) was first described by Gilling in 1998 (7) and was proven to be effective with no prostate size limitation with adequate haemostasis (8), recently it has been approved as a standard treatment for large prostatic adenoma (2), bipolar enucleation of the prostate (BPEP) has been introduced as an alternative energy source with a promising outcome with equal safety and efficacy (4,9,10).

Few studies evaluated both techniques, one study was done by Shoma et al. showing no statistical difference regarding safety and efficacy between both techniques(11), another study conducted by Enikeev et al. reported earlier recovery and catheter removal with HoLEP compared to BPEP (9). However, cost-effectiveness was never been evaluated before between both techniques especially in developing countries.

With such scarce information, we aimed through our study to compare these two energy sources in the enucleation procedure of the prostate in terms of safety, efficacy, and cost-effectiveness in the management of BPH in large prostatic adenoma more than 80 ml.

2. AIM/ OBJECTIVES

To compare the clinical outcome in the form of safety, efficacy and cost effectiveness between Holmium laser enucleation of the prostate versus bipolar transurethral enucleation of the prostate

3. METHODOLOGY:
Patients and Methods/ Subjects and Methods/ Material and Methods

Type of Study: prospective randomized clinical trial

Study Setting: Operation ward - Ain Shams University hospitals.

Study Period: 4/2018 till we finish the follow up period

Study Population: Egyptian male patients attending Ain Shams University hospitals Urology clinic

Sample size: It was dose using STATA program, setting alpha error at 0.05 and power at 90% based on results from previous study (Enikeev et.al,2018) that showed a mean catheter removal time in HoLEP group was 1.3 -/+0.6 while in Transurethral electrocautery enucleation group was 3.8 -/+1.7 (9), based on that, the needed sample is 50 cases per group taking in account 20% drop out rate.

Group A: 50 Patients will undergo prostatic resection using HoLEP

Group B: 50 Patients will undergo BPEP

Procedures: each procedure will be done by 2 expert surgeons who performed over 50 cases of enucleation with each energy source. In group 1, the HoLEP procedure will be done under either

general or spinal anesthesia, using a Holmium laser device (cyber Ho 100-watt, Quanta device, Milano, Italy) with a 50-watt power, 2.5 joules and 25 MHz frequency. A 550 nm flexible laser fiber. In group 2, the BPEP procedure will be done by a Karl Storz device, using a bipolar resection loop or button loop according to the availability and surgeon's preference, tissue morcellator with reusable blades (Ricjard Wolf Inc.) will be used to morcellate the prostatic adenoma.

The enucleation technique is nearly similar in both groups regardless of the energy source used, a 26 Fr continuous flow resectoscope (Karl Storz, Germany) with saline irrigation. The procedure will start by incision along the deepest prostatic groove using a bilobed technique where each lobe will be enucleated separately or a trilobed technique to separate a huge median lobe first then to continue as bilobed technique, the incision continues till verumontanum, then we will perform a circumferential marking proximal to the external urethral sphincter for demarcation, lateral incision will be done till the prostatic capsule and start enucleation using a mechanical force of the resectoscope with assisted energy source either Holmium laser or bipolar electrocautery, and then we will proceed anterolateral around the prostatic adenoma, aiming for early apical separation to avoid traction of the external sphincter with mucosal strip to be left intact more proximal to avoid dissemination of energy to the sphincter, anterior commissurotomy to be done to separate each lobe separately the procedure mimic figure enucleation in open surgery by using the resectoscope assisted energy source and then to proceed anteriorly till the bladder neck and then we complete the enucleation from anterior to lateral and move downward to finally separate the adenoma from posteriorly into the bladder, in this way we avoided the sub-trigonal injury or ureteric injury, then we perform the other lobe in the same way, after separation of each lobe we check the ureteric orifices and adequate hemostasis was done, finally morcellator will be used to cut down prostatic adenoma into small chips to be removed.

Inclusion criteria: Men who are fit for surgery and need a surgical resection of the prostate larger than 80 ml including:

1. Bothersome LUTS with an IPSS score over 19
2. Refractory hematuria
3. Upper urinary tract affection
4. Recurrent UTI secondary to prostatic enlargement
5. Maximum uroflow rate (Qmax) below 10 ml/sec.

6. bladder diverticula

7. Urinary retention whether recurrent acute attacks with failure of medical treatment or chronic retention.

Exclusion criteria: Patients with:

1. Neurogenic bladder
2. Previous prostate or urethral surgery
3. Associated urethral stricture
4. Prostate cancer diagnosed by TRUS biopsy
5. Bladder stones,

Ethical Considerations: Approval will be obtained from the ethical committee at Ain shams University before starting the research.

Study Procedures: The patients will undergo the following:

Preoperative:

1) History:

Including medical history, surgical history, drug history, International Prostate Symptom Score (IPSS) and quality of life score (QoL).

2) Clinical Examination:

Including abdominal, pelvic and digital rectal examination (DRE).

3) Laboratory investigations:

As Haemoglobin level, serum creatinine, urea, sodium, potassium and prostate specific antigen (PSA).

4) Radiological investigations:

As pelvi-abdominal ultrasound to assess prostate volume and postvoiding residual urinary volume (PVR).

5) Maximum Flow Rate (Qmax).

Intraoperative: Vital data monitoring, operative time and the need for blood transfusion

Postoperative Follow-up Protocol:

Patients will be evaluated immediately postoperative with vital signs (Blood pressure, Heart rate), abdominal examination, degree of haematuria, haemoglobin level drop and Sodium level changes.

Patients will be re-evaluated at 6 and 12 months postoperatively with the IPSS, QoL, Pelvic U/S (to assess prostate volume and post voiding residual urinary volume (PVR)) ,

Maximum Flow Rate (Qmax) and Total PSA .

Data collection and outcome measures:

Primary outcomes:

1. Catheter removal time

Secondary Outcomes:

1. Operative time, enucleation time
2. Intraoperative need of blood transfusion and hemoglobin drop
3. Conversion to other type of surgeries
4. Post-operative drop in hemoglobin level
5. Duration of hospital stay
6. Postoperative complication: urinary tract infection, stress incontinence, hematuria, urine retention
7. Post voiding residual urine, Qmax, PSA, Prostate volume, QoL and IPSS 1 and 12 months postoperative
8. Delayed complication up to12 months postoperative including urethral stricture, urinary retention, incontinence or bladder neck contracture.
9. Cost effectiveness of each procedure.

Statistical Analysis: The data will be collected, processed and statistically analyzed. Description of the quantitative variable will be done as mean and standard deviation and student t-test will be used to compare the two groups in parametric data while the qualitative data will be shown as frequency and compared using Chi square test. The results will be considered significant with P-value less 0.05 and high significant if less than 0.01, results with P-value ≥ 0.05 will be considered non-significant. Analysis of the data will be done using IBM SPSS software (Statistical program for social science version 21).

2. REFERENCES

1. Oelke M, Bachmann A, Descazeaud A, Emberton M, Gravas S, Michel MC, et al. EAU guidelines on the treatment and follow-up of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. Eur Urol. 2013;64(1):118–40.
2. Oelke M, Bachmann a, Descazeaud a, Emberton M, Gravas S, Michel MC, et al. Guidelines on the Management of Male Lower Urinary Tract Symptoms Benign Prostatic Obstruction (BPO). Eur Assoc Urol 2012. 2012;64:118–40.
3. Hiraoka Y, Akimoto M. Transurethral enucleation of benign prostatic hyperplasia. J Urol. 1989;142(5):1247–50.

4. Neill MG, Gilling PJ, Kennett KM, Frampton CM, Westenberg AM, Fraundorfer MR, et al. Randomized trial comparing holmium laser enucleation of prostate with plasmakinetic enucleation of prostate for treatment of benign prostatic hyperplasia. Urology. 2006;68(5):1020–4.
5. Herrmann TRW. Enucleation is enucleation is enucleation is enucleation. 2016;1–3.
6. Naspro R, Gomez Sancha F, Manica M, Meneghini A, Ahyai S, Aho T, et al. From “gold standard” resection to reproducible “future standard” endoscopic enucleation of the prostate: What we know about anatomical enucleation. Minerva Urol e Nefrol. 2017;69(5):446–58.
7. Fraundorfer MR, Gilling PJ. Holmium:YAG laser enucleation of the prostate combined with mechanical morcellation: Preliminary results. Eur Urol. 1998;33(1):69–72.
8. Elhilali MM. HOLMIUM LASER ENUCLEATION OF THE PROSTATE : MODIFIED TECHNICAL ASPECTS Abdulaziz S . Baazeem , Hazem M . Elmansy Hugh Mostafid , Raj Persad *, Roger Kockelbergh † and. 2010;584–5.
9. Enikeev D, Glybochko P, Okhunov Z, Alyaev Y, Rapoport L, Tsarichenko D, et al. Retrospective Analysis of Short-Term Outcomes After Monopolar Versus Laser Endoscopic Enucleation of the Prostate : 2018;32(5):417–23.
10. Koca O, Keleş MO, Kaya C, Güneş M, Öztürk M, Karaman Mİ. Plazmakinetik vaporizasyon ile transüretral prostat rezaksiyonu karşılaştırması; 6 yıllık sonuçlar. Turk Urol Derg. 2014;40(3):134–7.
11. Shoma A, Nageib M, Nabeeh A. Pd24-05 Holmium Laser (Holep) Versus Bipolar Enuclaetion (Tueb) of the Prostate. an Objective Evaluation Through a Prospective Randomize Study (Prt). J Urol [Internet]. 2016;195(4S):e512–3. Available from: http://dx.doi.org/10.1016/j.juro.2016.02.1770