PROTOCOL OF A Randomized controlled trial (1/10/2020)

Title of the Protocol*:*

Holmium versus Bipolar en bloc transurethral resection of urothelium carcinoma of the urinary bladder

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What is already known on this subject? AND What does this study add?
En bloc resection of bladder tumors (ERBT) may improve staging quality and perioperative morbidity and influence tumour recurrence.(1)

1. INTRODUCTION/ REVIEW

Urothelial carcinoma of the bladder (UBC) is the second most common urological malignancy and represents a growing healthcare problem worldwide [1]. An aging population in Western countries, as well as high tobacco consumption and poor occupational safety regulations in developing nations, has led to increasing incidence rates [2]. Although the vast majority of newly diagnosed bladder cancers are for nonmuscle-invasive disease (NMIBC) and may be treated with endourological procedures, correct initial staging is critical. The quality of transurethral resection of bladder tumors (TURBT) strongly determines patient prognosis and overall UBC treatment costs [3, 4].

Various research groups have already reported promisingresults for laser en bloc resection of bladder tumors (ERBT) [2, 6, 10]. However, not every hospital has access to laser devices, which are expensive. Using an electrical current instead of lasers may be a promising alternative. Indeed, one of the first research groups to show that ERBT is feasible used a modified J-shaped electrode needle [11].

Goals of new strategies should include avoiding second TURBTs and lowering overall treatment regimens. TURBT is one of the most established urological procedures. Modifications have mainly consisted of amendments designed to increase detection rates [5]. Modern laser technology has led to new alternatives to conventional TURBT (cTURBT). The advocates of ERBT have three goals: to improve resection quality, lower perioperative complication rates, and decrease recurrence rates at resection sites. The present study is the first to compare the results of laser and electric en bloc resection of bladder cancer with respect to the aforementioned goals.

To compare the clinical outcome in the form of safety and efficacy between Holmium and bipolar transurethral en bloc resection of urinary bladder tumors.

2. AIM/ OBJECTIVES

To compare the clinical outcome in the form of safety and efficacy between Holmium and bipolar transurethral en bloc resection of urinary bladder tumors.

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: 6/2020 till we finish the follow up period

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

Sample size: 75

Group A: 35 (represent Holmium en bloc resection)

Group B: 35 (represent bipolar en bloc resection)

After obtaining informed consent, patients will be randomized with a 1:1 ratio using sealed envelopes that will be prepared by the department's ethical committee into 2 groups, group 1 represent the Holmium en bloc resection procedure while group 2 represents bipolar en bloc resection. Patients will be blinded to the type of intervention as well as the data collector and the statistician.

Intervention: all procedures will be done by an expert surgeon who performed over 50 cases of en bloc urinary bladder tumor resection with each energy source. In group A, Holmium en bloc resection procedure will be done under either general or spinal anesthesia, using a Holmium laser device (Cyber Ho, Quanta device, Milano, Italy). We will use a 30-40-watt power, 1-2 joules and 20-30 MHz frequency for Group A and bipolar en bloc resection for Group B. A 550 nm flexible laser fiber will be used in group A and a bipolar resection loop for group B.

A circular incision will be made around the tumor; a distance will be maintained of approximately 5–10 mm from the tumor itself. Subsequently, the tumor will be bluntly dissected from the bottom while respecting the incision line. Care is to be taken to include detrusor muscle. HoLRBT will usually be set to 1.0–2.0 J and 15–30 Hz, generating total energy levels of 20–40 W.

All patients will receive a transurethral catheter for postoperative bladder irrigation. Bladder irrigation will be started immediately after finishing surgery. Patients will receive early instillation therapy (EI) received 40 mg of mitomycin C (MMC) within the first 12 h after surgery. Tumor specimen will be preserved in formalin solution and sent for histopathological examination.

1 month after the procedure, diagnostic cystoscopy will be performed for all patient to evaluate tumor complete resection and search for any residual tumors.

Inclusion criteria: Adult patients of both sexes presented with urinary bladder tumor aiming for complete resection as diagnosed by Ultrasound with or without CT prior

histopathological assessment.

Exclusion criteria: Patients with signs of extravesical tumor extension where complete resection will not beneficial or unable to proceed to complete resection due to huge tumor burden either huge single tumor more than 5 cm or multiple tumors that are not candidate for complete resection.

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, previous oncological history if present.

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, contrast enhanced CT scan on Abdomen and pelvis.

Intraoperative: Vital data monitoring, operative time and the need for blood transfusion, obturator reflex, conversion to trans-urethral resection of the bladder tumor. Ay intraoperative complication will be recorded like bladder perforation.

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.

Patients will be re-evaluated at 6 weeks and then regular follow up every 3 months for 1 year to evaluate tumour recurrence by ultrasound and diagnostic cystoscopy.

Data collection and outcome measures:

Primary outcomes:

main primary outcomes have been selected for our study

1. Conversion to the TURBT

Secondary Outcomes:

1. Operative time
2. Tumor size and stage
3. Presence of detrusor muscle in resected sample
4. Resected specimen's edge
5. Intraoperative complication like need for blood transfusion, bladder perforation
6. Incidence of obturator reflex
7. Post-operative drop in hemoglobin level, or hematuria
8. Post-operative catheterization time in hours
9. Postoperative irrigation time in hours
10. Recurrence rate of tumors according to time interval of postoperative follow up by diagnostic cystoscopy 1 month after enucleation.
11. Recurrence rate of tumors according to tumor location (same site recurrence Vs new site or both)

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).

4. REFERENCES

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