Ministry of Higher Education and Scientific Research University of Baghdad Institute of Laser for Postgraduate Studies



Efficacy and Safety of Ho:YAG Laser Used in Ureteroscopic Lithotripsy for Removal of Ureteral Stones in Iraqi Patients.

A dissertation submitted to the institute of laser for postgraduate studies/ Baghdad university, as a partial fulfillment of the requirements for the Diploma degree of laser application in medicine, (Urological surgery).

> By: Mohammad Jabbar Al-Rubayee M.B.ch.B, H.D.G.S, F.I.C.M.S. (URO). Supervisor: Dr. Dhergam Nihad Mohammed M.B.Ch.B., H.D.G.S., F.I.C.M.S., Hi.D.L.M.

2022 A.D.

1443 A.H.



سورة البقرة ايه 32

Certification

I certify that this thesis was prepared under my supervision at the Institute of Laser for Postgraduate Studies, University of Baghdad, as a partial fulfillment of requirements for the degree of "Higher Diploma in Laser in Medicine/ Urology".

Signatur	e:		
Name	: Dr. Dhergham Nihad Mohammed		
	M.B.Ch.B., H.D.G.S., F.I.C.M.S., H	i.D.L.M.	
Title	:		
Address	: Institute of Laser for Postgraduate of Baghdad.	Studies, University	
Date	: / / 2022		
(Supervis	sor)		

In view of the available recommendation, I forward this thesis for debate by Examining Committee.

Signature:Name: Dr. Hanan Jaafar TaherTitle: Asst. Prof. Head of the Scientific Committee.Address: Institute of Laser for PostgraduateStudies, University
of Baghdad.Date: 26 / 1 / 2022

Examining Committee Certification

We certify that we have read this dissertation (Efficacy and Safety of Ho:YAG Laser Used in Ureteroscopic Lithotripsy for Removal of Ureteral Stones in Iraqi Patients) as an examining committee.

We examined the study in its contents, and in our openion, it is adequate with the standards as a dissertation for the (Diploma Degree of Laser Applications in Medicine/ Urology).

Signature:	Signature:
Name :	Name :
Title :	Title :
Address : Institute of Laser for	or Address : Institute of Laser for
Postgraduate Studie	Postgraduate Studies,
University of Bagho	lad. University of Baghdad.
Date : / / 2022	Date : / / 2022

Approved by the Deanship of the Institute of Laser for Postgraduate Studies/ University of Baghdad.

Signature:

- Name : Dr. Hussein A. Jawad.
- Address : Dean of the Institute of Laser for Postgraduate Studies, University of Baghdad.

Date : / / 2022

Acknowledgments

* My deepest gratitude goes to professor Hussain Ali Jwad, dean of the institute of laser for post graduate studies, who has been an enormous help in many ways, as a teacher, in the planning and in the practical details of the study. His endless patience, supervision, advises, and cooperation were invaluable.

* I do very highly appreciate the important support given to me by Dr. Dhurgham Nihad, both as a teacher, and in connection with the study, particularly the assessment of the methodology and results in addition to the evaluation of the final draft. His kind supervision, advises and cooperation were invaluable to me. * I am grateful to Dr. Layla Muhammad Hassan and Dr. Ahmed Muhammad Hassan, lecturer in the institute, for her kind follow up and never ending patience during preparation of the thesis.

*My thanks to Mr. Ahmed Ghalib, chief of the theater sub staff, ENT department, Al Yarmook teaching hospital, for his particular skill helping in reproduction of photographs of the procedure .

Dedication

* To my late father, "may god bless his sole" *To the teaching staff of the institute of laser for postgraduate studies, who made it possible for medicine to join physics in a very pleasurable and fruitful experience.

List of Contents

List of contents	i
List of tables	ii
List of abbreviations	iii
Abstract	iv
introduction	2
Aim of the study	4
Material and methods	6
Laser Lithotripsy Equipment	8
Operative instrumentation and technique	8
Results	12
Discussion	18
conclusion	23
references	24

List of Tables

		Page
Table 1	Patients' and stones' characteristics: proximal versus distal ureteral calculi in 88 patients treated with ureteroscopicHo:YAG laser lithotripsy	13
Table 2	Operative characteristics, outcome and complications of ureteroscopicHo:YAG laser lithotripsy in 88 patients: proximal versus distal ureteral calculi	14
Table 3	Patients and Stones Demographics for 51 patients with proximal ureteric stones exposed to ureteroscopicHo:YAG laser lithotripsy classified as small (<10 mm) and large (>10 mm) stones	15
Table 4	Operative characteristics of 51 patients with proximal ureteric stones exposed to ureteroscopicHo:YAG laser lithotripsy classified as small (<10 mm) and large (>10 mm) stones	16

List of Abbreviations

HO/YAG	Holmium Yag
URS	Uretero-Reno Scope
EAU	European Association of Urology
AUA	American Urologic Association
SWL	Shock Wave Lithotripsy
CBC	Complete Blood Count
PCR	Polymerase Chain Reaction
SFR	Stone Free Rate
OR	Operation Room

Abstract

Background: Today, Laser lithotripsy is a cornerstone in endourological interventions . the use of Ho:YAG laser has led to capability of managing larger stone sizes throughout the whole upper urinary tract (ureters and pelvicalyceal system).

Aim of the study: to evaluate the efficacy and safety of Ho:YAG laser lithotripsy in ureteroscopic management of ureteral calculi in different locations along the ureters in a sample of Iraqi patients.

Patients and Methods:88 Iraqi patients with ureteric stones have been managed endoscopically with ureteroscopicHo:YAG laser lithotripsy in two private hospitals in Baghdad (Al Zahraa&Bayrut hospitals) between May 2021 and January 2022. Study endpoint was the number of treatments until the patient was stone-free. Patients were subdivided according to the location of their stones into Group I (distal ureteric stones, 51 patients) and group II (proximal ureteral stones, 37).

Results: Overall stone free rate for both groups was 95.8%. The mean number of endoscopic laser lethiotripsy was $1.1 \pm 0.1 (1-3)$ for proximal calculi and 1.0 ± 0.0 for distal calculi. The initial treatment in patients with distal ureteral calculi was more successful than initial treatment for patients with proximal calculi (100% vs. 82.40%, respectively, P = 0.008). However and after the second laser procedure no significant difference in the stone free rate was noticed for stones smaller versus larger than 10 mm (100% versus 94.1%, P = 0.13). complications were reported in Clavien grading and it was of an overall rate of 7.9% (Clavien II

und IIIb). Also stone location did not have an impact of the overall and grade-adjusted complication rates. No specific laser beam induced complications were reported.

Conclusions: according to our evidence we concludes that Ho:YAG laser shows the safety and efficacy for managing ureteral calculi and it appears to be an adequate tool to disintegrate these calculi independent of primary location. Using both semirigid and flexible ureteroscopes in additional to other required and appropriate endourologic tools could likely improve the stone clearance rates for proximal calculi regardless of stone-size as well.

CHAPTER ONE

Introduction and Basic Principles

Introduction

Laser history, physics, and applications:

A laser is a device that emits light through a process of optical amplification based on the stimulated emission of electromagnetic radiation. The word "laser" is an acronym for "light amplification by stimulated emission of radiation"^[1]. The first laser was built in 1960 by Theodore H. Maiman at Hughes Research Laboratories, based on theoretical work by Charles Hard Townes and Arthur Leonard Schawlow^[2].

A laser differs from other sources of light in that it emits light which is coherent. Spatial coherence allows a laser to be focused to a tight spot, enabling applications such as laser cutting and lithography. Spatial coherence also allows a laser beam to stay narrow over great distances (collimation), enabling applications such as laser pointers and lidar. Lasers can also have high temporal coherence, which allows them to emit light with a very narrow spectrum. Alternatively, temporal coherence can be used to produce ultra-short pulses of light with a broad spectrum but durations as short as a femtosecond^[2].

Lasers are used in optical disc drives, laser printers, barcode scanners, DNA sequencing instruments, fiber-optic, semiconducting chip manufacturing (photolithography), and freespace optical communication, laser surgery and skin treatments, cutting and welding materials, military and law enforcement devices for marking targets and measuring range and speed, and in laser lighting displays for entertainment. Semiconductor lasers in the blue to near-UV have also been used in place of lightemitting diodes (LEDs) to excite fluorescence as a white light source. This permits a much smaller emitting area due to the much greater radiance of a laser and avoids the droop suffered by LEDs; such devices are already used in some car headlamps^[3].

Laser medicine consists in the use of lasers in medical diagnosis, treatments, or therapies, such as laser photodynamic therapy, photo rejuvenation, and laser surgery^[4].

Lasers used in medicine include in principle any type of laser, but especially:

- CO2 lasers, used to cut, vaporize, ablate and photocoagulate soft tissue.
- Diode lasers.
- Dye lasers.
- Excimer lasers^[5].
- Fiber lasers.
- Gas lasers.
- Free electron lasers.
- Semiconductor diode lasers^[6].

Examples of procedures, practices, devices, and specialties where lasers are utilized include:

- Angioplasty.
- Cancer diagnosis.
- Cancer treatment^[7].

- Dentistry.
- Cosmetic dermatology such as scar revision, skin resurfacing, laser hair removal, tattoo removal^[8].
- Dermatology, to treat melanoma.
- Frenectomy.
- Lithotripsy.
- Laser mammography.
- Medical imaging.
- Microscopy.
- Ophthalmology (includes Lasik and laser photocoagulation).
- Optical coherence tomography.
- Optogenetics.
- Prostatectomy.
- Plastic surgery, in laser liposuction, and in treatment of skin lesions (congenital and acquired) and in scar management (burns and surgical scars)^[9].
- Surgery, to cut, ablate, and cauterize tissue^[10].

Laser technologies are well established and gold standard modalities for application on lithotripsy ^[11]. The introduction of the Ho:YAG laser have broadened the indications for ureteroscopic stone managements (URS) to include larger stone sizes throughout the whole upper urinary tract ^[12]. Furthermore, recent developments in the design of ureteroscopy and endoscopic instruments have enabled the URS to replace the open surgery treatments for urinary calculi over the last decade as a minimally invasive modality.

Stone Fragmentation by the Holmium Laser

Energy emitted from the laser fiber following holmium laser activation leads to the formation of a vapor channel (cavitation bubble) through which the laser radiation is transmitted. The size of the bubble formed is directly proportional to the pulse energy (PE) and laser fiber size. A photothermal mechanism and chemical decomposition are the major contributing factors for stone fragmentation. The energy produced during bubble collapse (shock wave) has a limited role in stone fragmentation. Recently, advances in pulse modulation have resulted in the development of the "Moses technology" in which the laser emits part of the energy to create an initial bubble, and the remaining energy is discharged once the bubble is formed, so that it can pass through the already formed vapor channel. This new technology was adopted from the previously described phenomenon of holmium vapor channel is created.

Stone management Guidelines of the European Association of Urology (EAU) and American Urological Association (AUA) have been continuously updating according to the development technologies in ureteral stone managements. According to these guidelines, management of symptomatic ureteral calculi is with extracorporeal shock wave lithotripsy (SWL) and URS and remains the two primary treatment modalities for this category ^[13]. This was based on the AUA and EAU meta-analysis. There was no difference in stone-free rates between SWL and URS after all primary procedures in the proximal ureter (82% versus 81%, respectively). This was dependent on the stone size. For small proximal stones (<10 mm), SWL stone free rate was higher than URS (90% versus 80%, respectively), however, for larger stones (>10 mm), URS stone free rate was superior (79% versus 68%, respectively). Interestingly, URS yields better stone-free rates for distal stones independent of the size (94.5%5 versus 74%, respectively) ^[13].

We assessed the safety and efficacy of Ho:YAG laser during endoscopic treatment of ureteral calculi whether with a semirigid or flexible ureteroscopy on the improvement of stone-free rates of proximal and distal ureteral stones. In addition, the influence of stone size on the outcome following this ureteroscopic laser lithotripsy was studied for proximal ureteral stones (≤10 mm vs. > 10 mm).

The safety of laser technology is dependent on the safety and skill of the surgeon operating it. It is important to allocate a suitable qualified technical assistant/ operator to ensure the safety use of lasers ^[35–37]. His duties include; review of protective measures taken by all staff, approving and maintaining all protective equipment, ensuring that all the staff is properly educated and trained. He is recommended to all operations of laser class 3B and 4 in most international regulations ^[35]. Safety behaviors include e.g. clear communications between personnel in the operating room and isolated field with closed doors, which should be marked with attention light signals. Safety equipment like goggles and fiber fixation tools and laser safety/emergency button should be available ^[38]. Personnel and surgeons should treat

operation equipment and catheters with caution to avoid any parallel damages ^[38].

Aim of the study

To assess efficacy and safety of Ho:YAG laser lithotripsy during retrograde ureteroscopic management of ureteral calculi in different locations in a sample of Iraqi patients.

CHAPTER TWO

Materials and methods

Material and Methods

Data of 88 patients (25 women and 63 men) who underwent Ho:YAG laser lithotripsy for ureteral stones over seven months from May 2021 to Januar 2022 at two private hospitals in Baghdad were prospectively reviewed by one experienced surgeon, informed consents were taken from all patients.

These were classified into 2 groups according to position of ureteric stones; distal ureteral stones below the pelvic brim (51 patients, group I) and proximal ureteral stones located above the pelvic brim (37, group II).

All patients underwent pre- and post-operative laboratory examinations, (urinalysis, renal function and electrolytes, CBC, virology, Covid-19 PCR test) . Patients with preoperative urinary tract infections received broad spectrum antibiotic therapy until urinalysis is obtained documenting no infection. Stone size was determined based on the preoperative plain abdominal x-ray or CT examinations. Total linear calculus diameter equals the measured largest linear dimension (transverse or cranio-caudal section) or the sum of the linear measurements of individual calculi for multiple ureteral calculi in one system.

Postoperative evaluation included plain abdominal films taken within few hours after treatment before leaving the hospital. Patients were followed up for a minimum of 3 months with abdominal ultrasonography, plain x-rays or CT scans to exclude complications and to verify the residual stone burden, if present.

Assessment of the procedure outcomes included stone free and complication rates. Stone freedom was defined as pulverization of all calculi to fine dust or fragments not larger than 2 mm in diameter on x-ray imaging at the end of procedure. This was considered to be too small to extract and was liable to pass spontaneously ^[13]. Patients requiring re-procedures or SWL during follow-up were considered as treatment failures. Operative time was calculated from begin of cystoscopy till the removal of all equipment.

Laser Lithotripsy Equipment

Ho:YAG laser system (Calculase III, Karl Storz, Tutlingen Germany) with laser fiber diameter of 365 μ m was used with the semirigidureteroscopes. Fibers with 220 μ m diameter were used for the flexible ureteroscopes to avoid compromising both irrigation flow and the maximal endoscope tip deflection.



Operative instrumentation and technique

The ureteroscopic manipulations of the upper urinary tract are adequately described ^{[12, 14, 15}.] here in brief;

Under general anesthesia, dorsal lithotomy position, and after sterilization and sterile coverings, a diagnostic 22 F cystoscopy was done. Spinal anesthesia are not a common approach in our department according to patients will and anesthists advice general anesthesia. This is followed with identification of the ureteral orifice and its cannulation with 0.038-inch hydrophilic guide wire under fluoroscopic guidance. A 16 F transurethral catheter is inserted for drainages to prevent bladder distension during continuous irrigation.

Ureteroscopic procedures were done either with semi-rigid ureteroscopes (Karl Storz, Tutlingen Germany); (diameter from 7 F to 9,5 F) or 7.5 F flexible ureteroscopes implying double active tip deflection mechanism and maintaining a 3.6 F-working channel (Zhuhai PUSEN Medical Technology Co.,Ltd., Zhuhai, China). The flexible ureteroscope was positioned via a 12 F ureteral access sheath that was placed over the guide wire. These ureteral access sheaths allow frequent passage of the ureteroscope to the upper urinary tract, enable optimal visualization, maintain low intra-renal pressure and hasten calculi fragments extraction. Ureteric manipulations were aiming to direct laser shock impulses to the middle of stones and their fragments under direct vision to allow fragmentation without ureteric injuries.





Different Ureteroscopy Stents Basket stone removal was considered for fragments >2 mm in size after laser fragmentation to achieve samples for stone composition analysis. Staged therapy after 6-8 weeks was considered in case of a bad visibility limiting further access to rest fragments or when remaining stone burden seems larger to still be removed at the same session. Bad visibility was mainly due to macrohematuria as well as stone dust leading to turbidity of fluid media and obscuring vision.

Ureteric stent was placed based on following criteria;

- 1. Prolonged procedures (>60 minutes),
- 2. Large amount of stone debris, or
- 3. Evident ureteral edema/trauma and prior insertion of an access sheath.

Complications were classified according to the modified Clavien grading system ^[16].

CHAPTER THREE

Results, discussion, conclusions and recommendations

Results

No significant difference in median patient's age between the two groups (53.9 vs. 53.3 year) was found. A part of patient cohorts had undergone previous interventions for calculus disease (39.2% vs. 40% for group I vs. II, respectively). Patients with proximal ureteral stones had larger calculi (median diameter = 10.70 mm) vs. those with distal ones (median 8.24 mm) and were more likely to have DJ-stent at presentation (37.3% vs. 16.2%, respectively). Multiple stones were found in three patients of 1st group versus five patients in 2nd group (Table 1). Table 1 Patients' and stones' characteristics: proximal versus distal ureteral calculi in 88 patients treated with ureteroscopicHo:YAG laser lithotripsy

Number of patients	Proximal stones 51	Distal stones 37	P value
Gender:			
male/female	40/11	23/14	0.095 NS
Age (years)*	53.9±1.8	53.3 ± 3.0	0.246 NS
Stone diameter (mm)*	10.7 ± 0.7	8.2 ± 0.6	0.0001 Sig.
Stone burden (mm ²)	110.7 ± 17.6	64.4 ± 11.6	0.0001 Sig.
Number of patients with multiple stone burden (%)	3 (5.9)	5 (13.5)	0.219 NS
Number of patients with prior treatments (%)	20 (39.2)	15 (40)	0.900 NS
Number of patients with preoperative double-J stents (%)	19 (37.3)	6 (16.2)	0.031 Sig.

Mean operative time was 81.3 ± 4.5 minutes (25–140 minutes) in the first group and 65.7 ± 3.8 minutes (25–120 minutes) in the 2nd group.

Operative characteristics are shown in Table 2. Complete fragmentation during single procedure was achieved in all patients of the 1st group (100%). In the 2nd group, only 42 patients (82.4%) were rendered stone free by a single laser lithotripsy procedure. A staged procedure was necessary in 9 patients due to large residual stone burden and constricted visibility. After a second laser lithotripsy procedure, 48 (94.1%) patients were rendered stone free. Third procedure was necessary in one patient. Three patients (5.8%) underwent SWL as they wished this trial before a third session and it was successful. Ureteral stents were placed at the end of 81 (86.2%) procedures to prevent transient obstruction.

Table 2 Operative characteristics, outcome and complications of ureteroscopicHo:YAG laser lithotripsy in 88 patients: proximal versus distal ureteral calculi

Number of patients	Proximal stones 51	Distal stones 37	P value
Ureteroscope number of procedures (%)			
Semirigid	12 (21.1)	37 (100)	
Flexible	2 (3.5)		
Combination	43 (75.4)	_	
Operation time (min)*	81,3+4,5	65.7 ± 3.8	0.0001 Sig.
Laser time (sec)*	379.8 + 50.8	154.3±38.1	0.0001 Sig.
Total energy (J)*	2528,8±422.6	1148.5±400. 7	0.0001 Sig.
Number of patients with postoperative stent (%)	50 (87.7)	31 (83.8)	0.014 Sig.
No of intra operative complications (%)	1 (1.8)	2 (5.4)	0.379 NS
No of early post-operative complications (%)	1 (1.8)	3 (8.1)	0.172 NS
Overall SFR per patient	48 (94.1)	37 (100)	
SFR after first treatment per patient (%)	42 (82.4)	37 (100)	
SFR after second treatment per patient (%)	48 (94.1)		
No of laser procedures*	1.1±0.1	1.0 ± 0.0	0.0028 Sig.

The overall stone free rate for both groups was 95.8%. The mean number of all laser procedures was 1.07 ± 0.003 , in the proximal ureter 1.1 ± 0.1 and in the distal ureter 1.0 ± 0.0 (P = 0.027). More successful initial treatments were done in the distal ureteral versus proximal calculi (100% vs. 82.40%, respectively).

There were no statistical significant differences in patients' demographics and operative characteristics when procedures done for proximal ureteral stones were compared as regards stones' sizes ($\leq 10 \text{ mm vs.} \geq 10 \text{ mm}$ in diameter) (Table 3). There was no statistical significant difference between stone free rates after the first versus second laser lithotripsy in 2nd group for stones smaller versus larger than 10 mm (94.1% vs. 100%, respectively, P =0.139) (Table 4).

Table 3 Patients and Stones Demographics for 51 patients with proximal ureteric stones exposed to ureteroscopicHo:YAG laser lithotripsy classified as small (<10 mm) and large (>10 mm) stones

	Proximal ≤ 10 mm (n = 31)	Proximal > 10 mm (n = 20)	P value
Gender (n)			
Male	24 (77.4)	16 (80)	P value
Female	7 (22.6)	4 (20)	0.827 NS
Age (years)	53.1 ± 2.2	55.3 ± 3.0	0.785 NS
Mean stone diameter (mm)*	7.4±0.3	15.8 ± 1.1	0.0001 Sig.
Mean stone burden (mm ²)*	45.2 ± 3.9	212.0 ± 34.0	0.0001 Sig.
No of patients with multiple stone burden (%)	2 (6.5)	1 (5)	0.830 NS
No. of patients with prior treatments (%)	11 (35.5)	9 (45)	0.500 NS
No. of patients with preoperative double-J stents (%)	12 (38.7)	7 (35)	0.789 NS

Table 4 Operative characteristics of 51 patients with proximal ureteric stones exposed to ureteroscopicHo:YAG laser lithotripsy classified as small (<10 mm) and large (>10 mm) stones

	Proximal ≤ 10 mm (n = 34)	Proximal > 10 mm (n = 23)	P value
Ureteroscope			
Semirgid	7 (20.6)	5 (21.7)	
Flexible	2 (5.9)	-	0.963 NS
Combination	25 (73.5)	18 (78.3)	
Mean OR time (min.)	80.7 ± 6.5	82.3±5.9	0.378 NS
Mean laser time	349.5±69.9	434.3 ± 66.9	0.0001 Sig.
Mean total energy (J)	2480.3 ± 585.8	2619.3±547.1	0.4002 NS
Postoperative stent (n)	31 (91.2)	19 (82.6)	0.830 NS
Intra operative complications (n)	1 (2.9)	0 (0)	
Post operative complications (n)	1 (2.9)	0 (0)	
Overall SFR per patient	28/31 (90.3)	20/20 (100)	
SFR after first treatment per patient	25/31 (80.6)	17/20 (85)	0.331 NS
SFR after second treatment per patient	28/31 (90.3)	20/20 (100)	
Laser rate	1,1±0,1	$1,2\pm0,1$	0.001 Sig

Overall complication rate was 7.9%. Perioperative complications were recorded in three and four patients in the 1st versus 2nd group, respectively (Table 2). There were no major perioperative complications noted in this series. All intraoperative complications were classified as clavien grade IIIa (small mucosal laceration without leakage), while all early postoperative complications were Grade II (febrile urinary tract infections). Ureteral mucosal injuries were seen in three patients (1 proximal, 2 distal stones) with impacted stones and were managed conservatively resolving within six weeks. Cases of urinary tract infection responded successfully to parenteral antibiotics. Overall and grade-adjusted complication rates did not depend on the stone location. None of these complications was due to laser energy (ureteroscopic tip laceration of mucosa during advancement, Dormia Baski retrieval of stone fragments, or due to submucosal passage of guide wire tip).

Stone analysis was available from 75 patients and revealed calcium oxalate monohydrate (COM) (78.7%), combination of calcium oxalate and phosphate (8.0%), pure calcium phosphate apatite (8%) and >50% uric acid stones (5.3%). Current study showed no influence of stone composition on laser efficacy or complication rates.

The Ho:YAG laser was capable to fragment all stone compositions to acceptable amounts of debris. Mean laser time per patient was longer in the proximal group (379.8 vs. 154.3 seconds)/ table 2. Accordingly, the meantotal energy was 2480.3 ± 585.8 vs. 2619.3 ± 547.1 J, respectively (P = 0.483).

Discussion

Over the last decade, lasers have been increasingly used for intracorporial lithotripsy ^[11]. Ho:YAG laser has become one of the most widely accepted lasers for this purpose as compared to ultrasonic, pneumatic and other laser devices (e.g. pulsed dye laser, Alexandrite laser and the frequency-double-doubled double-pulse neodymium:yttriumaluminium garnet (FREDDY) laser) ^[17].

Technical advancements in instruments (semi-rigid ureteroscopy), the advances of the new generation flexible ureteroscopes with greater angles of maximum active tip deflection and improved durability in addition to the introduction of laser lithotripsy with its precise and powerful thermal decomposition mechanism and its excellent safety profile with the ability of delivering laser energy through small, flexible fibers have blazed the trail for fragmentation of stones throughout the upper urinary tract ^[12, 18–21].

The meta-analysis of the EAU/AUA nephrolithiasis guideline panel demonstrated that URS yields significantly greater stone-free rates for the majority of stone stratifications ^[13]. There were a

change in trend in the nephrolithiasis guidelines, which recommended SWL for proximal ureter stones <10 mm (1997), to deeming the ureteroscopic management as a first choice therapy for those stones to improve efficacy and reduce morbidity. However, both guidelines still recommend SWL and ureteroscopy as an option for distal ureteric stones ^[13, 22].

The current study included cohort of patients with ureteral calculi requiring lithotripsy for stone retrieval. We showed a stone-free rate for calculi in the proximal ureter after one and two procedures of 82.4% and 94.1%, respectively. This confirms previous reports in literature about safety and efficacy of ureteroscopicHo:YAG laser treatment in treating proximal and distal ureteric stones ^[23–25]. In their meta-analysis, Tiselius et al. reported that re-treatment rates for ureteral stones using URS are lower than SWL (2.2% vs. 12.1%, respectively). This advantage was counter-balanced by the higher need for anesthesia (94.3% vs. 28.3%, respectively) ^[26].

The current stone-free rate of Ho:YAG laser lithotripsy in the proximal ureter was not significantly different when comparing stones with different sizes ($\leq 10 \text{ mm vs.} \geq 10 \text{ mm}$ in diameter or multiple stones) postulating that primary stone size does not influence the efficacy of the procedure. This is comparable to previous reports showing stone free rates of 78% to 96.5% after the first procedure and 88% to 100% after the second laser lithotripsy ^[13, 23–25]. The high success rate for distal ureter stones

in the current series after a single procedure is consistent with the literature that shows stone-free rates of 97-100% ^[20, 23, 25].

The current mean operative time (81.3 vs. 65.7 minutes, P = 0.017) and laser time (379.8 vs. 154.3 seconds, P = 0.009) was shorter for distal ureteral calculi than for proximal calculi. This could be explained with the larger stone burdens and our effort to completely "melt down" the calculi with laser and the effort to remove as much stone debris as possible leaving no significant fragments. Furthermore, combination of semirigid and flexible ureteroscopy in 75.4% of patients with proximal calculi may add another explanation.

A second procedure was indicated in some of our cases. Many causes attribute to the retrograde stone fragment migration occurring during the treatment of proximal ureteral stones. Gravitational forces, pressurized irrigation, stone retropulsion during lithotripsy, failure to access the calculi or large stone burden may bring the stone out of reach for the semi-rigid ureteroscope^[30, 33, 37, 38]. The use of the flexible ureteroscopes in combination with access sheaths provides consistent, reliable and unimpaired access to the upper urinary tract facilitating the treatment of complex proximal calculi and migrated stone fragments and ensuring the clearance of all stone fragments not deemed to pass spontaneously in the same ureteroscopic session ^[21, 29, 30]. Clear vision to ease direct access to the targeted stones is essential during ureteroscopic laser lithotripsy. Decreased

visibility leads to prolonged operative time and increase the potential risk of injuring the ureter or the flexible ureteroscope.

Generally, routine postoperative ureteral stenting after ureteroscopic laser lithotripsy is still a subject of debate. On one hand, stent-related morbidities like bladder irritation and mild back discomfort during urination were demonstrated to constrain postoperative quality of life. On the other hand, ureteral stenting was thought to prevent postoperative urinary sepsis by avoiding sudden ureteral obstruction by calculus fragments, blood clots or ureteral mucosal edema. The clear indications for stenting include ureteral injury/stricture, solitary kidney, renal insufficiency or large residual stone burden ^[13]. Furthermore, several prospective randomized controlled trails comparing a non-stented versus stented ureteroscopic lithotripsy reported the same result ^[31–33]. Ureteral stenting after uncomplicated ureteric procedures is not a routine at our institution. However, a transient ureteral stent is placed in all patients who had ureteral dilatation through the insertion of access sheath, presented with large and/or impacted calculi irrespective of the location. This explains the current high postoperative stenting rates (87.7% vs. 83.8%, respectively).

URS and laser lithotripsy have proved safety even where SWL is likely to fail or contraindicated. Major complications are not common during the procedure ^[13, 34]. Minor intra or postoperative complications were reported in a range from 0 to 13% and consist primarily of pain or urinary tract infection. Ho:YAG laser related complications are as low as 1% ^[18, 20, 23, 34]. There were no major

complications observed in the current series. Further, there was no significant difference of intra and postoperative complications between both groups. Both cases of ureteral mucosal injuries occurred in patients with impacted distal ureteric stones and were successfully managed conservatively within six weeks.

The wave length of the Ho:YAG laser varies from 2050 nm to 2100 nm depending on the apparatus(manufacturer technical preference). Pulse duration (150-800 µs) depends on the pulse energy, and could be selected only in the latest laser systems. Ho:YAG laser light is mainly absorbed by tissue water, so that it has a mean optical penetration depth of 0,2 mm. The mechanism of its laser induced effect for lithotripsy includes the "Moses" effect, (bubble formation in front of stones) and thermal vaporization of the stone water, thus during expansion fragmentation occurs. This mechanism is accompanied with small fragments and many pulses had to be applied, compared to short pulsed lasers (e.g. Q-switch) which produce large fragments in response to fewer pulses. The later laser lithotripsy is attributed to the shock wave effect of the laser resulting from cavitationcollapse mechanisms^[39]. Thus with using Ho:YAG laser pulses, the repulsion effect is reduced compared to the short-pulse laser lithotripsy ^[39].

Conclusion

Ho:YAG laser lithotripsy during URS appears to be an adequate tool to disintegrate all kinds of ureteral calculi with low complication rates. The combination of semirigid and flexible ureteroscopes ensures direct access to all migrated, repulsed or floated stone fragments. Destruction of large calculi may be time consuming prolonging operative time and general anesthesia, and could be an indication for staged therapy in some cases.

References

- 1. Taylor, Nick (2000). Laser: The Inventor, The Nobel Laureate, and The Thirty-Year Patent War. Simon & Schuster. ISBN 978-0684835150.
- Finley, J.J. (January 13, 2016). "Monolithically Integrated High-β Nanowire Lasers on Silicon". Nano Letters. 16 (1): 152–156. Bibcode:2016NanoL..16..152M. doi:10.1021/acs.nanolett.5b03404. PMID 26618638.
- Costela A, Garcia-Moreno I, Gomez C (2016). "Medical Applications of Organic Dye Lasers". In Duarte FJ (ed.). Tunable Laser Applications (3rd ed.). Boca Raton: CRC Press. pp. 293–313. ISBN 9781482261066.
- Popov S (2016). "Fiber Laser Overview and Medical Applications". In Duarte FJ (ed.). Tunable Laser Applications (3rd ed.). Boca Raton: CRC Press. pp. 263–292. ISBN 9781482261066.
- Duarte FJ (2016). "Broadly Tunable External-Cavity Semiconductor Lasers". In Duarte FJ (ed.). Tunable Laser Applications (3rd ed.). Boca Raton: CRC Press. pp. 203– 241. ISBN 9781482261066.
- Haub J G; He Y; White RT (2016). "Spectroscopic Applications of Pulsed Tunable Optical Parametric Oscillators". In Duarte FJ (ed.). Tunable Laser, Applications

(3rd ed.). Boca Raton: CRC Press. pp. 17–142. ISBN 9781482261066.

- Penzkofer A; Hegemann P; Kateriya S (2018). "Organic dyes in optogenetics". In Duarte FJ (ed.). Organic Lasers and Organic Photonics. London: Institute of Physics. pp. 13–1 to 13–114. ISBN 978-0-7503-1570-8.
- Przylipiak AF, Galicka E, Donejko M, Niczyporuk M, Przylipiak J (Oct 2013). "A comparative study of internal laser-assisted and conventional liposuction: a look at the influence of drugs and major surgery on laboratory postoperative values". Drug Design, Development and Therapy. 7: 1195–200. doi:10.2147/DDDT.S50828. PMC 3798112. PMID 24143076.
- 9. Jelinkova H, ed. (2013). Lasers for Medical Applications: Diagnostics, Therapy, and Surgery. Oxford: Woodhead. ISBN 978-0-85709-237-3.
- Chu, Steven; Townes, Charles (2003). "Arthur Schawlow". In Edward P. Lazear (ed.). Biographical Memoirs. Vol. 83. National Academy of Sciences. p. 202. ISBN 978-0-309-08699-8.
- 11. Breda A, Ogunyemi O, Leppert JT, Schulam PG: Flexible ureteroscopy and laser lithotripsy for multiple unilateral intrarenal stones. Eur Urol. 2009, 55: 1190-1196.
- Grasso M, Conlin M, Bagley D: Retrograde ureteropyeloscopic treatment of 2 cm. or greater upper urinary tract and minor staghorn calculi. J Urol. 1998, 160: 346-351.
- 13. Preminger GM, Tiselius HG, Assimos DG, Alken P, Buck C, Gallucci M, Knoll T, Lingeman JE, Nakada SY, Pearle MS, Sarica K, Turk C, Wolf JS: 2007 guideline for the

management of ureteral calculi. J Urol. 2007, 178: 2418-2434.

- Smith RD, Patel A: Impact of flexible ureterorenoscopy in current management of nephrolithiasis. CurrOpin Urol. 2007, 17: 114-119.
- 15. Busby JE, Low RK: Ureteroscopic treatment of renal calculi. UrolClin North Am. 2004, 31: 89-98.
- Dindo D, Demartines N, Clavian PA: Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004, 240: 205-213.
- 17. Bader MJ, Eisner B, Porpiglia F, Preminger GM, Tiselius HG: Contemporary management of ureteral stones. Eur Urol. 2012, 61: 764-672.
- Kijvikai K, Haleblian GE, Preminger GM, de la Rosette J: Shock wave lithotripsy or ureteroscopy for the management of proximal ureteral calculi: an old discussion revisited. J Urol. 2007, 178: 1157-1163.
- 19. Pierre S, Preminger GM: Holmium laser for stone management. World J Urol. 2007, 25: 235-239.
- 20. Sofr M, Watterson JD, Wollin TA, Nott L, Razvi H, Denstedt JD: Holmium:Yag laser lithotripsy for upper urinary tract calculi in 598 patients. J Urol. 2002, 167: 31-34.
- 21. Hollenbeck BK, Schuster TG, Faerber GJ, Wolf JS: Flexible ureteroscopy in conjunction with in situ lithotripsy for lower pole calculi. Urology. 2001, 58: 859-863.
- 22. Segura JW, Preminger GM, Assimos DG, Dretler SP, Kahn RI, Lingeman JE, Macaluso JN: Ureteral stones clinical guidelines panel summary report on the management of

ureteral calculi. The american urological association. J Urol. 1997, 158: 1915-1921.

- Tawfiek ER, Bagley DH: Management of upper urinary tract calculi with ureteroscopic techniques. Urology. 1999, 53: 25-31.
- 24. Leijte JA, Oddens JR, Lock TM: Holmium laser lithotripsy for ureteral calculi: predictive factors for complications and success. J Endourol. 2008, 22: 257-260.
- Cheung MC, Lee F, Yip SK, Tam PC: Outpatient holmium laser lithotripsy using semirigidureteroscope. Is the treatment outcome affected by stone load?.Eur Urol. 2001, 39: 702-708.
- 26. Tiselius HG: Removal of ureteral stones with extracorporeal shock wave lithotripsy and ureteroscopic procedures. What can we learn from the literature in terms of results and treatment efforts?.Urol Res. 2005, 33: 185-190.
- 27. Gupta PK: Is the holmium:Yag laser the best intracorporeal lithotripter for the ureter? A 3-year retrospective study.J Endourol. 2007, 21: 305-309.
- 28. Lee H, Ryan RT, Teichman JM, Kim J, Choi B, Arakeri NV, Welch AJ: Stone retropulsion during holmium:Yag lithotripsy. J Urol. 2003, 169: 881-885.
- 29. Xu C, Song RJ, Jiang MJ, Qin C, Wang XL, Zhang W: Flexible ureteroscopy with holmium laser lithotripsy: a New choice for intrarenal stone patients. Urol Int. 2014, [Epub ahead of print]
- Vanlangendonck R, Landman J: Ureteral access strategies: pro-access sheath. UrolClin North Am. 2004, 31: 71-81.

- Denstedt JD, Wollin TA, Sofer M, Nott L, Weir M, RJ DAH: A prospective randomized controlled trial comparing nonstented versus stented ureteroscopic lithotripsy. J Urol. 2001, 165: 1419-1422.
- 32. Cheung MC, Lee F, Leung YL, Wong BB, Tam PC: A prospective randomized controlled trial on ureteral stenting after ureteroscopic holmium laser lithotripsy. J Urol. 2003, 169: 1257-1260.
- 33. Shao Y, Zhuo J, Sun XW, Wen W, Liu HT, Xia SJ: Nonstented versus routine stented ureteroscopic holmium laser lithotripsy: a prospective randomized trial. Urol Res. 2008, 36: 259-263.
- 34. Pace KT, Weir MJ, Tariq N, Honey RJ: Low success rate of repeat shock wave lithotripsy for ureteral stones after failed initial treatment. J Urol. 2000, 164: 1905-1907.
- 35. IEC 60825–1 –Ed. 2.0:2007–03: Safety of laser products –Part 1: Equipment Classification and Requirments. Geneva, Switzerland: International ElectrotechnicalCommission.http://www.iec-normen.de,
- 36. Penny J, Smalley RN, CMLSO: Laser safety: risks, hazards, and control measures. Laser Ther. 2011, 20 (2): 95-106.
- 37. DIN EN 60825–1: 2008–05: Sicherheit von Lasereinrichtungen – Teil 1: Klassifizierung von Anlagen und Anforderungen (IEC 60825–1:2007). 2007, Berlin: BeuthVerlag: Deutsche Fassung EN, 60825-1. in German
- 38. Bader MJ, Gratzke C, Hecht V, Schlenker B, Seitz M, Reich O, Stief CG, Sroka R: Impact of collateral damage to endourologic tools during laser lithotripsy–in vitro

comparison of three different clinical laser systems. J Endourol. 2011, 25: 667-672.

 Ronald S, Nicolas H, Thomas P, Volkmar H, Derya T, Stief CG, Markus Jürgen B: In vitro investigations of repulsion during laser lithotripsy using a pendulum set-up. Lasers Med Sci. 2012, 27: 637-643. تم تقييم المضاعفات بواسطة تدريجات كليفن وكانت نسبة المضاعفات 7.9% (كليفن من الدرجة 11 ولغاية الدرجة طاا1). كذلك فان موقع الحصاة من الحالب لم يكن لها تاثير على نسبة حصول المضاعفات. لم كن هنالك اي مضاعفات من استخدام الليزر بحد ذاته.

الاستنتاج: نستنتج وحسب نتائج بحثنا ان الاستخدام العلاجي لليزر الهولميم ياك في تفتيت حصاة الحالب يتمتع بالكفاءة والسلامة, ويضهر لنا بانه اداة كفوءة لتفتيت هذه الحصوات في جميع اجزاء الحالب المختلفة. ان استخدام ناظور الحالب شبه الصلب والمرن كليهما بالاضافة الى الادوات الجراحية الملائمة لعمليات ناظور المسالك البولية سوف يحسن من النتائج المرجوة في نسبة تنظيف الملائمة لعمليات الواقعة في اعلى الحالب بغض النظر عن المرجوة في نسبة تنظيف الحالب شبه الصلب والمرن كليهما بالاضافة الى الادوات الجراحية الملائمة لعمليات الخور الحالب شبه الصلب والمرن كليهما بالاضافة الى الادوات الجراحية الملائمة لعمليات ناظور المسالك البولية سوف يحسن من النتائج المرجوة في نسبة تنظيف الحالب من الحصوات المرجوة في نسبة تنظيف الحالب من الحصوات الواقعة في اعلى الحالب بغض النظر عن حجم تلك الحصوات الحوات المربوة في نسبة الملائمة العالي من الحصوات الواقعة في اعلى الحالب بغض النظر عن حجم تلك الحصوات الحسوات المربوة في نسبة تنظيف الحالب من الحصوات الواقعة في اعلى الحالب بغض النظر عن حجم تلك الحصوات الحسوات المربوة في نسبة السالة النظر عن حصوات الواقعة في اعلى الحالب بغض النظر عن حرم تلك الحصوات الحسوات الحسوات الحسوات الخري المربوة في نسبة تنظيف النظر عن حدم تلك الحصوات الواقعة في اعلى الحالب بغض النظر عن حدم تلك الحصوات الواقعة في اعلى الحالب بغض النظر عن حدم تلك الحصوات الواقعة في اعلى الحالب بغض النظر عن حدم تلك الحصوات الولية الحسوات الولية الحسوات الولية المربون المرب

الخلاصة

خلفية عن البحث: في الوقت الراهن تعتبر تقنية تفتيت حصاة المسالك البولية بواسطة الليزر عنصر اساسي في تداخلات جراحة المسالك البولية الناضورية. ان استخدام ليزر الهولميم ياك قد فتح الطريق لامكانية معالجة حصاة المسالك البولية ذات الحجم الكبير على طول المسلك البولي (الحالب وحوض الكلية).

الهدف من البحث: الهدف من البحث هي تقييم كفائة وسلامة استخدام ليزر الهولميم ياك في تفتيت حصاة الحالب وعلى مختلف اجزاء الحالب في عينة من المرضى في العراق.

المرضى وطرق عمل البحث: تم معالجة 88 مريضا عراقي الجنسية يعانون من حصاة الحالب بواسطة ناظور الحالب وباستخدام طريقة تفتيت الحصى بالليزر نوع الهولميم ياك في مستشفتين اهليتين في بغداد وهن مستشفى الزهراء البتول الاهلي في مدينة الكاظمية المقدسة في ناحية الكرخ ومستشفى بيروت الاهلي في ناحية الرصافة وخلال المدة من شهر ايار لعام 2021 ولغاية شهر كانون الثاني من عام 2022. النتيجة النهائية في الدراسة كانت عدد مرات العلاجات التي احتاجها المريض لكل حالة للوصول الى تفتيت نهائي للحصاة. تم تقسيم المرضى الى مجموعتين حسب موقع الحصاة في الحالب, المجموعة الاولى كانت للحصاة اسفل الحالب وبعدد 15 مريضا, والمجموعة الثانية للحصاة اعلى الحالب وكان عدد المرضى 37 مريضا.

نتائج البحث: نسبة التفتيت الكلي كانت 95.8%. متوسط عدد التداخلات الناظورية كانت (3–1) 1.1 ± 1.1 للحصوات اعلى الحالب, و 0.0 ± 1.0 للحصوات اسفل الحالب. العلاج من المرة الاولى للمرضى ذوي الحصاة السفلى كان اكثر نجاحا من العلاج من المرة الاولى للمرضى الذين يعانون من حصاة اعلى الحالب (100% مقارنة ب 82.40% بالتسلسل, (100 هقارنة حسب الحجي وخاصة بعد التداخل التاني للحصاة حسب الحجي وخاصة بعد التداخل الثاني للحصاة ذات الحجم الاقل من 10 ملم عن الحصاة الاكبر من ذلك ليكون (100 للحصاة الاصغر من 10 ملم و 94 للحصاة الاكبر من 10 ملم (100 من 10 ملم).



وزارة التعليم العالي والبحث العلمي جامعة بغداد معهد الليزر للدراسات العليا

تقييم كفائة وسلامة ليزر الهولميم ياك في تفتيت حصاة الحالب بواسطة ناظور الحالب في عينة من المرضى في الحالب وال

اطروحة مقدمة الى معهد الليزر للدراسات العليا/ جامعة بغداد, لغرض اكمال متطلبات نيل شهادة الدبلوم العالي لتطبيقات الليزر الطبية والجراحية العامة

ميلادي 2021

هجرې 1442