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Original Article

Safety and efficacy of total intraluminal topical anaesthesia for ureteroscopy. Is success worth the pain?

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ABSTRACT

Background: Ureteroscopic management of ureteral calculi using topical anaesthesia has been described. Most studies topically anaesthetized the urethra or urinary bladder by instilling 2% of plain lignocaine. In addition to the success rate, the pain perception in these studies was reported subjectively using non-standard criteria. Topical anaesthesia of the ipsilateral ureter and the pelvicalyceal system (PCS), in addition to urethra and urinary bladder, and use of alkalinised lignocaine, for enhanced effect, has not been reported for ureteroscopy. Using these conceptual alterations, we tested the safety and efficacy of performing ureteroscopy and laser lithotripsy under our technique of total intraluminal topical anaesthesia (TILTA).

Methods: One hundred sixty-eight patients underwent ureteroscopic laser lithotripsy by topical instillation of alkalinised lignocaine into the urinary bladder and ipsilateral ureter and PCS. Self-assessed pain perception and changes in vital parameters were objectively scored at various times. The success rate, reasons for failure, maximum pain scores, complications, and willingness to undergo repeat procedure were recorded.

Results: The success rate was 91.3% with a mean duration of 14.7 minutes Double J Stent (DJS) was placed in 38.1%. 61.3% patients did not need any postoperative injectable analgesic, with 11.3% requiring more than a single dose. The intraoperative changes in vitals initially and at the height of pain were not statistically significant ($p > 0.05$). Self-assessed median pain scores between intravenous access placement and ureteroscopy were significantly different ($p < 0.05$). **Conclusions:** Ureteroscopy, effectively performed under TILTA, is safe with a high success rate. The acceptable pain tolerance and the shortened convalescence in addition makes the procedure's success worth the pain.

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Introduction

Symptomatic ureteral calculi cause considerable morbidity, often requiring operative ureteroscopy under anaesthesia. All anaesthesia techniques whether intubated general, spinal, or 'conscious sedation'¹ require preoperative fasting and intensive intraoperative and immediate postoperative monitoring. Adverse effects such as postdural puncture headaches occur in 0.1%–17.3% of patients, delaying convalescence.² The present study was aimed at finding the safety and efficacy of performing ureteroscopy and laser lithotripsy, using alkalinised local anaesthetic solution^{3,4} topically, in the entire accessible urinary tract. The perioperative analgesia was provided by a single intramuscular Non Steroidal Anti Inflammatory Drug (NSAID). The perceived advantages include the absence of mandatory fasting, absence of the requirement of the intense monitoring by an anaesthetist, and absence of sedation, allowing immediate ambulation at the termination of the procedure, thereby shortening convalescence.

The following objectives were contemplated. The primary objectives included the following: (1) safety and success of ureteroscopy under topical anaesthesia and (2) assessment of pain tolerance during laser lithotripsy by (a) subjectively noting significant changes in pain scores and (b) objectively noting significant differences in the measured pulse and blood pressures variables. The secondary objectives included the following: (1) assessment of the average postoperative analgesic requirement, (2) documentation of complications and (3) eliciting the percentage of patients willing to undergo a similar repeat procedure.

Materials and methods

The prospective single-arm interventional study was conducted at a tertiary-level hospital, from March 2016 until October 2017. The WMA Ethical Helsinki guidelines were followed.⁵ Permission from the institutional ethical review committee and an informed consent was obtained. The patients were informed of other available options and benefits and risks associated with each method. Patients with a single ureteral calculus less than 1 cm in size, as measured in maximum dimension on a digital radiogram or a non-contrast computed tomography, were included. An Intravenous Pyelogram (IVP) was obtained for documenting ureteral anatomy where necessary. All calculi were initially treated with medical expulsive therapy; in addition, the upper ureteral ones were initially subjected to extracorporeal shock wave lithotripsy. A standard pre-anaesthetic checkup was obtained, and American Society of Anaesthesiology (ASA) grades were documented. A sterile urine culture was ensured. The location of the calculus was documented as one for upper, two for middle, and three for lower ureteral calculi. Measurement variables included the charting of pain and vitals. All procedures were performed by a single operator.

Pain charting

The proforma sheet depicted a visually understandable Wong-Baker Faces Pain Rating Scale.⁶ After explaining to the patient, the self-perceived maximum pain response was documented on a scale of 0–10, labelled as the visual analogue scale (VAS) pain score. Pain was scored for a total of five times: during intravenous (IV) line placement at the baseline, during urethroscopy, cystoscopy, at ureteroscopy during laser lithotripsy, and finally, the pain score after 6 h for those admitted, or noted as perceived retrospectively during the next day's visit, for day-care cases. The procedure was proposed to be stopped whenever intolerable, not comfortable, or a score of 8 was reached to prevent inadvertent ureteral injury due to sudden patient movement.

Vitals charting

The baseline pulse and blood pressures were documented, initially at IV placement, and compared with those at the height of pain during laser lithotripsy.

Need for a control group

Patients with ureteral calculi, operated under anaesthesia, may not correctly document pain perception, and their procedure time will be inclusive of anaesthesia time, thus making comparison difficult. Therefore, historical data have been used for comparison.

Preparation of the standard solution

The available local anaesthetic solutions have an acidic pH, so alkalinisation of lignocaine was performed to increase its pH to 7.9, which is above its pKa (dissociation constant). It is achieved by adding 7.5% sodium bicarbonate solution, at the resultant pH, greater than 50% of the active drug remains in the non-ionic lipid-soluble form,^{4,7} capable of transmigrating across the intact cell membranes into the perivesical space giving rise to its anaesthetic effects. Serum levels of lignocaine after retaining 400 mg, equivalent of plain lignocaine in the urethra and bladder for an hour, have been documented to be around 200 ng/ml and 121 ng/ml, respectively.^{7,8} Alkalinisation increases levels to around 1060 ng/ml.^{9–11} This is much below the documented serum toxic dose of around 5000 ng/ml.¹⁰ To prepare the standard solution, about 30 ml of 2% plain lignocaine was diluted to 1% using 30 ml of 7.5% sodium bicarbonate solution using a sterile technique. The usually recommended ratio of dilution of 2% lignocaine with 7.5% sodium bicarbonate for alkalinisation is 20:1.5,⁴ otherwise excessive alkalinisation causes precipitation of the lignocaine base. To reduce the total dosage of lignocaine and to maintain the pH above its pKa, we used a ratio of 1:1 dilution. The mildly turbid suspension (standard solution) formed was subjected to ultraviolet spectroscopy to confirm the presence of active lignocaine. The peaks of 220 nm and 240 nm, depicted on the spectrum, of both pure lignocaine and the alkalinised form,

Fig. 1 – Ultraviolet spectroscopic waveforms between sodium bicarbonate, lignocaine hydrochloride and alkalinised lignocaine. Both peaks of 220 and 240 nm are visualised in the plain and alkalinised lignocaine.

respectively, confirmed the presence of active lignocaine comparable to that of the pure lignocaine solution (Fig. 1).

Operative procedure

After confirming the calculus location radiologically, an IV access was established, with recording of pain score and vitals. The urethra was anaesthetized with 10 ml of sterile 2% lignocaine jelly, and through a 5-Fr (French) feeding tube, about 20 ml of the standard solution was instilled into the collapsed bladder, the tube clamped and retained in situ. The patient was advised not to evacuate, until the start of the procedure. At this time, 3 ml of diclofenac injection (75 mg/3 ml) was administered intramuscularly. Approximately 20 to 30 min later, the patient walked inside the Operation Theater (OT) and was positioned for ureteroscopy. Non-invasive BP monitor and a pulse oximeter were attached. An IV lifeline was connected, and a single dose of amikacin injection 500 mg was administered. In those with deranged renal function, a suitable alternative was offered. A blinding screen over lower abdomen partitioned the operative site but permitted visualisation of the operative procedure on the monitor. The timing of the procedure was measured from the time of introduction of the ureteroscope until its final removal from the urethra.

Ureteroscopy

An 8- to 9.8-Fr semirigid ureteroscope (Karl Storz/Richard Wolf) was negotiated through the urethra into the bladder, guided by markings on the feeding tube, with minimal irrigation to prevent dilution of the standard solution. The ureteral orifice was visualised, and a 4/5-Fr straight tip ureteral catheter gently negotiated through the scope into lower ureter, using a 0.032-inch Terumo glide wire, occasionally. Also, a cystoscope was occasionally required for visualising the ureteral orifice. Subsequently in the Trendelenburg position, about 7–10 ml of the

standard solution was instilled through the ureteral catheter, into the ipsilateral pelvicalyceal system gently, until the patient complained of mild flank discomfort. Now, in the anti-Trendelenburg position, the ureteroscope was negotiated into the ureter, aided by the inserted glide wire, until the visualisation of calculus, a complaint of intolerable discomfort, or a maximum self-perceived pain score of 8 and above. Laser lithotripsy was performed using a 550 micron Holmium Laser end-firing fibre. Intraoperative clarity of vision was maintained by gentle saline flushing. The need for stenting was individualised. The visualisation of the procedure on the monitor permitted patient's active participation. After completion, the patient was taken back to the postoperative room by walk. Railroading over two guide wires was attempted if in the beginning, the ureteral orifice and the distal ureter appeared tight. If unsuccessful, the procedure was considered a failure and abandoned with or without stenting for a follow-up procedure. The procedure replicated the steps performed under spinal anaesthesia, and therefore, a generalisability bias was excluded.

The demographic data, ASA grades, location of calculus, and time for the procedure were documented. The pain scores and the vitals were recorded as per the protocol. The number of patients who underwent successful ureteroscopy was documented. The success rate of the procedure was calculated.

Sample size estimation

A sample size of 132 achieves 99% power to detect a mean and standard deviation of the pulse rate (of the paired differences), i.e. 2.0 and 4.00 with a significance level (alpha) of 0.001 using a two-sided paired samples t-test. The sample size was calculated using power analysis and sample size software, version 8 (PASS-8).

Statistical analysis

The normality of the continuous data was assessed using standard normal variate (z-score) of the skewness, and a variable was considered normal when the z-score was found between -3.29 and $+3.29$.¹³ Continuous data were presented using mean $\pm$ standard deviation/median (interquartile range), while categorical data were presented using frequency and percentage. To test the mean difference between pre-observations and postobservations, paired samples t-test was used. For three or more repeated groups, the Friedman test was used as data were ordinal in form. As p value < 0.05 , multiple comparisons were performed. A p value < 0.05 was considered as statistically significant. Statistical Package for the Social Sciences, version 23 (SPSS-23, IBM, Chicago, USA) was used for analysis of the data.

Results

A total of 204 patients were enrolled for the study (Fig. 2). Sixteen patients could not complete the procedure and were considered as failures. The reasons for failures are given in Table 1. Incomplete follow-up data for 20 after the operative procedure excluded them from the final analysis. Thus, data

Fig. 2 – Flowchart.

were analysed for those 168 patients who underwent a successful ureteroscopy.

Demography

The average age was 34.84 years. There were 135 (80.4%) males and 33(19.6%) females. The ASA grades of 1, 2, 3, and 4 were present in 146 (86.9%), 18 (10.7%), 3 (1.85%), and 1 (0.6%) of the population, respectively. One hundred eighteen (70.2%) had lower third calculi, 40 (23.8%) middle third and 10 (6%) upper third. The mean duration of surgery was 14.7 min. Our overall success rate was 91.3%. Individually, success rates were 66%, 90.9%, and 0.94.4%, respectively, in upper, middle, and lower third calculi.

None of the patients lost to follow-up had any documented complications. Ten (5.9%) patients, among those completely followed up, were noted to have complications which were documented as per the Clavien-Dindo grading criteria,¹² during a minimal follow-up of 3 months, by the author himself (Table 2). One hundred fifty-eight (94.1%) patients had an uncomplicated course. Sixty-four (38.1%) patients underwent double J stenting, whereas 104 (61.9%) remained unstented. One hundred three (61.3%) patients did not need any postoperative injectable analgesic, 46 (27.4%) needed one, 17 (10.1%) two, and 1 (0.6%) each needed three and four doses, respectively. One hundred forty (83.3%) patients felt that the procedural discomfort and pain was tolerable enough in view of the advantages and consented to

Table 1 – Reasons for stopping procedure.

S. No	No of Cases	Reason	Management
1	5	Inability to visualise ureteral orifices due to oedema	Antibiotics for a week, followed by successful localisation
2	3	Ureteral orifice/lower ureter appeared too tight	DJS and subsequent URS
3	3	False Passage	DJS placement
4	5	Pain	Subsequent surgery under GA at a later date

Table 2 – Complications (Clavien-Dindo) grading and management.

S. No	Grade	No of Cases	Complication	Management
Intraoperative				
1	I	1(0.6%)	Self-limiting transient slurring of speech	Conservative
2	II	1(0.6%)	Bradycardia	IV atropine
3	III a	2(1.2%)	False passage	DJS placement
4	III b	1(0.6%)	Perforation at site of impaction, with inability to negotiate DJS	Conversion to GA and DJS placement
Postoperative				
5	I	1(0.6%)	Persistent flank discomfort without fever	Conservative
6	II	3(1.8%)	Febrile UTI and acute pyelonephritis	As per the standard treatment guidelines
7	III b	1(0.6%)	Stricture	Laparoscopic reimplantation

a repeat procedure if had a recurrent ureteral calculus again, while 28 (16.7%) felt that the pain was significant and did not consent to a repeat procedure. Conversion to General Anaesthesia (GA) on table was performed on a single patient, who developed ureteral perforation at the impaction site, and conversion to GA helped in DJ stenting. He had an uncomplicated course after DJ removal.

Measured variables

The changes of the mean systolic and diastolic pressures between those at the baseline during IV placement and those at the height of pain during ureteroscopy were statistically insignificant, ($p = 0.612$) and ($p = 0.262$), respectively. The changes of the mean pulse rates, similarly, were also statistically insignificant ($p = 0.105$) (Table 3). The distribution of the VAS score was compared between the different time points using the Friedman test. Results showed that there was a highly significant ($p < 0.001$) difference in mean ranks of the VAS score among the different time points. Pairwise multiple comparisons were used to compare score between the time points. Similarly, the frequency distribution of the VAS score indicated that in most of the patients, the VAS score was within 1–2 range for the time points of IV access, urethroscopy, cystoscopy, and at 6 h; while in the ureteroscopy, maximum patients' (39.3%) score fell under 5–6 range (Table 4). Clinically felt observation of reduced pain at 6 h after stenting was not substantiated statistically ($p = 0.132$). The question of women having lesser pain due to a shorter urethra was not proven statistically. There was no significant

association between the location of the calculus and maximum pain intraoperatively ($p = 0.165$).

Discussion

The use of lignocaine jelly for providing topical urethral anaesthesia is well established. Topical bladder anaesthesia, using lignocaine itself¹⁴ or using electromotive technique,¹⁵ has also been described. Although ureteroscopy has been conventionally performed under GA or spinal or under conscious sedation, the procedure, for lower ureteral calculi, has also been described using only 2% lignocaine jelly topically in the urethra¹⁴ and bladder. Conceptually, the benefit of extrapolating this topical anaesthesia, from the bladder into the ureter including the PCS, has been studied by Roberts et al.³ for relief of post-Ureterorenoscopy (URS) stent-related pain. The same has not been studied with respect to performing ureteroscopy. We attempted to study the success of procedure, tolerance of pain, and acceptability under topical anaesthesia.

Using a comparable demographic profile, our mean duration of surgery of 14.7 min on the OT table is much lesser than that of 49 ± 16 min using anaesthesia.¹⁵ Our success rate of 91.3% using 8- to 9.8-Fr calibre scope under total intraluminal topical anaesthesia (TILTA) is comparable to 86–100% using conventional anaesthesia¹⁶ and to a success rate of 84.2% using similar calibre instrument by Shelbaia et al.,¹⁴ using only bladder lignocaine and a penile block. Using a lesser calibre 6- to 7.5-Fr ureteroscope, a success rate of 93.5%¹⁷ using only urethral lignocaine jelly has also been reported. Therefore, despite a higher calibre instrument, our success rates using TILTA are comparable to those under anaesthesia and comparable to thinner calibre instruments. Tolerance to pain has been documented in our study, noting maximal perceived pain at any stage of procedure. Others^{14,17} have documented the mean of individual scores at the same stage of the procedure, thus making head-to-head comparison difficult.

The average maximal self-perceived pain scores during cystoscopy and ureteroscopy in our study were 2.36 and 5.11 compared with 3.1 and 3.4, respectively, as studied by Park et al.¹⁷. A paradoxically greater value of 4.52 versus 3.6 at cystoscopy compared with ureteroscopy has also been documented.¹⁴ Subjectively, these pain scores during ureteroscopy were different statistically when compared with scores during cystoscopy, urethroscopy, at IV access, and that at 6 h

Table 3 – Comparison of vitals.

Variable	N	Mean $\pm$ SD	P value
Pulse rate at the baseline	168	85.28 $\pm$ 18.06	0.105
VAS pain score			
Pulse rate at the maximum	168	86.80 $\pm$ 16.65	0.612
VAS pain score			
Systolic BP at the baseline	168	138.13 $\pm$ 17.4	0.262
VAS pain score			
Systolic BP at the maximum	168	138.86 $\pm$ 20.07	0.262
VAS pain score			
Diastolic BP at the baseline	168	85.54 $\pm$ 10.80	0.262
VAS pain score			
Diastolic BP at the maximum	168	86.54 $\pm$ 14.82	0.262
VAS pain score			

VAS, visual analogue scale; SD, standard deviation.

Table 4 – Distribution of the VAS score.

Time	N	VAS score					
		Median (IQR)	0	1–2	3–4	5–6	>=7
IV access	168	2 (1–2)	26 (15.5)	115 (68.5)	21 (12.5)	6 (3.6)	0 (0)
Urethrosopy	168	2 (2–2)	12 (7.1)	120 (71.4)	23 (13.7)	12 (7.1)	1 (0.6)
Cystoscopy	168	2 (2–3)	5 (3)	120 (71.4)	34 (20.2)	9 (5.4)	0 (0)
Ureteroscopy	168	5 (4–6)	0 (0)	16 (9.5)	50 (29.8)	66 (39.3)	36 (21.4)
6 h	168	2 (2–4)	18 (10.7)	90 (53.6)	35 (20.8)	20 (11.9)	5 (3.0)

VAS, visual analogue scale; IQR, interquartile range.

Friedman test with multiple pairwise comparisons was used to compare the distribution of VAS score among different point of times.

Overall and all pairwise comparisons were significant at $p < 0.05$.

VAS score was presented in frequency (%).

(Table 4). Although statistically different, these higher scores during ureteroscopy did not clinically hamper the completion of the surgery. Although the pain scores were subjective, objectivity was provided by insignificant changes in the vital parameters at the height of pain compared with the baseline at IV access (Table 3). This was a measure of the efficacy of the topically instilled alkalinised lignocaine solution.

Critics may argue that a cut-off VAS score of 8 for termination of the procedure may appear high; as per the data, it was reached in 20 (11.3%) of successful cases only, and 14 (70%) of these 20 consenting for a reprocedure is paradoxical even with a high score. This also is an indicator of the subjectivity of the scoring system.

Despite dilution of lignocaine with sodium bicarbonate and urine over time, the topical effect permitted completion of the procedure. Postprocedure DJS was required by 38.7% of the population. There was no correlation between the dose of postoperative analgesic and presence or absence of the stent. Absence of correlation between the level of the calculus and the pain scores has also been brought out in our study. The ability to visualise the procedure on the monitor, acting via a positive feedback, may have reduced the self-assessed pain perception score at the height of pain. The mean pain score reduced to 2.65 at 6 h, permitting 61.3% of the patients to avoid any postoperative injectable analgesic. The remaining needed at least a single injection. A complication rate of 5.9%, comparable to conventional anaesthesia, was documented. Grade III complications were seen in four (2.3%) cases. Remedial measures taken have also been documented in Table 3. Ureteral stricture, managed with laparoscopic Boari flap, seen in a single case could be a sequela of preoperative calculus impaction as well.

The total dose of lignocaine instilled was 450–500 mg, which included 200 mg in the urethra in men and lesser quantities in women, 200 mg in the bladder and 50–100 mg in the PCS. Furthermore, the instilled lignocaine in the bladder, after acting topically, gets continuously diluted by urine, obviating possibility of any toxicity. Although no serum levels of lignocaine were measured, this alkalinised mixture was well tolerated without any toxicity, except probably in a single patient who had a transient self-limiting episode of slurred speech improving, before a decision to stop could be taken. Effectiveness of the procedure is concurred by absence of analgesic requirement in more than 60% of the patients

postoperatively and a willingness for a repeat procedure in 83.8% of the patients, in case of a subsequent recurrence.

Although ureteroscopy has been successfully completed with a high success rate using only urethral or only bladder topical anaesthesia, our's is the first study using ureteral and PCS topical alkalinised lignocaine, with the enhanced absorption permitting ureteroscopy and laser lithotripsy comfortably. In addition to lower ureteral calculi, we had a larger number of patients successfully completing the procedure in the middle ureteral segment as well. Because all patients walked out of the OT immediately at the end of the procedure, a reduced convalescence has the propensity to convert this procedure into a day-care and an office-based one.

The strengths of the study are a large sample size, objectivity of comparable variables, a high success rate and a high willingness for repetition in case of recurrence. The limitations include only 22 (13.9%) patients beyond ASA Grade 1 and only 10 (16.8%) patients with calculi in the upper third. So, generalisation of conclusions to these two categories may be inappropriate. Therefore, patients in risk categories beyond ASA Grade 1, because of safety concerns, should preferably undergo the procedure under conventional anaesthesia. Thus, our modification of ureteroscopy under TILTA should be accepted for patients in ASA Grade 1 and those with middle and lower ureteral calculi because we have matched the success and complications of the standard procedure, in addition to the benefits of reduced morbidity, immediate ambulation and reduced hospitalisation.

Conclusions

Ureteroscopic lithotripsy, effectively performed under TILTA, using alkalinised lignocaine is safe and feasible with a high success rate for both lower and middle ureteral calculi. The acceptable pain tolerance, minimal complications and shortened convalescence in addition make the procedure's success, worth the pain.

Conflicts of interest

The authors have none to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mjafi.2018.11.002>.

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