

Original Research Article

Effect of intraurethral instillation of cooled versus room temperature lignocaine gel on pain perception during outpatient rigid cystoscopy

Ravinder Singh*, Fredrick Paul R.

Department of Urology, Government Medical College, Kottayam, Kerala, India

Received: 27 March 2023

Revised: 02 May 2023

Accepted: 05 May 2023

*Correspondence:

Dr. Ravinder Singh,

E-mail: rsravinder0111@gmail.com

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ABSTRACT

Background: Reducing temperature of topically applied lignocaine gel for maximal anesthesia during cystoscopy in conscious patients have yielded mixed results. This prospective randomised controlled study was undertaken to compare pain mitigating effect of lignocaine gel at 4°C versus at room temperature during rigid cystoscopy in male patients.

Methods: The study consists of 126 consecutive patients (n=126) who were randomly assigned into two groups: Group 1 (control, n1=63) received 2% topical lignocaine at room temperature, Group 2 (L4, n2=63) received topical lignocaine cooled to 4°C prior to insertion of rigid cystoscope. Pain during instillation of lignocaine and during performance of rigid cystoscopy was measured by independent evaluator on non-graphical 100-mm visual analogue scale (VAS).

Results: Mean pain score for cystoscopy in L4 was lower (46.69 ± 10.38) than that in CONTROL (49.19 ± 12.47), this difference was statistically not significant (p value, one tail = 0.11, >0.05). Mean pain score for instillation in L4 was 14.80 ± 6.00 and that for control was higher at 17.04 ± 6.54 with difference in pain scores being statistically significant (p value, one tail = 0.02, <0.05).

Conclusions: With regard to reducing pain perception during rigid cystoscopy, cooled lignocaine gel at 4°C has no benefit over room temperature lignocaine gel, however cooling lignocaine gel to 4°C does significantly decrease pain of instillation of gel into urethra.

Keywords: Lignocaine gel, Temperature, Pain, Rigid cystoscopy

INTRODUCTION

In comparison to the age when only rigid instruments were available, since the introduction of flexible scopes, male patients now can bear cystoscopic examination under local anaesthesia for various indications without much suffering. Despite the fact that flexible cystoscopes are now readily available in India, many facilities still use rigid cystoscopes for diagnostic cystoscopy. Over the years 2% lignocaine aqueous gel has been the most preferred agent for topical analgesia prior to urethral instrumentation. Studies have looked into ways to reduce discomfort during cystoscopy in order to improve the

clinical effectiveness of lignocaine gel. Reducing the temperature of the lignocaine gel, increasing the delivery rate, volume of anesthetic gel, urethral exposure time and altering chemical composition are some of the strategies. Reducing temperature of tissues leads to augmented local anaesthesia is a well-established fact.¹⁻³

Search of existing literature showed only two studies, with contrasting findings, which tested the hypothesis that cooling lignocaine gel would enhance its pain mitigating effect and provide better tolerance during cystoscopy. Study by Bhoomi et al involved only 60 patients undergoing rigid cystoscopy and showed no

benefit of cooling lignocaine gel whereas Razdan et al had randomized 600 patients undergoing flexible cystoscopy to draw conclusion that cooling lignocaine provides additional analgesic benefit in men.^{4,5} Question whether patients undergoing rigid cystoscopy can be offered additional analgesia by cooling 2% lignocaine gel needed to be answered, so this prospective randomized study was designed with a larger sample size with primary outcome being to compare procedure related pain during outpatient rigid cystoscopy between two groups of males-one receiving cooled lignocaine gel while other group receiving room temperature lignocaine gel.

METHODS

Study design

This was a prospective, randomized, double-blind, controlled study conducted at a tertiary care facility-Kottayam Government Medical College and Hospital, Kerala from May 2021 to April 2022 (Figure 1). Ethical approval was taken from institutional review board prior to enrolling patients for study. A total of 126 males older than 18 years of age who required to undergo cystourethroscopy under local anaesthesia for either stent removal or check cystoscopy were enrolled, subject to exclusion criteria, in the present study.

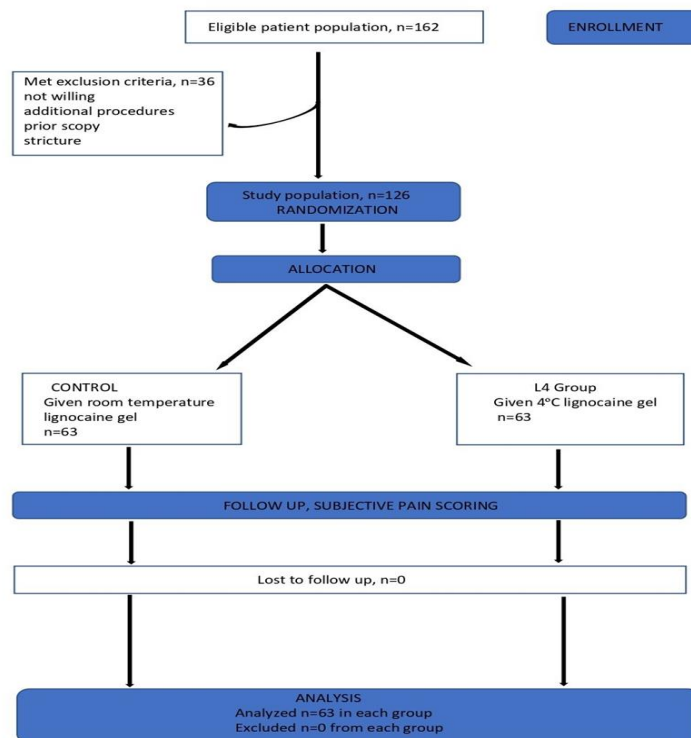


Figure 1: CONSORT diagram of the study.

Exclusion criteria

Patients were excluded if they were allergic to lignocaine, required immediate catheterization, had known structural abnormalities of urethra, had infection or were unable to cooperate with pain assessments (e.g., mental delay or an altered mental status) or had paraplegia or peripheral neuropathy or neurogenic bladder, had taken analgesics within last 24 hours or had undergone prior cystoscopy. Males in need for a simultaneous additional procedure during cystoscopy like urethral dilatation, unilateral or bilateral stenting or cold cup biopsy/clot evacuation were also excluded.

Women were excluded because they have been reported to experience less pain from urethral instrumentation than men do. Also, because of anatomic differences, it is not possible to place clamp on female urethra.

Procedure

After obtaining written informed consent, the next in a series of opaque consecutively numbered envelopes was opened to reveal the patient assignment into two groups. Residents not actively involved in the study counselled and explained the study procedure to all included patients without discussing the anticipated benefits of one allotment arm over the other, thus preventing any response bias. A prior urine culture confirmed absence of infection in all patients. Pre-procedural oral fluoroquinolone was given to each patient as prophylactic antibiotic.

In patients assigned to the group 1 (control, n=63) the urethra was pre-treated with 15 ml of room temperature 2% lignocaine gel, and patients assigned to group 2 (L4, n=63) with 15 ml of 4°C cooled 2% lignocaine gel. The

study gel was injected into the urethra over 10 seconds with a 20-cc syringe. After injection of the study gel, the end of the penis was held closed for 15 minutes with a gauze loop. We had chosen to wait 15 minutes to allow adequate time for onset of the lignocaine's anesthetic effect. Immediately after injecting the study gel, patients were asked to rate the pain of the injection on a previously validated 100 mm non graphical visual analogue scale (VAS) marked "most painful" at the high end.

After waiting period of 15 minutes all patients underwent rigid cystoscopy by single experienced urologist with a 20 Fr rigid cystoscope loaded with 30° 4 mm Karl Storz telescope. At the end of procedure each patient was asked to rate the subjective pain intensity of cystourethroscopy separately on a similar VAS. Administration of pain ratings were performed by urology nurses masked to the study intervention and their interaction with the patients was limited to instructing them on the use of the VAS. Patients were asked whether they would prefer similar pre-treatment of the urethra for future cystoscopies, whether they needed additional analgesics after procedure and whether they would prefer general or local anesthesia for future procedures. Relevant demographic and clinical data for each patient were recorded.

Data management and analysis

Data was numerically coded and entered into Microsoft Excel spread sheet. Analysis of data was done using online software. Pain scale ratings between the two groups were compared with two sample z-test with p value <0.05 being of statistical significance. Responses to need for analgesics after procedure, willingness for similar pre-treatment of urethra prior to scopy, preference for local or general anaesthesia for future scopies in two groups were compared using z-test for difference of two proportions.

RESULTS

Both groups, control and L4 contained 63 patients each. Demographic parameters of both the groups were comparable (Figure 2).

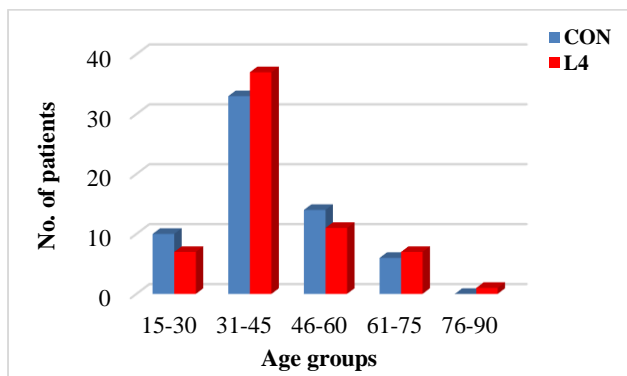


Figure 2: Age distribution across control and L4.

Mean age \pm SD for patients in control group was 41.5 \pm 13.21 years, while that in L4 group was 42.92 \pm 13.84 years. The difference was not statistically significant (p value =0.46). Youngest patient in control group was 20 years while oldest was 71 years; minimum age in L4 was 21 years while maximum age in L4 was 76 years.

Pain score distribution for injection and cystoscopy across control and L4 is displayed in (Figure 3). Two patients in L4 group for injection pain with pain score of 2 and 30 and one patient in control group for cystoscopy pain with pain score of 89 are depicted as outliers in the box plot. Comparison of the pain scores distribution in the two groups is shown in (Figure 4) for injection and (Figure 5) for cystoscopy. Although the mean pain score for cystoscopy in L4 was lower (46.69 \pm 10.38) than that in control (49.19 \pm 12.47), this difference was statistically not significant (p value, one tail =0.11, >0.05). On the other hand, mean pain score for injection in L4 was (14.80 \pm 6.00) and that for control was higher at (17.04 \pm 6.54) with difference in pain scores being statistically significant. (p value, one tail =0.02, <0.05).

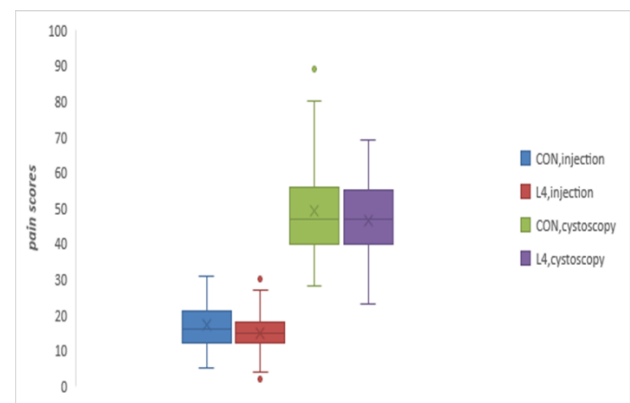


Figure 3: Comparison of pain distribution for injection and cystoscopy in both groups.

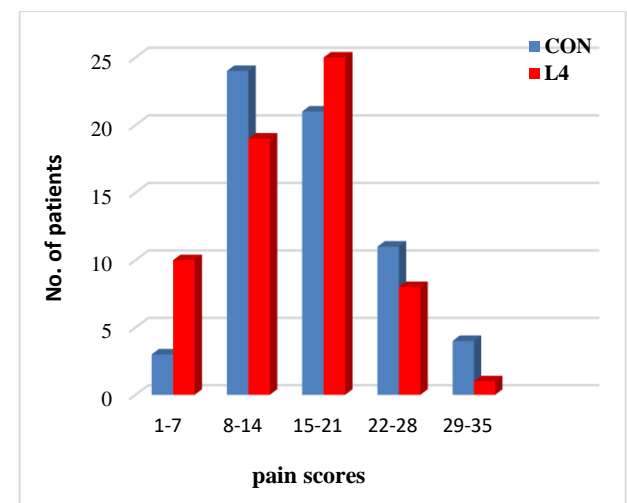


Figure 4: Pain distribution for injection across control and L4.

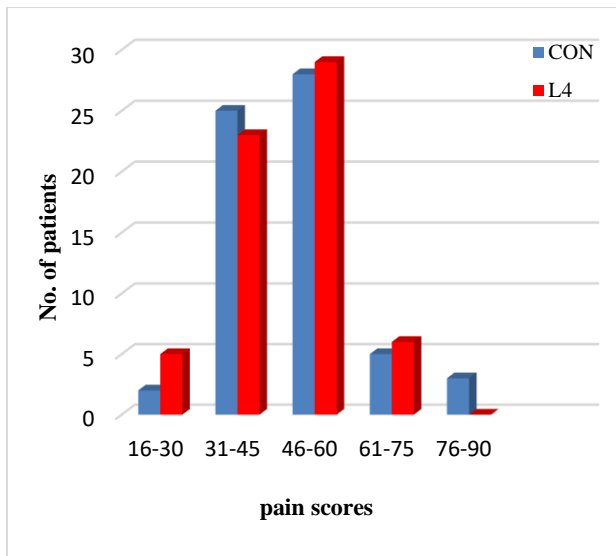


Figure 5: Pain distribution for cystoscopy across control and L4.

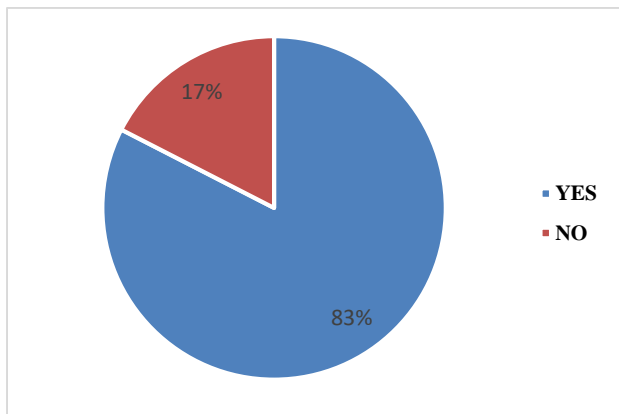


Figure 6: Preference for the same lubricant in control.

46.03% of total patients in control had undergone stent removal and remainder 53.97% had just diagnostic scopy whereas 50.79% patients in L4 had their stents removed and remaining 49.21% had diagnostic scopy (Table 1). Difference in proportion of each procedure between groups was not significant (stent removal p value =0.59, diagnostic scopy p value =1.41).

100 percent of the patients with cooled lignocaine wished to have same anesthetic for similar procedure in future whereas only 82.54% of the patients with room temperature lignocaine wished for the similar anesthetic (Figure 6 and 7). This difference was statistically significant (p value of 0.0005, Table 1).

Nearly sixty-eight percent patients in control preferred local anaesthesia for future procedures whereas eighty-three percent patients from L4 had given preference for local anesthesia (p value =0.062, not significant) Figure 8, Table 1.

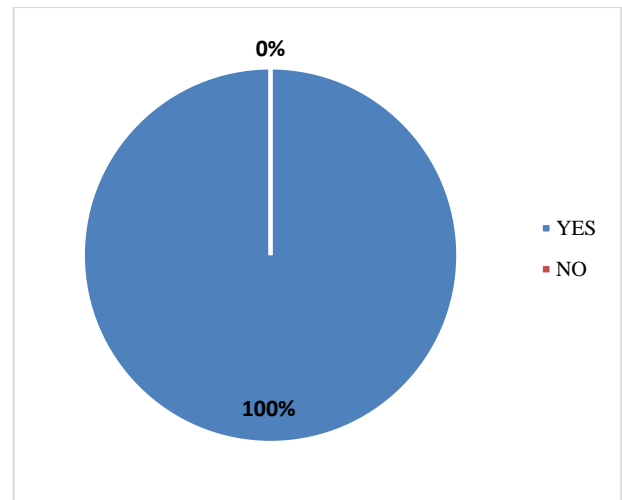


Figure 7: Preference for the same lubricant in L4.

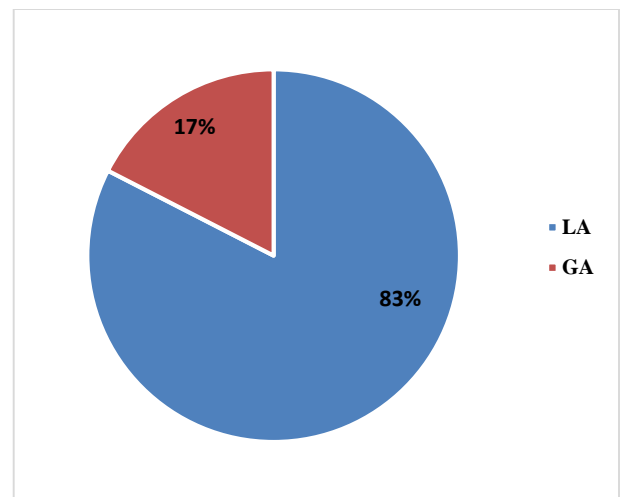


Figure 8: Preference for the local/general anesthesia (LA/GA) for future cystoscopy in L4.

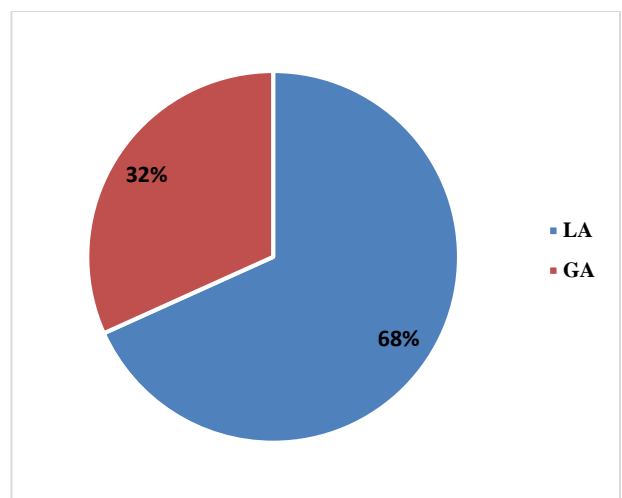


Figure 9: Preference for the local/general anesthesia (LA/GA) for future cystoscopy in control.

Table 1: Demographics and other procedural data summary.

Parameter	Control	L4	P value
Age, Mean±SD	41.5±13.21	42.92±13.84	0.46
Injection pain, Mean±SD	17.04±6.54	14.80±6.00	0.02
Cystoscopy pain, Mean±SD	49.19±12.4	46.69±10.38	0.11
Stent removal (%)	46.03	50.79	0.59
Diagnostic scopy (%)	53.97	49.21	1.41
Willingness for same lubricant (%)	82.54	100	0.0005
Preference for LA (%)	68.25	83	0.062
Preference for GA (%)	31.75	17	1.94

31.75% patients in control had given preference for general anaesthesia for future scopies, while 17 percent patients from L4 would like to have general anaesthesia for future cystoscopy. [p value =1.94] Figure 9, Table 1.

None of the patients in both groups needed analgesic in post cystoscopy period, had undergone any prior cystoscopy and no adverse reactions occurred during and after instillation of lignocaine gel.

DISCUSSION

Many patients have been hesitant to undergo office cystoscopy because of their perceptions of discomfort, anxiety, and pain. Urologists now use a variety of pain control techniques, with intraurethral lignocaine, being the most popular.⁶

Lignocaine is a lipid-soluble amide that penetrates the neural membrane's hydrophobic component, blocking the transmembrane flow of sodium ions essential for action potential initiation and propagation. Several studies have been undertaken on various elements of intraurethral instillation of lignocaine gel into males undergoing cystoscopy, including volume, rates of instillation, time of exposure, and temperature of lignocaine gel.

In our experiment, we used 15 ml of lignocaine gel and waited 15 minutes before putting the cystoscope in. Using ultrasonography to measure the amount of gel needed to pass past the bladder neck, Dawkins and colleagues discovered that conscious men had a mean urethral volume of 16 ml (range 12–20 ml).⁷ 10 ml of gel

doesn't seem to be enough to completely lubricate the whole urethra in male patients. Brekkan et al and Holms et al came to the conclusion that injecting 20 ml of anesthetic gel is preferable to injecting 10 ml, whereas McFarlane et al observed no difference in pain reduction between 10 ml and 20 ml of anesthetic gel instillation.⁸⁻¹⁰

Thompson et al compared the discomfort produced by intraurethral instillation of lignocaine gel at three different temperatures: 4, 22, and 40 degrees Celsius.¹¹ They discovered that lowering lignocaine gel's temperature to 4°C significantly lessened the pain produced by injecting it into a man's urethra. In addition, Goel and colleagues discovered that lignocaine gel was less uncomfortable when frozen to 4°C than when it was 22°C.¹² In the current study, we discovered that injecting cooled lignocaine gel into the urethra caused significantly less discomfort than injecting room-temperature lignocaine gel, and that a higher percentage of patients who received cooled lignocaine gel expressed a desire to use the same anesthetic agent for subsequent procedures. Reduced temperature has been shown to lessen nociceptor sensitivity, which might account for the decreased pain associated with cooled lignocaine gel.¹³

In contrast, the current study found no significant difference in pain levels for cystourethroscopy between the groups who got lignocaine gel at room temperature and those who received it at 4°C. Because of the complicated innervation of the external sphincter, topical anesthetic does not effectively block pain feeling throughout the whole urethra, and passing through the membranous urethra is regarded as the most painful phase of cystoscopy.¹⁴⁻¹⁶

It has been discussed how long lignocaine should stay in contact with urethral mucosa for the best analgesic effect after intraurethral instillation. Pharmacokinetically, topical lignocaine absorbs slowly, with a peak level being reached in 15 to 60 minutes.¹⁷ Choong et al found that doing a cystoscopy 25 minutes after gel instillation improved pain management.¹⁸ Nevertheless, Herr et al found no difference in pain perception between cystoscopy conducted immediately and 15 minutes later, and Burke et al found that cystoscopy performed 30 to 60 seconds after lignocaine gel instillation was well tolerated.^{19,20}

According to Yung et al and McFarlane et al even lignocaine gel does not significantly improve pain perception during cystoscopy over plain lubricating gel.²¹ In a meta-analysis of clinical trials that were published between 1950 and September 2006, Patel and colleagues compared 2% lignocaine gel to plain lubricant for flexible cystoscopy.²² A pooled analysis of over 800 male patients from nine studies demonstrated no statistically significant difference in pain reduction efficacy between 2 percent lidocaine and plain gel during flexible cystoscopy. These contradicting data imply that additional elements, including lignocaine gel, may be at play. Factors such as

surgeon's expertise, patient counselling, the patient's age, prostate volume, BMI, associated comorbidities and pain sensitivity may influence patient's pain tolerance during cystoscopy.

Limitations

Majority of the participants in this study came from a single southern state, restricting the applicability of our findings to other ethnic groups. To further account for possible genetic propensity to pain perception among individuals, future studies should include a more ethnically diverse group. The likelihood of visual diversion resulting in eased pain, anxiety, or discomfort cannot be ruled out because the study did not control for patient's observation of the surgery on monitor.

CONCLUSION

Cooled lignocaine gel at 4°C has no advantage over room temperature lignocaine gel in terms of lowering pain perception during rigid cystoscopy. The pain of instilling lignocaine gel into the urethra is greatly reduced when the gel is chilled to 4°C. Patients who received cooled lignocaine gel were more likely than those who received room temperature lignocaine gel to want to employ the same anesthetic agent for future procedures.

ACKNOWLEDGEMENTS

Dr. Haris CH, Professor and Head, Department of Genitourinary Surgery and Dr. Suresh Bhat, former Professor and Head, Department of Genitourinary Surgery, Govt. Medical College Kottayam. Dr. Apurvi Kaler, Senior Medical Officer, Govt. BDK Hospital, Jhunjhunu.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Singh R, Fredrick PR. Effect of intraurethral instillation of cooled versus room temperature lignocaine gel on pain perception during outpatient rigid cystoscopy. *Int Surg J* 2023;10:1002-8.