Systematic Review and Meta-Analysis

Analgesic effect of intravesical lignocaine in urology surgery: A systematic review and meta-analysis

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ABSTRACT

Background and Aims: Recent trials showed that transurethral lignocaine for bladder irrigation provides excellent analgesic effects and can minimise catheter-related bladder discomfort. The primary objective was to determine the efficacy of intravesical lignocaine on the incidence of catheter-related bladder discomfort in adult patients undergoing urologic surgery. **Methods:** The MEDLINE, EMBASE, and CENTRAL databases were searched from their start date until December 2024. Randomised clinical trials (RCTs) were included, comparing intravesical lignocaine and control for bladder irrigation in adults undergoing urological surgery. The odds ratio (OR) of the incidence of severe, moderate, and mild catheter-related bladder discomfort and the incidence of rescue analgesia were assessed. The revised Cochrane risk-of-bias tool for RCTs was applied to evaluate the risk of bias in all included studies. GRADEpro was used to evaluate the quality of the evidence. **Results:** Compared to the control group, our pooled analysis of three RCTs showed that intravesical lignocaine significantly reduced the incidence of severe catheter-related bladder discomfort (OR: 0.27, 95% confidence interval (CI): 0.12, 0.58, $P = 0.0008$, grade of evidence: low) and the incidence of moderate catheter-related bladder discomfort (OR: 0.31, 95% CI: 0.14, 0.67, $P = 0.003$, grade of evidence: low). It also statistically decreased the incidence of rescue analgesia (OR: 0.06, 95% CI: 0.02, 0.15, $P < 0.00001$, grade of evidence: low). **Conclusions:** The intravesical administration of lignocaine statistically reduced moderate and severe catheter-related bladder discomfort. There was a significant decrease in the number of patients requiring rescue analgesia in the intravesical lignocaine group.

Keywords: Analgesia, bladder irrigation, catheter-related bladder discomfort, intravesical, lignocaine, meta-analysis, percutaneous nephrolithotomy, prostatectomy, rescue analgesia, transurethral resection of bladder tumour, urology

INTRODUCTION

Various analgesic modalities, such as tramadol, ketamine, hyoscine, and antimuscarinic agents such as oxybutynin, tolterodine, and butyl scopolamine, are administered to reduce postoperative pain and discomfort from catheter, or bladder spasms in urological surgery.[1] Continuous bladder irrigation is an ongoing infusion of normal saline to prevent intravesical blood clot formation, wash out blood clots and prevent short term voiding failure. Thus, it allows proper monitoring of postoperative bleeding.[2,3] However, it is associated with catheter-related bladder discomfort, which is highly prevalent, ranging from 47% to 90% due to a variety of risk factors.[1] Catheter-related bladder discomfort may manifest itself as a burning sensation or urinary urgency[4] and pain in the suprapubic and penile areas, resulting in aggravation of postoperative pain, emergence agitation, and prolonged hospital stay.[1] The incidence of moderate and severe catheter-related bladder discomfort is reported among

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38%–57% of patients at the post-anaesthesia care unit, necessitating rescue treatments.[1]

Current evidence indicates that catheter-related bladder discomfort is resistant to traditional opioid treatments.[4] Several studies have investigated the impact of various medications, namely dexamethasone, tramadol, and anticholinergics such as solifenacin, atropine, oxybutynin, tolterodine, in the management of catheter-related bladder discomfort.[5] However, these pharmacological agents may not effectively reduce the incidence of catheter-related bladder discomfort, owing to their lack of efficacy and unwanted adverse effects, namely increased risk of seizure, visual impairment, and dry mouth.[6] Therefore, a safe and effective pharmacological agent is essential to attenuate catheter-related bladder discomfort in adults undergoing urological surgery.

Lignocaine is a short-acting local anaesthetic agent that is one of the safest, cheapest and commonly used in surgeries.[7] Recently, there has been a growing interest among anaesthesiologists to utilise of a non-opioid anaesthetic adjunct, lignocaine, which is added to the irrigation fluid to reduce the incidence of catheter-related bladder discomfort. Some randomised clinical trials (RCT) have revealed that the intravesical lignocaine approach for bladder wash is associated with a lower incidence of catheter-related bladder discomfort.[8,9] This meta-analysis explores, for the first time, the effects of lignocaine through bladder irrigation on the incidence of catheter-related bladder discomfort in patients undergoing urologic surgery.

We hypothesised that intravesical lignocaine reduces the incidence of catheter-related bladder discomfort. The primary objective of this systematic review was to examine the effects of intravesical lignocaine on the incidence of severe catheter-related bladder discomfort among adults undergoing urologic procedures.

METHODS

This systematic review was carried out by the guidelines based on the Cochrane Handbook of Systematic Reviews.[10] The study protocol of this review was registered with PROSPERO (ID: CRD42023426862) before the commencement of the literature search. Research questions were created based on the population-intervention-comparison-outcome (PICO) approach. The PICO applied in the current review is as follows: (1) population: adult patients undergoing urologic surgery [prostatectomy, percutaneous nephrolithotomy, and transurethral resection of bladder tumour (TURBT)]; (2) intervention: intravesical lignocaine; (3) comparator: placebo or any other active drug. The primary outcome of this systematic review was the incidence of catheter-related bladder discomfort among adult patients undergoing urologic surgery. Secondary outcomes included the incidence of needing rescue analgesia.

Search strategy and study identification

The search strategy was developed to perform a comprehensive search to identify eligible studies. The databases of MEDLINE, EMBASE, and CENTRAL (Cochrane Central Register of Trials) were searched extensively from its starting date till 22 December 2024 (updated date from the initial search on May 2023). The ClinicalTrials.gov.my and the WHO International Clinical Trial Registry were searched for ongoing or unpublished clinical trials. No restrictions were applied regarding the publication date and language of publication. Thus, publications in languages other than English were translated with the help of the authors. The search strategy included keywords such as 'bladder irrigation', 'transurethral resection', 'transurethral', 'bladder washout', 'bladder irrigation', 'lidocaine', and 'lignocaine' [Supplementary Table 1].

Inclusion and exclusion criteria

We included articles from RCTs that involved adult patients aged ≥18 years who underwent urological surgery. Urological surgery such as prostatectomy, percutaneous nephrolithotomy, and TURBT were included. Observational studies, case series, case reports, letters to editors, and conference abstracts were excluded. In addition, published studies comparing intravesical lignocaine and control *in vitro*, animal, or cadaver studies were excluded.

Study selection and data extraction

The review was reported according to the Preferred Reporting Items for Systematic Review and Meta-Analyses Statement (PRISMA) 2020 reporting guidelines.[11,12] Eligibility screening was done using a two-step method, namely title or abstract screening and then full-text screening—two authors screened articles separately. The titles and abstracts of studies were screened separately based on the inclusion criteria by two authors (WT and WL). These studies were then classified into 'Yes', 'No', and 'Maybe'. Studies that were categorised as 'Yes' were retrieved, and the full texts were retrieved. The screening of the full text was carried

out by both authors (WT and WL) separately. Studies classified as 'No' were excluded, whilst studies under the 'Maybe' category were discussed with the third author (KN). The final selection of all the included RCTs was discussed until an agreement was reached among the three authors (KN, WT, and WL). The two authors (WT and WL) extracted data (list of authors, publication year, total sample size, and baseline characteristics of patients) from relevant studies using a standardised data collection form. Clinical characteristics of all the included studies were documented and tabulated by both authors (WT and WL) separately and cross-checked to prevent discrepancies. The following data were extracted [Table 1]: author, year of publication, type of surgery, dose of lignocaine, type of control drug, mean age of both control and intervention group, total sample size, and primary and secondary outcomes detailed in the included RCTs.

The primary outcome of this review was the incidence of severe catheter-related bladder discomfort. The incidence of each study as n/N was calculated, with n being the number of patients who developed severe catheter-related bladder discomfort and N being the total number of patients in the respective control and intervention. The findings from all included studies for two specific time intervals were extracted, which is the immediate time period and 6 hours after drug administration. These two points were chosen to investigate the effects of intravesical lignocaine immediately after drug administration and after the elimination half-life period of lignocaine, which is 1.5–2 hours. The distinction between the presence and absence of the occurrence of severe, moderate, and mild catheter-related bladder discomfort and the occurrence of requiring rescue analgesia was retrieved as a dichotomous outcome. Any conflicts were solved by the third author (KN) until a consensus was achieved. Authors were contacted at least three times for additional information on incomplete data on the clinical characteristics of the patients, such as age, duration of surgery, and duration of anaesthesia.

Risk of bias assessment

Two authors (WT and WL) independently assessed the included RCTs for the risk of bias by using the Cochrane Collaboration Risk of Bias Assessment Tool 2.0.[15] The risk of bias assessment was evaluated based on the randomisation process, deviations from the intended intervention, outcome data, measurement of the outcome, and selection of the reported results.[16] The principles of the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) system were applied to evaluate the quality of evidence of primary and secondary outcomes.[17] Both authors (WT and WL) used the GRADEpro/GDT software to conduct separate summaries of findings and assessments of the level of evidence.[18] The level of evidence was evaluated based on five major criteria (risk of bias, inconsistency, indirectness, imprecision, and publication bias). Any conflicts were discussed with the principal author (KN).

Summary measures and synthesis of results

Statistical meta-analysis was conducted using the software application Review Manager version 5.4 (The Cochrane Collaboration, Copenhagen, Denmark).[19] Quantitative analysis was performed on the data extracted. In general, the cut-off value for statistical significance of two-tailed *P* values was less than 0.05. Regarding dichotomous outcomes, odd ratios (OR) and 95% confidence intervals (CI) were calculated. The heterogeneity of the pooled results was assessed using the I-square (I^2) test, with values of 40%, 40%–60%, and >60% classified into low, moderate, and high, respectively. Due to anticipated significant heterogeneity and small sample size, a random-effect model was applied to analyse the data. When the values were reported as median or interquartile range, these values were calculated and then converted to mean and standard deviation.[20] According to Peters *et al*.,[21] evaluating publication bias for reported outcomes using the funnel plot method lacks accuracy when there are less than 10 included studies. Thus, this current meta-analysis did not evaluate the publication bias due to a limited number of included studies. Subgroup analysis was performed for the primary outcome (the incidence of severe catheter-related bladder discomfort) and secondary outcomes (the incidence of moderate and mild catheter-related bladder discomfort) to explore the factors contributing to heterogeneity across the included studies.

RESULTS

The study selection process is illustrated in the PRISMA diagram [Figure 1]. Our search strategy yielded a total of 540 studies. After 106 duplicates were removed, 434 studies were identified for title and abstract screening. Ten articles were retrieved for full-text screening. Upon applying the inclusion and exclusion criteria, five articles were excluded. The list of excluded articles with their respective justification of exclusion is shown in Supplementary Table 2.

Table 1: Clinical characteristics of included studies

Author (s)/ Year	Country	Type of Surgery	Dose of Lignocaine	Type of Control Drug	Mean Age[1]		Total Sample Size	Primary Outcome	Secondary Outcomes
					Control	Intervention			
Wang *et al*./2003[9]	China	Prostatectomy	100 mg lignocaine in 500 mL saline	Normal Saline	65.2 (5.1)	64.9 (4.1)	36	To determine the incidence of cysto-spasm	To determine the incidence of cysto-spasm (in a day) and the duration of continued cysto-spasm (days)
Zeng *et al*./2004[13]	China	Prostatectomy	0.04% lignocaine diluted with normal saline for 3–4 times a day. Each bladder washing session lasts for 3–4 hours. Then, normal saline is used for bladder washing for the rest of the time.	Normal Saline	67.2	67.2	179	To determine the incidence of cysto-spasm	To determine the duration of cysto-spasm (seconds) and the duration of continued cysto-spasm (days)
Guo *et al*./2021[14]	China	Percutaneous nephrolithotomy	0.5% lignocaine was continuously infused at a rate of 5 mL/h	Sufentanil	58.0 (6.0)	57.0 (8.0)	40	To determine the incidence of catheter-related bladder discomfort	To determine the severity, SAS score, QoR-9 score, cortisol, norepinephrine, epinephrine, and glucose concentrations. To study the incidence of postoperative rescue analgesia, first off-bed time, exhaust time, and length of hospital stay after surgery, as well as the incidence of postoperative nausea and vomiting, respiratory depression, hypotension, and skin itching.
Singh *et al*./2023[8]	India	Transurethral resection of bladder tumour	Normal saline with preservative free 0.01% lignocaine (2% Lignocaine injection, 100 mg in 1 L Normal Saline]	Normal Saline	54.4 (14.1)	59.3 (11.1)	94	To determine the incidence of catheter-related bladder discomfort	To determine the severity of catheter-related bladder discomfort, pain scores (NRS), and satisfaction scores
Lin *et al*/2023[22]	Taiwan	Transurethral Surgery	0.05% lignocaine (2% lignocaine 25 mL in 1000 mL saline)	Normal Saline	63.5 (6.9)	63.9 (6.6)	79	To determine the incidence of catheter-related bladder discomfort	To determine consciousness level, ANI score, and the incidence needing rescue analgesia

[1]Data are calculated in mean (standard deviation)

A total of five studies (n = 428) were included in this review.[8,9,13,14,22] Searching the main registries identified two ongoing studies [Supplementary Table 3].

The clinical characteristics of all included studies are depicted in Table 1. Four studies[8,9,13,22] administered normal saline as a placebo, whereas one study gave sufentanil as a control drug.[14] In terms of the type of surgery, one of the studies involved percutaneous nephrolithotomy,[14] whereas the other types of surgery were prostatectomy, TURBT,[8,9,13] or elective transurethral surgery.[22] The age range of the

control group was 40.27–70.40 years. Similarly, the intravesical lignocaine group had an age range of 48.2–70.50 years. The body mass index of the control and intravesical lignocaine groups was 18.0–29.2 kg/m^2 and 14.0–29.0 kg/m^2, respectively. Table 2 describes data analysis of the primary and secondary outcomes. Table 3 shows a list of summary findings and the level of evidence.

Based on the overall risk of assessment, one of the included studies was evaluated as having a low risk of bias,[8] whereas the rest of the studies were assessed as having an unclear risk of bias[9,13,14,22] due to a lack of blinding of participants, personnel, and outcome assessors [Supplementary Figure 1].

Primary outcome: Incidence of severe catheter-related bladder discomfort

Pooled analysis showed that patients who were randomised to receive intravesical lignocaine for bladder washing had a statistically significant decrease in the incidence of severe catheter-related bladder

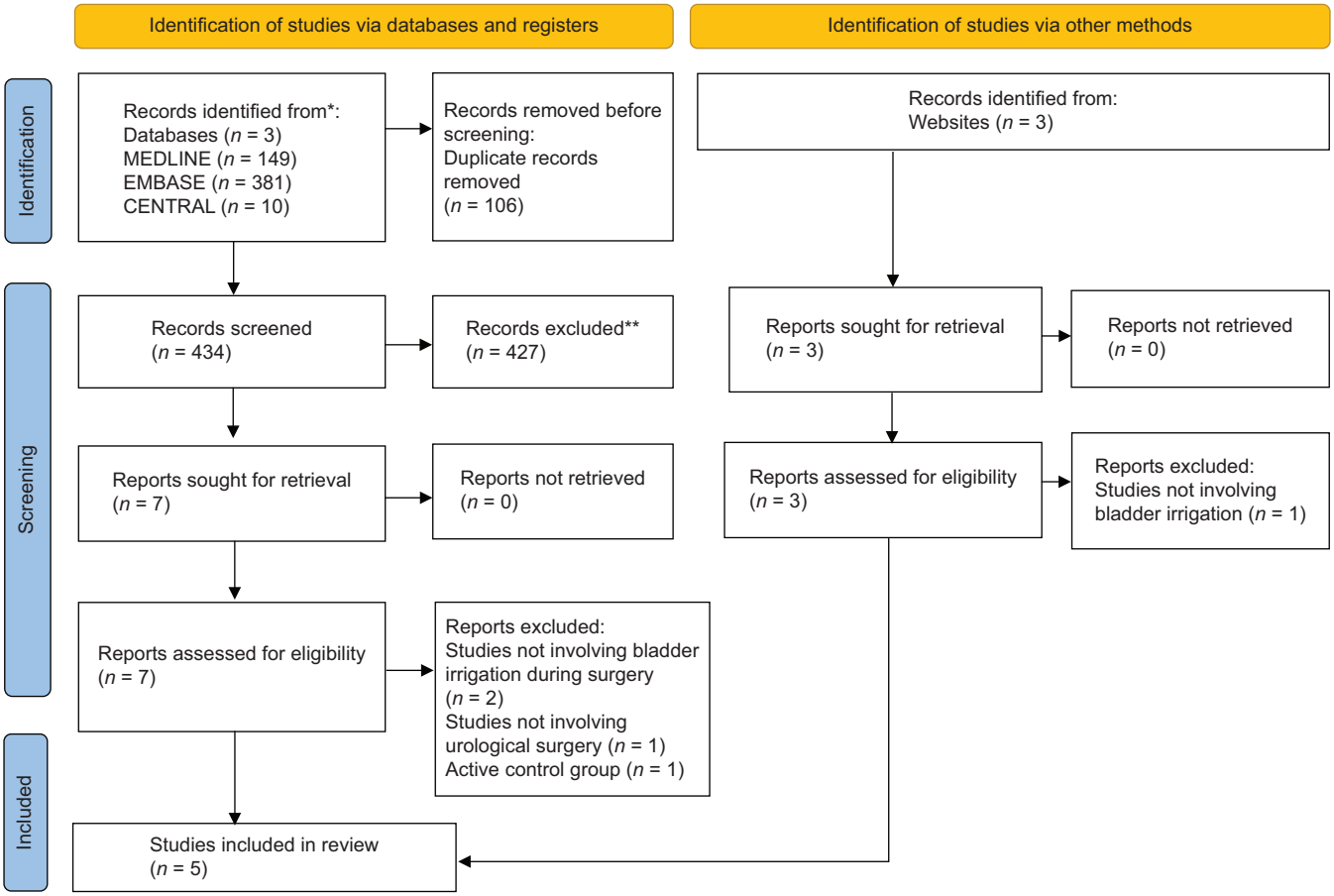

Figure 1: PRISMA diagram

Table 2: Data analysis of primary and secondary outcomes

Outcomes	Trials	Total sample size	I^2 (%)	MD/OR (95% CI)	*P*
Incidence of Severe Catheter-Related Bladder Discomfort	3	426	0	0.27 [0.12, 0.58]	0.0008
0 h	3	213	0	0.21 [0.08, 0.53]	0.001
6 h	3	213	0	0.49 [0.12, 2.01]	0.32
Incidence of Mild Catheter-Related Bladder Discomfort	2	374	73	1.11 [0.37, 3.34]	0.85
0 h	2	134	79	1.58 [0.18, 13.92]	0.68
6 h	2	134	48	0.78 [0.26, 2.33]	0.65
Incidence of Moderate Catheter-Related Bladder Discomfort	2	374	1	0.31 [0.14, 0.67]	0.003
0 h	2	134	55	0.26 [0.05, 1.40]	0.12
6 h	2	134	0	0.15 [0.02, 0.90]	0.04
Time Taken to Request for Analgesia	3	213	0	0.06 [0.02, 0.15]	<0.00001

1I2=Heterogeneity; MD=Mean Difference; OR=Odds Ratio; CI=Confidence Interval

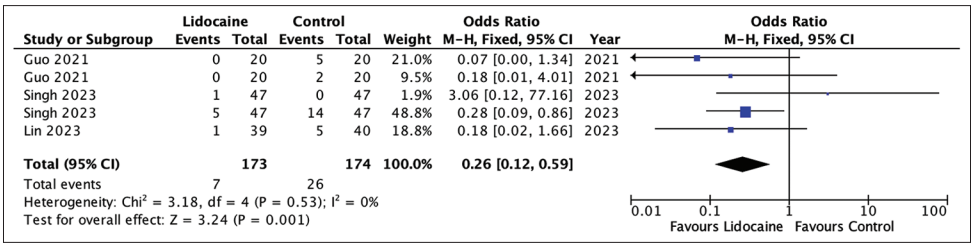

Figure 2: Forest plot of the incidence of severe catheter-related bladder discomfort. Transurethral Lignocaine is associated with significant reduction in the occurrence of severe catheter-related bladder discomfort. M-H=Mantel-Haenszel (M-H); Random=Random-effects model. CI=confidence interval

Table 3: Level of evidence based on GRADE certainty of evidence

Certainty assessment							№ of patients		Effect		Certainty
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Lignocaine	Control	Relative (95% CI)	Absolute (95% CI)	
3	randomised trials	serious[a]	not serious	not serious	serious[b]	none	8/212 (3.8%)	29/214 (13.6%)	OR 0.27 (0.12 to 0.58)	95 fewer per 1,000 (from 117 fewer to 52 fewer)	⊕⊕◯◯ Low[a,b]
2	randomised trials	serious[a]	serious[c]	not serious	serious[b]	none	66/134 (49.3%)	54/134 (40.3%)	OR 1.11 (0.37 to 3.34)	25 more per 1,000 (from 203 fewer to 290 more)	⊕◯◯◯ Very low[a,b,c]
2	randomised trials	serious[a]	not serious	not serious	serious[b]	none	12/134 (9.0%)	33/134 (24.6%)	OR 0.31 (0.14 to 0.67)	154 fewer per 1,000 (from 203 fewer to 67 fewer)	⊕⊕◯◯ Low[a,b]
3	randomised trials	serious[a]	not serious	not serious	serious[b]	none	16/106 (15.1%)	55/107 (51.4%)	OR 0.06 (0.02 to 0.15)	454 fewer per 1,000 (from 493 fewer to 377 fewer)	⊕⊕◯◯ Low[a,b]

GRADE certainty of evidence for five study outcomes. GRADE = Grading of Recommendations, Assessment, Development, and Evaluations. CI=confidence interval; OR=odds ratio. a. Half of the studies possess unclear risk of bias. b. Sample size of each arm <300. c. High degree of heterogeneity

discomfort compared to the control group (OR: 0.27, 95% Cl: 0.12, 0.58, $P = 0.0008$) [Figure 2].[8,14,22] All the included studies showed a low degree of heterogeneity ($I^2 = 0\%$).[8,14,22] The subgroup analysis on the severity of catheter-related bladder discomfort indicated that the intravesical lignocaine group was associated with a lower incidence of severe catheter-related bladder discomfort in the immediate postoperative period (OR: 0.21, 95% CI: 0.08, 0.53, $P = 0.001$, $I^2 = 0\%$) [Supplementary Figure 2].[8,14,22]

Secondary outcomes: Incidence of mild catheter-related bladder discomfort, incidence of moderate catheter-related bladder discomfort, and incidence of needing rescue analgesia

Two trials showed no significant differences in the occurrence of mild catheter-related bladder discomfort between patients who received intravesical lignocaine and the control group (OR: 1.11, 95% CI: 0.37, 3.34, $P = 0.85$) Supplementary Figures 3 and 4].[8,14] The pooled analysis indicated that compared to placebo, intravesical lignocaine statistically reduced the incidence of moderate catheter-related bladder discomfort (OR: 0.31, 95% CI: 0.14, 0.67, $P = 0.003$, $I^2 = 1\%$) [Supplementary Figure 5 and Supplementary Figure 6].[8,14] The three RCTs, including 213 patients, revealed that bladder irrigation with lignocaine resulted in a lower incidence of the patients needing rescue analgesia, which was statistically significant (OR: 0.06, 95% Cl: 0.02, 0.15, $P < 0.00001$) [Supplementary Figure 7].[8,14,22] A low degree of heterogeneity was noted across the studies ($I^2 = 0\%$).[8,14,22]

DISCUSSION

This paper highlighted the potential role of intravesical

lignocaine in reducing the incidence of catheter-related bladder discomfort and the number of patients requiring rescue analgesia after urologic surgery. The general quality of evidence for all measured outcomes varied from very low to low due to the risk of bias, inconsistency, indirectness, and imprecision.

To our knowledge, this is the first meta-analysis investigating the analgesic effects of bladder washing with lignocaine versus control in adult patients undergoing urological surgery. The urinary bladder receives innervation from the parasympathetic nerves and hypogastric sympathetic nerves.[23] During urological procedures, the irritation of the urethra and bladder stimulates the afferent nerves of the bladder. It releases acetylcholine to stimulate the muscarinic receptors, resulting in detrusor muscle contraction[24] to cause catheter-related bladder discomfort. Lignocaine is believed to be responsible for non-competitive inhibition of muscarinic type 3 receptor (M3) signalling,[25] which can translate into reducing the incidence of catheter-related bladder discomfort. Although the proportion of muscarinic type 2 (M2) receptors and M3 receptors is 3:1 in the urinary bladder,[25] a high proportion of M3 receptors has also been found in the urothelium and efferent nerves to cause direct contraction of the detrusor muscle.[26] Another possible explanation by Mikhailidis *et al*.[27] asserts that urologic procedures cause injury to the mucosal layers, which stimulate the local inflammatory process of the cyclo-oxygenase (COX) pathway and the production of prostaglandin to trigger the contraction of the detrusor muscle. The administration of lignocaine is reported to suppress the production of mucosal COX-2 and plasma prostaglandin PGE_2, the most important mediators for the contraction of the detrusor muscle.[28] The analgesic effects of intravesical lignocaine on severe catheter-related bladder discomfort are better manifested compared to mild and moderate discomfort. Of all included studies, severe catheter-related bladder discomfort involved strong behavioural responses, such as flailing limbs, trying to remove the catheter, and loud vocal responses.[8,14] However, the criteria for mild and moderate catheter-related bladder discomfort were discomfort reported by patients during questioning by the assessor and self-reported discomfort without questioning, respectively,[8,14] both of which are subjective to the individual patient's tolerance to pain and discomfort,[29] consequently resulting in the introduction of bias in measuring our primary outcome. In addition, based on the guidelines from acute pain management by the Australian and New Zealand College of Anaesthetists, self-reported pain is, by definition, subjective. It may be unreliable as patients may refrain from complaining of pain or discomfort due to language barriers, reluctance to cooperate, and severe anxiety upon completion of surgery,[30] thus making the interpretation of the impact of intravesical lignocaine on catheter-related bladder discomfort difficult.

However, several confounding factors could affect the occurrence of catheter-related bladder discomfort. For example, it may be influenced by variations in the diameter of the Foley catheter and the use of adjuvant analgesia.[4,31] Li and co-workers reported that patients older than the age of 50 years ($P = 0.001$) and inadequate use of analgesics at the end of the surgery ($P = 0.02$) were independent risk factors for the development of the incidence and severity of catheter-related bladder discomfort.[31] The administration of different types of analgesics, such as sufentanil[14] and fentanyl,[8] in all the included studies and the inclusion of patients over 50 years of age can convey a high degree of variability to our pooled estimates. A multivariate regression analysis performed by Binhas *et al*.[4] reported that a large diameter of Foley catheter, notably 18 French gauge (Fr) or greater (OR =2.2), was an independent predictor of catheter-related bladder discomfort. Therefore, the lack of standardisation of the diameter of the Foley catheter used across the included studies may introduce variances to our findings, making the interpretation of the effects of bladder irrigation with intravesical lignocaine difficult. Hence, future trials are warranted on the study of intravesical lignocaine in more homogeneous conditions with similar sizes of urinary catheters and local analgesia content of lubricants.

Similar analgesic benefits have been reported by Singh *et al*.[8] in their work on bladder irrigation with lignocaine. Similarly, our pooled estimates found that intravesical lignocaine significantly reduced the incidence of moderate and severe catheter-related bladder discomfort after urological surgery. Bolus infusion of the bladder with irrigation fluid of lignocaine is shown to significantly improve catheter-related bladder discomfort immediately after surgery due to its quick onset of action (5–20 minutes).[32] However, lignocaine has a short half-life, which ranges between 1.5 and 2 hours.[33] As reported in previous RCTs, the poor absorption of intravesical lignocaine from the bladder into the bloodstream[34,35] limits its systemic absorption and clinical benefits for an extended period. The observed lack of systemic absorption of lignocaine via the intravesical route could be attributed to the transitional epithelium of

the bladder, which is joined by tight junctions, densely packed plaques, and an anti-adherent glycosaminoglycan mucin layer, forming an impermeable barrier to slow the absorption of lignocaine.[36] Hence, continuous irrigation of fluid with lignocaine may provide better pain control to overcome the short half-life of bolus intravesical lignocaine. Including RCTs that administered bolus infusion of lignocaine[8] may cause bias in evaluating the incidence of catheter-related bladder discomfort 6 hours after surgery. Hence, due to the variability of infusion methods and the limited number of studies with small sample sizes, the true effects of adding lignocaine to the irrigation fluid on the development of catheter-related bladder discomfort remain inconclusive.

Our review showed that there was a decrease in incidence of needing rescue analgesia in the intravesical lignocaine group in comparison to the control group. Nickel *et al*.[37] emphasised that intravesical lignocaine significantly improved pain relief in patients suffering from interstitial cystitis or bladder pain syndrome. In terms of plasma concentration of intravesical lignocaine, an RCT conducted by Birch summarised that the average peak plasma concentration of intravesical lignocaine in patients who were given 400 mg of lignocaine for 1 hour was 121 ng/mL,[34] which is far below the toxicity threshold of 5 μg/mL.[38] The dosage of intravesical lignocaine used in our included studies varied from 100 mg[8] to 25 mg/h,[14] with no incidence of lignocaine-related toxicity reported. The main mechanism of the analgesic effects of lignocaine lies in its anti-inflammatory and anti-nociceptive effects.[39,40] To illustrate, *in vitro* studies by Lan showed that lignocaine attenuates the production of pro-inflammatory cytokines, such as interleukin-1 (IL-1), and IL-6, IL-8, and reduces the expression of Intracellular Adhesion Molecule-1 (ICAM-1), which plays a key role in transporting neutrophils to the inflammatory site.[40] Hence, the suppression of the inflammatory process by lignocaine is hypothesised to reduce the excitation of afferent nerves, subsequently terminating the transmission of nociceptive information of pain to the brain,[39] which reduced postoperative pain and the number of patients needing rescue analgesic. However, the low certainty of evidence and limited sample size warrants more adequately powered studies to assess the effects of intravesical lignocaine on the incidence of needing rescue analgesia.

Our study has several limitations. Firstly, there was a lack of standardisation for defining our primary outcome across all the included studies, which may introduce a substantial degree of heterogeneity. Some major confounding factors were common to other meta-analyses, namely different clinical characteristics of patients, the dosage of intravesical lignocaine for bladder irrigation, the timing or duration of intravesical lignocaine, and various protocols of analgesia used, which are unadjusted in this review. Most of the included RCTs were small in sample size and might be underpowered to detect the clinical benefits of intravesical lignocaine. In addition, the certainty of the evidence is low for all measured outcomes.

CONCLUSION

The meta-analysis indicated the potential benefit of intravesical lignocaine in reducing the incidence of moderate and severe catheter-related bladder discomfort. Given the substantial degree of heterogeneity with a low level of evidence and limited small sample size, strong recommendations for adding lignocaine into irrigation fluid for urological patients are limited. Thus, future adequately powered RCTs are warranted to evaluate intravesical lignocaine's efficacy and safety profile on catheter-related bladder discomfort.

Study data availability

The data for this systematic review and meta-analysis may be requested with reasonable justification from the authors (email to the corresponding author) and shall be shared.

Supplementary material

Visit journal website for supplementary tables and figures associated with this article.

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Conflicts of interest

There are no conflicts of interest.

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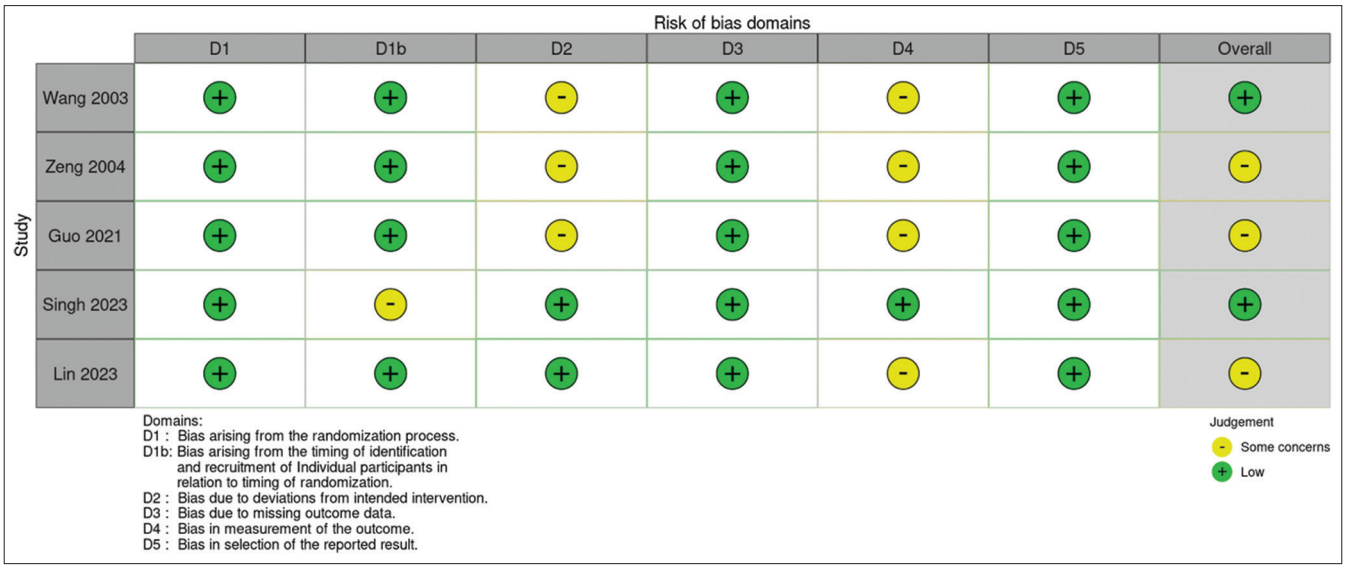
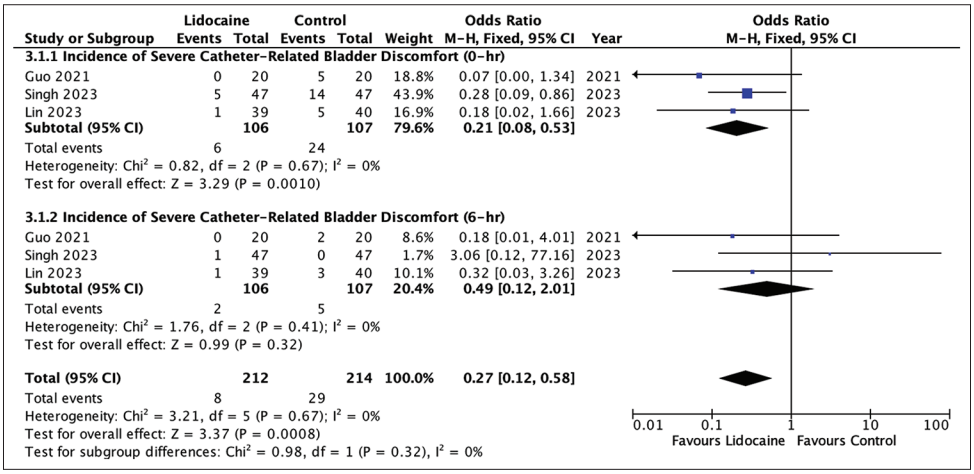
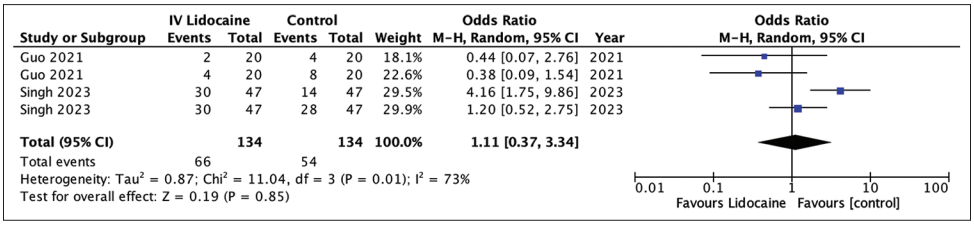


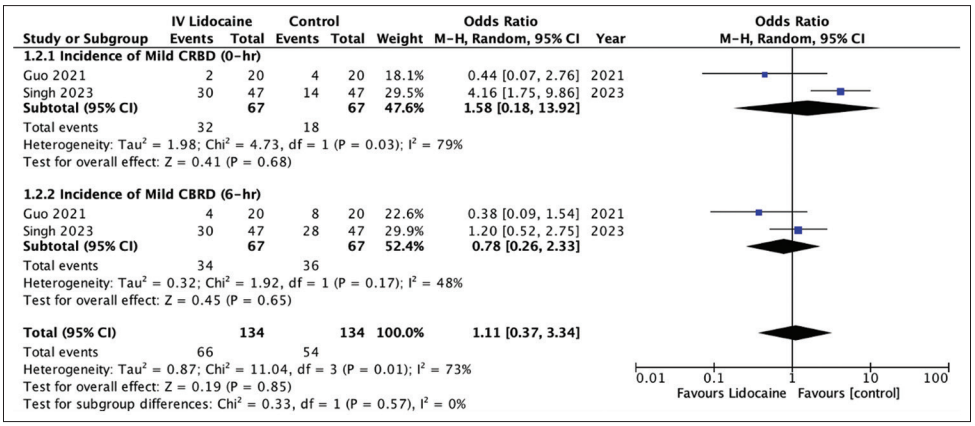
Supplementary Figure 1: Risk of Bias Assessment of all the Included Studies



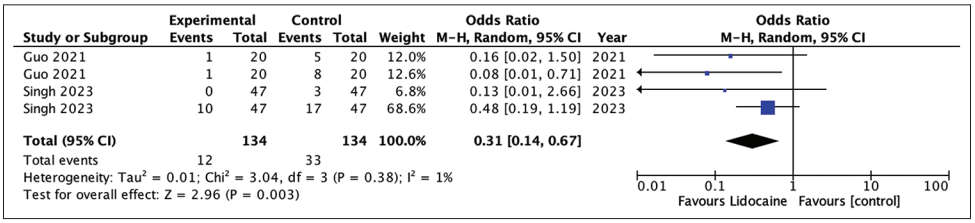
Supplementary Figure 2: Forest Plot of Incidence of Severe Catheter-Related Bladder Discomfort (Subgroup Analysis). Transurethral Lignocaine significantly reduced the incidence of severe catheter-related bladder discomfort in the immediate period after drug administration. M-H=Mantel-Haenszel (M-H); Fixed=Fixed-effects model



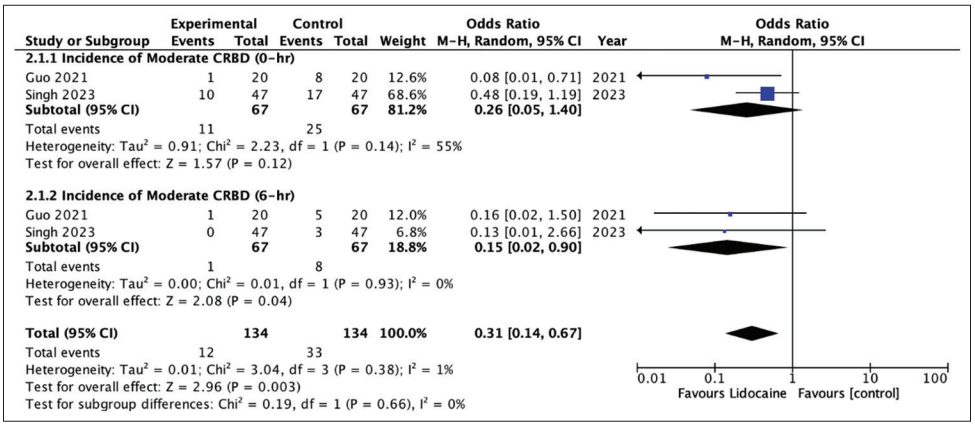
Supplementary Figure 3: Forest Plot of Incidence of Mild Catheter-Related Bladder Discomfort. No significant differences found between transurethral lignocaine and control on the incidence of mild catheter-related bladder discomfort. M-H=Mantel-Haenszel (M-H); Random=Random-effects model



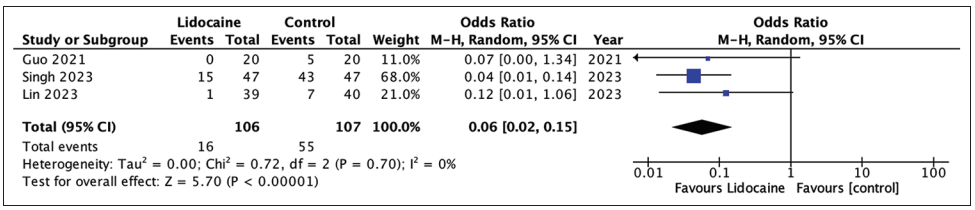
Supplementary Figure 4: Forest Plot of Incidence of Mild Catheter-Related Bladder Discomfort (Subgroup Analysis). No significant differences between transurethral lignocaine and control on the incidence of mild catheter-related bladder discomfort at the 0-hour and 6-hour after drug administration. M- H=Mantel-Haenszel (M-H); Random=Random-effects model



Supplementary Figure 5: Forest Plot of Incidence of Moderate Catheter-Related Bladder Discomfort. Transurethral Lignocaine significantly reduced the incidence of moderate catheter-related bladder discomfort. M-H=Mantel-Haenszel (M-H); Random=Random-effects model



Supplementary Figure 6: Forest Plot of Incidence of Moderate Catheter-Related Bladder Discomfort (Subgroup Analysis). Transurethral Lignocaine significantly reduced the incidence of moderate catheter-related bladder discomfort at the 6-hour after drug administration. M-H=Mantel-Haenszel (M-H); Random=Random-effects model



Supplementary Figure 7: Forest Plot of Incidence of Needing Rescue Analgesia. Transurethral Lignocaine is associated with a statistical decrease in the incidence of needing rescue analgesia. M-H=Mantel-Haenszel (M-H); Random=Random-effects model

Supplementary Table 1: Search strategy for EMBASE and MEDLINE

Search Strategy for EMBASE databases (1974–December 2024)

Steps	Search String
1	Bladder irrigation.mp. or exp bladder irrigation/3069
2	exp transurethral resection/or transurethral.mp. 36958
3	bladder washout.mp. or exp bladder irrigation/2839
4	lignocaine.mp. or exp lidocaine/85664
5	1 or 2 or 3 39337
6	4 and 5 372

Search Strategy for MEDLINE databases (1946–December 2024)

Steps	Search String
1	Bladder irrigation.mp. or exp bladder irrigation/676
2	exp transurethral resection/or transurethral.mp. 20210
3	bladder washout.mp. or exp bladder irrigation/89
4	lignocaine.mp. or exp lidocaine/27040
5	1 or 2 or 3 20770
6	4 and 5 100

Supplementary Table 2: Characteristics of excluded studies and reasons for exclusion

Author	Year	Design	Reason	Country	Total sample size
Nickel	2008	RCT	Wrong Design	United States	102
Offiah	2019	RCT	Wrong Design	Ireland	46
Evans	2021	RCT	Wrong Design	United States	190
Zhang	2020	RCT	Wrong Design	China	60
Yang	2012	RCT	Wrong Design	China	120

RCT=randomised controlled trial

Supplementary Table 3: Characteristics of ongoing studies. There is a total of 2 ongoing trials

Author	Year	Status	Title	Total sample size	Clinical Trial Number
Lin	2020	Unknown	Bladder Irrigation 0.05% Lignocaine Decreases Postoperative CRBD	80	NCT04133571
Singh	2023	Not Yet Recruiting	Relief in post-operative catheter-related bladder discomfort after using lignocaine or dexmedetomidine in irrigation fluid in patients undergoing percutaneous nephrolithotomy (PCNL) or ureteroscopic lithotripsy (URSL): A double-blinded randomised controlled trial	Not stated	CTRI/2023/09/058151