ORIGINAL ARTICLE

Randomized Double-Blind Controlled Trial Comparing Safety and Efficacy between Plain Lubricant and Lidocaine Gel during Ambulatory Cystoscopy

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Background: Cystoscopy is a basic procedure for urologists to visualize the urethra, the prostate gland, and the urinary bladder. However, ambulatory cystoscopy may be associated with pain and discomfort. Accordingly, varied types and amounts of lubricating gels were studied to relieve these symptoms.

Objective: To compare the efficacy and safety between plain lubricant and lidocaine gel during ambulatory cystoscopy.

Materials and Methods: The present study was a double-blind randomized controlled trial conducted to evaluate pain during cystoscopy. One hundred patients were randomized into two groups. Group A, 20 mL of 2% lidocaine hydrochloride gel and Group B, 20 mL of plain lubricant gel were instilled into urethra 15 minutes before the procedure. Pain was assessed by an independent data collector using a numerical rating scale (NRS) and visual analog score (VAS). Blood pressure and pulse rate were compared before and after the procedure. Complications were recorded by telephone within several days.

Results: The mean NRS of Group A was lower (3.8±2.38) than that of Group B (4.22±2.65) (p=0.407) and the mean VAS of Group A was 2.7±1.36, Group B was 2.66±1.27 (p=0.880). Additionally, the present study found no difference in the change in mean arterial blood pressure (MAP) (Group A 6.69±11.18 mmHg, Group B 4.84±11.45 mmHg, p=0.416) and pulse rate (Group A 6.4±11.9 BPM, Group B 3.73±13.67 BPM, p=0.302). Gross hematuria was seen in one patient (2%) in Group A and three patients (6%) in Group B. Dysuria was equal in both groups.

Conclusion: The plain lubricant gel used for cystoscopy without otherwise manipulation has similar safety and efficacy compared to the lidocaine gel.

Keywords: Lubricant gel; Ambulatory cystoscopy; Cystoscopy without otherwise manipulation

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Cystoscopy is the basic procedure in urology that is routinely performed both in the office and operating room. It allows direct visualization of the urethra and bladder and can be used to diagnose and treat conditions such as hematuria, lower urinary tract symptoms, and malignancy[1,2]. However, it is associated with pain and discomfort. Varying materials such as plain lubricant gel, ether, and lidocaine gel can be used to relieve pain and discomfort during the procedure.

Plain lubricant gel is inexpensive, widely available, and can be instilled into the urethra immediately before performing the procedure. However, it has been used in varying concentrations, volumes, and instillation time. Furthermore, there is still controversy in the literature regarding the potential benefits of lidocaine gel[3,4].

In most studies, cystoscopy was performed 10 to 15 minutes after instillation of 10 to 20 milliliters of the lubricant[5-10]. Accordingly, the aim of the present study was to compare the efficacy and complications between plain lubricant and lidocaine gel during ambulatory cystoscopy. In the present study the protocol was to instill 20 milliliters of lubricant for 15 minutes. After that, the pain scores, blood pressure, and pulse rate will be recorded to compare between the two groups.

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Complications after cystoscopy varied, such as gross hematuria, dysuria, urinary tract infection, and urinary frequency. From the literature, the rate of severe urinary tract infection was low[11-14]. In the present study, the authors will record complications between using lidocaine gel and plain lubricant gel during cystoscopy.

Materials and Methods

Study population

The present study population consisted of patients who underwent cystoscopy for diagnostic or surveillance purposes between June and September 2020 at the urology outpatient clinic, Phramongkutklao Hospital. According to the study of Mcfarlane et al.[6], they found that the mean ± standard deviation (SD) of Group B was 3.93±0.64 and the mean±SD of Group C was 3.57±0.63, thus using this data, the calculated sample size for our study was 50 cases per group.

The inclusion criteria consisted of all healthy patients aged 18 years old and older that undergone cystoscopy without active genital inflammation or infection. Additionally, patients must be able to follow the instructions as well as discontinue anticoagulants and antiplatelet agents for seven days. The present study excluded patients with allergic history to lidocaine, urethral stricture, and associated procedures such as bladder biopsy, urethral dilatation, or bladder irrigation, along with cystoscopy.

After obtaining informed consent, patients were randomized into two groups by block randomization. Group A received intraurethral instillation of 2% lidocaine hydrochloride 20 mL and Group B received plain lubricant gel 20 milliliters. Patients were prepared in lithotomy position and intraurethral instillation agents were then prepared by the assistant. The operator and the patients were double-blinded. In male patients, penile clamps and gauze loops were used to compress the glans of the penis for 15 minutes (Figure 1)[15]. In contrast to the female patients, only intraurethral instillations were performed for 15 minutes before the procedure. Regarding the instillation agent preparation protocol, 25-milliliter syringes were used to contain 20 milliliters of lubricant gel (Figure 2).

Cystoscopy was performed with a rigid 17-French KARL STORZ cystoscope and a flexible 16.5 French Olympus cystoscope under video-camera guidance with sterile saline irrigation. A single urologist performed all the cystoscopies.

After the procedure, the independent data collector used a numerical rating pain scale (NRS) with 0 for no pain and 10 for severe pain, and visual analog score (VAS) (0=no pain and 6=severe pain)[16]. The difference in blood pressure and pulse rate before and after cystoscopy were recorded. Several days after the procedure, the independent data collector called the patient to record the

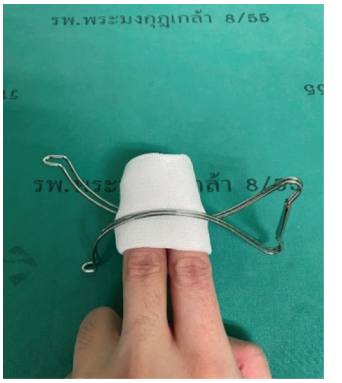

Figure 1. Penile clamp.

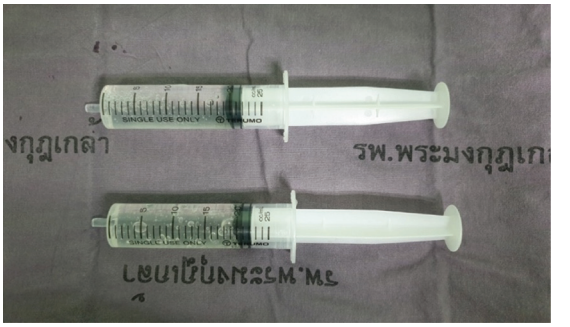

Figure 2. Lubricant gel.

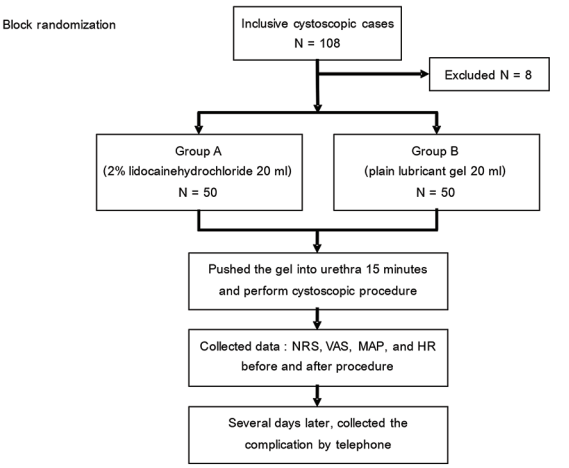

Figure 3. Research methodology.

Table 1. Demographics data of study population

	Group A: Lidocaine gel (n=50)	Group B: Plain lubricant (n=50)	p-value
Sex; n (%)			0.668*
Female	15 (30)	17 (34)	
Male	35 (70)	33 (66)	
Age (years); mean±SD	65.3±12.12	63.78±14.13	0.565**
Body mass index (kg/m^2); mean±SD	26.52±14.71	23.9±4.32	0.230**
Underlying diseases; n (%)			
Diabetes mellitus	8 (16)	9 (18)	0.790*
Dyslipidemia	24 (48)	22 (44)	0.668*
Hypertension	22 (44)	23 (46)	0.841*
Other	14 (28)	9 (18)	0.235*
Causes of procedure; n (%)			
Gross hematuria	4 (8)	9 (18)	0.175*
Lower urinary tract symptoms	16 (32)	9 (18)	0.106*
Malignancy	16 (32)	13 (26)	0.509*
Other	14 (28)	19 (38)	0.288*
Cystoscopy types; n (%)			0.603*
Rigid	40 (80)	42 (84)	
Flexible	10 (20)	8 (16)	
Procedure duration; n (%)			0.169*
<5 minutes	46 (92)	49 (98)	
5 to 10 minutes	4 (8)	1 (2)	

SD=standard deviation

* Chi-square, ** t-test

complications (Figure 3).

Statistical analyses were done using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA). Frequencies and percentages were calculated for the categorical variables while continuous variables were reported as means and standard deviations. Differences were assessed using chi-square and independent t-test where applicable. A p-value less than 0.05 was considered statistically significant.

Ethical approval was obtained from the Institutional Research Ethics Committee (approval No. IRBRTA 669/2563).

Results

Eight patients were excluded from the study with three patients due to history of urethral stricture and five patients due to additional procedures.

Each group was consisted of 50 patients and included 35 male patients in Group A (70%) and 33 male patients in Group B (66%). The mean age of patients in Group A was 65.3±12.12 years and in Group B was 63.78±14.13 years. There were no statistical differences between the two groups in terms of gender, age, BMI, causes of procedure, device type, and procedure duration (Table 1).

The mean NRS in Group A was 3.8±2.38, which was lower than Group B with a score of 4.22±2.65, but this was not statistically significant (p=0.407). Similar to NRS, the mean Visual Analog Score were 2.7±1.36 in Group A and 2.66±1.27 in Group B without being statistically significant (p=0.880). In objective pain assessment, the present study found no difference in the change in mean arterial blood pressure (MAP) with Group A at 6.69±11.18 mmHg and Group B at 4.84±11.45 mmHg (p=0.416), and pulse rate with Group A at 6.4±11.9 BPM and Group B at 3.73±13.67 BPM (p=0.302) (Table 2).

Furthermore, complications were gross hematuria in one patient in Group A (2%) and three patients in Group B or 6%, dysuria in one patient in both groups or 2%. However, there were no statistical differences between the two groups, (p=0.140 and 1, respectively) (Table 2).

In the subgroup analysis, the present study found no difference in NRS for male patients with Group A at 4.17±2.37 and Group B at 4.76±2.65 (p=0.339), and VAS in Group A at 2.91±1.34, Group B 2.94±1.25, p=0.937). Similar to males, no difference in NRS was observed in female patients with Group

Table 2. Pain score, difference in the change in mean arterial blood pressure (MAP), and pulse rate between lidocaine gel and plain lubricant during cystoscopy

	Group A: Lidocaine gel (n=50)	Group B: Plain lubricant gel (n=50)	Mean difference (95% CI)	p-value
Numeric rating pain scale (0 to 10); mean±SD	3.8±2.38	4.22±2.65	−0.42 (−1.42 to 0.58)	0.407**
Visual analog score (1 to 6); mean±SD	2.7±1.36	2.66±1.27	0.04 (−0.48 to 0.56)	0.880**
Mean arterial blood pressure (mmHg); mean±SD				
Pre procedure	91.92±9.4	92.63±10.96	−0.71 (−4.76 to 3.34)	0.727**
Post procedure	97.54±10.34	96.36±9.4	1.18 (−2.74 to 5.1)	0.552**
Difference (mmHg)	5.62±9.87	3.73±9.53	1.89 (−1.96 to 5.74)	0.331**
Difference (%)	6.69±11.18	4.84±11.45	1.85 (−2.64 to 6.34)	0.416**
Pulse rate (beats per minute); mean±SD				
Pre procedure	77.84±13.53	79.34±13.49	−1.5 (−6.86 to 3.86)	0.580**
Post procedure	81.96±11.42	81.78±14.82	0.18 (−5.07 to 5.43)	0.946**
Difference (mmHg)	4.12±7.81	2.44±10.41	1.68 (−1.97 to 5.33)	0.363**
Difference (%)	6.4±11.9	3.73±13.67	2.66 (−2.42 to 7.75)	0.302**
Complications; n (%)	2 (4)	4 (8)	-	0.218*
Gross hematuria	1 (2)	3 (6)	-	0.140*
Dysuria	1 (2)	1 (2)	-	1*

SD=standard deviation; CI=confidence interval

* Chi-square, ** t-test

Table 3. pain score between lidocaine gel and plain lubricant during cystoscopy in male and female groups

	Group A Lidocaine gel (n=50); mean±SD	Group B Plain lubricant gel (n=50); mean±SD	Mean difference (95% CI)	p-value
Male				
Rigid	n=25	n=26		
• NRS (0 to 10)	4.36±2.61	5.15±2.56	−0.79 (−2.25 to 0.66)	0.278*
• VAS (1 to 6)	2.96±1.49	3.19±1.23	−0.23 (−1 to 0.53)	0.546*
Flexible	n=10	n=7		
• NRS (0 to 10)	3.7±1.64	3.29±2.63	0.41 (−1.78 to 2.61)	0.693*
• VAS (1 to 6)	2.8±0.92	2±0.82	0.8 (−0.12 to 1.72)	0.085*
Total	n=35	n=33		
• NRS (0 to 10)	4.17±2.37	4.76±2.65	−0.59 (−1.8 to 0.63)	0.339*
• VAS (1 to 6)	2.91±1.34	2.94±1.25	−0.03 (−0.65 to 0.6)	0.937*
Female				
Rigid	n=15	n=16		
• NRS (0 to 10)	2.93±2.25	3.13±2.47	−0.19 (−1.93 to 1.55)	0.823*
• VAS (1 to 6)	2.2±1.32	2.06±1.18	0.14 (−0.78 to 1.06)	0.762*
Flexible	n=0	n=1		
• NRS (0 to 10)	-	4	N/A	1*
• VAS (1 to 6)	-	3	N/A	1*
Total	n=15	n=17		
• NRS (0 to 10)	2.93±2.25	3.18±2.4	−0.24 (−1.93 to 1.45)	0.771*
• VAS (1 to 6)	2.2±1.32	2.12±1.17	0.08 (−0.82 to 0.98)	0.853*

NRS=numerical rating pain scale, VAS=visual analog score; N/A=not applicable; SD=standard deviation; CI=confidence interval

* Chi-square, ** t-test

A at 2.93±2.25 and Group B at 3.18±2.4 (p=0.771), and VAS with Group A at 2.2±1.32 and Group B at 2.12±1.17 (p=0.853) (Table 3).

Discussion

Ambulatory cystoscopy is a common procedure in urology that allows direct visualization of the

urethra and bladder for diagnosis and treatment[1,2]. Nowadays, both rigid and flexible cystoscopes are widely available. Although, utilization of flexible cystoscope was increasing to reduce pain and discomfort compared to rigid cystoscopy, rigid cystoscopy is still necessary and has potential benefits in some cases.

Anyway, varying lubricant agents were used to relieve symptoms during procedure, with lidocaine gel still being the most popular agent. Accordingly, studies have been conducted to compare the efficacy of these different agents in terms of pain, discomfort, and complications. Furthermore, the data from previous studies is still controversial in terms of lubricant agent type, instillation amount (5 to 30 mL), instillation duration (5 to 25 minutes)[5-8], and lubricant agent temperature(9,10). Therefore, the authors conducted this double-blind randomized controlled study using 20 mL of lubricant agent at room temperature, 15 minutes before the procedure to compare the safety and efficacy between plain lubricant gel and 2% lidocaine gel.

Moreover, the results of the present study showed no difference in pain, discomfort, blood pressure, and pulse rate between these two groups. Similarly, subgroup analysis showed no differences between genders, and type of instruments regarding symptoms and complications. Therefore, ambulatory cystoscopy can be safely done using plain lubricant gel at room temperature, especially in disease surveillance purposes. This knowledge can be applied in clinical use in appropriately selected patients to reduce the cost and duration of the procedure.

In aspect of cost-effectiveness, although the cost of plain lubricant (0.59 USD/20 mL) is lower than that of lidocaine lubricant (3.13 USD/20 mL), the former agent may be an appropriate option for national reimbursement, especially in underdeveloped countries. To answer this question, further study concerning cost-effectiveness study should be conducted.

A limitation of the present study is that it included too few cases of flexible cystoscopy. Therefore, future studies may require more cases of flexible cystoscopy to increase the power of the study.

Conclusion

Plain lubricant gel was not inferior to lidocaine gel and could be used for ambulatory cystoscopy without urinary tract manipulation, with similar safety and efficacy, to save cost and time.

What is already known on this topic?

There is still a controversy between intraurethral instillation agents, amount, and duration.

What this study adds?

Intraurethral instillation with plain lubricant gel is safe and effective for ambulatory cystoscopy without otherwise manipulation.

Funding disclosure

The present trial had no source of funding. According to the study protocol, all the samples were covered by civil servant rights, which were routinely scheduled for ambulatory cystoscopy. Furthermore, all prepared lubricating agents were covered by civil servant rights.

Conflict of interest

The authors declare no conflict of interest.

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