

Investigation of a New Catheter on Relieving Pain During Male Cystoscopy – A Randomized Clinical Trial

Xiong Yongjiang, Liu Jiaji, Zhao Tao*

Purpose: To investigate the pain intensity and tolerability of a new catheter applied for urethral surface anesthesia during rigid cystoscopy in male patients, and explore the prospects of its application and the anesthetic method in hospitals at primary levels.

Materials and Methods: 252 adult male patients were randomly divided into the experimental group and the control group. 1% lidocaine solution was irrigated into the posterior urethra of the experimental group using the new catheter before cystoscopy, while the control group was administered with lidocaine gel. Both groups were assessed by visual analogue scale (VAS) with their pain perceived during administration of lidocaine (control group) / during insertion of catheter and administration of lidocaine (experimental group) (T1), during the insertion of cystoscope (T2), at the beginning of cystoscopy (T3), the third minute of cystoscopy (T4), during the first urination after the procedure (T5), as well with the maximum pain (Pmax) perceived during the whole procedure. The fluctuations of blood pressure and heart rate in each group before, after and during the procedure were recorded, and the anesthesia costs in both groups were calculated.

Results: Except a slightly higher score in T1, the scores of VAS in experimental group were lower than those of control group in T2, T3 and T4. The Pmax of the control group was 4.92 (SD=1.20), which was higher than in the experimental group of 3.89 (SD = 0.95, $P < 0.01$). There was no significant difference on blood pressure variation in both groups. While heart rate variation in experimental group was lower than that in control group (16.3%, SD=3.4 vs. 22.6%, SD=5.0, $P < 0.01$). No obvious complications were found in both groups. The anesthesia cost of the experimental group is about 1.53 dollars, with 1.75 dollars lower than that of the control group.

Conclusion: It is tolerable and beneficial to apply the new catheter for male urethral anesthesia. It can significantly relieve the pain during rigid cystoscopy in male patients, and is low in cost and easy in operation. Thus this method is worth being recommended to hospitals, especially at community hospitals or primary hospitals.

Keywords: cystoscopy; male; catheter; anesthesia; pain

INTRODUCTION

The most basic endoscopic technique in urology, cystoscopy is an essential step for operations such as ureteral retrograde catheterization, retrograde pyeloureterography, ureteral stent extraction, etc⁽¹⁾. However, cystoscopy has been reported by patients to maintain an inevitable pain. Pain is more intense in male patients than in female patients⁽²⁾. During cystoscopy, the most painful part is the insertion of cystoscopy into the urethra, especially when the cystoscopy passes through the external urethral sphincter⁽³⁾. However, the commonly used clinical methods for perfusion through the external urethral orifice or application of drug to the surface of the sheath cannot take sufficient effect on the posterior urethra, resulting in unsatisfactory pain relief⁽⁴⁻⁶⁾. It has always been the topic of discussion for urologists as for how to reduce the patient's pain during cystoscopy. Our aim was to explore a new method by using a new catheter technology to fully apply the topical anesthetic

to the male urethral mucosa before performing cystoscopy.

PATIENTS AND METHODS

Study population

Ethical approval for the study was granted by the institutional review board at Yongchuan Hospital of Chongqing Medical University. According to the design formulas, we calculated the sample size by considering the expected accuracy, attrition rate and the cost of the experiment.

230 adult male patients from June 2016 to August 2017 who underwent cystoscopy in our department were selected as the research objectives, and were randomly divided into the experimental group (120 patients) and the control group (110 patients) based on a randomization generator available at randomization.com by a nurse. Exclusion criteria: those who are allergic to anesthetic

Department of Urology, Yongchuan Hospital of Chongqing medical university, Xuan Hua Road, Yongchuan District, Chongqing, 402160, China.

Correspondence: Department of Urology, Yongchuan Hospital of Chongqing medical university, Xuan Hua Road, Yongchuan District, Chongqing, 402160, China.

Ph: +8613527491151, email: zhaotao_1999@163.com.

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Table 1. Comparison of patients in experimental and control group

Characteristics	Control	experimental	P value
Mean age, years (SD)	52.2(15.3)	54.0(14.2)	0.29
Hematuria(%)	20/122(16.4)	26/130(20.0)	0.34
Bladder tumor(%)	31/122(25.4)	28/130(21.5)	
Retrograde ureteral catheterization(%)	13/122(10.7)	20/130(15.4)	
Postoperative re-examination(%)	31/122(25.4)	22/130(16.9)	
Urethral stent extraction(%)	27/122(22.1)	34/130(26.2)	
Operation time >3min(%)	77/122(63.1)	68/130(52.3)	0.08
Operation time (min)	5.83 ± 0.66	5.19 ± 0.37	0.28

Abbreviation: SD = standard deviation

lidocaine; those who have used analgesics within the past 24 hours; those with sensory deficits (such as paraplegia); patients with severe cardiovascular and cerebrovascular diseases; other patients who were not eligible for cystoscopy, such as those suffering from acute cystitis, urethritis, prostatitis, urethral stricture, severe bladder contracture and so on. A total of 41 patients in both groups had undergone transurethral operation with general anesthesia or spinal anesthesia before, such as TURP and TURBT, while the rest were examined for the first time. The clinical data of the two groups of patients were not statistically significant and hence were comparable.

Surgical technique

Control group: 10g of lidocaine gel was injected into the urethra, and the perineal urethra was massaged slightly. The cystoscopy was performed 5 minutes later. **Experimental group:** Using a new Fr16 catheter (**Figure 1 and Figure 2**) for urethral surface anesthesia, and the method is as follows: the catheter is fully lubricated, then inserted into the patient's urethra until it enters the bladder. Afterwards, 5mL of physiological saline was injected from the channel so as to fill the balloon. When gently pulled back, the balloon would be stuck at the bladder neck. 10mL 1% lidocaine solution was further injected into the channel and the solution gradually overflowed from the small holes into the prostatic and membranous urethra. 1 minute later, the physiological saline in the balloon was completely withdrawn. And then, the catheter was pulled out slowly while 2 mL of lidocaine solution was injected into the channel so as to take effect on the mucosa in other area. Cystoscopy was performed 5 minutes later.

Both groups of patients underwent rigid cystoscopy were operated by two urologists. They worked together to confirm that the same procedures were practiced on each group. The amount of bladder perfusion was not more than 200 mL. Each cystoscopy was performed with a rigid cystoscope with 22 Fr sheet and 30 degree

lens.

Data collection and analysis

Both groups of patients were evaluated by a specialized nurse using the Visual Analogue Scale (VAS) to assess the analgesic effect in urology cystoscopy room. The nurse recorded the VAS scores during different moments, i.e. T1: during administration of lidocaine (control group) /during insertion of catheter and administration of lidocaine (experimental group), T2: during the insertion of cystoscope, T3: at the beginning of cystoscopy, T4: the third minute of cystoscopy, T5: during the first urination after the procedure, and the maximum pain score (Pmax) experienced by the patient during the whole operation. All the data were accurate to the nearest tenth. The VAS scores were: 1-3 for mild pain, 4-6 for moderate pain, 7-9 for severe pain, and 10 for extreme pain. The fluctuations of blood pressure and heart rate before and during the examination were monitored. Blood pressure variation = (maximum systolic blood pressure - systolic blood pressure at rest before examination) / systolic blood pressure at rest before examination × 100%. Heart rate variation = (maximum heart rate - static heart rate before examination) / static heart rate before examination × 100%. 24 hours later, the patient was followed up by telephone and asked if he had taken analgesic drugs and developed other complications such as dysuria, urinary retention, and systemic allergy. The patient's required anesthesia costs were calculated separately.

All patients were informed and signed consent to participate in the study. Randomization was performed by a nurse before the patient went into the operating room. When the preoperative anesthesia was performed by the nurse, the urologists, but not the patient, were informed of which group the patient in. The two doctors did not participate in the randomization, and they were unaware of the study-group assignments. During the operation, both groups of patients were evaluated by another nurse using the Visual Analogue Scale (VAS) to assess the analgesic effect.

Continuous variables are presented as means and standard deviations, and binary variables as numbers and percentages. VAS scores of two groups are response variables of multiple paired samples. Friedman test was used to compare the VAS scores of two groups at different time points. Student-t test was used to compare the mean age and operation time. Pearson's chi-square test was used for counts, as appropriate. Two-sided P values of less than 0.05 were considered to indicate statistical significance. All calculations were performed with the use of Excel 2013 (Microsoft), SAS software.

Table 2. VAS scores of two groups at different time points.

	Control	experimental	P value
T1(SD)	3.02(1.09)	3.44(0.89)	0.21
T2(SD)	4.61(1.82)	3.51(1.48)	<0.01
T3(SD)	3.57(1.44)	2.67(0.95)	<0.01
T4(SD)	2.96(1.38)	2.07(1.01)	<0.01
T5(SD)	1.28(0.76)	1.16(0.59)	<0.01
Pmax	4.92(1.20)	3.89(0.95)	<0.01

Abbreviations: SD=standard deviation, VAS=visual analogue scale

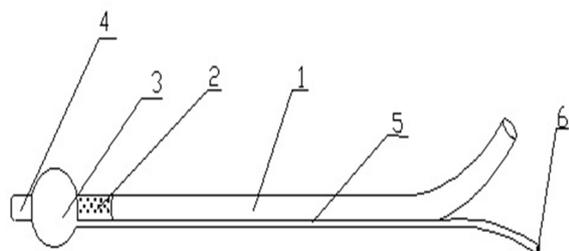


Figure 1. Sketch of the new catheter. The perimeter of the catheter is 14mm and the tip is a closed end. There is a Non-return Valve at the end of channel.

RESULTS

A total of 252 male patients were enrolled and underwent randomization from June 2016 to August 2017. The baseline characteristics of the patients were similar in the two groups (**Table 1**). All of them completed the operation without serious complications such as systemic anaphylaxis, induced asthma, urinary retention, hypertensive crisis, severe arrhythmia and other serious adverse reactions. No postoperative analgesic drugs were administered. Two patients in each group had urinary frequency and dysuria on the second day after operation, and their urine routine indicated a significant increase in white blood cells. They were cured after oral antibiotic was administered.

Overall comparison (two-factor repeated measures analysis of variance) showed that there was a significant difference among different time points on VAS ($P < 0.05$). Except that at T1, the VAS score of the control group was slightly lower than that of the experimental group, those of control group at other time points were invariably higher than those of the experimental group (**Table 2**).

The Pmax VAS score of the control group was 4.92 (SD = 1.20), which was higher than that of the experimental group with 3.89 (SD = 0.95, $P < 0.01$).

The blood pressure variation in control group was 12.9% (SD = 3.7), similar with the experimental group of 11.2% (SD = 3.2, $P = 0.12$). While heart rate variation in experimental group (16.3%, SD = 3.4) was lower than that in control group (22.6%, SD = 5.0, $P < 0.01$).

As per calculation, the anesthetic cost per patient in the control group was about 3.28 dollars, which was higher than the 1.53 dollars in the experimental group.

DISCUSSION

As a commonly used examination item in urology, cystoscopy can be used to observe the presence of stones,

tumors, foreign bodies, and deformities in the bladder and urethra. It can also be used for ureteral retrograde catheterization, retrograde pyeloureterography, ureteral stent extraction, etc. Due to the long male urethra, there are three physiological stenoses and flexions. Male patients often experience pain during cystoscopy and even fear of examination. The pain caused by cystoscopy is mainly due to (1) the pain caused by the squeezing of the urethra by the endoscope. In the anterior urethra, this pain is mainly caused by the somatosensory afferent nerve, and when the endoscope sheath is inserted into the posterior urethra, it is mixed with the stimulation of the visceral nerves and hence the more severe pain, which cannot be avoided nor be effectively relieved without drug intervention(3). (2) The pain caused by the pulling and stimulation of the visceral nerves, which is a result of the full bladder due to the use of large amount of perfusate(7). This pain can be relieved by improving the operation skills and reducing the intravesical pressure. At present, the commonly applied clinical practice includes general anesthesia, spinal anesthesia, pre-loaded analgesics, urethral surface anesthesia, etc., which are used to relieve pain in patients during cystoscopy(8). For the first two methods, due to their complicated operation, high requirements for cardiopulmonary function, more complications, high cost, etc., it is not easy to be widely used, especially in outpatient patients. Pre-treatment pain medications are not sufficiently effective and are accompanied with significant gastrointestinal side effects. The urethral surface anesthesia works by directly acting on the urethral mucosa through local anesthetic drugs, and has the advantages of simple and convenient operation and small side effects. David et al. found that intraurethral instillation of lidocaine gel reduced the likelihood of moderate to severe pain during cystoscopy(9). Shahram et al. performed a double-blind, randomized clinical trial in 2016. They concluded that combined glandular lidocaine injection and intraurethral lidocaine gel significantly reduced pain perception after cystoscopy compared to the use of intraurethral lidocaine gel alone(10). However, other scholars demonstrated no benefit from the use of an anesthetic gel in cystoscopy(4). Although the debate over the use of lidocaine for urethral surface anesthesia continues, the commonly used clinical methods for perfusion through the external urethral orifice or application of drug to the surface of the sheath cannot take sufficient effect on the posterior urethra, resulting in unsatisfactory pain relief(4-6). Poletajew's study of anesthesia of the posterior urethra indicated that after 6 h patients in the experimental group were more likely to declare that the cystoscopy was painless (81.8% vs. 70.2%, relative risk = 1.17)(11). Some scholars claim



Figure 2. Photo of the new catheter.

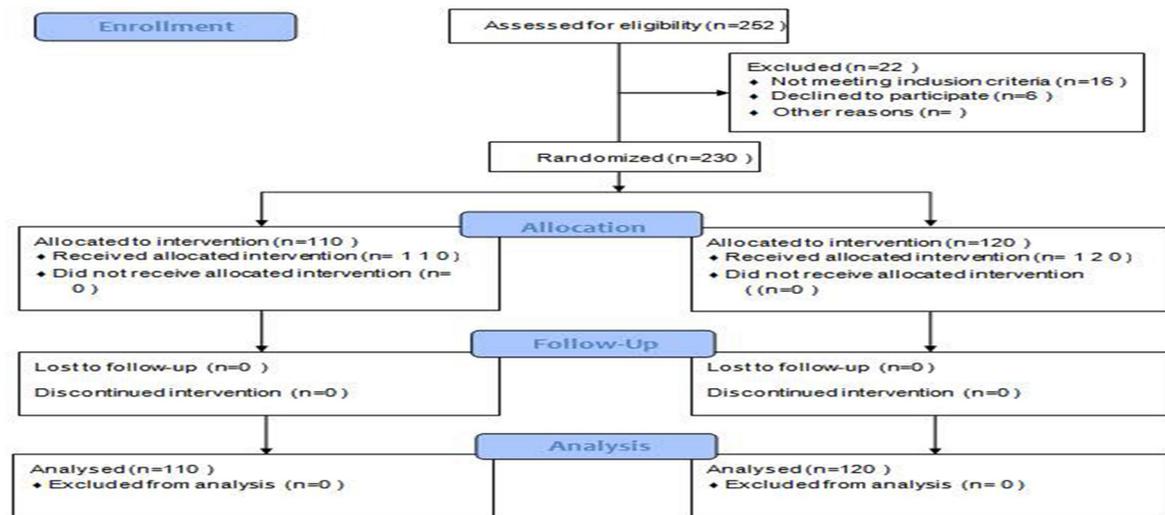


Figure 3. Patients' enrolment algorithm.

that flexible cystoscopy, compared with rigid cystoscopy, can reduce pain in patients⁽¹²⁾. However, no matter flexible or rigid cystoscope, it will invariably cause significant pain and discomfort when passing through the urethra, especially the posterior urethra⁽¹³⁾. Neither is flexible cystoscopy ideal for relieving the pain of patients. Gee GR⁽¹⁴⁾ observed the pain degree of flexible and rigid endoscope examination via VAS score, which of flexible endoscope group and rigid group were 1.4 and 1.8 respectively, without significant difference. In addition, flexible cystoscopes are expensive, easily damaged, and unsuitable for beginners. It is more difficult to promote them in basic medical institutions.

A simple, easy-to-apply technology that facilitates its promotion among basic medical institutions to enable effective anesthetic agents to act on the entire urethra, especially the posterior urethra, and to minimize patient suffering is thus a subject worthy of exploring. For these reasons, we designed and invented a new type of catheter. The tip of the catheter is a blind end. There are numerous small holes near the distal end of the balloon within 5 cm. The anesthetic agent can evenly act on the posterior urethra through the small holes; the role of the balloon is to close the inner urethra and prevent the anesthetic from rapidly leaking into the bladder so as to extend the drug action time. In this study, the VAS score of the control group at T1 was slightly lower than of the experimental group, which may be related to the increased urethral pressure after catheter stimulation of the urethra and insufficient smoothness around the small holes of the catheter due to the technical reasons of the manufacturer, but the difference was not statistically significant. Although the patients in the experimental group increased the process of urethral catheterization, the pain caused by the urethral catheterization was very slight and did not cause special discomfort to the patient, the main disadvantage of which was a slight increase the time for anesthesia. While at T2, T3, T4, and T5, the moments when the patients are more sensitive to the pain perceived, the scores of the experimental group were significantly lower than those of the control group, and so was Pmax, the maximum pain value during the examination. It is indicated that

the anesthetic can be fully applied to the posterior urethra through the new catheter, hence effectively relieve pain in patients with cystoscopy. We also found that in both the experimental group and the control group, the Pmax for most patients occurred when the sheath was inserted into the posterior urethra, while for a small proportion of the patients, it occurred in the initial stage of the examination when the endoscope moved in large amplitude. This indicates that the urinary tract stimuli are the most important cause of pain in cystoscopy, as reported by Losco G⁽¹⁵⁾. It also shows that although the use of new catheters can significantly reduce the pain of patients, the operation skills are still factors that cannot be ignored⁽¹⁶⁾.

Most of the patients who underwent cystoscopy were middle-aged or elderly patients and often had hypertension, diabetes, arrhythmia, and atherosclerosis. Severe pain can lead to a dramatic increase in blood pressure, heart rate, and even fecal incontinence, triggering cardiovascular events even serious adverse reactions⁽¹⁷⁾. This experiment showed that there was no significant fluctuation in blood pressure between the two groups during the examination, but the heart rate change was lower in the experimental group than that in the control group. This fact not only shows that the analgesic effect of the experimental group is better, but also confirms that the method used in the experimental group is safe and reliable, and has less impact on the cardiovascular function of the patient, hence lower potential risk. In addition, the new catheter used in the experimental group is simple and novel in design, low in cost, and can reduce the economic burden of patients to some extent.

We know that our study have limitations about the lack of smoothness around the small holes of the catheter, so it is necessary to improve the technical process after communicating with the manufacturer to avoid bias and to obtain a definitive conclusion.

CONCLUSIONS

Application of this new catheters can effectively relieve pain in the cystoscopy of male patients. The operation is simple and convenient, and it is safe and economical. It is worthy of promotion and adoption in the majority

of primary medical institutions.

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CONFLICT OF INTEREST

We declare that we have no conflicts of interest.

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