BJMS
Borneo Journal of Medical Sciences

ORIGINAL ARTICLE

POUR-UP: Power of Urination in Relieving Urethral Pain During Flexible Cystoscopy in Males

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Received: 10 July 2023

Accepted: 29 August 2023

Published: 30 September 2023

DOI: https://doi.org/10.51200/bjms.v17i3.4389

Keywords: *flexible cystoscopy, micturition, urethral pain, intraurethral application, POUR-UP*

ABSTRACT

This study aimed to investigate the effectiveness of micturition (urination) during flexible cystoscopy in alleviating urethral pain in males. A single-blinded, randomized controlled trial was conducted with 103 male outpatients at a tertiary care hospital in Malaysia. Participants, aged 18–80, undergoing flexible cystoscopy were randomly assigned to either a control or interventional group. The interventional group was instructed to urinate during the procedure, while the control group received no such instructions. All patients received standard lidocaine gel before the examination. Patient discomfort was assessed using Visual Analogue Scores (VAS) at three points: before gel instillation (baseline), immediately after the procedure, and 15 minutes post-examination. Age, BMI, duration of the examination, and examiner experience were also recorded to explore their correlation with the immediate post-procedure pain score. The interventional group reported significantly lower pain scores immediately after the procedure ($p < 0.001$) and 15 minutes later ($p < 0.005$) compared to the control group. However, there was no statistically significant difference in age, BMI, examination duration, or examiner experience level between the two groups regarding the pain score immediately post-procedure. These findings suggest that urination during flexible cystoscopy can substantially alleviate urinary discomfort and lead to a significant reduction

in urethral pain in males. This approach may provide a valuable method to improve patient comfort during the procedure.

INTRODUCTION

Flexible cystoscopy examination is a routinely performed office procedure in any urological consultation. Since its introduction in 1984, it has become a common procedure with almost no/minimal reported side effects. In comparison with a rigid cytoscope, it has no blind spots, clear vision, and can be performed as an outpatient procedure for most diagnostic/surveillance procedures (Pillai & Sooriakumaran, 2009). Urethral pain or discomfort has been one of the most challenging factors that urologists have faced while performing this procedure (Krajewski et al., 2016). Many patients, particularly men, refuse this examination for this reason.

There have been many methods described in the literature on how to manage pain among patients undergoing CE, especially male adults. Instillation of local analgesic agents (LA) such as Lignocaine/Bupivaicaine/ Tetracaine gels as a gelatinous mix of lubricant and LA has been common practice for years (Akkoç et al., 2016; Patel et al., 2008). In recent years, many studies have been performed to explore the role of behavioral/psychological interventions to reduce urethral pain, for example, watching examination procedures via television (Patel et al., 2007; Zhang et al., 2011) or squeezing pressure balls while listening to music (Zhang et al., 2014; Raheem et al., 2015).

Techniques to reduce urethral pain during cystoscopy are still a controversial topic, as most studies use the patient's perception of pain. The role of urination in reducing urethral pain is relatively new, and the only randomized study that has been performed to support this idea was by Xie et al. (2020) with the concept that micturition should relax the sphincters, which in turn should open the urethral lumen wider, and reduce the painful sensation of cystoscopic examination.

The primary objective of this study is to assess the effectiveness of micturition (urination) during flexible cystoscopy in relieving urethral pain in males. Additionally, the study aims to identify any other factors that might contribute to a higher pain score among the Malaysian population during this procedure.

METHODOLOGY

Study Population

Male patients between 18 and 80 years old undergoing elective CE in Hospital Sultanah Aminah from May 2022 – Dec 2022 and requiring diagnostic/surveillance cystoscopy were recruited. Exclusion criteria included using analgesics within 24 hours of the study period, having a known urethral stricture, a history of urethral dilation, an acute urinary tract infection, an indwelling urethral catheter, and having existing urethral pain (including chronic pelvic inflammatory disease and interstitial cystitis).Patients as well as those who are unable to cope with pain assessment due to a mental disorder or who are treated as neurogenic bladder failure or bladder failure or who are unable to void on command were excluded from this study. Potentially vulnerable subjects were also excluded from the study (prisoners, cognitively impaired subjects, and critically ill subjects).

Randomization

After being reviewed by the medical officers-in-charge, by using Random Allocation Software, version 1.0.0, a random number is built, which then randomly divides patients into experimental and control groups with a 1:1 ratio. This process is carried out by another medical officer who is not involved in the subject's recruitment process. To ensure concealment of allocation, only sealed opaque envelopes were used. Only participants in the intervention group in the trial know the grouping; however, the data collectors (staff nurse who qualified to assess pain scores)

were blinded to avoid bias. The operator of the cystoscopy only knew the grouping of the patient when he opened the sealed envelope prior to performing the procedure.

Design

We performed a prospective, randomized, controlled trial (single-blinded) designed to compare pain scores between patients in the interventional and control groups. Patients who are deemed eligible to join this study underwent routine urinalysis to rule out the presence of any active infection. Prior to cystoscopy, a routine bladder scan was performed to ascertain a minimal volume of 100 ml of urine present so the patient was able to void on command. Patients in the test group were instructed to urinate during the procedure, while those in the control group were not given any instructions.

All cystoscopies were performed by experienced urologists, surgeons, or trainees who have a minimum of 2 years of experience in the field of urology. Pain scores are assessed using the Visual Analogue Score (VAS), where patients where are asked to mark their intensity of pain with a range from "0" indicating no pain, to "10" on the other end, indicating severe pain. Patient's pre-procedure pain score, immediate post-procedure pain score (after entering bladder), and 15 minutes post procedure pain score recorded by data collectors. In this study, a standard cystoscopy system, including 16F flexible cystoscopy (Olympus CYF-5A), a digital camera (Olympus OTV-S7), and color video monitor (Olympus OEV-191H), was used.

Intervention

All patients underwent preliminary bladder scans immediately prior to the procedure to ascertain that at least a minimum of 100 ml of residual urine was present in order to be able to void on command. Patients were positioned supine as per any cystoscopic examination. The area of interest was disinfected with routine antiseptic solutions. Prior to the examination, 10 ml of 2% lidocaine gel was instilled into the urethra and squeezed gently for a duration of 5 minutes. For the control group, the penis is stretched and the cystoscope introduced through the meatus with examiner's left hand while introducing a flexible cystoscope into the urethra with the guide of his left thumb and index finger. The cystoscope held with his right hand, with his thumb used to control the adjusting lever. Under direct vision and with the help of continuous irrigation fluid flow, the examiner observes the urethra, which is transmitted into video surveillance. Upon reaching the external urethral sphincter, the examiner stays 1 – 2 seconds and attempts to enter the bladder. Meanwhile, for the experimental group, similar steps repeated and patients were instructed to void upon reaching external urethral sphincter. Cystoscopy advanced to enter the bladder as the patient attempts to voids, when visual relaxation of sphincter happens completing the examination.

Collection of co-variate data

A few other data points such as age, height, weight, indication for examination, and duration of examination were also recorded. Performing examiners are distributed by random selection. This data was collected to support the secondary objective of this study.

Follow-up

Prior to discharge, patients were reviewed by the medical officer in charge, and the findings of the procedure were explained in detail. Follow-up is given to review the patient at one-month's duration to record any adverse effects. Routine clinic follow-up appointments were given according to the nature of the illness.

Data Analysis

Sample size of this study calculated based on two-sample t-test: $n = (2 * (Z\alpha/2 + Z\beta) / d)^2$. Where: n = sample size per group $Z\alpha/2$ = critical value of the standard normal distribution at a

significance level (α/2) Zβ = critical value of the standard normal distribution at the desired statistical power (1 – ß) d = Cohen's d effect size.

We used results from Taghizadeh et al. (2006) 2.82 ±1.2 VAS (presuming with minimally clinically important pain difference as 0.9 (Kelly, 1998). Given the effect size of Cohen's d = 0.5, and a two-sided 5% level t-test with a statistical power of 1 – ß = 80%, 32 patients would be needed to detect this group difference. We recruited 103 patients in this trial (n = 51 control, n = 52 interventional); recognizing a potential loss of analytical power due to patient withdrawals of 10%.

SPSS 20.0 software was used for all data analysis. Numerical data are presented as mean ± standard deviation (SD), median, and interquartile range (IQR). Categorical are presented as frequency and percentage. The mean pain score between the 2 groups (control and intervention) was compared using an independent t test. A p-value less than 0.05 was considered to be statistically significant. The correlation between factors is analyzed with Pearson correlation.

RESULTS

As shown in Table 1, 103 patients included in this study which were randomized into control, (n = 51) and interventional (n = 52). Mean age, BMI, and examination time are analyzed with an independent t-test showing no statistical significance among the control and interventional groups empowering our study population, which are similar in nature.

Table 1 Demography of study population

Variables	Control (n = 51) Mean (SD)	Interventional (n = 52) Mean (SD)	Mean diff (95% CI)	t-statistic (df)	p-value
Age (years)	59.37 (9.35)	59.00 (9.68)	–0.37 (-4.09,3.34)	–0.20 (100)	0.843
Body Mass Index	30.17 (2.45)	30.15 (3.49)	–0.14 (-1.19,1.17)	–0.02 (101)	0.983
Examination time (min)	14.61 (1.04)	14.67 (1.26)	0.07 (–0.39,0.52)	0.29 (101)	0.776

Between interventional and control groups, patients were equally examined by either Consultant, Surgeon, Senior or Junior trainee (Table 2). Statistical analysis by one-way ANOVA showed a p value that was not significant between and within groups, as shown in Table 3 below, the same as for all our other demographics in both groups.

Table 2 Examiner's experience among control vs interventional groups

Examiner's experience	Control group N (%)	Interventional group N (%)
Consultant	13 (25.4)	13 (25.0)
Surgeon	12 (23.5)	14 (26.9)
Senior trainee (UT2)	13 (25.4)	12 (23.1)
Junior Trainee (UT1)	13(25.4)	13 (25.0)

Table 3 Comparison between surgeons experience and pain recorded one-way ANOVA analysis

	Sum of squares	df	Mean square	F	Sig.
Between groups	0.289	1	0.289	0.229	0.633
Within groups	127.264	101	1.260		
Total	127.553	102			

The majority of our patients undergo cystoscopy as part of preoperative evaluation for bladder calculus, followed by a benign prostatic hyperplasia workup prior to surgical interventions. The third largest group of patients were those on regular surveillance for malignant neoplasm of non-muscle invasive bladder carcinoma/upper tract urothelial carcinoma after radical nephro-ureterectomy with bladder cuff excision. The other indications are tabulated in the bar chart below (Figure 1).

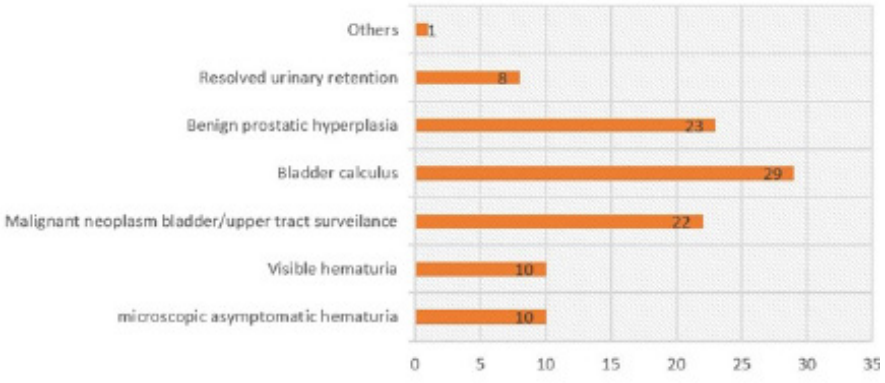

Figure 1 Indication for urethro-cystoscopy

In terms of VAS, neither group experienced pain at the start of the test (score = 0).Score at immediate post-procedure was lower among the interventional group: 4.35 ± 1.05, while the control group score was 5.20 ± 1.23, with a statistically significance difference of p = 0.00001. Similar findings noted for score 15 minutes post procedure whereby interventional group recorded score = 2.06 ± 1.02 while control group score = 2.63 ± 1.00 with statistically lower score with $p < 0.005$. Table 4 shows statistical analysis while box and whisker in Figure 2 showing interquartile range of both test and control group at 2 different time of pain score recordings.

Table 4 VAS difference Control vs Interventional at immediate and post procedure (15 min)

Visual analogue score (VAS)	Control mean (SD)	Interventional mean (SD)	Mean diff (95% CI)	t-statistic (df)	p-value*
Immediate	5.20 (1.23)	4.35 (1.05)	–-0.85 (–1.30, –3.97)	–3.72 (101)	0.00001
15 min post procedure	2.63 (1.00)	2.06 (1.02)	–0.06 (–0.96, –1.78)	–2.89 (101)	0.005

*Independent t-test

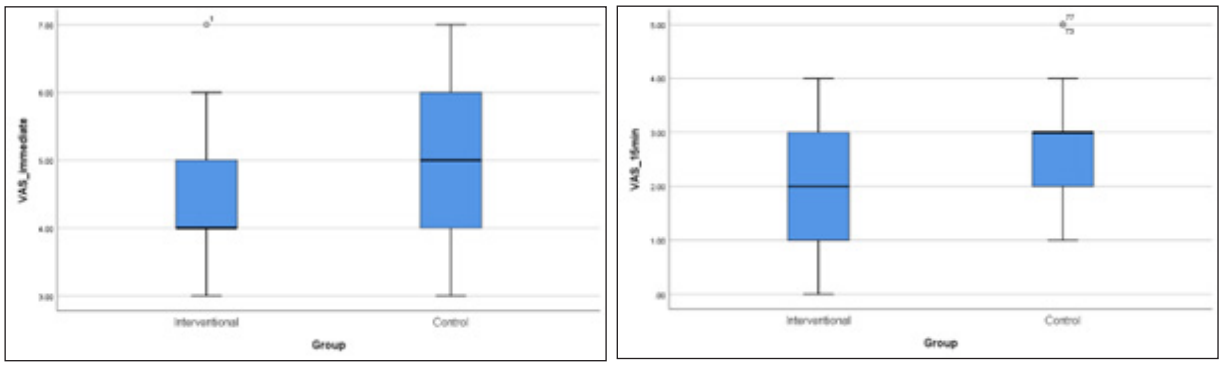

Figure 2 VAS comparison immediate and 15 minutes post procedure

Age, BMI, procedure duration (time), and operator experience are found to have no significant effect on pain score (VAS) at the immediate post procedure ($p>0.05$). Result of the Pearson correlation are tabulated in Table 5 below.

Table 5 Secondary factors associated with VAS (immediate)

	Pearson Correlation	Sig (2-tailed)
Age	0.187	0.06
BMI	–0.01	0.99
Time	0.127	0.20
Operator experience	0.057	0.570

DISCUSSION

Flexible cystoscopy is widely used in urological investigations for direct visualization of lower urinary tract pathologies. However, urethral pain and discomfort have been significant limitations, particularly in males undergoing this procedure. Previous studies have highlighted that the most painful part of flexible cystoscopy occurs when the scope tip passes the external sphincter (Taghizadeh et al., 2006; Chen et al., 2005), which is rich in nerve endings and comes into contact with the urethral mucosa.

Studies by Xie et al. (2009) demonstrated that during urine storage, the external sphincters remain contracted to maintain continence, and they relax during voiding. These findings have led to the exploration of various methods to reduce pain during cystoscopy. Non-pharmacological strategies, including psychological and behavioral techniques, have gained popularity, as they allow active control of the cerebral cortex through intentional urination, leading to relaxation of the external urinary sphincter and smoother passage of the cystoscope.

In our study, we aimed to replicate these findings within our local population as this may lead to better treatment modality for future references. We were successful in recruiting 109 patients to participate in this study. After recruitment, total of 6 patients were excluded from further data analysis. 4 patients from interventional arm withdrawn due to failure to void with instruction. This event might be related in the earlier phase of study whereby more medical personnels than needed were present that contributed shyness to perform needed act. The other 2 patients (1 from each arm) refused to undergo this procedure due to personal reasons. Degree of relaxation of sphincter is subjective to each performing surgeons however all agreed upon only to advance cystoscopy further once urine is seen gushing out at level of external sphincter in interventional arm. Verbal assurances, the bag squeeze technique, listening to music were allowed for both while maneuvers that might lead to sphincter relaxation (verbal order to relax sphincter, wiggling toes, cough, etc.) was not performed in control group. Retroflexion however not performed in any of the cases as we believed bladder pain might arise with friction of endoscope. We observed significantly lower pain scores in the interventional group compared to the control group immediately post-procedure (5.20 ± 1.23 vs 4.35 ± 1.05, $p = 0.000$) and 15 minutes post-procedure (2.63 ± 1.00 vs 2.06 ± 1.02, $p = 0.005$). Although statistically significant, we acknowledge that clinical difference of VAS 1 does not seem much in real world data. First experience with painful episode of cystoscopy examination will affect compliance of further surveillance follow up (Chen et al., 2005) and affects overall quality of life in patient care.

One of the strengths of our study is the even distribution of the study population between the interventional and control groups, with no significant differences in age, BMI, duration of examination, or examiner experience. This minimized bias and reduced the impact of confounding factors. Surprisingly, our analysis did not find any correlation between age, BMI, examination duration, examiner experience, and higher pain scores immediately post-procedure.

However, our study does have limitations. One limitation is the uncertainty regarding the degree of relaxation of the external sphincters in the control group. Objective assessment of sphincter relaxation using techniques such as electromyography (Xiyu & Bo, 2002) could be considered in future studies. Furthermore, a more comprehensive analysis of other potential confounding factors and their influence on pain scores could provide additional insights. It would be interesting to explore if there is any association between pain scores and race, considering that Malaysia is a multiracial country. This could be a potential avenue for future research.

CONCLUSION

In conclusion, our study supports previous findings that micturition during flexible cystoscopy significantly reduces urethral pain in males. This non-pharmacological approach, allowing active relaxation of the external urinary sphincter, shows promise in enhancing patient comfort during the procedure. Further research is warranted to explore additional factors and refine the techniques used to alleviate pain and discomfort during cystoscopy.

CONFLICT OF INTEREST AND FUNDING

The authors declare they have no conflict of interest to publish this article. This research received no specific grant from any funding agency in the public, commercial or non-profit sectors.

ACKNOWLEDGEMENTS

The authors would express their gratitude to all medical personnel involve either directly or indirectly for assisting during this study period.

DISCLOSURE

This study was conducted in compliance with ethical principles outlined in the Declaration of Helsinki and Malaysian Good Clinical Practice Guideline. Approval was obtained from Medical Research and Ethics Committee (MREC) and this study is registered as RSCH ID-21-01155-Z2F with National Medical Research Register (Malaysia) prior to recruitment. All participants signed consent agreeing to be involved in this study. There was no animal involved in this study.

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