

Anaesthesia of the posterior urethra and pain reduction during cystoscopy – a randomized controlled trial

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Abstract

Introduction: Standard intra-urethral instillation of anaesthetic gel may not sufficiently exclude pain perception during cystoscopy.

Aim: To evaluate the impact of the anaesthesia within the posterior urethra on pain intensity related to cystoscopy in men.

Material and methods: One hundred and twenty-seven men undergoing cystoscopy were prospectively enrolled in the study. Patients were randomly assigned to the experimental or control group (66 vs. 61 patients). Intra-urethral instillation of 2% lidocaine gel was done in both groups. In the experimental group, the posterior urethra was additionally anaesthetized with distribution of the lidocaine gel by catheterisation. The study endpoints were pain intensity at successive time points of the procedure assessed on a numeric rating scale, overall pain intensity assessed on a Likert scale, the need for analgesics during 6 h after the procedure, and the frequency of urinary tract infections (UTIs) during 14 days after the procedure.

Results: Pain perception during cystoscopy did not differ significantly between the two groups ($p > 0.05$). However, 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). The need for analgesics and the incidence of UTI were similar in both groups ($p > 0.05$). Statistically significant differences regarding pain perception were observed depending on patients' age and the number of transurethral procedures performed in the past, with no relation to type of anaesthesia ($p < 0.05$).

Conclusions: Anaesthesia of the posterior urethra is not more efficacious in reducing pain related to cystoscopy than standard instillation of anaesthetic gel. However, it improves the general perception of the procedure, and hence may positively influence patients' compliance.

Key words: bladder cancer, cystoscopy, anaesthesia, urethra.

Introduction

Bladder cancer is the most common urinary tract malignancy [1]. About 75% of patients undergo transurethral resection of the bladder tumour (TURBT) due to the presence of non-muscle-invasive bladder cancer (NMIBC). Afterwards they all need close follow-up based on cystoscopy repeated every 3–12 months for at least 5 years [2].

Cystoscopy remains an uncomfortable procedure with inevitable pain reported by patients. The pain is usually classified as mild or moderate, may be reduced by the use of a flexible instrument, but still remains consistently reported by all patients [3, 4]. Moreover, while patients report less pain related to cystoscopy than they anticipate before the procedure, conversely physicians are likely to underestimate actual pain perceived by patients [5, 6]. The

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pain is more intense in men than in women [4]. The most painful part of the procedure is insertion of a cystoscope, especially at the moment when it passes the external urethral sphincter [7, 8].

While the body of literature on the optimisation of urethral anaesthesia is growing, it is still questionable whether standard installation of anaesthetic gel or plain lubricant through the external urethral orifice can sufficiently exclude pain perception within the posterior urethra in men. Simultaneously, none of already published studies was aimed at design and evaluation of anaesthesia in this region before diagnostic cystoscopy.

Aim

The aim of the study was to evaluate the effect of the anaesthesia within the posterior urethra on the pain intensity during and after rigid cystoscopy in men.

Material and methods

One hundred and twenty-seven men with a mean age of 71.4 years and a history of TURBT, undergoing routine follow-up cystoscopy, were prospectively enrolled in the study. Patients were randomly assigned to the experimental or control group (66 vs. 61 patients) based on a randomization generator available at randomization.com. The institutional review board approved the study protocol. All patients gave written consent to participate in the study. Detailed characteristics of the study population are presented in Table I. Figure 1 presents the CONSORT diagram.

Twelve ml of 2% lidocaine gel, administered through the external urethral orifice, was used for local anaesthesia in both groups. In the experimental group, after the initial analgesic effect was achieved, additionally a 10 Fr Tieman bladder catheter (coude-

tipped catheter) was inserted to distribute the lidocaine gel along the entire length of the urethra, and hence to anaesthetize the posterior urethra. The time from gel administration to urethra instrumentation with the cystoscope was 5 min in both groups.

Urinary tract infection (UTI) was excluded before the procedure in all cases. Six residents in urology participated in the study and performed uniform anaesthesia and cystoscopies. No dedicated patient preparation for the procedure was adopted. All the cystoscopies were performed with a 17 Fr rigid cystoscope in a lithotomy position.

The primary study endpoint was the pain intensity at different time points during and after the procedure assessed on a 10-point numeric rating scale (NRS). Secondary study endpoints were overall intensity of pain related to the procedure assessed on a Likert scale, the need for analgesics within 6 h after the procedure, and the frequency of UTI within 14 days after the procedure.

We hypothesized that anaesthesia of the posterior urethra would be superior to standard local anaesthesia with respect to pain intensity at the time of insertion of the cystoscope and non-inferior with respect to other study end-points. We also assumed that the NRS score at the time of insertion of the cystoscope would be at least 30% lower in the experimental group. Considering a mean visual analogue scale (VAS) score of 3.0 in the control group based on literature data, a sample size of 50 patients in each study arm was planned to detect a 30% difference in NRS score and obtain 80% power using a one-sided α value of 0.05.

Statistical analysis

Statistical calculations were performed with Statistica 10.0 software. The Shapiro-Wilk test con-

Table I. Characteristics of the studied groups

Parameter	Experimental group	Control group	P-value
Number of patients	66	61	
Mean age [years]	73.0	71.2	> 0.05
Mean time interval from the last TURBT [days]	497	494	> 0.05
Mean number of TURBT performed per patient	4.6	4.5	> 0.05
Number of patients who received adjuvant intravesical BCG therapy after TURBT	11	9	> 0.05
Mean time interval from last intravesical instillation of BCG [days]	1419	818	> 0.05

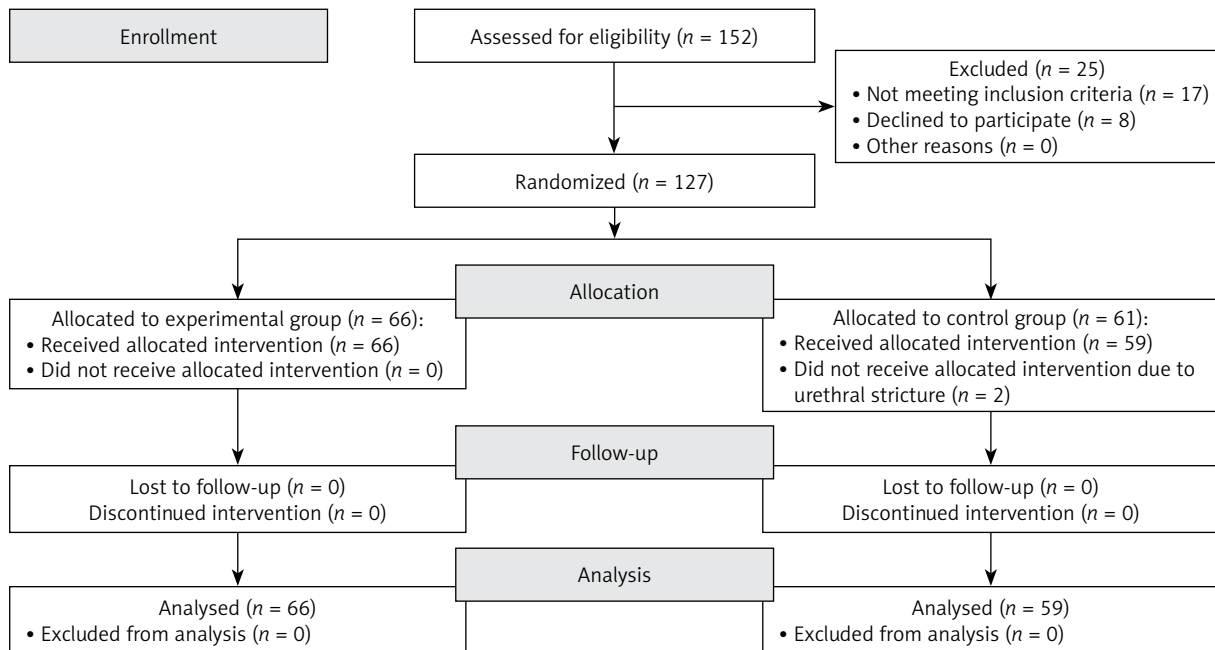


Figure 1. Flow diagram of the progress through the phases of the trial (based on diagram available on <http://www.consort-statement.org>)

firmed the normal distribution of all variables. The Levene test was applied for assessment of the equality of variances. For the comparison of results between study groups, the χ^2 test with the Pearson formula and *t*-test were used for non-parametric and parametric variables, respectively. The differences were considered statistically significant when the *p*-value was < 0.05.

Results

The final analysis was based on 125 patients with the mean age of 71.7 years. Two patients from the control group were excluded from the study due to the presence of urethral strictures preventing cystoscopy.

Primary endpoint

Pain perception assessed directly during the cystoscopy, as well as that assessed after the procedure, did not differ between the two groups. Detailed results are presented in Table II. Each step of the procedure was associated with similar discomfort independently of the anaesthesia of the posterior urethra.

Secondary endpoints

When evaluated 6 h after the cystoscopy, patients in the experimental group were less likely to classify pain related the procedure as mild (10.9 vs. 17.5%, relative risk (RR) = 0.60) or moderate (7.3% vs. 12.3%, RR = 0.59) and more likely to declare

Table II. Pain perception during cystoscopy assessed on 10-point numeric rating scale, mean values and standard deviations

Time point/study group	Insertion of catheter	Insertion of cystoscope	Second minute of cystoscopy	Five minutes after completion of cystoscopy
Experimental	2.75 ±2.16	2.93 ±2.17	2.38 ±1.92	1.59 ±1.60
Control	–	3.34 ±2.22	2.00 ±1.65	1.58 ±1.25
Absolute difference	–	0.41	–0.38	–0.01

that the cystoscopy was painless (81.8% vs. 70.2%, RR = 1.17). The percentage of patients demanding analgesics within 6 h after the procedure was 0% in the experimental group and 1.8% in the control group ($p > 0.05$). During 14 days after the procedure, UTI was diagnosed in 8.1% of patients in the experimental group and 7.3% of patients in the control group ($p > 0.05$). The incidence of symptomatic UTIs was 1.6% vs. 5.4%, respectively ($p > 0.05$). The most common pathogen isolated from urine was *Escherichia coli* (75% of symptomatic UTIs), followed by *Klebsiella pneumoniae* (25% of symptomatic UTIs).

Post-hoc analysis

Statistically significant differences regarding pain perception were noted depending on the patients' age and number of procedures performed in the past with no relation to the type of anaesthesia. Patients aged < 75 years declared significantly higher NRS scores at the time of insertion of the cystoscope into the bladder (3.61 vs. 2.62, $p < 0.05$). With an increasing number of TURBTs performed in the past, NRS scores declared by patients during cystoscopy decreased. The pain perception was significantly lower during catheterisation in patients with a history of at least 2 TURBTs (2.33 vs. 3.44, $p < 0.05$), at the second minute of cystoscopy in patients with a history of at least 3 TURBTs (1.92 vs. 2.62, $p < 0.05$) and during insertion of the cystoscope into the bladder in patients with a history of at least 10 TURBTs (2.21 vs. 3.29, $p < 0.05$).

Discussion

Bladder cancer is the most common malignancy occurring within the urinary tract. According to GLOBOCAN data, the incidence in Central Europe is 15.1 new cases per 100 000 habitants per year [1]. About 75% of patients are diagnosed with non-muscle invasive bladder cancer (NMIBC) [9]. They undergo TURBT followed by intravesical chemo- and/or immunotherapy. Due to the significant risk of recurrence and progression, these patients need close, often lifelong, follow-up with numerous cystoscopies performed every 3–12 months [2]. Despite significant technological improvement, including wide implementation of flexible cystoscopies, the procedure remains uncomfortable for patients.

We performed a prospective, randomised controlled study aimed at optimisation of anaesthesia in men undergoing cystoscopy. As patients report

that the most painful step of the procedure is the moment when the cystoscope passes the posterior urethra [7, 8], we focused on improvement in anaesthesia of this particular region. To our knowledge, this is the first study that presents a method of anaesthesia of the posterior urethra and assesses its clinical significance.

Our study did not reveal a direct and statistically significant effect of anaesthesia of the posterior urethra at the time of cystoscopy; however, it did find an important improvement in overall perception of the procedure in the experimental group. This fact can be crucial for patients' compliance. In everyday clinical practice it is not uncommon that patients abandon follow-up because of pain related to cystoscopy. In a historical study by Schrag *et al.* the incidence of suboptimal frequency of follow-up cystoscopies was over 60% of NMIBC patients, while almost 10% of patients did not even have a single follow-up cystoscopy done [10].

Numerous research groups have already attempted to optimise the cystoscopy protocol, especially to reduce pain perception. There have been many prospective, randomized and controlled trials on this issue published in recent years. Thompson *et al.* and Goel and Aron independently proposed to cool the gel to 4°C [11, 12]; however, the benefit of lower temperature was not confirmed by Bhomi *et al.* [13]. Brekkan *et al.* and Holmes *et al.* independently suggested increasing the volume of lidocaine gel to 20 ml before cystoscopy in men, especially in patients younger than 55 years [14, 15]. Khan *et al.* outlined the importance of the delivery rate of lidocaine gel, indicating that slow administration within 10 s reduces patient discomfort compared to 2-second administration [16]. Vasudeva *et al.* and Losco *et al.* independently examined the optimal dwell time of intraurethral lidocaine gel before insertion of the cystoscope. The first group concluded that 15 min is more effective than both 5 and 10 min for patient as well as physician assessment of pain intensity [17], while the second group did not observe significant differences between immediate insertion of the cystoscope and after a 3-minute delay [18]. Moharari *et al.* added ketamine to lidocaine gel and observed significantly lower scores on the visual analogue scale compared to lidocaine alone [19]. The analgesic effect can also be strengthened when lidocaine gel is combined with oral

medication. Komiya *et al.* proposed administering orally a 160 mg single dose of zaltoprofen 60 min before cystoscopy, which resulted in lower pain scores compared to no premedication [20]. Gunendran *et al.* described a “bag squeeze” technique, during which a member of the nursing staff gently squeezes the irrigating fluid bag until the opening of the external sphincter visible on the video camera before the scope passes through the posterior urethra [21]. Zhang *et al.* recently improved this technique. They confirmed that higher irrigation pressure is associated with less discomfort during cystoscopy and proposed to raise the irrigation solution bag and adjust the height in order to easily improve patients’ satisfaction [22]. Apart from technical tips and tricks, Yeo *et al.* found that listening to classical music during rigid cystoscopy is a simple, economical and effective means of enhancing patient comfort and reducing feelings of pain, anxiety, and dissatisfaction [23].

Finally, numerous research groups have questioned the value of the analgesic effect of lidocaine gel for cystoscopy. In 2008 two meta-analyses on this issue with contradictory results were published. While Aaronson *et al.* concluded that intraurethral instillation of lidocaine gel provides control of moderate to severe pain and benefit to male patients undergoing cystoscopy [24], Patel *et al.* provided no evidence of a statistically significant difference in pain scores between lidocaine gel and plain gel instillation [25]. Apart from uncertainty regarding effectiveness, some authors report that delivery of lidocaine gel can cause significant discomfort compared to plain lubricant [26]; however, this finding is not consistent within the literature [15]. None of the already published studies have focused on optimization of anaesthesia of the posterior urethra.

In the present study we found that age and number of cystoscopies performed in the past were inversely correlated with pain intensity during the procedure. This finding was not universal, as statistically significant differences were not observed at all assessed time points, or in all examined groups. However, there is a trend to worse pain scoring during the first cystoscopy and in younger men, which is also described by other authors [3–5, 20–22]. While the aim of our study was to optimise local anaesthesia for cystoscopy, these findings are clinically useless despite their relevance. However, being fully consistent with previously published data, they

confirm that our methods and protocol are sound, despite the negative findings.

Our study has some limitations. First, nowadays flexible cystoscopy is becoming a standard procedure, while rigid instruments are used less commonly. However, in our institution we still use both rigid and flexible cystoscopes. What is more, we think that in many urological centres rigid cystoscopes are still in use due to their simplicity, reliability and cost-effectiveness. Finally, the character of the instrument does not impact the significance of the results obtained in our study, although one could expect lower NRS scores if a flexible cystoscope were used [27]. Second, as this study is not a blind one, the level of evidence is limited. However, from a practical point of view, it is impossible to plan a blind and especially double-blind study of such character. Last but not least is the fact that as many as six physicians were involved in conducting the experiment. The significance of this fact is substantially reduced by standardisation of the procedure and inclusion of a similar number of patients in both study groups by each resident.

Conclusions

Anaesthesia of the posterior urethra does not decrease the pain at the time of introducing a cystoscope and has no influence on the overall feeling of pain during the procedure. However, it improves the general perception of the procedure, and hence may positively influence patient compliance. Standard injection of anaesthetic gel through the external urethral orifice to exclude pain perception within the posterior urethra is as sufficient as extended gel distribution to the posterior urethra.

Conflict of interest

The authors declare no conflict of interest.

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