

ANALGETIC EFFICACY OF FLURBIPROFEN AXETIL IN RIGID CYSTOSCOPY FOR MEN: A PROSPECTIVE STUDY

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Objective: To evaluate the analgesic effect of preprocedural flurbiprofen axetil on rigid cystoscopy-associated pain for men.

Methods: Fifty-two men scheduled for cystoscopy were recruited in this study. The effects of oxybuprocaine jelly alone or in combination with preprocedural flurbiprofen axetil, were compared. The pain intensity was assessed using visual analogue scale (VAS) scores during injecting oxybuprocaine jelly into the urethra, during inserting rigid cystoscope into the urethra, during viewing inside the urinary bladder, at the first urination after cystoscopy and at the first urination on the following morning at home.

Results: VAS scores with preprocedural flurbiprofen axetil were significantly lower as compared with the control group at the time periods of inserting rigid cystoscope into the urethra, viewing inside the urinary bladder, the first urination after cystoscopy and at the first urination on the following morning at home. No side effects associated with flurbiprofen axetil were observed.

Conclusion: Preprocedural flurbiprofen axetil can decrease cystoscopy-associated pain.

Keywords: non-steroidal anti-inflammatory drug; pain; preventive analgesia; rigid cystoscopy; flurbiprofen axetil.

Introduction

Cystoscopy is painful examination. Despite the availability of flexible cystoscope in clinical practice, the use of rigid cystoscope is still common because it is less expensive, easier to handle and maintain and has a better visual field¹. Instillation of analgesic jelly into the urethra several minutes before the procedure has shown little significant effect for reducing pain²⁻⁵. Patients complain for not being able to stand the pain even with the assistance of analgesic jelly when undergoing

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rigid cystoscopy. Moreover, patients also complain of great pain during urination after cystoscopy²⁻⁶. Thus, more effective methods are necessary to reduce pain associated with rigid cystoscopy.

Preprocedural administration of non-steroidal anti-inflammatory drug (NSAID) such as flurbiprofen by the oral route has been reported to have a positive effect on cystoscopy-related pain⁷. However, to our knowledge no study about the analgesic effect of this injectable NSAID drug on cystoscopy-related pain has been conducted.

The aim of this prospective, double-blinded and randomized study is to evaluate the efficacy of flurbiprofen axetil by the intravenous route on cystoscopy-related pain.

Methods and Materials

This prospective and randomized study was approved by the institutional ethical committee. Male patients who were scheduled to undergo rigid cystoscopy in the outpatient urology clinic of our hospital were asked to participate in this study and 52 male patients were enrolled after written informed consents were obtained. Exclusion criteria were American Society of Anesthesiologists (ASA) physical status more than II, a history of cystoscopy, active urinary tract infection, allergic reaction to the study drugs, peptic ulcer, liver or renal insufficiency and mental disorder. All patients were instructed of the visual analogue scale (VAS: 0- no pain; 1, 2, 3-mild pain; 4, 5, 6-moderate pain; 7, 8, 9-severe pain; 10-worst imaginable pain) for measuring pain intensity before cystoscopy.

Venous access was achieved after the patients were taken to the clinic without premedication. The patients were equally assigned to one of the two treatment groups according to a computer-generated schedule. Group F received 50 mg flurbiprofen axetil (flurbiprofen axetil, Beijing Tide Pharmaceutical CO LTD, Beijing, China) and Group C received 20% fat emulsion injection (medium and long chain fat emulsion injection C8-24Ve, B. Braun Melsungen AG, Suzhou, China) diluted with normal saline to achieve the concentration of 2% as control agent. The study drugs were administered intravenously slowly over 1 minute. Fifteen minutes later, 20 ml 0.3% oxybuprocaine

jelly (oxybuprocaine hydrochloride jelly, Shenyang Luzhou Pharmaceutical CO. LTD, Shenyang, China) was injected transurethrally. A penile clamp was placed for 10 minutes. The patient lay supine during the 10-minute interval, and then cystoscopy began. The study drugs were prepared by an independent researcher who was not involved in the procedures, so neither the physician performing cystoscopy nor the patients knew the grouping situation.

Cystoscopy was done by the same urologist using a rigid 22 F cystoscope (27005CA HOPKINS II Telescope 70°, STORZ, Tuttlingen, Deutschland). All patients were observed for 1 hour after cystoscopy before they went home. Patients rated pain perceived based on VAS at various time periods, including T1—during injecting oxybuprocaine jelly into the urethra; T2—during inserting rigid cystoscope into the urethra; T3—during viewing inside the urinary bladder; T4—at the first urination after cystoscopy and T5—at the first urination on the following morning at home. One of the researchers who was not involved in the procedures recorded VAS scores. The overall patient satisfaction was evaluated using a four-point scale (1: poor; 2: moderate; 3: good and 4: excellent). Side effects were evaluated.

Based on previous studies, pain score during inserting cystoscope into urethra is considered the primary outcome^{2,7}. To detect a standard deviation of 30% (estimated from initial pilot observations) in VAS score during inserting rigid cystoscope into the urethra between the two groups with an 80% power and two-sided 5% α a sample size of 20 patients per group was required. We enrolled 22 patients per group for possible dropouts.

SPSS 17.0 (SPSS Inc, IL, US) was used for statistical examination. The normally-distributed data were compared by student's t-test. Differences in VAS scores were calculated using Mann-Whitney U test. The categorical variables were analyzed with Fisher's exact test or Chi-square test, as appropriate. The level of statistical significance was set at $P < 0.05$.

Results

The pain examination forms were collected from all of the participants. The characteristics of the patients

were comparable between the two groups (Table 1). The VAS scores of the two groups were given in Figure 1. Pain scores in Group F were significantly lower than those in Group C at the time periods of inserting rigid cystoscope into the urethra, viewing inside the urinary bladder, the first urination after cystoscopy and the first urination on the following morning at home. Preoperative flurbiprofen axetil did not result in any significant change in pain during injecting 0.3% oxybuprocaine jelly into the urethra. The patients were more satisfied in Group F than in Group C (Table 2). No adverse events associated to flurbiprofen axetil were observed.

Discussion

In the present study, significant decreases in pain are observed with preprocedural flurbiprofen axetil at various time periods except when injecting 0.3% oxybuprocaine jelly into the urethra as compared with the control group. As similar to the findings by Matsuda *et al.* and Komiya *et al.*, the pain intensity during inserting the cystoscope into the urethra was largest, followed by the pain at the first urination after cystoscopy, during viewing inside the urinary bladder and at the first urination on the following morning at home^{2,3,7}. Our findings indicate that preprocedural

Fig. 1

Box plots of VAS scores at various time points. Results are expressed as median. The top and bottom of each box indicate 75th and 25th percentiles and the error bars maximum and minimum values. VAS, visual analogue scale; T1—during injecting oxybuprocaine jelly into the urethra; T2—during inserting rigid cystoscope into the urethra; T3—during viewing inside the urinary bladder; T4—at the first urination after cystoscopy and T5—at the first urination on the following morning at home; Group F, the flurbiprofen axetil group; Group C, the control group. * indicates $P < 0.05$.

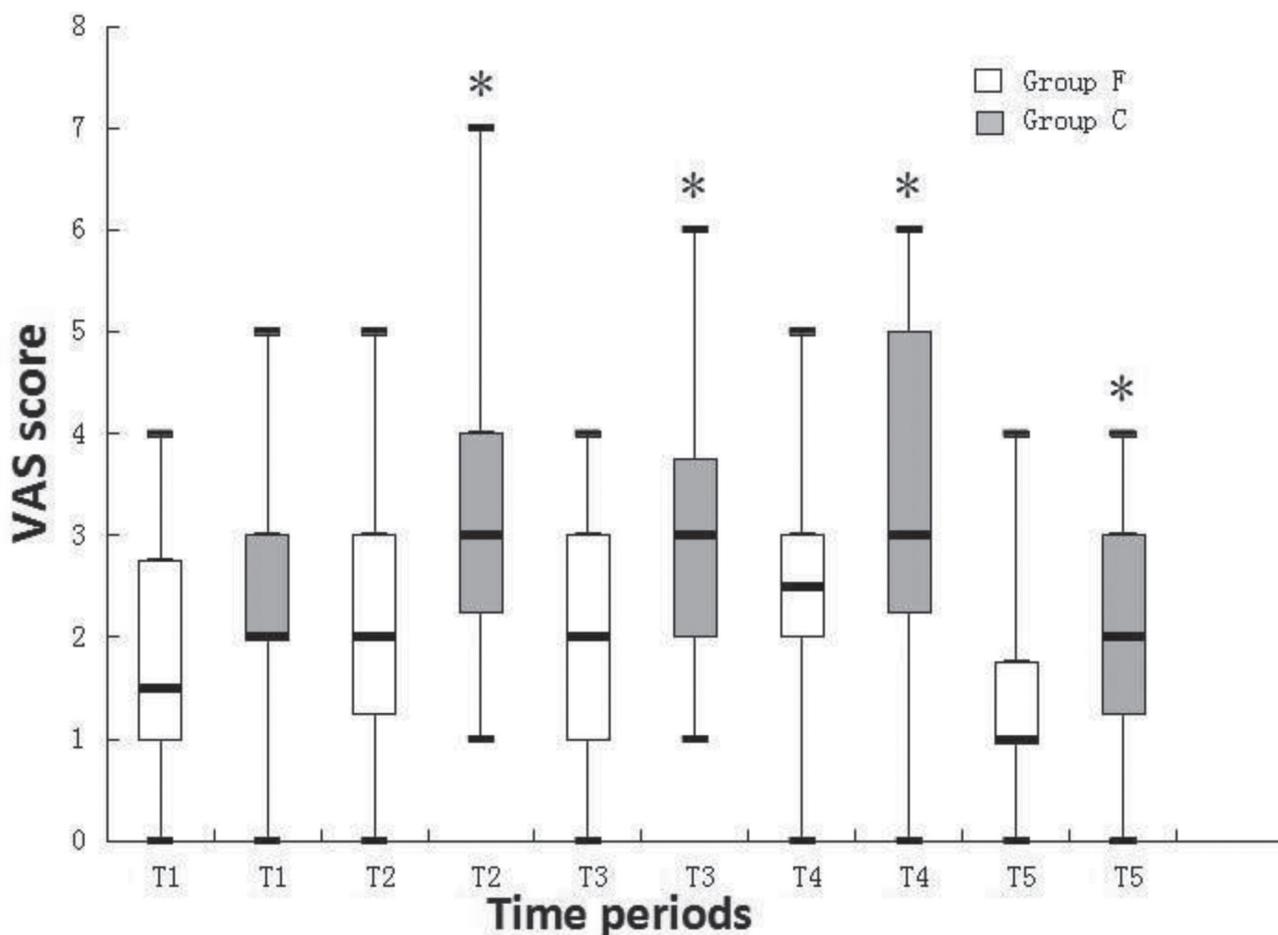


Table 1
Patients' characteristics

	Group F (n=22)	Group C (n=22)	<i>P</i> -value
Age (yr)	56.4±9.5	58.8±8.7	0.387
Weight (kg)	62.7±13.3	61.1±11.9	0.676
ASA I/II (n)	18/4	16/6	0.720
The procedure duration (min)	11.3±4.3	12.4±5.1	0.443

Data are presented as mean ± standard deviation.

Table 2
Patient overall satisfaction

	Group F (n=22)	Group C (n=22)
Poor	1 (4.5%)	5 (22.7%)
Moderate	7 (31.8%)	12 (54.5%)
Good	12 (54.5%)	4 (18.2%)
Excellent	2 (9.1%)	1 (4.5%)

P=0.039, data are presented as number of patients (%). Abbreviations: n, number of patients; Group F, the flurbiprofen axetil group; Group C, the control group.

flurbiprofen axetil can reduce pain at these four time periods. Preoperative intravenous administration of flurbiprofen axetil provides preemptive analgesia for transurethral resection of the prostate, tonsillectomy, spinal fusion surgery, hysterectomy and arthroscopic rotator cuff repair surgery⁸⁻¹². Flurbiprofen axetil is not only a NSAID drug, but also an injectable nonselective cyclooxygenase inhibitor with peripheral analgesic effect which is also called targeted analgesia. The patented technology of flurbiprofen axetil uses emulsified lipid microspheres which have a high affinity for injured tissues to achieve targeted drug therapy¹³. Thus, preoperative flurbiprofen axetil can decrease or even eliminate the peripheral sensitivity resulting from physical stimulation of the urethra by the cystoscope. The results of our study are mostly

consistent with Komiya's findings. In their study, no significant decreases are detected in pain at the first urination on the following morning at home⁷. In our study, the pain decreases in the flurbiprofen axetil group at this time period.

The present study is conducted only in male patients, so further study is necessary to evaluate the effect of flurbiprofen axetil for women who also suffer cystoscopy-associated pain.

Conclusion

Preprocedural flurbiprofen axetil can decrease rigid cystoscopy-associated pain and is recommended for use in clinical practice.

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^{*} Train-of-four
[†] Post tetanic counts
[‡] Second twitch

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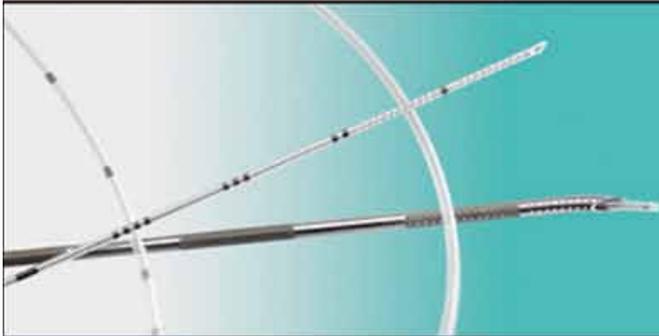
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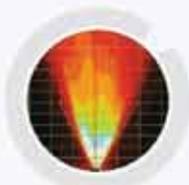
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