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

JINGUO WANG¹, HAICHUN MA², LEI WANG³, HONGLAN ZHOU⁴, YANG GAO⁵ AND NA WANG**

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...
rigid cystoscopy. Moreover, patients also complain of
great pain during urination after cystoscopy. 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 pain. 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
effects were evaluated.

Based on previous studies, pain score during
inserting cystoscope into urethra is considered the
primary outcome. 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% a 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.
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 surgery. 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 therapy. 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 home. 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.

### Table 1

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patients’ characteristics</th>
<th>Group F (n=22)</th>
<th>Group C (n=22)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td></td>
<td>56.4±9.5</td>
<td>58.8±8.7</td>
<td>0.387</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td></td>
<td>62.7±13.3</td>
<td>61.1±11.9</td>
<td>0.676</td>
</tr>
<tr>
<td>ASA I/II (n)</td>
<td></td>
<td>18/4</td>
<td>16/6</td>
<td>0.720</td>
</tr>
<tr>
<td>The procedure duration (min)</td>
<td></td>
<td>11.3±4.3</td>
<td>12.4±5.1</td>
<td>0.443</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation.

### Table 2

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Patient overall satisfaction</th>
<th>Group F (n=22)</th>
<th>Group C (n=22)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor</td>
<td></td>
<td>1 (4.5%)</td>
<td>5 (22.7%)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td>7 (31.8%)</td>
<td>12 (54.5%)</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td></td>
<td>12 (54.5%)</td>
<td>4 (18.2%)</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td></td>
<td>2 (9.1%)</td>
<td>1 (4.5%)</td>
<td></td>
</tr>
</tbody>
</table>

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.

Conclusion

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

BRIDION is indicated for the reversal of neuromuscular blockade induced by vecuronium or rocuronium. In children and adolescents (aged 2-17 years), BRIDION is only recommended for routine reversal of moderate rocuronium-induced neuromuscular blockade.

Important safety information
BRIDION is not recommended in patients with severe renal impairment. Studies in patients with hepatic impairment have not been conducted and, therefore, patients with severe hepatic impairment should be treated with great caution. Lactation should be exercised when administering BRIDION to pregnant women. No clinical data on exposed pregnancies are available.

BRIDION has not been investigated in patients receiving rocuronium or vecuronium in the intensive care unit (ICU) setting.

The neuromuscular blockade is required within 24 hours of BRIDION administration, a non-depolarizing neuromuscular blocking agent should be used instead of rocuronium or vecuronium. The most commonly reported adverse reactions were dysgeusia (metallic or bitter taste) and anesthetized complications (movement, coughing, stimulating, or sucking on the endotracheal tube). Impairments treated with BRIDION, a few cases of awareness were reported. The relation to BRIDION is uncertain. In a few individuals, allergic-like reactions (e.g., flushing, erythematous rash) following BRIDION were reported. Patients should be prepared for the possibility of allergic reactions and take the necessary precautions. In a trial of patients with a history of pulmonary complications, bronchoconstriction was reported in 2 patients, and a causal relationship could not be fully excluded.

Voluntary studies have demonstrated a slight (<1%–2%) and transient (<36 minutes) prolongation of the prothrombin time under partial thromboplastin time (PT/PTT) with BRIDION; however, clinical studies have demonstrated no clinically relevant effect on pre- or postoperative bleeding complications with BRIDION alone or in combination with anticoagulants. As BRIDION has demonstrated an in vitro pharmacodynamic interaction with anticoagulants, caution should be exercised in patients on anticoagulants for a pre-existing or coexisting condition. This pharmacodynamic interaction is not clinically relevant for patients receiving routine postoperative prophylactic anticoagulation. Although formal interaction studies have not been conducted, no drug interactions were observed in clinical trials. Preclinical data suggest that clinically significant drug interactions are unlikely with the possible exception of terfenadine, hystolic acid, and hormonal contraceptives.

REFERENCES:
1. BRIDION Summary of Product Characteristics (SPC)

Please see summary of product characteristics for full prescribing information.

MSD
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