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Randomized controlled trial of NSAID prior to cystoscopic ureteral stent removal in a pediatric population

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Keywords
Ureteral stent; Ureteral spasm; Postoperative pain; Nonsteroidal anti-inflammatory; Ibuprofen

Abbreviations
NSAID, nonsteroidal anti-inflammatory; FPS-R, Faces Pain Scale-Revised; VAS, visual analogue scale; COX, cyclooxygenase; UPJO, ureteropelvic junction obstruction

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Summary

Introduction
Ureteral spasm, common with ureteral stents, is partially mediated by prostaglandins and may be suppressed by cyclooxygenase inhibitors like nonsteroidal anti-inflammatory (NSAIDs). Practices currently vary widely for pain management in patients with ureteral stents, sometimes including opioids.

Objective
We aimed to determine if NSAID given prior to stent removal would reduce postoperative pain. We hypothesized there would be at least a 75% reduction in postoperative severe pain (pain score $\geq$7) in patients receiving ibuprofen compared to placebo.

Study design
We performed a double-blind, placebo-controlled randomized controlled trial on pediatric urology patients with an indwelling ureteral stent undergoing removal in the operating room from 2014 to 2019. 20 patients in each arm were needed to achieve 80% power to detect a 75% reduction in the estimated 55% incidence of severe postoperative pain ($\alpha = 0.05$). Patients $\geq$4 years old who had a unilateral stent placed after treatment of urolithiasis or ureteropelvic junction obstruction were randomized to NSAID or placebo in a 1:1 ratio at least 15 min prior to scheduled stent removal. Patients estimated pain using Faces Pain Scale-Revised (FPS-R) or visual analogue scale (VAS) prior to and 24 h after stent removal.

Results
254 patients undergoing stent removal were assessed for eligibility, and 44 randomized patients were analyzed using intention to treat analysis. The cohorts were demographically similar and received similar anesthesia treatment. There was no significant difference in maximum post anesthesia care unit pain score ($p = 0.269$) or use of in-hospital opioids ($p = 0.626$) between the two groups. No difference was seen in the incidence of severe postoperative pain ($p = 1.0$), thus rejecting the hypothesis. Significant worsened postoperative pain (pain score increases of $\geq$2 between time points) decreased from 22.7% to 13.6% between placebo and NSAID, but this did not reach significance ($p = 0.410$).

Discussion
There was no difference in postoperative pain for patients undergoing ureteral stent removal given preoperative NSAID versus placebo. The incidence of severe pain before and after stent removal was low, ranging from 4.5 to 9.1%.

Conclusion
Research to understand the etiology of pain after stent removal and techniques to minimize or prevent discomfort should continue in order to optimize patient outcomes.

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Summary Table Primary and secondary outcomes from the study demonstrated no significant difference in postoperative pain between placebo and NSAID given prior to stent removal.

	Placebo	NSAID	Effect size	P value
Patients	22 patients	22 patients	—	—
Severe pain (≥7)	1 (4.5%)	2 (9.1%)	4.6% (−10.3−19.4%)	1.000
Significantly worsened postoperative	5 (22.7%)	3 (13.6%)	−9.1% (−31.7−13.5%)	0.696

Introduction

Ureteral stents are commonly used after treatment of urolithiasis and after surgical repair of ureteropelvic junction obstruction (UPJO) [1]. Stents can be very bothersome, affecting more than 80% of patients, resulting in flank and loin pain, dysuria, urinary frequency, even prompting unexpected emergency room visits [2,3]. Medications such as α-blockers (e.g., tamsulosin) have been previously shown in studies to ameliorate some of this effect while the stent is in situ, but its use in children remains off-label in the United States and other jurisdictions [4,5]. Despite these options, a number patients still experience some discomfort and decreased quality of life. Very few clinical studies of how best to treat discomfort from ureteral stents have been performed in children, limiting guidance for best practices.

Urologists have long commented on the anecdotal evidence that some patients experience severe, debilitating pain in the period following stent removal [6,7]. While some hypothesized that stent size and positioning may influence symptoms while the stent is in place, the physiologic mechanism behind pain after removal of the foreign body from the ureter is not well-understood [8]. *In vitro* and *in vivo* studies have demonstrated ureteral spasm in response to stretch, which may occur with removal and cause discomfort felt by patients [9]. This spasm has been shown to be partially mediated by the generation of prostaglandins and hence blocked by cyclooxygenase (COX) inhibitors like non-steroidal anti-inflammatory (NSAID) medications [10]. To date, there have been no studies in children around preventing post-stent removal pain nor standardized care pathways for stent removal. There have been studies examining ways to avoid general anesthesia in children, including use of a string for extraction and magnetically-tipped stents, which one group found to be less painful than cystoscopic removal [11]. These methods may not always be available nor preferred.

A randomized controlled trial of a COX-2 inhibitor given to adults prior to outpatient stent removal in the urology clinic demonstrated significant improvements in severe pain [12]. For pediatric patients with an indwelling ureteral stent, ambulatory clinic awake cystoscopy to remove a stent is not generally tolerated and rarely performed. Patients are typically brought to the operating room for a brief general anesthetic to allow for removal. Thus, it remains unclear if general anesthesia in children modulates the effect of pretreatment with NSAIDs shown in adults. Additionally, variability in components of a balanced general anesthetic could be an additional factor in observed clinical outcomes. Use of NSAIDs pre-, intra-, or postoperatively is inconsistently applied, and increasingly, urologists are avoiding opioids and using non-opioid analgesic options (e.g, acetaminophen and an NSAID) [13−15].

The incidence of "post-stent syndrome" in children is unknown, and treatment and prevention have not been studied [16]. We hypothesize that children who have a temporary, indwelling ureteral stent as part of care received during surgical treatment for either urolithiasis or ureteropelvic junction obstruction will experience a decrease in the incidence of severe postoperative pain (pain score ≥7) if given an NSAID prior to removal of the ureteral stent when compared to placebo.

Methods

Study design and setting

Institution review board approval was obtained (COMIRB 14-0514) for this research and the study was registered with ClinicalTrials.gov (NCT02140970) [17]. The Consolidated Standards of Reporting Trials (CONSORT) checklist was used in the preparation of this manuscript [18]. The study was conducted at a single, free-standing children's hospital, consisting of a randomized, placebo-controlled, double-blind study of 1:1 ratio of NSAID versus placebo administered prior to stent removal in the operating room.

Participants

Pediatric patients between 4 and 17 years of age with an indwelling ureteral stent placed for treatment of either urolithiasis or upper tract ureteral surgery (e.g., pyeloplasty) were considered for enrollment. Full inclusion criteria included presence of a unilateral ureteral stent for treatment of urolithiasis or ureteropelvic junction obstruction with removal under general anesthesia in the operating room. Exclusion criteria were: patients undergoing other concomitant surgical procedures at time of ureteral stent removal, patients with bilateral stents, patients with complicated stent removal (encrustation requiring ureteroscopy and/or laser lithotripsy, proximal migration of ureteral stent), pregnant patients, patients with developmental delay who were unable to report pain scores, and patients with contraindications to receive NSAIDs (documented or stated allergy to NSAIDs, chronic kidney disease, prior renal transplantation, history of nasal polyps, history of asthma).

Patients were assessed for eligibility preoperatively using the stated inclusion and exclusion criteria. Eligible patients were approached by the coordinator and parental

consent was obtained for those who agreed to participate (and assent for children between the ages of 7 and 17). Reasons for ineligibility or declination to enroll were recorded in the study database along with basic demographic data.

Exposures

After enrollment, an order for the study drug was placed by the study team in the electronic medical record, and the research pharmacy randomized patients between a 10 mg/kg oral liquid dose of the non-selective NSAID ibuprofen or a similar volume liquid placebo formulated to have similar taste, smell, consistency and visual appearance. Randomization was performed using a prepared block randomization scheme by age (4–8 years or 9–17 years), sex (female or male) and indication for ureteral stent (urolithiasis or upper urinary tract ureteral surgery) to ensure balance of these covariates between the two study arms. The study drug was administered in the preoperative area no fewer than 15 min prior to going back to the operating room for induction of anesthesia and ureteral stent removal. Study medication was only given after completion of the preoperative questionnaire noted above. Allocation concealment was maintained by the research pharmacy, who kept randomization tables inaccessible to the study team until the analysis phase. By design, the electronic medical record also aided with allocation concealment by virtue of only indicating a study drug was administrated without information regarding drug composition.

Adverse events were reported to an independent safety monitor (author ARB), who had discretion to access study arm assignment for patients and attribute any such events to the intervention. The safety monitor did not participate in enrollment, parental or patient consent or assent, randomization, anesthesia administration for patients in the study, data collection or analysis. Parents, patient, surgeons, investigators, and the study coordinator were blinded to study arm assignment.

Procedure

Cystoscopy and stent removal occurred per standard of care under a short general anesthetic (typically mask with or without IV access) without administration of NSAID intraoperatively. Stent size, brand, and sidedness were recorded. Cystoscopy was performed with an age-appropriate sized scope to minimize discomfort. Scope size and configuration were recorded. A weight-based dose of 2% viscous lidocaine (0.2 mL/kg up to maximum of 10 mL) was given intraurethrally per usual care to facilitate stent removal. No opioid or NSAID medications were given postoperatively. Patients were instructed to take acetaminophen (15 mg/kg up to 500 mg) and ibuprofen (10 mg/kg up to 400 mg) orally as needed every 6 h for 24 h after hospital discharge.

Outcomes

The primary outcome was incidence of postoperative severe pain, defined as any pain score $\geq$7 on a 10 point scale. Secondary outcomes included incidence of significantly worsening pain ($\geq$2 point increase in pain between pre- and postoperative assessments), postoperative opioid usage converted to milligrams intravenous morphine equivalents [19], emergency room visits, readmissions and need to replace a ureteral stent in the operating room.

To assess outcomes, patients filled out a questionnaire (with the assistance of a study investigator), which included either the Faces Pain Scale – Revised (FPS-R) or the visual analogue scale (VAS) depending on age to assess pain, prior to stent removal and administration of the study drug. FPS-R was administered to children between 4 and 8 years of age, and VAS was given to patients between 9 and 17 years of age. A similar pain questionnaire was then filled out 24 h later (i.e., the day after surgery) that also collected information on opioids in the last 24 h, use of tamsulosin, and any returns to a hospital. The postoperative survey was performed with assistance from research personnel via phone on paper by the patient with parental assistance (and delivered by mail or email) or via direct, secure electronic means.

Statistical analysis

A sample size of 20 patients in each arm (total 40 patients) was calculated to be needed to achieve 80% power ($\beta = 0.80$) to detect a 75% reduction in the estimated 55% incidence of severe pain noted in adults on the postoperative pain assessment (two-sided test, $\alpha = 0.05$) [12]. An intention to treat analysis was performed. The placebo and NSAID arms were compared using Student's t-test for normally-distributed continuous data, Mann–Whitney U test for non-normal continuous covariates, and chi-square test for categorical data. Effect estimates or risk differences were calculated and 95% confidence (CI) interval provided. Patients who did not complete the postoperative pain assessment were excluded from the analysis. A post-hoc power analysis was performed for both primary and secondary outcomes. Two tailed tests were used. Results were considered statistically significant at $p < 0.05$.

Results

254 patients undergoing stent removal were assessed for eligibility between 7/2014 and 12/2019 at a single free-standing children's hospital. 51 patients were enrolled and 49 randomized. Two patients presented after research pharmacy hours and were unable to be randomized and receive the drug and were withdrawn from the study. Three patients were excluded for loss to follow and incomplete postoperative surveys (two from the placebo arm and one from the NSAID arm). One patient was excluded from the final analysis from each arm for other issues (one patient did not meet the inclusion criteria and another was removed at the request of the Institution Review Board for a misplaced patient consent that the study team could not re-obtain). The trial was stopped after meeting enrollment target and accounting for exclusions. 44 randomized patients were analyzed, noting that no patients received treatment for which they were not assigned. Fig. 1 shows the CONSORT study flow diagram for this study.

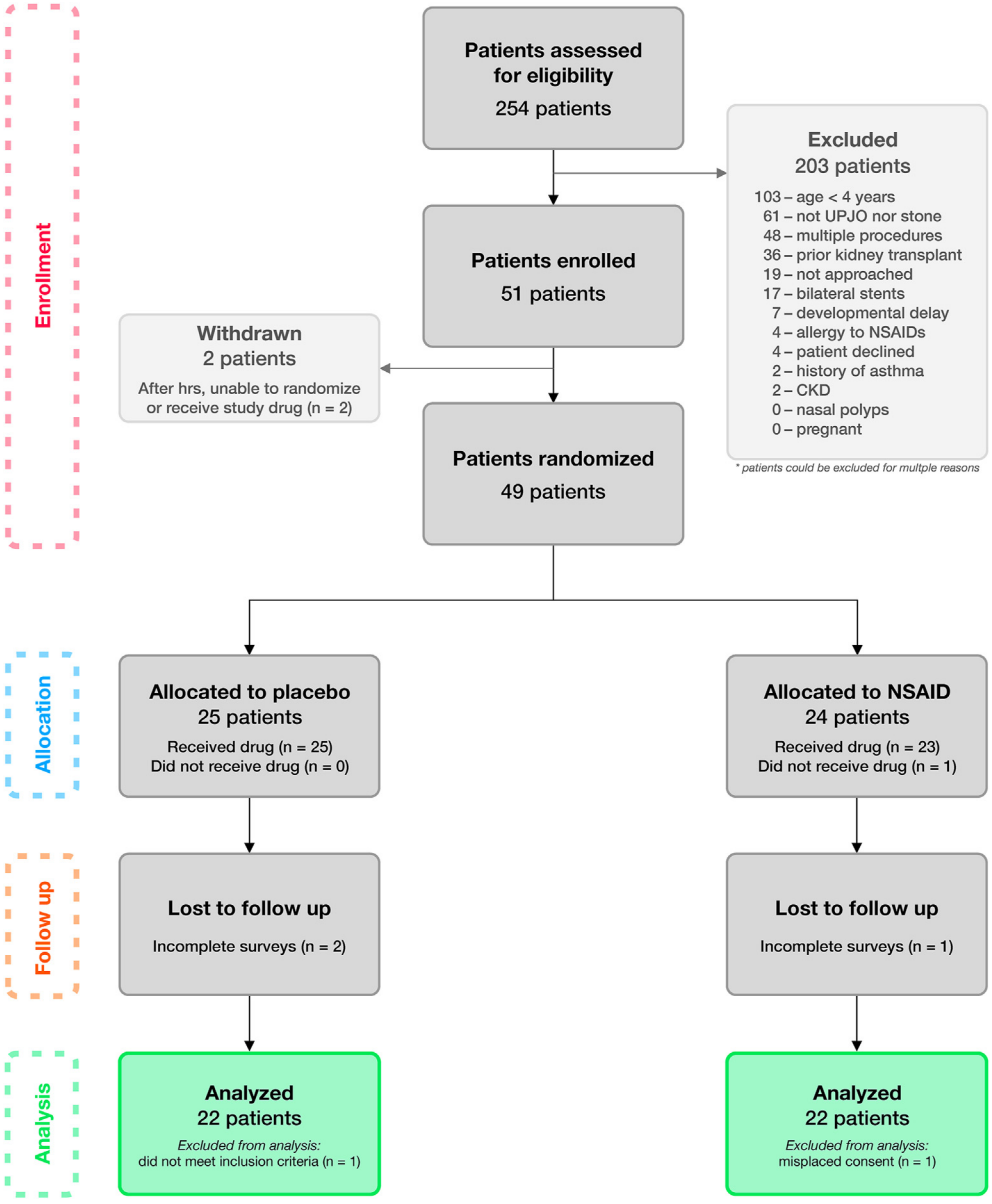

Fig. 1 CONSORT study flow diagram of patients assessed, enrolled, randomized, allocated, followed up, and ultimately analyzed. Intention to treat analysis was used. Reasons for exclusion at various stages are listed. One patient did not receive the drug in the NSAID arm secondary to ordering and pharmacy delays. This same patient had an incomplete survey and was thus lost to follow up. Two patients in the placebo arm had incomplete surveys and were categorized as lost to follow up. One patient from each arm was excluded from the final analysis for logistical reasons: one for improper enrollment and another for misplaced consent. In the case of the misplaced consent, family was contacted multiple times unsuccessfully and ultimately withdrawn at the request of the Institutional Review Board.

Table 1 shows demographic and medical history information, demonstrating the two study arms were well balanced with the exception of driving distance from the hospital (mean 50.7 miles in placebo arm vs 127.2 miles in NSAID arm, $p = 0.036$). There were no differences in the numbers of patients with preoperative urine cultures (82% versus 86.4%, $p = 1.000$) or positive urine cultures requiring treatment before the procedure (16.7% versus 5.3%, $p = 0.557$).

There are a number of potential factors that might confound a study related to perioperative pain control including anesthesia technique, medications administered, stent related factors like duration, size and length, and postoperative pain management. Table 2 demonstrates there were no observed differences in any of these factors that might otherwise confound or bias the study results.

Regarding outcomes shown in Table 3, the primary outcome of incidence of severe pain ($\geq$7 out of 10) was not significantly different between the placebo and NSAID arms (4.5% vs 9.1%, risk difference +4.6%, 95% CI -10.3—19.4%, $p = 1.000$). This was unexpectedly different than the rate of severe pain reported in adults undergoing ambulatory

Table 1 Demographics and medical history of pediatric patients presenting for ureteral stent removal in the operating room enrolled in the study and analyzed.

	Placebo	NSAID	P value
Number of patients	22 patients	22 patients	—
Demographics			
Age (years)	12.2 (4.7—18.0)	10.5 (4.2—17.3)	0.186
Gender			1.000
Female	11 (50.0%)	10 (45.5%)	
Male	11 (50.0%)	12 (54.5%)	
Race			0.521
Non-Hispanic White or European-American	14 (63.6%)	16 (72.7%)	
Black, Afro-Caribbean, or African American	1 (4.5%)	0 (0.0%)	
Latino or Hispanic American	6 (27.3%)	5 (22.7%)	
East Asian or Asian American	0 (0.0%)	1 (4.5%)	
Middle Eastern or Arab American	1 (4.5%)	0 (0.0%)	
BMI (kg/m^2)	19.6 (13.3—38.6)	18.8 (13.7—42.8)	0.661
BMI z-score	4.2 (−0.2—17.3)	3.8 (0.3—19.8)	0.686
Triponderal mass index (kg/m^3)	13.4 (9.4—24.6)	13.4 (8.4—25.8)	0.995
Patient primary language			0.599
English	19 (86.4%)	20 (90.9%)	
Spanish	2 (9.1%)	2 (9.1%)	
Other	1 (4.5%)	0 (0.0%)	
Insurance			0.453
Medicaid/Medicare	10 (45.5%)	8 (36.4%)	
Commercial	11 (50.0%)	14 (63.6%)	
Self Pay	1 (4.5%)	0 (0.0%)	
Distance from hospital (km)	50.7 (3.4—168.0)	127.2 (2.7—571.2)	**0.036**[a]
Medical history			
Primary underlying diagnosis (reason for stent)			0.591
urolithiasis	10 (45.5%)	9 (40.9%)	
UPJ obstruction	12 (54.5%)	12 (54.5%)	
Ureteral stent side/location			0.543
left	14 (63.6%)	11 (50.0%)	
right	8 (36.4%)	11 (50.0%)	
Preop urine culture performed	18 (81.8%)	19 (86.4%)	1.000
Preop urine culture positive	3 (16.7%)	1 (5.3%)	0.557
Preop urine culture treated	2 (66.7%)	0 (0.0%)	1.000

[a] denotes significant difference ($p < 0.05$).

cystoscopy with stent removal (55%) reported by Tadros et al. [12] As such, the hypothesis was rejected. Fig. 2 depicts pain score transitions between the two time points for both groups. There were no significant differences in baseline preoperative pain scores (mean 1.0 versus 0.8, $p = 0.677$), number who completed postoperative survey electronically (4 versus 3, $p = 1.000$), or pain scale used (6 versus 9 used the FPS-R scale, $p = 0.525$) between the two study groups. The *a priori* defined secondary outcome of significantly worsened postoperative pain ($\geq$2 point increase between pre- and postoperative time points) improved from 22.7% to 13.6% but also did not reach significance (risk difference −9.1%, 95% CI -31.7—13.5%, $p = 0.696$). Other secondary outcomes such as in-hospital and post-discharge opioid usage, emergency department visits, readmissions and reoperations were not significantly different between the two study arms. Post-hoc power analysis demonstrates there was only 8.7% power for the primary outcome and 11.8% power for the secondary outcome of significantly worsened postoperative pain. No adverse events or unintended effects were identified during the study.

Discussion

Ureteral stents can be particularly troublesome for some patients, but remain a key part of urologic practices in the management of urolithiasis and UPJ obstruction, among other conditions. While it is possible to avoid their use safely in some circumstances, there are situations where they represent a key therapeutic intervention (relieving obstruction or managing poorly draining upper tract infections) [20,21]. The wide range of symptoms patients exhibit (from no symptoms to intractable flank and pelvic pain) can frustrate the urologist given their unpredictable nature. The underlying etiology of pain in pediatric patients after stent removal remains undefined—is it related to cystoscopy, ureteral spasm, edema, or something else? [7] Defining etiology and risk factors for ureteral stent related symptoms and strategies to prevent unwanted effects would be highly beneficial.

The authors asked if a simple preoperative pharmacologic intervention could improve pediatric patient outcomes after cystoscopic ureteral stent removal in the

Table 2 Study drug, stent, and operative details, including perioperative medications and pain-related details for both study arms. A single opioid prescription was given to a patient in the NSAID arm, but was not filled according to a query of the Colorado Prescription Drug Monitoring Program database. NSAID, non-steroidal anti-inflammatory drug.

	Placebo	NSAID	P value
Number of patients	22 patients	22 patients	—
Study details			
Study drug dose (mg/kg)	9.0 (6.2—10.5)	8.7 (3.4—10.7)	0.633
Ureteral stent information			
Stent diameter (Fr)			0.083
3.7	4 (18.2%)	5 (22.7%)	
4.7	1 (4.5%)	6 (27.3%)	
5	17 (77.3%)	11 (50.0%)	
Stent length (cm)			0.234
12	1 (4.5%)	0 (0.0%)	
14	0 (0.0%)	3 (13.6%)	
16	2 (9.1%)	5 (22.7%)	
18	3 (13.6%)	2 (9.1%)	
20	1 (4.5%)	2 (9.1%)	
22—32	15 (68.2%)	10 (45.5%)	
Stent duration (days)	33.4 (7.0—78.0)	35.0 (14.0—61.0)	0.700
Operative details and perioperative medications			
Cystoscope configuration			1.000
offset	21 (95.5%)	22 (100.0%)	
unknown	1 (4.5%)	0 (0.0%)	
Cystoscope diameter (Fr)			0.442
7	2 (9.5%)	1 (4.5%)	
9	0 (0.0%)	1 (4.5%)	
9.5	9 (42.9%)	12 (54.5%)	
10.5	8 (38.1%)	8 (36.4%)	
11	2 (9.5%)	0 (0.0%)	
Dexmedetomidine	1 (4.5%)	0 (0.0%)	1.000
Intravenous lidocaine	1 (4.5%)	1 (4.5%)	1.000
Anxiolytic	1 (4.5%)	0 (0.0%)	1.000
Steroid	12 (54.5%)	12 (54.5%)	1.000
Antiemetic	14 (63.6%)	17 (77.3%)	0.509
Pain medications			
Acetaminophen in hospital	5 (22.7%)	7 (31.8%)	0.735
Opioid prescription	0 (0.0%)	1 (4.5%)	1.000
Opioid prescription filled	—	0 (0.0%)	—

operating room under general anesthesia. Pediatric patients generally do very well with stent removal, but this effort was undertaken after several patients were seen back after stent removal with pain that was managed with tamsulosin, NSAIDs, and, in one instance, an oral steroid burst. While the study itself was negative, a post-hoc power analysis demonstrated the study was underpowered for both primary and secondary outcomes, rendering it difficult to understand if this was a true negative (that preoperative NSAID therapy does not help) or rather a false negative. With hindsight, general anesthesia likely reduced the incidence of severe post-stent removal pain measured in awake adults by Tadros et al. from 55% to 7% [12]. This observation suggests future studies might focus on those pediatric patients who use a string for ureteral stent extraction at home and any immediate changes in discomfort or anxiety.

Although the study result was negative, we have better information about the incidence of postoperative severe pain and significantly worsening pain in pediatric patients undergoing ureteral stent removal. The cost and risks of NSAID as part of a stent removal protocol are low (our hospital cost per dose is $<$ \$1 for oral ibuprofen). This report demonstrates that most pediatric patients undergoing ureteral stent removal do very well with few issues. This is corroborated by a recent National Surgical Quality Improvement Program Pediatric analysis that demonstrated ureteral stent usage during the treatment of urolithiasis did not increase 30-day unplanned readmission rates as compared to patients without stents [22]. A randomized controlled trial of 114 patients in Korea of stent removal with and without an extraction string found that pain scores on the VAS scale were significantly lower in those with a

Table 3 Study outcomes, pre- and postoperative patient questionnaire responses, and 30-day chart review results for both study arms. Proportions were compared with chi-squared test. Mean pain score differences are shown (minimum—maximum) and were compared with Student's t test. Median PACU pain scores are reported (minimum—maximum) and were compared with Mann—Whitney U test. NSAID, non-steroidal anti-inflammatory drug; CI, confidence interval; PACU, postanesthesia care unit; IV, intravenous.

	Placebo	NSAID	Effect estimate or risk difference (95% CI)	P value
Number of patients	22 patients	22 patients	—	—
Study outcomes				
Severe postop pain (≥7)	1 (4.5%)	2 (9.1%)	4.5% (−10.3—19.4%)	1.000
Significantly worsened postoperative pain (increase ≥2)	5 (22.7%)	3 (13.6%)	−9.1% (−31.7—13.5%)	0.696
Mean change in pre- and postoperative pain scores	0.2 (−4.0—4.3)	0.4 (−3.9—8.0)	0.2 (−1.4—1.8)	0.824
Median maximum PACU pain score	0 (0.0—6.0)	0 (0.0—6.0)	0 (0—0)	0.269
Opioid usage in hospital (mg/kg IV morphine equivalent)	0.015 (0.000—0.055)	0.019 (0.000—0.116)	0.004 (−0.017—0.010)	0.626
Preprocedure questions				
Tamsulosin in last 24 h	4 (18.2%)	2 (9.1%)	−9.1% (−29.2—11.0%)	0.660
Opioid in last 24 h	1 (4.5%)	1 (4.5%)	—	1.000
Postprocedure questions				
Tamsulosin in last 24 h	0 (0.0%)	0 (0.0%)	—	—
Opioid in last 24 h	0 (0.0%)	0 (0.0%)	—	—
Emergency department visit in the last 24 h	0 (0.0%)	0 (0.0%)	—	—
Admitted to a hospital in the last 24 h	0 (0.0%)	0 (0.0%)	—	—
Unexpected procedures or surgeries in the last 24 h	0 (0.0%)	0 (0.0%)	—	—
Chart review				
Emergency department visits within 30 days	0 (0—1)	0 (0—0)	—	0.329
Readmissions within 30 days	0 (0—0)	0 (0—0)	—	—
Reoperations within 30 days	0 (0—0)	0 (0—0)	—	—

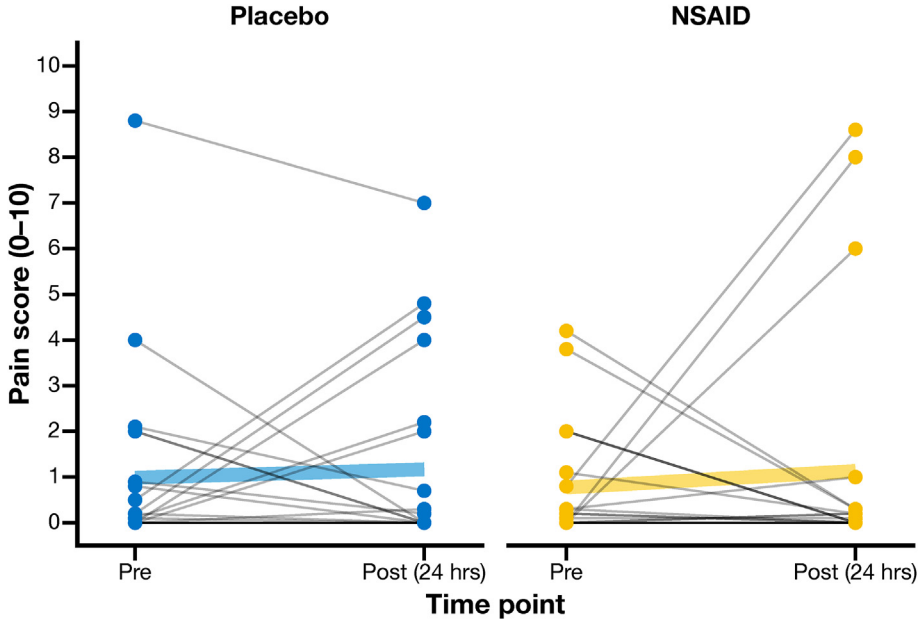

Fig. 2 Comparison of preoperative to postoperative pain scores in placebo and NSAID groups. Significant worsened postoperative pain (≥ pain score increase of 2 between the two time points) decreased from 22.7% to 13.6% between placebo and NSAID, but this did not reach significance ($p = 0.696$).

string (thus obviating the need for cystoscopy), suggesting that if possible, pediatric urologists should endeavor to use an extraction string for both patient benefit and resource stewardship when it makes clinical sense [23]. Similar findings to this study were shown in a 2005 study of preoperative NSAID prior to a broad range of pediatric urologic procedures, which did not show clinically-significant differences in postoperative nausea, pain, or resumption of normal activities [24]. A NIDDK (National Institute of Diabetes and Digestive and Kidney Diseases) funded prospective observational student entitled Study to Enhance Understanding of sTent-associated Symptoms (STENTS) recently got underway which plans to examine stent-related symptoms in adolescents and adult patients in detail, which should provide better insight into future research needs [25].

Limitations

The study population was small and selected, and the incidence of severe pain proved to be more rare than in adults. This led to underpowering. Given the lack of published data on the incidence in children, however, this appeared to be a reasonable starting point. Assessment the day after ureteral stent removal via various means (paper or electronic entry with aid of research personnel via phone) may have influenced the answers in unknown ways (although no significant difference between paper vs electronic assessment between the two arms) and may have missed changes in discomfort between last pain assessment (post-anesthesia care unit) and 24 h later. Pain-related outcomes tend to be very patient-specific and are notoriously difficult to study, particularly absolute scores. While the primary outcome used absolute pain scores at a single point in time, the secondary outcome compared pre- and postoperative pain scores differences for the same patient, offering a degree of internal normalization. Larger sample sizes are often necessary to see clinically significant changes in pain score (which have been reported to be a low as a single point change) [26]. The use of two pain scales can also be criticized, although the authors felt this was necessary given each pain scale was validated in different age pediatric groups. Comparison of the two scales demonstrates strong interscale correlation ($r = 0.93$, $p < 0.001$), thus we do not believe this constitutes a significant source of bias [27].

Conclusion

There was no difference in postoperative pain for a small number of pediatric patients undergoing ureteral stent removal given preoperative NSAID versus placebo. The incidence of severe pain before and after stent removal was lower in a pediatric population (4.5—9.1%) than reported in adults (55%). Research to minimize pain and physiologic stress of surgical procedures, even "minor" ones, should continue in order to standardize care and optimize patient outcomes.

Conflicts of interest

KOR is a site investigator for Abbvie research.

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