Initial Experience with Narcotic Free Ureteroscopy: A Feasibility Analysis.

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Abstract:

Background and Purpose: In the United States, there is an opioid abuse epidemic fueled by prescription medications. Concerns that uncontrolled pain after surgical procedures will result in poor patient satisfaction and increased work load for ancillary staff are potential factors that influence provider prescription habits. Currently, there is a paucity of literature on analgesic requirements after ureteroscopy (URS) for nephrolithiasis. Our study objective was to evaluate the safety of narcotic free URS (nf-URS) and assess its impact on provider work load.

Methods: We performed a retrospective chart review of 104 patients, between October 2017 and May 2018, who underwent ureteroscopy and who required a stent post procedure. Starting February 2018, patients without absolute contraindication or allergies to NSAIDs received a prescription for diclofenac instead of hydrocodone or oxycodone. Postoperative phone calls to nurses and residents, emergency room visits, and prescription monitoring reports were evaluated for all patients and compared between the narcotic free URS (nf-URS) and the standard URS (s-URS).

Results: There were 52 nf-URS and 52 s-URS procedures. In the postoperative period, 9(17%) nf-URS and 10 (19%) s-URS called with postoperative pain issues. 5 (10%) nf-URS versus 9 (17%) s-URS patients obtained narcotics after seeking additional medical care after URS because of insufficient pain control. There were no post-operative complications in our cohort. Compared to s-URS, 6,871.5 mg morphine equivalent doses (1,375 hydrocodone tablets) less were administered to nf-URS patients immediately after surgery.

Conclusions: Attempts to reduce the number of narcotic prescriptions is paramount in the fight against narcotic addiction in the United States. Although our initial cohort is small, this feasibility study provides compelling evidence that nf-URS is a safe and effective practice. Furthermore, nf-URS resulted in a dramatic decrease in the number of narcotics circulating in the community.

Introduction:

The United States (U.S.) saw the introduction of prescription (Rx) opioids in the late 1990s as an effort to improve the quality of life for patients suffering from chronic pain. Since that time the number of prescriptions for opioid pain medication has progressively increased and their use has expanded beyond the management of chronic pain into most areas of medicine including post-procedural pain control[1]. Despite the number of narcotic prescriptions peaking in 2010 with a slow decrease since, the impact of the opioid epidemic is still being felt throughout the country. Overdose and death from prescription narcotics continues to rise. There was a 70% increase in opioid overdoses in the Midwestern region of the U.S. and an estimated 50,000 deaths from opioids (synthetics 20,145; heroin 15,446; natural prescription opioids 14,427) between July 2016 - 2017[1]. The Center for Disease Control and Prevention identified prescription narcotics as a gateway into opioid drug addiction and has directed providers to question the need, duration, and patient appropriateness before prescribing narcotic pain medication[2].

From a urologic perspective, prescription opioids have been routinely used to control post ureteroscopy (URS) pain; especially pain associated with ureteral stents. URS is progressively being adopted by urologists as the mainstay surgical therapy for nephrolithiasis $\leq$ 1.5cm and suspected upper tract malignancy[3]. Although it is not common practice globally, urologists in the U.S. routinely prescribe narcotic medication for obstructing nephrolithiasis during medical expulsive therapy, after intervention to decompress the collecting system, or after endoscopic laser fragmentation with or without stone removal and ureteral stent placement. How prescription opioid usage for minimally invasive urologic surgery (MIS) was initially adopted is uncertain; however, they are commonly used for MIS across multiple surgical specialties[4]. Fujili *et al.* contacted 330 patients who underwent general, orthopedic, gynecologic, or urologic (cystoscopy biopsy/stent, TURP, robotic prostatectomy) surgery and found that 92% had received a prescription for narcotic pain medication. The average morphine equivalent dosage

(MED) received in the cohort was 120mg (24 hydrocodone pills); however, 34% of patients did not fill or use their narcotic prescription.

The prescription habits of most surgeons are largely influenced by a general concern for the well-being and satisfaction of patients after surgery; two factors affected by post-procedural pain control. Despite good intentions, these practices can have detrimental effects as evidence by a Canadian study which showed that after undergoing MIS such as cataract replacement, varicose vein stripping, a laparoscopic cholecystectomy or a transurethral resection of the prostate (TURP), patients who received a narcotic prescription within 7 days of surgery were 44% more likely to become a long-term opioid user compared to matched patients who did not receive narcotics[5]. Since stent related pain is possibly related to inflammation and irritation, post procedure analgesia centered around non-steroidal anti-inflammatory (NSAIDs) medication such as diclofenac may offer significant benefits. We hypothesize that after undergoing URS, patients can be discharged home without narcotic medication and still have adequate pain control. Furthermore, we hypothesize that a narcotic free approach to post-URS pain control would not generate significant additional work for ancillary staff or providers. In 2018, we changed our clinical practice to narcotic-free ureteroscopy (nf-URS) and present our experience.

Methods:

We performed a retrospective chart review of patients undergoing URS by a single surgeon (AEK) at a high-volume stone institution between October 1, 2017 and May 1, 2018. On February 1st 2018, a change in clinical practice was adopted for all patients undergoing URS by this surgeon; patients were no longer provided narcotics for post-operative pain after nf-URS. Before the change in practice, patients would receive hydrocodone or oxycodone-based prescription narcotics after standard ureteroscopy (s-URS). During the study period, it was standard intraoperative practice to administer IV ketorolac and a belladonna-and-opium (B&O) suppository to every patient at the conclusion of the procedure except those with renal insufficiency (GFR $\leq$ 10mL/min/1.73m^2) or symptomatic benign prostatic hyperplasia

respectively. As part of the nf-URS practice, patients were counselled in the office about the dangers of narcotics, and informed of the risks, benefits and alternatives of NSAIDs. After nf-URS, in addition to our stent cocktail (Tamsulosin, Oxybutynin, Phenazopyridine), a prescription for 20 tablets of Diclofenac-50mg were provided in place of a narcotic. Patients with allergies to diclofenac or NSAIDs, with renal insufficiency, or heart disease were offered 20 tablets of tramadol-25mg; a weak opioid with 1/10 the potency of morphine. If patients declined tramadol, acetaminophen was recommended for post procedural analgesia. Between the study dates, 178 URS procedures were performed, of which 64 were nf-URS and 114 were s-URS. Patients were excluded if they underwent a combination percutaneous nephrolithotomy (PCNL)-ureteroscopy or a secondary ureteroscopy for residual stone fragments after PCNL. The groups were consecutively accrued in a 1:1 fashion progressing chronologically in an antegrade and retrograde fashion for nf-URS and s-URS respectively with a total of 52 patients in each group. The groups were matched based on age, gender, diagnosis. We obtained demographics and medical history from the electronic medical record (EMR). Prescription opioid usage 12-months before and 60 days post-URS was obtained using our state's prescription monitoring program (PMP- INSPECT) which partners with 43 states to provide a national PMP. All phone calls to our clinic, nurses line, on-call residents and visits to a patient's local or our institution's emergency or primary care facilities were documented in our EMR and reviewed. Any call or clinical consultation because of insufficient pain control was recorded along with any narcotic prescription provided. Statistical analysis including t-test, chi-squared and multivariate analysis comparing nf-URS and s-URS was performed by a biomedical statistician using STATA data analysis software.

Results:

Demographic comparison of the nf-URS and s-URS group is presented in table 1, of which there were no significant differences. URS was performed for nephrolithiasis in 99/104 patients with the remaining 5 patients undergoing diagnostic URS for hematuria. For 39% of nf-URS and 35% of s-URS patients, this was their first stone event. Prior psychiatric diagnoses (anxiety/depression 23 patients, bipolar 1 patient,

ADHD 2 patients, Borderline personality disorder 1 patient) were present in 25% nf-URS and 32% s-URS. 30 patients (57%) and 35 patients (67%) who underwent nf-URS and s-URS, respectively, had received narcotics within 12 months leading up to URS. Patients were distributed evenly between right, left and bilateral cases with most patients having multiple stones (41% nf-URS vs 44% s-URS) with an average largest stone size of 6.5 mm. There were significantly more patients who were pre-stented in the s-URS (38% vs 25% - p=0.01) compared to the nf-URS cohort; however, use of a sheath, laser, basket and postop stent placement and duration of stenting (table 2) were equivalent between the groups. Discharge medications differed significantly between the two cohorts. In the nf-URS group, 48 patients were discharged with diclofenac-50mg alone, 2 patients had both diclofenac-50mg and tramadol-25mg, and 3 had only tramadol-25mg compared to 100% of s-URS patients receiving hydrocodone(oxycodone)-acetaminophen (p=0.001). The two recipients of both diclofenac and tramadol specifically requested tramadol because of concern for breakthrough pain despite using diclofenac. Compared to s-URS, 6,871.5 mg less of MED were administered to nf-URS patients immediately after surgery. There was no significant difference between the groups in the number of phone calls to ancillary staff or on-call personnel regarding inadequate pain control (9 nf-URS vs 10 s-URS patients). Overall, 5 nf-URS versus 9 s-URS patients obtained an initial (nf-URS), or additional (s-URS), narcotic prescription, with a median MED of 135mg vs 150mg, respectively. These additional prescriptions were provided by our clinic (1 Rx), local pcp/urologist (9 Rx) and emergency department (4 Rx). Of note, the only patient who received a narcotic prescription from our urology clinic presented when the staff surgeon was out of the country and an advanced practice provider, who was unaware of the clinical practice change to nf-URS, provided the patient with hydrocodone for flank pain 4 days after stent removal with a negative urinalysis and normal renal/bladder ultrasound. Additionally, the four patients who presented to an ED with pain control issues had CT scans without evidence of pyelonephritis, residual stones, or hydronephrosis of which 2 had stents still in place and 2 had recently removed their stents. There were no other postoperative complications noted in either cohort. On multivariant analysis prior psychiatric condition was associated with 1.9-fold increase in filling additional prescriptions (p = 0.05); however, such an

association was not true for other variables of interest such as patient age (0.22 p=0.8), gender (female -0.52 p=-0.6), stone characteristics, stent duration (0.68 p=0.3), prior stone event (0.02 p=0.9), or prior narcotic use (0.87 p=0.4).

Discussion

There are multiple publications outlining the opioid crisis and the physician's role in controlling the distribution of the controlled substances[6]. Government control has attempted to impact narcotic prescribing habits as exemplified by Ohio and Kentucky who mandated that all pain clinic providers review PMP data on patients. Despite limited evidence, common explanations for the over use of narcotics after surgery, in this case URS, centers around anticipating patient analgesic needs and preventing pain related issues that may require additional efforts to resolve. The availability of the primary surgeon, surgeon's nurse or assistant, and other ancillary staff or providers is limited and for many providers there are no extra resources to deal with additional stressors such as post procedural pain. These influences have led to overuse of narcotics, however, the practice of PMP review can reduce narcotic prescriptions, which was see in 85% of counties in Ohio and 62% of counties in Kentucky[7] after implementing the PMP review requirements. In our experience of attempting to decrease narcotic prescriptions, we saw that 91% of patients underwent URS and did not require narcotic pain medication. Furthermore, we showed that a narcotic free pain control protocol did not increase workload for the physician's office staff or other providers. Other surgical specialties are re-evaluating the need for narcotics after surgery. A group of orthopedic surgeons from Illinois showed less time to first bowel movement, first oral intake, first unassisted ambulation and a 1 day reduction in hospital stay for 275/559 patients receiving only ketorolac vs 284/559 patients receiving narcotic analgesics after spine and joint procedures.[8] Another group showed that diclofenac was superior to morphine for the management of post cesarean section pain with lower pain scores (3.63±0.96 vs 5.66 ±1.36, $p<0.05$) and that those receiving morphine were more likely to request, and sooner to request (3.28±2.16 vs 5.24 ±4.07 hrs, $p<0.05$), breakthrough intravenous merperidine[9].

In fact, there are studies evaluating medical therapies to alleviate post-URS and ureteral stent related pain which have shown that NSAIDs and α-blockers are superior to opioids[10]. However, concerns with NSAIDs have focused on their potential to cause renal insufficiency and cardiovascular events. Diclofenac, when used for postoperative pain control, was found to have equivalent adverse renal events (0.9% vs 0.7%; p=0.75) and cardiovascular adverse events (11.6% vs 12.2%; p= x) compared to placebo in phase III double blinded prospective studies. In our experience, at 6 weeks follow up after taking diclofenac, none of our patients experienced a cardiac event. Prior to receiving diclofenac, labs validating that all patients had GFRs >30mL/min/1.73m^2 or no evidence of renal failure based on clinical interaction and chart review. We found it useful to inform patients that the use of Diclofenac after URS, although not without risk, appears to be safe and effective at controlling postoperative pain. Furthermore, NSAIDs remove all potential risk of developing a narcotic dependence.

Despite our multivariate analysis showing only prior psychiatric conditions as predictors for additional prescription drug use after URS, there are clearly two patient groups captured in our study– opioid naïve and opioid exposed. Adopting nf-URS prevented the exposure of opioids to the opioid-naïve patient population, eliminating the risk of dependencies forming at this point which is especially important in our adolescent population who made up 5% of this cohort. The benefit of nf-URS in the opioid exposed or baseline narcotic depend group is less obvious. This group has been described by Stephen Kappa *et al.* who identified 48/200 patients who underwent URS that received narcotic prescriptions from 2 or more different providers. Compared to patients receiving narcotics from one source, these patients were more likely to have a history of mental illness (37.5 vs 16% p<0.01), have undergone prior stone procedures (66 vs 42% p<0.01), require longer postoperative opioid use (39.1 vs 6.0 days) and necessitate higher doses of narcotics (44.7 vs 35.2 MED/day)[13]. By performing nf-URS in this group, we

limit the access to excessive narcotic and decreased the potential motivation to contact the medical providers to request additional narcotic medication. The addition of more patients undergoing nf-URS will hopefully identify more pre and post-operative risk factors for patients developing or with opioid use disorder (OUD). A recent publication in the New England Journal of Medicine outlines the priority, effort and funding by the National Institute of Health to develop preventative techniques (such as nf-URS), novel treatments for dependence and overdose, and new non-opioid based analgesics[14]. This paper emphasizes the complexity of the opioid epidemic but should also empower more groups to report techniques such as nf-URS; a simple practice change that reduced narcotic use in our practice by 91%.

This study is not without limitations. It is a retrospective review from a single institution involving patients cared for by a single surgeon and therefore it may not translate into all types of urologic practices. As this was a retrospective feasibility trial, we did not perform a formal power analysis. However, the goal of demonstrating the feasibility of nf-URS is achieved here and will hopefully motivate other providers to adopt this practice for endoscopic procedures. Guidelines for postoperative opioid usage[15] are being established in other subspecialties, and with enough feasibility studies similar guidelines could be developed for urologic procedures to provide support for urologists attempting to avoid narcotic prescription use. Secondly, we could not control for prior narcotic prescription and as such 57% and 67 % of the nf-URS and s-URS patients had a history of filling a narcotic prescription within 12 months of undergoing URS. Therefore, our conclusion, may be overstated, that there is no additional work load associated with nf-URS as patients could potentially have used old prescription pain medication rather than call for additional analgesia. Never-the-less, 51 prescriptions, 8141 morphine equivalents, 1628 tablets of hydrocodone-acetaminophen, or 1085 tablets of oxycodone-acetaminophen were removed from circulation within 4 months of adopting nf-URS. Finally, since this was a feasibility study, a standardized pain questionnaire was not utilized.

Additional patient accrual and multi-center collaboration is needed to further investigate the feasibility and role of nf-URS in all type of urologic practice settings. With a broader adoption of nf-URS, there is a potential to motivate the field to develop narcotic free analgesic protocols for more invasive GU-surgeries and as a specialty, discontinue the practice of over-prescribing of narcotics.

Conclusion

Narcotic-free ureteroscopy is achievable, based on this study, with pre-operative counselling, a zero tolerance for providing narcotics, and support from ancillary and supporting staff. By managing patient expectations, along with their pain, and being honest about the unnecessary use of opioids in endoscopic surgery, there appears to be minimal need for narcotic prescriptions after uncomplicated ureteroscopy.

Author Disclosure Statement:

No competing financial interests exist. Dr. Krambeck is a consultant for Thermedx, Boston Scientific and Lumenis.

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