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General

Opioids in Urology: How Well Are We Preventing Opioid Dependence and How Can We Do Better?

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Urologic procedures (both open and minimally invasive) can cause pain due to the surgery itself, devices placed, and post-operative issues. Thus, pain management is important for every post-procedure recovery period. Opioid use post-surgery is common and often over-prescribed contributing to persistent use by patients.

In this article, we review the extent of opioid use in pediatric urologic procedures, vasectomy, endourologic procedures, penile implantation, urogynecologic procedures, prostatectomy, nephrectomy, cystectomy, and scrotal/testicular cancer surgery.

Generally, we have found that institutions do not have a standardized protocol with a set regimen to prescribe opioids, resulting in more opioids being prescribed than needed and patients not properly disposing of their unused prescriptions.

However, many institutions recognize their opioid overuse and are implementing new multimodal opioid-sparing analgesics methods such as non-opioid peri-operative medications, minimally invasive robotic surgery, and nerve blocks or local anesthetics with varying degrees of success. By shedding light on these opioid-free methods and prescription protocols, along with improved patient education and counselling, we hope to bring awareness to institutions and decrease unnecessary opioid use.

INTRODUCTION

In this literature review, we hope to shed more light on the need to better address the opioid crisis, specifically in the field of urology. In the past 30 years, we have seen a significant uptick in not only the number of opioid related deaths, but also the increased abuse and prescribing of opioids.[1] We will delve into discussion of opioid usage in several distinct procedures and patient populations within urology such as in pediatric urology and endourology. Within our discussion of opioid usage, we will aim to focus on the prescribing of opioids post-operatively. Furthermore, we will talk about the importance of the patient-provider relationship when it comes to prescribing opioids and the expected patient feelings post-operatively in terms of pain.[2,3]

Another key aspect for our consideration regarding opioid usage in urology will be to discuss the potential for developing recommended courses of action for opioid administration for different specific urological procedure guidelines.[2] In fact, one study looking at different urological procedures noted that 11 out of the 16 procedures displayed a reduction in opioid use with the remaining 5 procedures expressing no change.[2] The results suggest that diagnostic endoscopy and transurethral resection interventions do not recommend using opioids in the treatment plan along with minimally invasive urological surgeries as a different study concluded.[2,4]

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Despite recent encouraging results of decreased opioid prescriptions being fulfilled, we have witnessed an alarming amount of opioid related deaths and opioid misuse. For instance, in 2015 approximately 11.5 million Americans didn't responsibly use opioids with an estimated 1.9 million having an opioid disorder.[5]

To better address the misuse of opioids specifically in urology, it might be beneficial to develop and utilize a standardized post-operative opioid prescribing protocol.[6] In a study analyzing urology resident opioid prescribing habits, it was noted that only 15.5% of residents use a structured algorithm in prescribing opioids post-operatively. Additionally, not even half of residents (51.6%) had formal training on how to appropriately prescribe opioids with 42.1% of residents regularly examining for opioid abuse in their patients.[6] In a similar study assessing opioid prescribing habits in residents of different specialties including urology it was noted that just 35% of residents noted they had formal training regarding appropriate opioid prescribing.[7] The study also found that residents did not use standardized order sets at a high rate and that patient education and expectations with opioid prescription were not met well.[7] Ultimately, when considering the next generation of physicians, building a standardized protocol might have potential to better address the opioid crisis.

OPIOIDS IN PEDIATRIC UROLOGY

According to one study, 85.8% of pediatric urology patients did not receive a prescription for opioids following surgery.[8] Patients that were more likely to receive a prescription for opioids tended to be older in contrast to younger patients.[8] Furthermore, a different study with

102 pediatric urologists answering a 23-question survey noted that 48% prescribe opioids for all of their ambulatory pediatric cases. A mere 16% of providers thought that their patients would use most of the opioids they prescribed post-operatively.[9] With such variation in the results of both studies and a limited pool of research on the topic in pediatric urology specifically, it is important to acknowledge that formulating better education and appropriate practice guidelines could yield positive results in the current opioid crisis specifically within the field of urology.[9]

When it comes to outlined appropriate practice patterns for the use of opioids in the surgical care and treatment of pain, not many formal guidelines exist. This has impacted physicians with not having very concrete guidelines towards how much if any opioid prescription is appropriate and beneficial to the patient post-operatively.[10] A retrospective survey of 587 urological surgery patients 2-4 weeks post-operatively noted that 67% of the patients had excess opioids available. Additionally, looking at a different study measuring the oral morphine equivalents (OMEQ) prescribed to urological patients after robotic or open prostatectomy revealed that from the median 225 mg OMEQ, just 10% was used with 87% of patients keeping the excess. This can be problematic not only for the patient, but for those who now have easy access to opioids and further manifesting the opioid crisis.[10] Additionally, looking at a strictly pediatric patient population in a different study, it was noted that 78% held on to the excess opioids and only 62% of the patient population finished all the prescribed opioids.[11]

One key strategy that could help lower opioid prescribing and help move away from the opioid epidemic is the Prescription Drug Monitoring Programs (PDMP). PDMP has been established for each U.S. State and despite mixed findings from given states, it could help give a more holistic understanding on how opioids are being inappropriately prescribed or misused.[10]

A valid question for us to consider is if opioids are even necessary in many urological procedures for pediatric patients. A study was conducted to assess parents of pediatric patients' satisfaction with how their child did following circumcision.[12] Compared to the opioid group, the nonopioid group's parents were satisfied with the pain control their child received 61% compared to 53%. The study results implicate minimizing opioid use for patients post-operatively for circumcision and addressing pain following the surgery with nonopioid solutions could be an appropriate treatment intervention.[12] Continually, a different study was performed to try and reduce opioid use in pediatric patients who underwent hypospadias repair. The researchers set a goal of a 30% reduction in opioids over a 4-month timeframe.[13] A prospective study was completed while adhering to the Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) guidelines. The results of the study displayed a 35% complete reduction in opioid use in a 6-month timeframe. The researchers also concluded opioid use in hypospadias patients is not completely necessary and should be cautiously considered within post-operative treatment.[13]

This further emphasizes the importance of formulating more structured practice guidelines to address the current opioid crisis and how not all procedures have the same protocol.[14] In a study to analyze opioid prescribing practices between 2018 and 2019, the results expressed a significant drop in the prescribing and administering of opioids.[15] In 2018 61% of patients were prescribed opioids compared to 34% in 2019. Of the patients prescribed opioids, 55% and 28% respectively utilized the opioids between each year.[15] The study also mentions that halfway into the project the progress was discussed within the urology department with the goal to lower opioid prescribing in 2019. This assists the point of addressing and educating not only patients but providers towards safer practice of medicine specifically in appropriate opioid prescribing.[15] Lastly, a prospective study was conducted to analyze opioid use in pediatric urologic surgeries. Of a patient population of 202, an opioid prescription was distributed to each patient with 10 available doses. The results showed that most patients took 0-2 opioid doses of the 10 available. The researchers concluded the results support greater work towards building specific procedure-based guidelines and improved communication among everyone involved in the treatment process.[16]

OPIOIDS IN VASECTOMY

Comparing patients prescribed opioids versus non-opioid analgesics post-vasectomy, there are no race, marital status, insurance, or BMI differences between the groups, even when considering prior opioid usage or history of chronic pain.[17] Giving opioids for immediate post-vasectomy analgesia is seen to confer a marginal benefit in terms of needing an additional opioid prescription, where 2% to 4% of patients required an opioid prescription within 30 days after vasectomy.[17,18] This is in contrast to the nearly 10% of patients who received non-opioid analgesics (such as ibuprofen and ice) needing an additional opioid prescription within 30 days post-vasectomy.[18]

However, the benefits of using opioids as a post-vasectomy analgesic are seen to be outweighed by their risks. Most notably, between non-opioid and opioid-treated vasectomy patients, there is no difference in unplanned visits to the emergency room, frequency of secondary clinic appointments, or additional phone calls for pain.[18,19] For patients who receive opioids, Baker et al. found at their institution that 75% of patients received excess medication than what was needed, and 51% of patients did not dispose of their excess medication.[3] Importantly, Barham et al. found that 8% of their patients receiving opioids for post-vasectomy pain continuously used the medication 3 to 6 months following surgery,[18] which significantly exceeds the typical 5-day pain-free recovery period.[19] While the risk of opioid misuse can be mitigated by better patient education and physician prescribing protocols for opioids,[19] the issue can be significantly reduced if post-vasectomy pain was managed by non-opioid approaches.

OPIOIDS IN ENDOUROLOGY

Endourologic procedures are designed to be minimally invasive and thus have the goal of reducing post-operative pain as compared to an open approach. However, in endourologic procedures such as ureteroscopy, according to Awad et al. nearly 50% of US endourologists surveyed in their study reported prescribing opioids more than half the time.[20] Indeed, Tam et al. used a claims-data approach to find that 6.2% of patients discharged post-ureteroscopy with opioids had persistent use of opioids 3 to 6 months later.[21] There are a number of factors that predict a patient's persistent use of opioids, from prior opioid prescription and previous ureteroscopy, to mental illness and younger age.[22] Even when implementing an opioid-free approach to manage post-ureteroscopy pain, it has been found that about 14% to 17% of patients end up procuring an opioid prescription within 30 days of their surgery.[23] Surprisingly, 91% of these patients acquired the opioid prescription from other sources such as urgent care or the emergency department.[23]

However, the benefits of a non-opioid post-ureteroscopy analgesic approach are evident, as Sobel et al. found that patients who did not receive opioids did not have additional unexpected encounters to the emergency room or clinic, nor extra phone calls for pain.[24,25] And this opioid-free strategy is seen to be feasible in nearly 75% of patients.[24] In addition, robotic-assisted laparoscopic approaches or regional anesthetics and peripheral nerve blocks have been used as tools in other endourologic procedures (such as prostastectomies) to reduce intraoperative and postoperative opioid use.[26] These non-opioid approaches paired with patient education and counseling on expectations have further facilitated post-operative pain control.[25]

OPIOIDS IN PENILE IMPLANTATION

Inflatable penile prosthesis (IPP) surgery is the current treatment of choice for people suffering from erectile dysfunction who are resistant to noninvasive therapies. However, adequate postoperative pain control is challenging for penile implants recipients, and opioid use may be inevitable. During the postoperative period, patients are given a rigorous schedule for every non-opioid pain medication, and oxycodone should be taken only as needed for any breakthrough pain. There are studies investigating pre- and intra-operative strategies that reduce opioid use after penile implantation. One strategy is preoperative prophylactic analgesia through a combination of NSAIDSs, acetaminophen, gabapentin, pregabalin, or meloxicam. Another strategy is administering nerve blocks to the pudendal and dorsal penile nerves during IPP surgery using local anesthetics such as lidocaine and ropivacaine.[27] These strategies are part of the multimodal analgesia (MMA) protocol for improved pain control and reduced opioid use.[28] There are yet to be studies comparing the effectiveness of different IPP placement approaches at reducing opioid consumption. Novel approaches such as analgesic-coated implants, though exist, have not been extensively proven to be more effective than conventional implants.[27]

OPIOIDS IN UROGYNECOLOGY

Studies have shown that opioid use is more prevalent among urogynecology patients than among general gynecology patients.[29] According to a 2022 prospective multicenter study sponsored by the American Urogynecologic Society, urogynecology patients were on average prescribed 3 times the amount of oxycodone tablets that they consumed.[30] Preventing opioid over-prescription is thereby crucial after urogynecologic surgeries. Linder et. al recommends that clinicians follow a procedure-specific opioid-prescribing approach for pelvic organ prolapse surgeries, since their study showed that this approach reduced urogynecologic opioid use by about one half at Mayo Clinic.[31] Reagan et al. recommends no more than 15 tablets of opioids (about 112.5 morphine milligram equivalents) at discharge for pelvic reconstruction patients who have not taken opioids previously; providers shall aim for no opioid prescription at discharge for patients who used little or no opioids during postoperative hospitalization.[32] Solouki et al. reports that a multimodal analgesia regimen at Montefiore Medical Center resulted in reduced opioid consumption after urogynecologic procedures and maintained similar patient satisfaction levels.[33] Moskowitz *et al.*

demonstrated that a provider educational intervention was successful in reducing opioid prescription, while maintaining patient satisfaction.[34] In conclusion, there are multifaceted approaches that urogynecologists can adopt to prevent over-prescription and overconsumption of opioids after procedures.

OPIOIDS IN PROSTATECTOMY

In an era of multimodal analgesia during perioperative management and advent of the minimally invasive robotic prostatectomy, there has been a growing number of studies recommending an opioid-free pain management protocol for patients' post-prostatectomies.

Robot-assisted radical prostatectomy (RARP) continues to be the norm for urologists based in the United States, accounting for 85% of all radical prostatectomies compared to other operative techniques such as open radical prostatectomies or laparoscopies.[35] RARP allows for decreased operative time, blood loss, and pain level post-operatively leading to associative findings such as decreased postoperative opioid usage for patients who underwent RARP compared to other operative prostatectomy measures.[36,37] One pre-post interventional study concluded that a structured opioid-free pain regimen post-RARP was not inferior when compared to the traditional opioid-based standard of care.[38] Another study further concluded that the DaVinci SP® robotic platform (Intuitive Surgical, Inc., Sunnyvale, CA, USA) assisted procedure with an extraperitoneal approach and lower body mass index of the patient was associated with opioid-free management over the standard multi-port Da Vinci Si robotic platform with a transperitoneal approach.[39] As such, continued operative treatment discoveries within urology may lend a change in the standard of care post-prostatectomies.

Opioid prescription protocols post-discharge after prostatectomies also appear to be more commonly done by healthcare providers in the United States and Canada, whereas they are used sparingly when compared to the rest of the world.[40] North American figures are not only high with the amount of prescriptions, but also with the ratio of opioid naïve surgical patients transitioning to chronic opioid use after a single prescription – some studies revealing figures of 3% to 7%.[41,42] One Swedish register study reported a rate of less than 1% for patients that filled an opioid prescription post radical prostatectomy whom became chronic opioid users.[43]

Given the rise of the opioid epidemic in the United States, surgeons are encouraged to pursue medication alternatives for operative pain management such as regional blocks preoperatively or intravenous acetaminophen and nonsteroidal anti-inflammatory drugs postoperatively.[44] Future work is needed to apply similar regimens broadly for opioid-free standard of care post-prostatectomies.[38,44]

OPIOIDS IN NEPHRECTOMY

Laparoscopic minimally invasive radical or partial nephrectomies and open radical or partial nephrectomies to treat pathologies such as kidney cancer, have also been under scrutiny on if there is appropriate opioid prescriptions being made for perioperative pain management. There have been multiple studies conducted for urology patients' post-operative recovery including nephrectomy patients which concluded too many opioid prescriptions were being made for pain control and a range of 60-77% of such medications went unused.[45-47]

Consistent with other urologic operative treatment, open surgeries were oftentimes associated with increased odds of opioid based pain management. One Canadian population level study concluded that open nephrectomy was associated with higher odds of early opioid use compared to a minimally invasive nephrectomy (Odds Ratio [OR] 1.36, 95% Confidence Interval [CI] 1.19-1.55).[48] However, surgery type for the nephrectomy was not associated with prolonged opioid use in this study.[48] Additionally, another American retrospective cohort study analyzing Medicare data over 9 years concluded that higher prescribed opioids at discharge was associated with prior exposure to opioids, young age, rural location, and open nephrectomies.[49] For this cohort, there were no observable differences in prescribing patterns after kidney surgery by race/ethnicity, however Black and Hispanic patients were more likely to have long term opioid exposure independent of the procedure.[49]

Striking the balance between the amount of postoperative opioid for pain control continue to be a challenge at the provider level. While the review netted a few studies on how opioids are heavily prescribed and open nephrectomies may lead to greater opioid use post surgeries, the wide variability in postoperative opioid prescriptions for nephrectomies continue to be a focus of future research studies.[48,49]

OPIOIDS IN CYSTECTOMY

Radical cystectomy with lymph node dissection continue to remain as the recommended treatment in high risk muscle invasive and non-muscle invasive nonmetastatic bladder cancer.[50] However, radical cystectomy represents a significant surgical challenge in urology with development of morbidities at 30-64%.[51] Given the higher risk, enhanced recovery after cystectomy (ERAC) pathways, modeled after the enhanced recovery after surgery (ERAS) pathways in colorectal procedure complications, have been recommended development by urologic associations.[52,53] Perioperative analgesia is one component of this ERAC protocol recommending multimodal opioid-sparing analgesics such as non-steroidal anti-inflammatory drugs, epidural blocks, and locoregional blocks to enhance recovery.[52,53] One global survey study found half of the respondents still used opioids with or without non-steroidal anti-inflammatory drugs and limited use of epidural analgesia.[53] There have been a couple retrospective studies demonstrating epidural usage in radical cystectomy patients to be associated with longer hospital stay times and increased complications.[54,55] Another prospective implementation of a nonopioid perioperative pain management protocol for patients undergoing robot-assisted radical cystectomy demonstrated fea-

sibility allowing for minimal narcotic usage post-surgery.[56] With a higher variability in perioperative management for radical cystectomy patients alongside the higher morbidity risk that come with the operation, adherence to a still maturing ERAC protocol to phase out opioids may prove to be more difficult for urologists. As such, more research need to be conducted to determine if a nonopioid protocol is beneficial for radical cystectomies (open vs minimally invasive) alongside clarification of the ERAC protocols.

OPIOIDS IN SCROTAL & TESTICULAR SURGERY

There are several reasons that may lead to scrotal or testicular surgery including but not limited to hydroceles, spermatoceles, testicular torsion, or testicular cancer.[57,58] Needless to say, opioid usage post-surgery for pain management remains a significant factor to consider for recovery. One prospective study compared postoperative pain control among men receiving different quantities of narcotic prescriptions after scrotal surgery.[59] In this study, reducing total prescription for narcotic/non-narcotic medication was not associated with increased postoperative pain; limited prescription alongside non-steroidal anti-inflammatory drugs and ice were adequate for pain control.[59] In another study, celecoxib started twice daily preoperatively netted a significant decrease in postoperative pain and opioid use for patients who underwent microsurgical testicular sperm extraction procedures.[60] As such, alternative modems of pain control may yield the same results as opiates for pain management post-scrotal or testicular surgeries.

CONCLUSION

Preventative education on opioids and the present risk to patients and the general population is still a very present concern when considering an estimated 1.9 million Americans having an opioid disorder.[5] With not many formal guidelines in place for providers to glean appropriate regimens on prescribing of opioids to patients, more research is recommended. A mere estimation of 48.4% of residents obtained formal training on appropriate opioid prescribing in their residency training and just 42.1% of residents analyze for opioid abuse in their patients.[6] These stats reiterate the importance of establishing stronger and more comprehensive safe practice guidelines for the administering of opioids specifically post-operatively.[6] Additionally, one study noted that only 16% of providers figured their patients will finish all of the opioids prescribed and another result noting 67% of pediatric urology patients had extra opioids leftover in the post-operative period.[9,10]

Building upon the concept of improved education and awareness regarding the safe prescribing and use of opioids, we did witness effective change in our analysis when goals and open discussion among healthcare professionals took place.[13] In one study that set the goal to decrease opioid use post-operatively, a decrease in opioids prescribed from 2018 to 2019 of 61% to 34% $P < .0001$ was observed. It is encouraging to see an effective change in a short amount of time and the results were also likely related to halfway into the study the researchers' educated members of the urology department on lowering opioid use. Ultimately, the study also concluded that following pediatric urologic surgery, opioids are not always necessary for each patient.[13,15]

To further address the opioid crisis: increased formal education, better practice guidelines on prescribing opioids, and an improved patient-provider relationship could further positively impact the current opioid crisis.

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