

Opioid use after uro-oncologic surgeries in time of opioid crisis

Bruno Turcotte, Emma Jacques, Samuel Tremblay, Paul Toren, Yves Caumartin, Michele Lodde

Division of Urology, Department of Surgery, CHU de Québec—Université Laval, Quebec, QC, Canada

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Abstract

Introduction: Recent literature emphasizes how overprescription and lack of guidelines contribute to wide variation in opioid prescribing practices and opioid-related harms. We conducted a prospective, observational study to evaluate opioid prescriptions among uro-oncologic patients discharged following elective inpatient surgery.

Methods: Patients who underwent four surgeries were included: open retropubic radical prostatectomy, robot-assisted radical prostatectomy, laparoscopic radical nephrectomy, and laparoscopic partial nephrectomy. The primary outcome was the dose of opioids used after discharge (in oral morphine equivalents [MEq]). Secondary outcomes included: opioid requirements for 80% of the patients, management of unused opioids, opioid use three months postoperative, opioid prescription refills, and guidance about opioid disposal.

Results: Sixty patients were included for analysis. Patients used a mean of 30 MEq (95% confidence interval 17.8–42.2) at home and 80% of the patients used 50 MEq or less. A mean of 40.4 MEq per patient was overprescribed. Fifty percent of the patients kept the remaining opioids at home, with only 20.0% returning them to their pharmacy. After three months, 5.0% of the patients were using opioids at least occasionally. Three patients needed a new opioid prescription. Forty percent reported having received information regarding management of unused opioids.

Conclusions: We found 60% of opioids prescribed were unused, with half of our patients keeping these unused tablets at home. Our results suggest appropriate opioid prescription amounts needed for urological cancer surgery, with 80% of the patients using 50 MEq or less of morphine equivalents.

Introduction

Opioid overdose and addiction are two contemporary, growing problems in North America. Opioid overdoses killed more people than car accidents in the U.S. in 2015.^{1,2}

Canada is less affected but has its share of responsibility, being the second-largest opioid prescriber.^{3,4} In the province of Quebec, the opioid problem remains relatively low compared to the rest of Canada, especially when compared to British Columbia (9.4 vs. 25 opioid-related hospitalizations/100 000 population, respectively).⁵ Preventing the problem from worsening and improving the current situation rest, in large part, with surgeons as regular prescribers of opioids. In Canadian universities, medical students spend an average of 16 class hours on pain control, while veterinary students spend around 87 hours.⁴ Thus, there is clearly room for more education.

Worldwide, opioid prescriptions doubled between 2001 and 2013.⁶ This is particularly alarming since overprescribing is one of the most dominant factors influencing the development of opioid addiction.^{3,7} It is estimated that opioid-naïve patients who take a single opioid dose have a 6% chance of becoming addicted after one year and a 3% risk after three years.⁸ After minor or major surgery, it is estimated about 5–8% of opioid-naïve patients can become addicted.^{1,2,6,9} It is also known that the total amount of opioids prescribed is associated with misuse (defined as the use of opioids in a different manner or dose than prescribed by the physician) and need for prescription refills.¹⁰ In 2019, according to a *Lancet* review on opioid prescriptions after surgery, 67% of patients had an excess of prescribed opioids and 91% kept them at home.⁶ Similarly, many studies revealed that nearly 50% of the total prescribed opioids are unused and less than 10% of those are correctly disposed of.^{2,3,9} Among regular consumers, 60% are consuming non-prescribed opioids obtained from a close family member.¹¹ The World Health Organization indicates that being a family member of someone prescribed opioids is a risk factor for opioid overdose.¹²

As physicians, there are actionable factors identified to decrease prolonged opioid use after surgery: the dosage of prescriptions and the duration of the initial prescription are risk factors for opioid abuse. Therefore, the role of physicians, residents, and nurses is crucial.^{6,12}

Considering the above information, we believe there is a lack of local guidelines regarding the correct amount of analgesic opioid medication to prescribe in the postoperative

period. In this study focusing on uro-oncologic patients, we evaluated prescribing practices for common operations at our hospital. To do so, we conducted a prospective, observational study to assess how many opioids uro-oncologic patients received after hospital discharge and how many they really used at home.

Methods

In this study, approved by our local ethics committee (#2020-4880), we prospectively enrolled patients having oncologic surgery at Hotel-Dieu de Québec. Patients included in the study were men and women 18–80 years old having one of four common urologic cancer surgeries: open retropubic radical prostatectomy (RP), robot-assisted laparoscopic radical prostatectomy (RALP), laparoscopic radical nephrectomy (LRN), or laparoscopic partial nephrectomy (LPN). In our center, every RP includes standard or extended bilateral pelvic lymph nodes dissection. Patients were excluded if they chronically took opioids preoperatively, had an alcohol or drug use disorder, experienced a perioperative or early postoperative complications (Clavien-Dindo >2), had another concomitant surgery, or had laparoscopic surgery converted into open surgery.

Our primary outcome was to find the dose of opioids used in oral morphine equivalent (MEq) at home after each urologic surgery. MEq is a standardized measure for opioid content corresponding to the equivalent milligrams of morphine. In order to get the equivalent of morphine tablets, a division of MEq value by five is necessary. The secondary outcomes included the dose of opioids required by 80% of patients for each surgery, management of unused opioids, number of patients still consuming opioids three months after surgery, number of patients who needed an opioid prescription refill, and number of patients who had information about opioid disposal.

Participants were met the day before or the day of discharge. We had two clinical nurses who participated subsequently in opportunistic recruitment. No urology resident or attending staff other than the authors were aware of the study to eliminate the Hawthorne effect, whereby individuals change prescribing practices knowing they are observed. Three questionnaires were completed during the study. The first questionnaire assessed patient demographics immediately after signing the consent form. A second questionnaire was sent one month after surgery, in which was included an instruction form to help patients answer questions about the prescribed drug, dose, and quantity. Three months after surgery, a third and final form was sent to collect information on patients' opioid consumption to date and how they disposed of the remaining pills. Patients were contacted if we did not receive their questionnaire one month after sending it.

Results

From October 2019 to August 2020, 77 patients were approached to participate in the study and 68 patients accepted and were enrolled. Eight were excluded for analysis because of postoperative complications or the absence of followup. Fifteen patients had RP, 28 had RALP, five had LRN, and 11 had LPN. We also included one patient who had a robotic partial nephrectomy (RPN). This group of patients includes patients from 10 urologists. The mean length of stay was 2.1 (standard deviation [SD] 0.95) days.

Participants were aged between 43 and 84 years old (Table 1). Most of the patients were either married (53.3%) or with a common-law partner (30%). The highest educa-

Table 1. Patient demographics

Age, mean	63.2	
	n	%
Surgery		
RP	15	25.0%
RALP	28	46.7%
LRN	5	8.3%
LPN	11	18.3%
RPN	1	1.7%
Marital status		
Married	32	53.3%
Common-law partner	18	30.0%
Single	7	11.7%
Divorced	1	1.7%
Widowed	2	3.3%
Educational attainment		
Primary	3	5.0%
High school	20	33.3%
College	9	15.0%
University	17	28.3%
Professional diploma	10	16.7%
Other	1	1.7%
Annual income		
0–30 K	5	8.3%
30–50 K	23	38.3%
50–80 K	13	21.7%
80–100 K	6	10.0%
>100 K	9	15.0%
Undeclared	4	6.7%
Ethnicity		
Caucasian	50	83.3%
First Nations	1	1.7%
Metis	1	1.7%
Other	6	10.0%
Undeclared	2	3.3%

LPN: laparoscopic partial nephrectomy; LRN: laparoscopic radical nephrectomy; RALP: robot-assisted laparoscopic radical prostatectomy; RP: radical prostatectomy; RPN: robotic partial nephrectomy

tional attainment included 33.3% with a high school degree, 15.0% with a college degree, 28.3% with a university degree, 16.7% with a professional diploma, 5.0% with a primary degree, and 1.7% reporting other schooling. Patients' annual incomes were divided as 0–30 K (8.3%), 30–50 K (38.3%), 50–80 K (21.7%), 80–100 K (10.0%), >100 K (15.0%), and undeclared (6.7%). Most patients identified themselves as Caucasian (83.3%) and 1.7%, 1.7%, 10.0%, and 3.3% of the patients identified themselves as First Nations, Metis, other, and undeclared, respectively.

In the three months before their enrollment, 8.3% of patients had used opioids but less than once a month. Seven patients (11.7%) reported drinking alcohol every day and 21 patients (35.0%) reported drinking alcohol weekly. Two patients (3.3%) reported using recreational drugs weekly.

Hydromorphone was prescribed for 53 patients (88.3%), morphine for two patients (3.3%), and four patients (6.7%) did not take their opioid prescription (Table 2). In total, 3510 MEq (702 tablets), a mean of 65 MEq (13 tablets) per patient, were prescribed at discharge. At home, patients used a mean of 30 MEq (95% confidence interval [CI] 17.8, 42.2) and a median of 15 MEq. Fifty MEq (10 tablets) correspond to the 80th percentile of opioids used in our population. When asked to rate their pain control at home on a scale out of 10 (10 being pain-free), patients rated it at a mean of 8.8/10 (95% CI 8.2, 9.4) compared to a mean of 8.5/10 (95% CI 7.9, 9.2) in hospital. The dose of opioids used at home was not associated with the type of surgery ($p=0.8$)

or the total opioids used, including those consumed during hospitalization ($p=0.68$). We did not find a correlation between the length of stay and discharge opioids use (0.09, Kendall Tau b); however, patients who used 27.5 MEq or less during hospital stay were 4.5 times more prone to use no opioid at home ($p=0.01$, Bivariate logistic regression). There were no statistically significant association between opioid use after discharge and marital status ($p=0.3$), education ($p=0.44$), annual income ($p=0.81$), ethnicity ($p=0.54$), alcohol consumption before surgery ($p=0.88$), or preoperative drug consumption ($p=0.55$).

A total excess of 2220 MEq was prescribed (the equivalent of 444 morphine 5 mg tablets) with a mean of 40.4 MEq per patient. At one month postoperative, half the patients (50.0%) kept their overprescribed opioids at home, while only 13.3% returned them to their pharmacy. Others either disposed of them themselves (3.3%), had no excess opioids (10.0%), or did not fill their opioid prescription (10.0%). At three months, half the patients still had excess unused opioids at home (48.3%), while 20.0% of the patients returned them to their pharmacy, 1.7% had given them to someone, 5.0% used them for other reasons, and 15.0% had no excess opioids (Table 3). At three months postoperative, one patient (1.7%) reported using opioids regularly, two patients (3.3%) reported using opioids occasionally, and three patients (5.0%) rarely. Three patients (5.0%) needed an opioid refill. Instruction received for management of excess opioids was reported by 26.7% and 40.0% of the patients at one month and three months, respectively.

Discussion

Within our sample of uncomplicated oncologic surgeries, we found a mean of 30 MEq (six tablets) use following hospital discharge. In our sample, the opioid need did not vary significantly according to the surgery. Patients rated good pain control at home with a mean of 8.8/10. Our results suggest that to decrease potential for opioid-related harms, MEq prescribed at discharge for uncomplicated surgeries should be less than 50 MEq (10 tablets of hydromorphone 1

Table 2. Opioid use after uro-oncologic surgeries

	n	%
Opioid		
Hydromorphone	53	88.3%
Morphine	2	3.3%
No opioid	4	6.7%
Dose prescribed (n=54)	MEq	
Mean	65	95% CI 55.1, 74.9
Median	55	50.0; 100.0 (Q1; Q3)
Total	3510	
Dose used (n=55)		
Mean	30.0	95% CI 17.8, 42.2
Median	15.0	0.0; 40.0 (Q1; Q3)
Dose unused (n=55)		
Mean	40.4	95% CI 30.5, 50.2
Median	35.0	0.0; 75.0 (Q1; Q3)
Total	2220	
Co-analgesia		
Acetaminophen	49	89.1
Naproxen	3	5.5
Ibuprofen	1	1.8
Pregabalin	1	1.8
Oxybutinin	2	3.6

CI: confidence interval.

Table 3. Patient-reported management of unused opioids

Unused opioids management	1 month		3 months	
	n	%	n	%
Returned to pharmacy	8	13.3	12	20.0
Kept at home	30	50.0	29	48.3
Disposed	2	3.3	0	0.0
No unused opioids	6	10.0	9	15.0
Prescription not fulfilled	6	10.0	0	0.0
Given to someone	0	0.0	1	1.7
Used for other reason	0	0.0	1	1.7
Other	0	0.0	3	5.0
No detail	8	13.3	5	8.3

mg or morphine 5 mg), as this dose or less was required by 80% of our patients, and only three patients (5.0%) needed a new opioid prescription.

Other studies looking at opioid needs after RP found mean patient requirements between 50.5 and 58.6 MEq.^{10,13} According to our results, 80% of our patients would need 50 MEq or less (10 morphine 5 mg tablets equivalent) after discharge. This is higher opioid requirements than reported by Theisen et al, where 80% of their patients needed between 17 and 23 oxycodone-equivalent (25–34.5 MEq) after RP, laparoscopic/robotic nephrectomy, and RALP;² however, in-hospital analgesia protocols were different and co-analgesia was not captured in their study, limiting the comparisons. Still, these doses are significantly lower than the 100 MEq often prescribed after discharge. We did not find an association between any demographic factors studied and the dose of opioids used; however, Loeb et al found a higher risk of new chronic opioid use with patients having higher cancer risk, greater comorbidity, unmarried status, and low educational level.¹⁴

Overall, an excess of 2220 MEq (63.2%) were prescribed in only 60 patients. This dose corresponds to 444 tablets of morphine 5 mg being potentially available for misuse. These results are similar to the 60% and 77% reported by Theisen et al and Patel et al, respectively.^{2,9} On the other hand, we found that patients using 27.5 MEq or less during hospital stay were 4.5 times more prone to use no opioids at home ($p=0.01$), so adjusting patients' opioid prescriptions before discharge according to the dose received during hospitalization could be a strategy to reduce opioid overprescription.

We observed half of our patients kept the excess opioids at home, while only 13.3–20.0% reported having returned them to their pharmacy. These trends were also highlighted by similar studies, where 9% of the patients disposed of their excess opioids correctly and 74–92% of the patients reported keeping the excess opioids at home,^{10,15} increasing the risks of misuse.⁸ The latter phenomenon could also be related to the fact that at one and three months postoperative, only 26.7% and 40.0% of the patients, respectively, reported having received information about excess opioid disposal. Evaluating the prolonged use of opioids after surgery, we observed that at three months, three patients (5.0%) still reported using opioids regularly or occasionally. This is in line with Brummett et al, who reported 5.9–6.5% new persistent opioids use after major surgery.¹⁶ Looking at some causes of overprescription and possible improvement strategies, we considered concentrating our attention on different facts. In our university-affiliated centers, prescriptions are often written immediately prior to the surgery using pre-filled prescriptions including 20 tablets of hydromorphone 1 mg (100 MEq). This is a common practice among many surgical specialties. Patient satisfaction and hospital performance are often related to the absence

of pain after surgery as a high-stakes indicator.¹⁷ As doctors, we wish to achieve this outcome for our patients, avoiding the inconvenience of returning to the hospital for a prescription refill. Moreover, prescriptions may often be written by residents who were not principally involved in the surgery or perioperative care, reducing the possibility of individualized prescription adjustment.

The main limitation of this study is the small sample size. We had difficulties enrolling patients because of our opportunistic-based recruitment. Our recruiting nurse worked part-time on the project with a variable schedule and a full-time job as a clinical nurse in the urology department. The COVID pandemic also significantly impacted recruitment possibilities. Nonetheless, our results largely correspond with similar existing literature and can support future prospective studies in the postoperative period. Despite relatively few patients included, it is nonetheless striking that there was an excess of 2220 MEq of prescribed opioids in our study. Extrapolated annually, where greater than 400 of the four surgeries included in our study are performed, approximately 14 800 MEq (2960 tablets) of excess opioids could be available with the potential for abuse.

The lack of control on the co-analgesia was the second limitation. Ziegelmann et al compared the prescription of opioids in MEq before and after introducing evidence-based guidelines to surgeons for postoperative urologic surgery and found the median MEq prescribed decreased by 33%, with refill rates unchanged.¹⁸ Similar results were obtained by Patel et al, where patients decreased opioid use after prostatectomy by 26.5% after implementing evidence-based co-analgesia interventions.¹⁹ Co-analgesia may even be sufficient to eliminate postoperative opioid use.^{20–22} With their protocol, Hallway et al found high satisfaction and good pain control for 47% of robotic prostatectomy patients with no opioid use.²³

Other key points to decrease opioid needs include appropriate counselling, preoperative co-analgesia (gabapentin, acetaminophen with or without nonsteroidal anti-inflammatory drugs), regional or local anesthetic before incision, opioid-free protocol during surgery, and postoperative co-analgesia (ketorolac, gabapentin, and acetaminophen).²⁴ The Centers for Disease Control also suggests reducing opioids use to three days or less to reduce the chance of addiction, side effects, and misuse by relatives.⁸ A shared decision-making approach to opioid prescriptions may also play a role in diminishing opioid prescriptions.⁶

Conclusions

In our cohort, we found 60% of opioids prescribed were in excess of patient needs. Nearly 50% of our patients kept their unused tablets, probably due to lack of counselling

at hospital discharge. After uncomplicated urologic cancer surgery, patients generally require 30–50 MEq of opioids at home. A reduction and personalization of the dose of opioids prescribed is warranted, while the optimization of co-analgesia could further decrease opioid requirements. Multidisciplinary consensus meetings for local guidelines and educational meetings for healthcare stakeholders should be considered.

Competing interests: Dr. Toren has been an advisory board member for Abbvie, Bayer, and Knight; has received grants and/or honoraria from AstraZeneca; and has participated in clinical trials supported by Janssen, Merck, and Roche. The remaining authors do not report any competing personal or financial interests related to this work.

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Correspondence: Dr. Bruno Turcotte, CHU de Québec—Université Laval, Quebec, QC, Canada; bruno.turcotte.1@ulaval.ca