AUCTORES
Globalize your Research

International Journal of Clinical Nephrology

Syed N. Rahman *

Open Access

Research Article

Retrospective Evaluation of a Novel Perioperative Opioid Sparing Protocol for Patients Undergoing Robotic Assisted Laparoscopic Radical Prostatectomy or Partial/Total Nephrectomy: A Case Control Study

Syed N. Rahman [1*], Mursal Gardezi [1], Jonathan Coronado [2], Katelyn Johnson [1], Jamil Syed [1], Soum D. Lokeshwar [1], Benjamin H. Press [1], Christopher S. Hayden [1], Ankur U. Choksi [1], Amir I. Khan [1], Michael S. Leapman [1], Joseph F. Renzulli II [1]

[1] Department of Urology, Yale University School of Medicine, New Haven, CT, United States.

[2] Touro College of Medicine, Harlem, NY, United States.

***Corresponding Author:** Syed N. Rahman, Department of Urology, Yale School of Medicine.

Received Date: January 17, 2023; **Accepted Date:** January 30, 2023; **Published Date:** February 03, 2023

Citation: Syed N. Rahman, Mursal Gardezi, Jonathan Coronado, Katelyn Johnson, Jamil Syed, et all (2023), Retrospective Evaluation of a Novel Perioperative Opioid Sparing Protocol for Patients Undergoing Robotic Assisted Laparoscopic Radical Prostatectomy or Partial/Total Nephrectomy: A Case Control Study. *International Journal of Clinical Nephrology*. 5(1); DOI:10.31579/2834-5142/050

Abstract

Background/Aim: We aimed to evaluate the clinical effect and outcomes of an opioid-sparing perioperative regimen among patients treated with minimally invasive abdominal urologic surgery.

Materials and Methods: We conducted a retrospective study to evaluate the efficacy of a perioperative opioid sparing protocol. Patients enrolled in the treatment group received a pre-specified regimen of meloxicam, gabapentin, omeprazole, oxybutynin, and acetaminophen. Average length of stay, numeric pain scores, amount of opioids utilized in the inpatient post-operative period, the necessity of an opioid prescription at discharge, and outpatient 7-day post-operative phone calls were collected. Descriptive statistics were utilized to measure significant differences between cohorts.

Results: The study consisted of 197 patients enrolled between 2018-2020, including 70 (35.5%) who received the intervention and 127 (64.5%) controls. 106 patients out of 127 (83.5%) patients in the control group were discharged with an opioid prescription as compared to 2 of 70 (2.9%) patients in the treatment group ($p< 0.01$). There were also significant differences in total inpatient oral milligram morphine equivalents (44.14 mg vs 17.38 mg, $p=0.01$) in patients with no history of chronic opioid use, inpatient pain score at post-operative days 2-3 (3.84 vs 2.75, $p<0.01$) and average outpatient pain scores seven days after discharge (3.73 vs 1.67, $p<0.01$). No difference was observed regarding length of stay (1.74 vs 1.49, $p=0.17$)

Conclusion: A non-opioid perioperative regimen can result in similar post-operative pain control and length of stay while leading to fewer opioid prescriptions being written at discharge. By decreasing the number of patients requiring opioids post operatively, there is the potential to have a positive impact on the opioid epidemic.

Keywords: opioids; opioid sparing; robotic surgery; eras

Introduction

Worldwide the use of post-operative opioid analgesia has resulted in numerous harms including opioid overuse, increased incidence of opioid dependence and opioid use disorder, and opioid diversion [1]. Such outcomes can be linked to the growing opioid epidemic in the United

States resulting in up to 120 deaths per day as a result of both non-synthetic and synthetic opioids [2]. Given the development of such

deleterious outcomes from excess opioid prescriptions, a growing amount of research has started to investigate patterns in opioid prescriptions.

It has previously been demonstrated that there exists high variability in outpatient surgery opioid prescriptions even amongst the same procedure [3]. Additionally, longitudinal data has demonstrated that opioid prescriptions for both low risk and high risk surgery have increased steadily [4]. Given this increase there has been growing interest and research into adopting different approaches to treat pain while reserving the use of opioid analgesics as a last resort. Some of these different approaches include novel surgical techniques and procedures as well as the implementation of multimodal analgesia, defined as using medications to target multiple areas in which pain originates in order to provide a more synergistic effect than using any one agent alone [5].

An opioid-sparing regimen was originally developed at our institution to reduce the amount of pain medications utilized by patients in orthopedic surgeries. Slight modifications to the regimen given to the orthopedic patients were made to tailor the regimen to patients undergoing robotic-assisted laparoscopic radical prostatectomy or partial/total nephrectomy. These minimally invasive procedures allow a surgeon to perform a prostatectomy or nephrectomy with decreased blood loss and typically result in better pain control as well as shorter lengths of stay [6]. The purpose of this study is to investigate the effectiveness of a pre-defined opioid sparing pathway by observing a reduction in the amount of prescriptions written at discharge by targeting multiple pathways of pain for patients undergoing a robotic-assisted laparoscopic radical prostatectomy or partial/total nephrectomy.

Materials and Methods

Patient Selection and Cohort Design

A retrospective cohort study was conducted to determine if there is a significant impact in the prescribing of opioid analgesics in both the inpatient and outpatient setting while still maintaining adequate pain control. Data was collected from the medical records of 97 consecutive patients who had a robotic-assisted laparoscopic radical prostatectomy or partial/total nephrectomy performed by the same surgeon at the same facility.

The control group consisted of patients undergoing one of these procedures from the beginning of June 2018 to the end of January 2020 and did not receive an opioid-sparing packet. The treatment group consisted of patients undergoing one of these procedures from September 2018 to November 2019 that received a blister-pack of medications containing three days of meloxicam 7.5mg daily and gabapentin 300mg at bedtime as well as omeprazole 40mg, oxybutynin ER 5mg, and acetaminophen 1000mg the morning of the procedure. These medications were continued immediately after the surgery and during the rest of the hospitalization. Patients were then discharged with these medications for seven days post-operatively.

Outcomes

The primary outcomes were opioid prescriptions needed at time of discharge and average inpatient MME in the control group vs the treatment group. Secondary outcomes included average length of stay, average daily numeric pain scores, number of opioid medications utilized in the inpatient post-operative period and outpatient 7-day post-operative pain scores. Average length of stay was calculated by using the number of midnights spent in the institution. Average daily numeric pain scores were collected via nursing assessment on a scale from 0-10 (0 = no pain, 10 = worst pain). The amount of opioids utilized in the post-operative period was converted to oral milligram morphine equivalents (MME) to account for different type of opioids used, see **Table 1** for conversions. Outpatient 7-day post-operative pain scores were collected via telephone interview.

	Oral (mg)	IV (mg)
Buprenorphine	0.4 (SL)	N/A
Hydrocodone	30	N/A
Hydromorphone	7.5	1.5
Fentanyl	N/A	0.1
Meperidine	N/A	100
Methadone*	10	N/A
Morphine	30	10
Oxycodone	20	N/A

*While some sources use a conversion of 1:4.7, 1:3 is an appropriate conservative conversion.

Table 1: Milligram Morphine Equivalents

All patients that underwent surgery from June 2018 to November 2019 were included in the study. If a patient was non-compliant with the opioid-sparing pathway before and after the surgery, they were automatically placed into the control group. Patients were only excluded if they did not undergo the surgical procedure. If a patient in the opioid sparing group had an allergy to any component to the opioid-sparing packet, that component was removed and they received the other medications. No regional blocks were utilized for these procedures. It was documented if patients chronically took opioids or had a history of any kind of alcohol or drug abuse, but they were not excluded if they did use chronic opioids. The baseline characteristics are listed in **Table 2**.

	No Opioid Sparing Pathway/ Control Group (n=127)	Opioid Sparing Pathway/ Treatment Group (n=70)
Age	63 [55-73]	65 [56-78]
Gender		
Male (#)	124	66
Female (#)	3	4
Allergy to Opioid-Sparing Regimen	0% (0/127)	3% (2/70)
Chronic Use of Opioids	5% (7/127)	4% (3/70)
Prior History of Any Substance Abuse (including marijuana)	8% (10/127)	11% (8/70)
Alcohol Usage	35% (45/127)	40% (28/70)
Type of Surgery		
Prostatectomy (#)	90% (116/127)	83% (58/70)
Nephrectomy (#)	10% (11/127)	17% (12/70)

Table 2: Baseline Characteristics

The protocol was reviewed and approved by the Institutional Review Board of South County Hospital and the research was conducted according to the principles of the Declaration of Helsinki, seventh revision (*JAMA*. 2013; 310:2191-4).

Statistical Analysis

Statistical analysis was performed using Microsoft Excel 2010 software. The statistical significance threshold was set at p-value ≤ 0.05 using 95% confidence intervals (CIs). An unpaired t-test assuming equal variances was used to compare the differences in length of stay, average pain scores on post-op days 0, 1 and 2, pain scores 7 days post-op, average oral milligram morphine equivalents utilized inpatient and number of opioid prescriptions at discharge (given independent groups).

Results

Baseline characteristics

From 2018 to 2020, 197 patients were ultimately eligible for analysis, including 127 patients in the control cohort and 70 patients in the opioid sparing cohort (Table 2). The majority of patients enrolled were men (97.6% in control cohort and 94.2% in opioid sparing cohort) and underwent prostatectomy (90% and 83% respectively). No significant differences in terms of chronic opioid use or prior substance use were identified between cohorts (5% vs. 4% p=0.87, 8% vs. 11% p=0.46).

Pain Score and Length of Stay

The average length of stay did not significantly differ between both cohorts (1.74 days compared to 1.49 days in the non-opioid sparing cohort and opioid sparing cohort respectively, p=0.17). Pain scores did not significantly differ between the non-opioid sparing and opioid sparing cohort on POD1 (2.90 vs. 2.58, p=0.28). However, pain scores were significantly reduced in the opioid sparing cohort compared to the non-opioid sparing cohort on POD2 and POD3 (3.84 vs. 2.75 p<0.01 and 4.45 vs. 3.18 p=0.03 respectively). Additionally, pain scores at home on POD7 continued to be significantly lower in the opioid sparing cohort (3.73 vs. 1.67, p<0.01).

Opioid Utilization

Overall, 106 patients out of 127 (83.5%) in the control group were discharged with an opioid prescription as compared to 2 of 70 (2.9%) patients in the opioid sparing cohort (p< 0.01). Additionally, a significantly lower amount of total oral milligram morphine equivalents (MME) was documented in the opioid sparing cohort compared to the control (1.92 vs. 14.40, p<0.01). When isolating for patients that utilized opioids while inpatient, although a statistically significant difference in MME was not identified between the two groups (44.64 mg MME vs 71.91 mg MME, p = 0.74), there was a clinically significant difference when patients with a history of chronic opioid use were excluded (44.14 mg MME vs 17.38 mg MME, p=0.01). See **Table 3** for a complete list of all results.

	No Opioid Sparing Pathway (n=127)	Opioid Sparing Pathway (n=70)	P value
Percent Discharged with Opioid Prescription	83.5% (106/127)	2.9% (2/70)	<0.01
Average Length of Stay (days)	1.74 (CI = 1.46–2.14) (n=127)	1.49 (CI = 1.24–1.73) (n=70)	0.17
Average Pain Score Post-Op Day 0	2.90 (CI = 2.34-3.26) (n=127)	2.58 (CI = 2.20–2.97) (n=70)	0.28
Average Pain Score Post-Op Day 1	3.84 (CI = 3.52–4.18) (n=127)	2.75 (CI = 2.32–3.15) (n=70)	<0.01
Average Pain Score Post-Op Day 2	4.45 (CI = 4.01–5.07) (n=20)	3.18 (CI = 2.37–3.99) (n=7)	0.03
Average Inpatient Total Oral MME (mg)	34.40 (CI = 22.29–41.93) (n=127)	1.92 (CI = 0.15–3.43) (n=70)	<0.01

Average Inpatient Total Oral MME (for those that utilized opioids) (mg)	44.64 (CI = 38.81–101.34) (n=127)	71.91 (CI = 8.63–135.19) (n=11)	0.74
Average Inpatient Total Oral MME Excluding those with Chronic Opioid Use history (for those that utilized opioids)	44.14 (CI = 36.14–52.26) (n=126)	17.38 (CI = 4.27–30.29) (n=8)	<0.01
Average Pain Score at Home 7 Days Post-Op	3.73 (CI = 3.32–4.15) (n=15)	1.67 (CI = 1.26–2.09) (n=61)	<0.01

Table 3: Results

Discussion

This retrospective analysis revealed a non-opioid perioperative regimen can result in the equivalent length of stay, improved pain control POD1 onwards and lead to fewer opioid prescriptions being written at the time of discharge. The amount of opioid prescriptions written at discharge had an absolute reduction of 80.6%. The amount of opioids required in the post-operative period for patients who do not chronically use opioids was reduced by more than 50%.

However, the notable takeaway from our results is that a reduction in opioid prescriptions and inpatient use of opioids with our opioid sparing pathway led to similar pain scores in POD0 and actually improved pain scores POD1 and beyond. Length of stay was noted to be decreased in the opioid sparing group, although not a statistically significant reduction. Additionally, pain scores remained improved until postoperative day 7 in the opioid sparing cohort. The overall sample size across both cohorts remained low preventing further generalizability of such results.

To our knowledge this is the first study focused on achieving a profound reduction in opioid prescriptions and leading to improved pain control with an opioid-sparing regimen in patients undergoing urologic procedures. Multiple studies have investigated opioid prescriptions being filled after robotic assisted laparoscopic urologic procedures. Studies have identified that in certain cohorts over 50% of patients following radical prostatectomy fill a prescription for opioids [6-7]. However, it has become evident now that in those cohorts over 70% of prescriptions ultimately remain unused and add potential opioids to the community that may subsequently contribute to the growing opioid epidemic [8]. Although prior trials aimed at developing and testing opioid-sparing regimens had different results based on the time of procedure, our results demonstrate the need for a randomized prospective trial comparing an opioid sparing pathway to the traditional opioid pain regimen. Modifications to the existing pain regimen identified in our study, such as the utilization of Toradol inpatient and incorporating regional blocks, should additionally be investigated. Additionally, proper patient educations regarding medication administration, such as discussing each element of the blister pack given to the patient in our study, may lead to improved patient satisfaction and post-operative pain scores that may directly affect opioid requirements.

There are a few notable strengths to this study. All surgeries were performed by the same two surgeons at the same institution. Since the same surgeons performed these procedures, the outcomes are more likely to reflect differences in the medical management rather than differences in the surgical techniques. In addition, all patients that received the surgery in the specified timeframe were included in the study. Lastly, all patients received the same preoperative and post-operative regimen, except for two patients, both of which reported an allergy to non-steroidal anti-inflammatory drugs.

The greatest limitation to this study was the retrospective nature and small sample size of patients as it relates to average pain scores at seven days after discharge. Since pain scores were recorded via telephone interview, we were unable to include pain scores for patients that were unable to be reached after discharge. Additionally, it is important to note that this is a descriptive study and that further refined statistical analyses with larger sample sizes will be required to understand optimal combinations of perioperative pain regimens. Future randomized controlled trials investigating opioid sparing protocols are warranted.

Conclusion

A non-opioid perioperative regimen can result in equivalent length of stay, similar or even improved post-operative pain control and fewer opioid prescriptions being written at the time of discharge. By decreasing the number of opioids required in the post-operative recovery period and the number of patients requiring opioids at discharge, the utilization of an opioid-sparing regimen has the potential to have a substantial impact on the opioid epidemic by reducing drug availability.

Disclaimer: All authors have no financial interests to disclose

References

1. Neuman MD, Bateman BT, Wunsch H. Inappropriate opioid prescription after surgery. *Lancet*. 2019;393(10180):1547-1557. doi:10.1016/S0140-6736(19)30428-3
2. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and Opioid-Involved Overdose Deaths – United States, 2013-2017. *WR Morb Mortal Wkly Rep*. ePub: 24 June 2019.
3. Hill MV, McMahon ML, Stucke RS, Barth RJ Jr. Wide variation and excessive dosage of opioid prescriptions for common general surgical procedures. *Ann Surg* 2017; 265: 709–714.
4. Wunsch H, Wijeysundera DN, Passarella MA, Neuman MD. Opioids prescribed after low-risk surgical procedures in the United States, 2004—2012. *JAMA* 2016; 315: 1654–1657.
5. Ladha KS, Patorno E, Huybrechts KF, Liu J, Rathmell JP, Bateman BT. Variations in the Use of Perioperative Multimodal Analgesic Therapy. *Anesthesiology*. 2016;124(4):837-845. doi:10.1097/ALN.0000000000001034
6. Carlucci JR, Nabizada-Pace F, Samadi DB. Robot-Assisted Laparoscopic Radical Prostatectomy: Technique and Outcomes of 700 Cases. *Int J Biomed Sci*. 2009; 5: 201–208.

7. Loeb S, Cazzaniga W, Robinson D, Garmo H, Stattin P. Opioid Use after Radical Prostatectomy: Nationwide, Population Based Study in Sweden. J Urol. 2020 Jan;203(1):145-150. doi: 10.1097/JU.0000000000000451. Epub 2019 Jul 17. PMID: 31584849.

8. Patel HD, Srivastava A, Patel ND, Faisal FA, Ludwig W, Joice GA, Schwen ZR, Allaf ME, Han M, Herati AS. A Prospective Cohort Study of Postdischarge Opioid Practices After Radical Prostatectomy: The ORIOLES Initiative. Eur Urol. 2019 Feb;75(2):215-218. doi: 10.1016/j.eururo.2018.10.013. Epub 2018 Oct 21. PMID: 30352714.

DOI: 10.37579/ijcn.2022/050