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Optimizing post-operative opiate prescribing following gynecologic surgery

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ARTICLE INFO	A B S T R A C T	
Keywords: Opiate prescribing Gynecologic surgery Enhanced recovery after surgery	<i>Background:</i> Post-operative opiate prescribing has traditionally been stratified by procedure type with little re- gard for patient opiate utilization. We sought to evaluate peri-operative factors associated with patient opiate utilization post-operatively to develop, implement, and assess a discharge prescribing intervention. <i>Study design:</i> This was a quality improvement study of opiate prescribing practices for patients undergoing gy- necologic surgery on an enhanced recovery pathway (ERAS) pre- and post-discharge prescription intervention. In the pre-intervention cohort (12/2018 to 05/2019), peri-operative factors (demographic, procedure, and pain scores) associated with post-operative patient opiate usage and quantity of opiate prescribed were identified. A discharge planning intervention based solely on opiate usage was implemented. The pre- and post-intervention cohort (07/2020 to 09/2020) were compared to assess changes in post-operative opiate prescribing and refill requests.	
	<i>Results:</i> There were 220 patients in the pre-intervention cohort and 120 patients post-intervention. Post-operative opiate usage in the pre-intervention cohort was correlated only with pain score and age ($p < 0.001$, $p = 0.04$). Quantity of opiate prescribed was correlated only with procedure type and not reflective of patient opiate usage. Using this information, a discharge planning intervention for opiate prescription informed by opiate usage in the twenty-four hours prior to discharge was added to the discharge order set. Post-intervention, adherence to recommended prescription was 40.8%. Opiate prescriptions decreased from a mean 27.3 tablets to 14.8 tablets ($p < 0.001$). <i>Conclusions:</i> A tailored, patient specific approach to post-operative opiate prescribing can significantly decrease the quantity of opiates prescribed.	

1. Introduction

In 2018, there were an estimated 10.3 million Americans who misused opioids and an estimated 2.0 million Americans with opioid use disorder. (Substance Abuse and Mental Health Services Administration, 2018) The majority of these patients report first exposure to opiates through a prescription for treatment of acute pain. (Lamvu et al., 2018) Surgery remains one of the most common indications for opiate prescribing with upwards of 50 million ambulatory surgeries performed annually in the United States. (Hall et al., 2017) While efforts have been made to limit opiate requirement in the immediate post-operative period through programs like Enhanced Recovery after Surgery pathways (ERAS), this has not been fully operationalized with individualized and patient centered prescribing practices at time of hospital discharge. (Modesitt et al., 2016)

While the portion of patients who progress to chronic opiate use following surgery can be as high as 6.5%, recent literature suggests the rate of persistent opiate use post hysterectomy is less than 0.1%. (Brummett et al., 2017; Young et al., 2020 Jan) The greater concern from excess opiate prescribing is the contribution to opiates in the community as 40–70% of all opioids prescribed after surgery are unused for management of postoperative pain. (Bicket et al., 2017) Excess tablets should be disposed of using Center for Disease Control guidelines, so that they do supply line to those with prescription use disorder in the community. Reportedly, 74% of those with prescription use disorder obtained their prescriptions from friends and family. (Lamvu

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et al., 2018) To stem the flow of opiates into the community, altering practice to tailor prescriptions to individual opiate need following surgery could minimize the opiate excess generated post-operatively.

There is a growing body of evidence that opiate use prior to discharge is the best predictor of post discharge opiate use. This has been shown for minimally invasive surgery (MIS) hysterectomy, and is the foundation for one study of ultra-restrictive opiate prescribing in gynecologic surgery. (Weston et al., 2019; Mark et al., 2018) This has also been shown in general surgery where patient opiate use while admitted along with age were the best predictors of opiate usage at home following discharge. (Hill et al., 2018) In this study, which included open and laparoscopic procedures, post discharge opiate usage was not significantly affected by procedure type. This challenges the practice of procedure-based prescribing. Current expert panel recommendation which was published in 2018 in the Journal of American College of Surgeons for gynecologic procedures recommends prescribing stratifying based on procedure type with abdominal procedures receiving 0-20 tablets of opiates and 0-10 tablets for a major gynecologic laparoscopic procedure. (Overton et al., 2018; Freiden and Houry, 2016)

These guidelines do not individualize opiate prescribing recommendations based on individual perception of pain. The experience of post-operative pain is unique to a person. We sought to evaluate our post-operative opiate prescribing practices and identify factors that correlate with patient opiate usage prior to discharge. Using this information, as a quality improvement at our institution, we developed a guideline for opiate prescribing post operatively, implemented and then prospectively followed to assess for change in quantity of opiate prescribed. As a secondary outcome, we evaluated number of refill requests from patients as a surrogate marker for the adequacy of the quantity prescribed.

2. Methods

This was a quality improvement study performed under institutional review exempt protocol (University of Virginia IRB for Health Science Research, Protocol 21585 and 22960). Fig. 1 details the timeline of this quality improvement intervention. Patients who underwent gynecologic surgery utilizing the ERAS protocol from December 2018 through May 2019 at The University of Virginia Health System were identified using the existing prospectively enrolled ERAS database. This time period was selected as it captured current prescribing practices during the opioid epidemic for procedures performed utilizing an ERAS protocol, which was fully adopted at our institution in 2015. Patients were excluded if they were currently incarcerated, had a history of opiate abuse, chronic pain including cancer pain requiring opiate at baseline, post-operative complication requiring additional pain medication including reoperation, or a length of stay less than twenty-four hours. Utilizing the demographic and clinical information obtained from the ERAS database and additional chart review, multivariable regression modeling was performed to evaluate for patient factors correlating with opiate use in the twenty-four hours prior to discharge and for factors correlating with prescribing practices post-operatively.

The ERAS protocol at our institution is divided into a light pathway (minimally invasive surgery) and a full pathway (abdominal surgery). Both pathways utilize pre-operative celecoxib, acetaminophen, and gabapentin, intra-operative continuous lidocaine infusion, and post operatively scheduled acetaminophen and celecoxib with as needed oxycodone. Under the ERAS full pathway, patients also receive an opioid spinal with Duramorph 250 mcg and the lidocaine infusion is continued for the first 24 h after surgery. Our ERAS database includes demographic and clinical information including date of birth, age, race, ethnicity, division, date of surgery, CPT codified surgical procedure, length of stay, average pain score prior to discharge, highest pain score, and morphine equivalent (MME) usage in the operating room from the electronic medical record.

Additional information for each patient was obtained from chart

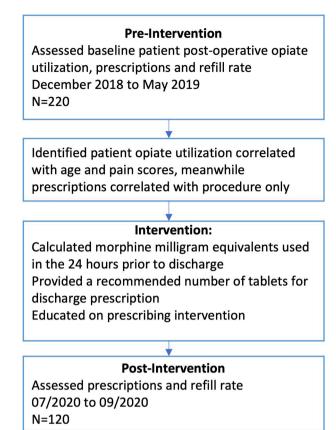


Fig. 1. Timeline of evaluation, development, implementation, and assessment of quality improvement intervention/tool.

review including mailing address to calculate distance lived from the hospital, procedure type, indication for surgery, substance usage including tobacco, cocaine, marijuana, or opiates, and prior opiate use. Each operative report was reviewed to assess for the procedure type. Laparotomy for any indication was considered a laparotomy. Major laparoscopic procedures included laparoscopic or robotic hysterectomy, minimally invasive sacrocolpopexy, or minimally invasive adnexal surgery with additional procedure including hernia repair, colon resection or cholecystectomy. Vaginal hysterectomy included those undergoing concomitant urogynecologic procedures. Vaginal prolapse surgery encompassed those with a prior hysterectomy undergoing apical suspension, anterior and/or posterior repair, sling, or colpocleisis. The Medication Administration Record summary was reviewed to calculate morphine milligram equivalents (MME) used for the twenty-four hour period prior to discharge as well as the number tablets of 5 mg oxycodone or 2 mg hydromorphone used. Pharmacy utilized for discharge prescriptions identified those who had their prescriptions conveniently sent to the hospital pharmacy and delivered via "Meds to Beds" service. Chart review identified patients requiring additional opiate prescriptions.

With the results of the multivariable regression and national prescribing guidelines, we developed a prescribing guideline that calculated MME usage in the previous twenty-four hours and provided a recommendation of the number of tablets prescribed (0, 10, or 20 tablets). This patient specific opiate prescribing practice was implemented in March 2020 amidst the coronavirus pandemic. There were alterations in surgical volume so review of our post intervention cohort did not begin until our institution returned to routine operative volumes in July 2020. House-officers prescribe all of the post-operative pain medications at our institution. Prior to the implementation of opiate discharge tool/ intervention, house officers were educated on this new prescribing recommendation/tool. They were encouraged to use this patient specific approach along with clinical information and discussion with the patient to determine the appropriate amount of opiate to prescribe.

We planned to follow our post-intervention cohort for 3 months, which based on our pre-intervention group, would include approximately 108 patients. We anticipated that this would give us the ability to detect a mean 10 tablet decrease in post-operative opiate prescribing with 80% power and a two-sided alpha of 0.05. Patients were prospectively followed from July 2020 to September 2020 collecting the same information from chart abstraction as was initially collected in the pre-intervention cohort. Statistical analysis was performed using RStudio Team (RStudio, Boston, MA). The pre and post intervention cohorts were compared with a p-value of 0.05 considered statistically significant. Continuous variables were compared using Student's *t*-test. Multiple continuous variables were compared using ANOVA with post-hoc Tukey analysis. Categorical variables were compared using Chi Square test or Fisher's Exact test as appropriate.

3. Results

In the pre-intervention cohort, 220 met inclusion criteria and in the post intervention cohort, 120 met inclusion criteria. The two groups were of similar age, body mass index and had surgery performed for similar indication by similar departments. The majority of surgeries

Table 1

Demographic and clinical information pre- and post- intervention.

	Pre n = 220	$\begin{array}{l} \text{Post} \\ n=120 \end{array}$	
Age (Years)	54.7 (CI:	56.0 (53.3,	p =
	52.7, 56.6)	58.7)	0.45
BMI (kg/m ²)	32.1 (CI:	32.1 (30.5,	p =
	30.9, 33.4)	33.7)	0.96
Miles from hospital	50.9 (CI:	67.5 (54.0,	p =
	45.5, 56.4)	80.9)	0.02
Race			p =
			0.29
White or Caucasian	160 (72.7%)	85 (47.2%)	
African American	36 (16.4%)	28 (23.3%)	
Other	19 (8.6%)	5 (4.2%)	
Asian	4 (1.8%)	2 (1.6%)	
American Indian or	1 (0.5%)	0 (0.0%)	
Alaskan Native			
Division			$\mathbf{p} =$
			0.23
Gynecologic	135 (61.4%)	85 (70.8%)	
Oncology			
Benign Gynecology	51 (23.2%)	21 (17.5%)	
Urogynecology	34 (15.5%)	14 (11.7%)	
Procedure Type			p =
			0.005
Major Laparoscopy	116 (45.5%)	59 (49.2%)	
Laparotomy	76 (34.5%)	44 (36.7%)	
Vaginal Hysterectomy	22 (10.0%)	7 (5.8%)	
Vaginal Prolapse	6 (2.7%)	3 (2.5%)	
Vulvectomy	0 (0.0%)	7 (5.8%)	
Duramorph Spinal	67 (30.5%)	39 (32.5%)	p = 0.70
In direction for Course and			0.72
Indication for Surgery			p = 0.28
Domine	151 (69 60/)	75 (63 50/)	0.28
Benign Cancer	151 (68.6%)	75 (62.5%)	
	69 (31.4%)	45 (37.5%)	-
Length of Stay	1.8 (CI: 1.7,	1.7	p =
MME prior to discharge	2.0) 25.0 (CI:	(1.6,1.9)	0.33
MME prior to discharge		27.8 (22.6,	p = 0.37'
No opieto teleon in the 24 h prior to	21.6, 28.3) 61 (27.2%)	32.9) 35 (29.2%)	
No opiate taken in the 24 h prior to discharge	01 (27.2%)	33 (29.2%)	p = 0.80
Greater than 10 tablets of opiate taken	15 (6 8%)	15 (12 5%)	0.80 n –
in the 24 h prior to discharge	15 (6.8%)	15 (12.5%)	p = 0.06
Average Pain Score	3.3 (CI: 3.0,	3.7 (3.3,	
AVELASE PAILI SCOLE	3.5)	3.7 (3.3, 4.1)	p = 0.10
	3.3)	4.1)	0.10

were performed by gynecologic oncology and over a third of procedures were for a diagnosis of cancer (Table 1). These groups differed only in distance lived from the hospital which was a mean 16.6 miles further in the post intervention arm and a higher number of vulvectomies in the post intervention group (p = 0.04, p = 0.005).

In the pre-intervention cohort, the potential contributing factors to inpatient opiate requirement were evaluated and only pain score and age were significantly associated with opiate use (Table 2). Notably, a

Table 2

Multivariable analysis of factors associated with inpatient opiate usage in the twenty-four hours prior to discharge.

		Estimated Contribution to Number of Tablets	95% Confidence Intervals	P- value
Procedure	Laparotomy	0		
Туре	Major Laparoscopy Vaginal Hysterectomy Vaginal Prolapse	0.724	(-0.434, 1.882)	p =
		1.596	(-0.265, 3.457)	0.22 p = 0.09
		1.464	(-1.332, 4.260)	p = 0.30
Division	Benign	0		
	Gynecology Gynecologic Oncology Urogynecology	-0.111	(-1.217, 0.994)	p = 0.84
		-0.142	(-1.590, 1.873)	p = 0.87
Age		-0.036	(-0.071, -0.002)	p = 0.04
Distance Lived from Hospital		0.0001	(-0.009, 0.009)	p = 0.97
Hospital History of Prior Abdominal	No	0		
Surgery	Yes	0.661	(-0.120, 1.441)	p = 0.09
Length of Stay (days)		0.061	(-0.477, 0.602)	p = 0.82
Body Mass Index (kg/ m2)		0.008	(-0.034, 0.051)	p = 0.70
Pain Score Prior to Discharge		1.063	(0.853, 1.273)	p < 0.001
Cancer	Yes No	0 0.198	(-0.769,1.165)	p = 0.69
Race	African	0		
	American American Indian/Alaska Native	-1.174	(-6.569, 4.222)	p = 0.67
	Asian	-1.698	(-4.511,1.115)	p = 0.24
	White or Causasion	-0.612	(-1.605, 0.579)	0.24 p = 0.43
	Other	-0.513	(-2.137, 0.914)	0.43 p = 0.36

cancer diagnosis or a laparotomy were not significantly associated with increased opiate utilization in the twenty-four hours prior to discharge. For each point increase in average pain score prior to discharge, patients took an estimated 1.06 tablets of opiate (p < 0.001, 95% CI (0.8, 1.2)). For each year of age, an estimated 0.03 fewer tablets were taken (p = 0.04, CI (-0.07, -0.002). No other factors were associated with significant variation in opiate utilization. Opiate prescribed on discharge was correlated with procedure type (p < 0.001) and remained significantly correlated even after controlling for patient demographic information, length of stay, pain scores, and opiate taken by the patient. We found that regardless of how much opiate patients took prior to discharge, they received a prescription for a mean 25–30 tablets of opiate.

Using this information in conjunction with CDC and American College of Surgeon prescribing guidelines, we developed a prescribing recommendation based on MME usage while admitted. This can be seen in Table 3, which also shows adherence to these prescribing guidelines post intervention. Following implementation, there was a decrease in number of tablets prescribed from 27.3 to 14.8 tablets. (mean difference of 12.5 tablets CI: 10.9, 14.1; p < 0.001) Refill rate was not statistically different between the two arms at 3.7% v 8.1 % (p = 0.07). Of the 10 requiring a refill in the post-intervention cohort, one reported side effects from the oxycodone requiring a change to hydromorphone, two were prescribed less opiate than was recommended by the new algorithm, one reported their prescription was run over by a car, and four required more than 10 tablets prior to discharge. Only two patients received the recommended prescription and required a refill.

4. Discussion

The transition from a standardized prescribing practice influenced predominately by procedure to one reflective of actual patient opiate usage, significantly decreased our post-operative opiate prescribing. This was possible even in a patient population that predominately underwent complex laparotomy and major laparoscopic procedures with gynecologic oncology with a third of all patients having a cancer diagnosis. This was accomplished in a rural setting where patients travel on average more than 50 miles to receive care. All prescription refills in both arms were e-prescribed which has more recently become available in all 50 states and Washington D.C.

Our intervention addresses two likely contributing factors to our preintervention prescribing practices that are likely experienced at other institutions: (1) the electronic medical record had a pre-populated prescription for 30 tablets of opiate in the discharge order set (2) MME use prior to discharge could not be readily accessed. Removing the prepopulated 30 tablet prescription and replacing it with two unselected options for 10 or 20 tablets, prompts physicians to consciously choose the amount of opiate to prescribe with objective data for the individual patient. The strategy of changing EMR preset opiate prescriptions alone has previously shown a 15% reduction in opiate prescribing. (Chiu et al., 2018)

Our pre-intervention prescribing practices are consistent with national prescribing patterns where median post hysterectomy prescription is 30 tablets. (Young et al., 2020) While we greatly improved, compliance with the exact recommended algorithm was poor, at best 55% in the 20 tablet group and worst in the group recommended to receive no opiate. The number of tablets prescribed was still decreased by nearly 50%, but our data is reflective of hesitancies to forego opiate prescribing with only 6 patients receiving no opiates on discharge postintervention. The post intervention group had an even higher percentage of patients utilizing hospital delivery of prescriptions likely reflective of limiting unnecessary contact during the pandemic. This translates to an additional 15% of patients receiving the quantity of opiate prescribed and not having the option to partially fill or selectively fill a prescription only if necessary. This further highlights the importance and timeliness of optimizing opiate prescribing practices.

Table 3

Post-operative opiate prescribing recommendations and post-intervention adherence.

Milligram Morphine Equivalents used in the last 24 h	Recommended Opioid Prescription	Number in Post Intervention Meeting Criteria	Number in Compliance
0	0 Tablets	35	6 (17.1%)
1-23	10 Tablets	25	10 (40.0%)
≥ 24	20 Tablets	60	33 (55%)

Though refill rate pre- and post-intervention increased from 3.7% to 8.1%, it remained lower than published rates of up to 16% and was not statistically significant (p = 0.07). (Weston et al., 2019; Mark et al., 2018) The subset of patients requiring more than 10 tablets of opiate prior to discharge accounted for 33% of refills pre-intervention and 50% of refills post-intervention. The proportion of patients with this opiate need trended toward a significant increase post-intervention (12.5% v 6.8% pre-intervention, p = 0.06), which likely accounts for the majority of the change in refill rate.

The strengths of this study were that it evaluated a large number of patients undergoing surgery using current ERAS practices. We were able to quantify actual morphine use prior to discharge for all patients. The limitations were that it is a retrospective study at a single institution. There was no follow up to evaluate for adequate pain control and actual opiate use was not quantified. There was no follow up data to determine which patients actually filled their prescription potentially overestimating the amount of opiate given. Some patients could have received additional opiate from local providers not in our system.

Opiate prescriptions following gynecologic surgery should be tailored to specific patient needs and providers should feel empowered to change their post-operative opiate prescribing practice to better reflect the inpatient opiate requirement. This study highlights the ability to accommodate refill requests through electronic prescription even in a practice setting with a large catchment area where patients travel an average of 50 miles for their procedure and alleviate provider concern about under prescribing opiates.

Author contribution section

Study Concept and Design: Croft, Sarosiek, Muthusubramanian, Hedrick, Modesitt.

Acquisition of Data: Croft, Sarosiek, Muthususubramanian.

Analysis and Interpretation of Data: Croft, Sarosiek, Muthusubramanian, Trowbridge, Modesitt.

Drafting of manuscript: Croft, Sarosiek, Trowbridge, Muthusubramanian, Hedrick, Modesitt.

Critical revision: Croft, Sarosiek, Trowbridge, Muthusubramanian, Hedrick, Modesitt.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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