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Validating an opioid prescribing algorithm in post-operative pediatric surgical oncology patients☆

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ABSTRACT

Purpose: We developed an algorithm to decrease opioid prescriptions for pediatric oncology patients at discharge following surgery, based on a retrospective analysis to decrease variability and over-prescribing. The aim of this study was to prospectively test the algorithm.
Methods: Opioid-naïve patients undergoing surgery for tumor resection at a single institution were included. A prescribing algorithm was developed based on surgical approach, day of discharge, and inpatient opioid use. Prospectively collected data included outpatient opioid consumption and patient/family satisfaction. Total home dose prescribed was equal to that used in the 8 or 24 h, depending on length of stay and operative approach, prior to discharge, divided into 0.15 mg/kg doses.
Results: The algorithm was used in 121 patients and correctly predicted outpatient opioid requirements for 102 patients (84.3%). For 15 (12.4%) patients, the algorithm over-estimated opioid need by an average of 0.38 OME/kg. Four (3.3%) patients required additional opioids. Using this algorithm, we decreased overall opioid prescriptions from 6.17 to 0.21 OME/kg ($p < 0.001$), and all but one patient/family reported being satisfied with post-operative pain control.
Conclusion: Using an algorithm based on inpatient opioid use, outpatient opioid needs can be accurately predicted, thereby reducing excess opioid prescriptions without detriment to patient satisfaction.
Type of Study: Prospective Quality Initiative Study.
Level of Evidence: Level III.

Inappropriate prescriptions have played a contributing role in the opioid epidemic. We and numerous other centers have demonstrated that opioid prescriptions for children after surgery are variable and often excessive [1–8]. Additionally, prescribed opioids are frequently unused, kept in unsafe locations, and not disposed of properly [9–13]. Because post-operative patients often require opioid administration and outpatient opioid prescriptions, surgeons play a critical role in safe opioid stewardship and minimizing the risk for diversion [14].

Numerous quality improvement initiatives have been implemented to decrease pediatric opioid prescriptions after common surgical procedures, such as hernia repair [15–17], appendectomy [1,16], and tonsillectomy [18]. However, these prior initiatives do not address larger operations with more variable post-operative courses. Algorithms that can be used on a broader scale are needed to help identify selective patient populations who might need opioids at discharge and to determine how much should be given.

We and others have shown that inpatient opioid use can be used to predict outpatient opioid needs and guide outpatient prescriptions [7,19]. In our prior study, we analyzed baseline opioid prescribing patterns after pediatric oncologic surgeries over a two-year period. We then initiated a quality improvement program to educate staff and families about opioid side-effects, alternative pain control options, and standardized use of multi-modal analgesia. We prospectively gathered data on outpatient opioid use between July 2018 through December 2018 and used that data to create a prescribing algorithm (Fig. 1) for pediatric oncology patients after thoracic and abdominal operations. We hypothesize that our algorithm can predict opioid needs after discharge. The aim of this study was to test this hypothesis by prospectively evaluating its accuracy.

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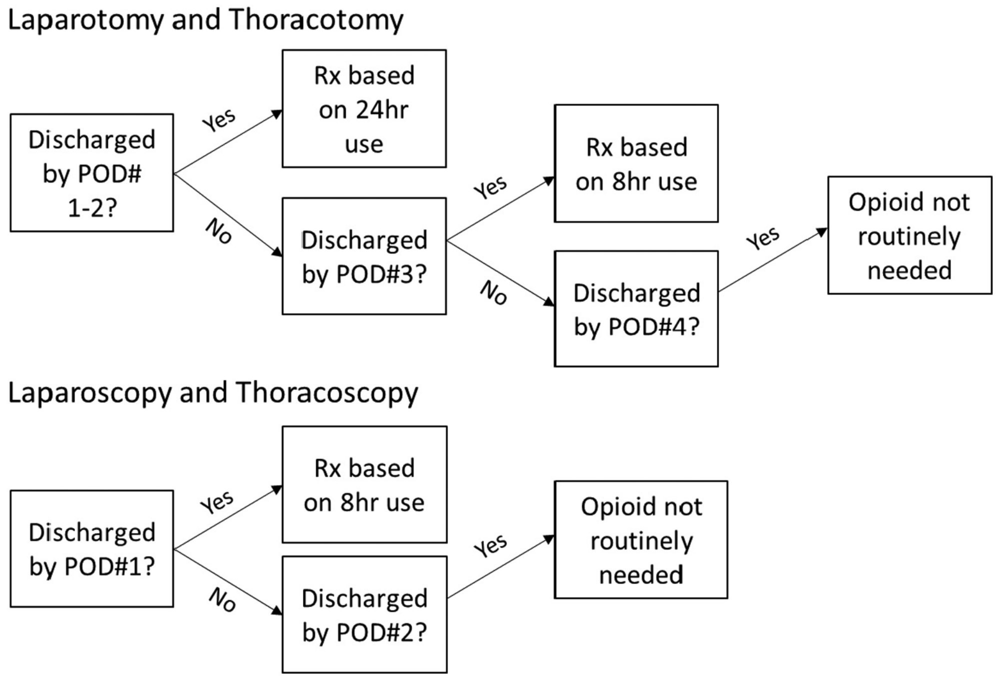

Fig. 1. Prescribing algorithm based on operative approach and the post-operative day (POD) of discharge. Opioid prescriptions are created based on inpatient use during either the 24 h prior to discharge, or 8 h prior to discharge.

1. Methods

1.1. Retrospective post-operative analgesia data collection – baseline cohort

As part of a quality improvement (QI) initiative, the current study was deemed exempt by our institutional review board and waiver of informed consent was therefore obtained. We previously performed a retrospective review of opioid prescribing and usage in patients undergoing thoracotomy, thoracoscopy, laparotomy, and laparoscopy for tumor resections between July 2016 and July 2018 at a single children's cancer hospital. These patients comprised the baseline cohort and are shown for comparison in this study. Starting July 2018, we began a quality improvement initiative to improve multi-modal analgesia use, and patient/parent education on pain control regimens. At the pre-operative visit and during the post-operative stay, we reviewed the options for non-opioid pain medicines and the side-effects of opioids. For inpatient pain regimens, the pain intensity was described based on an age-appropriate pain scale (1–10) and used for analgesic medications. Indications for inpatient analgesic administration were explicitly stated and discussed with nursing for every patient (example: acetaminophen 10–15 mg/kg prn pain 1–3 every 6 h, ibuprofen 10 mg/kg prn pain 4–6, opioid prn pain 7–10). Contraindications to acetaminophen and ibuprofen included: allergies to the medication or component, liver impairment (acetaminophen), and renal insufficiency or thrombocytopenia (ibuprofen). These contraindications were documented. We reviewed cases weekly and made adjustments or added educational components via multiple iterative "plan, do, study, act" (PDSA) cycles with input from outpatient and inpatient personnel.

1.2. Prospective post-operative analgesia data collection – Prescription algorithm development

As part of our QI initiative, we asked every patient/family to document their postoperative outpatient opioid consumption and data was collected at their post-operative surgery clinic visit and recorded. We prospectively collected this data from July 2018 to December 2018. This cohort of patients comprised the algorithm development cohort. We collected daily opioid use and calculated the average consumption decrease by day of surgery. We used multiple Pearson correlations to compare inpatient opioid requirements during the 24 h prior to discharge and 8 h prior to discharge compared to the subsequent outpatient use, after adjusting for post-operative day and type of operative approach. This led to the development of our prescribing algorithm in Fig. 1. A description of our algorithm development has been reported previously [7].

As an example, consider a patient who is discharged on post-operative day (POD) two following a laparotomy. If the patient used 10 mg (mg) of oral morphine equivalents during the 24 h prior to discharge, then a prescription was created totaling 10 mg oral morphine equivalents (OME) in divided doses. We prefer to provide equivalents of morphine doses of less than 0.15 mg/kg with instructions to try the smaller dose first, but an additional dose is allowed if pain control is not adequate. Acetaminophen and ibuprofen are also provided to every patient with specific instructions to try non-opioid medications first. If the patient in this example were 13 kg, then we would prescribe 2 mg morphine po for 5 doses every 4 h prn pain not relieved by prn acetaminophen and ibuprofen. We do not provide a duration but rather use the total amount divided into the smallest doses (0.1–0.15 mg/kg). We typically start with 4-h intervals but discuss with patients and/or their parents that they may take the opioids more frequently if pain is not well controlled or less frequently as pain subsides. We use oral morphine, hydromorphone, or oxycodone based on the available formulations and dosing needed. For younger patients, we used morphine as our liquid formulation (10 mg/5 ml) because this allowed easier dosing of small amounts.

1.3. Prospective post-operative analgesia data collection – testing and validation of algorithm – prospective cohort

The algorithm was then used to prospectively guide discharge opioid prescriptions for every patient following abdominal or thoracic surgery for tumor resections from January 2019 to January 2020 (the prospective cohort). At the post-operative clinic appointment, we continued to collect data on outpatient opioid consumption. We also asked every patient or parent about their satisfaction with the pain control regimen. Satisfaction was classified as one of the following: very satisfied with little to no pain, satisfied with pain control but did have pain that did not impact normal activities, or dissatisfied with pain control regimen. For each patient, the algorithm prediction was deemed "correct" if it accurately predicted their outpatient consumption within 0.01 OME/kg, which allows for some discrepancies in oral dosage type available. The algorithm was deemed to "over-estimate" if the prediction resulted in excess doses of opioid given, but not consumed. The algorithm was deemed an "under-estimate" if the prediction resulted in not enough opioid dispensed compared to what was consumed.

Data were analyzed using Graphpad Prism 8.0 (La Jolla, CA, USA) and presented as mean ± standard deviation or median (interquartile range), as appropriate. Univariate analysis of continuous variables was performed using Student's *t* test, and Fisher's exact test or chi-square test were used to compare categorical variables. Analysis of variance (ANOVA) was used to compare multiple continuous variables and detect patient differences based on algorithm performance. Non-morphine opioid dosing was converted to oral morphine equivalents (OME) using standard conversion factors [20]. OME is reported per kilogram based on the patient weight at time of surgery (OME, mg/kg). Amount of opioid prescribed at discharge is reported as total amount of OME/kg prescribed.

2. Results

The algorithm was used prospectively in 122 patients (33 laparoscopy, 46 laparotomy, 25 thoracoscopy, 17 thoracotomy). It was found to accurately predict outpatient consumption in 102 patients (84.3%) (Table 1). The algorithm over-estimated outpatient consumption in 15 (12.4%) patients. In this subset, the average amount of over-estimation was 0.38 OME/kg. There were 4 patients (3.3%) where the algorithm under-estimated outpatient consumption. One patient was not provided an opioid prescription based on the algorithm and returned on day of discharge for complaints of pain. This patient had been discharged on post-operative day one after a laparoscopic adrenalectomy after using no opioids for > 12 h prior to discharge. After returning, he was provided with 5 doses of morphine and consumed a single dose (0.18 OMG/kg). He required no further pain medication. The remaining 3 patients were prescribed an opioid beyond post-operative day 4 due to continued inpatient opioid use and all three used two doses of opioid after discharge (average 0.29 OME/kg). Because the algorithm had called for no opioids to be dispensed for patients discharged after post-operative day 4, these patients would have been underdosed by the algorithm. All were discharged on post-operative day 4 following open procedures. The average age of these patients was 14.5 years (range 12–19).

Analysis of variance (ANOVA) revealed a difference in age among patients for whom the prescribing algorithm accurately, over-estimated, or under-estimated outpatient opioid requirements ($p < 0.004$). Patients where the algorithm was accurate were significantly younger (6.6 years ±6.0) than patients where the algorithm over estimated (10.7 ± 6.7 years, $p = 0.017$) and under-estimated (14.5 ± 3.1 years, $p = 0.011$) outpatient opioid requirements. There was also a difference between length of stay among the groups (ANOVA $p = 0.002$). The length of stay in patients with correct algorithm prediction was longer than in patients who were over-estimated (3.0 ± 1.7 days vs 1.3 ± 0.7 days, $p = 0.004$), but not different from those who were under-estimated (2.8 ± 1.5 days, $p = 0.970$) (Table 1).

Inpatient epidural use was lower in the prospective cohort compared to baseline cohort (69.8% of thoracotomies and laparotomies vs 84.6%, $p = 0.03$). Acetaminophen and ibuprofen were prescribed at discharge more often compared to the baseline cohort (115 (96.6%) acetaminophen and 93 (86.1%) ibuprofen, $p < 0.001$ for both) after correcting for contraindications. Significantly more patients were discharged with only non-opioid analgesia (n = 93, 76.9%) compared to baseline (n = 11, 5.4%, $p < 0.001$). The average OME/kg prescribed was significantly lower in the prospective cohort (0.22 (±0.52) OME/kg) compared to baseline (6.17 ± 7.71 OME/kg, $p < 0.001$) (Table 2). There was a single readmission for pain (described above) resulting in a readmission rate of 0.8%, which was significantly lower than the baseline cohort (8.8%, $p = 0.002$). Fig. 2 demonstrates the average OME/kg prescribed per operative type over time. The educational aspect of the QI initiative with increased use of multi-modal pain control is marked at July 1st, 2018. Over the following 6 months opioid prescriptions decreased as a result of the educational campaign. During this time data was collected on outpatient opioid usage and satisfaction which allowed us to create our algorithm. Starting January 2019 all discharge prescriptions were created using the algorithm.

Satisfaction results were recorded for 119 patients in the prospective cohort. A total of 105 (88.2%) patients reported they were "very satisfied with little to no pain". There were 13 (10.9%) who reported they were "satisfied with pain control with some pain that did not impact normal activities". The one patient described above, was "dissatisfied with the pain control regimen".

3. Discussion

Inpatient opioid use can be used to predict outpatient needs using an algorithm based on surgical type and time from surgery. By using the algorithm, opioid prescriptions decreased and over-prescribing opioids in excess of actual patients' needs was minimized. This was done without compromising patient satisfaction and may have contributed to a reduced readmission rate.

It is difficult to quantify the success of this algorithm given the lack of a similar comparisons in the literature. The dramatic decreases in opioid prescriptions are likely attributed to our QI initiative which included patient and parent education. The algorithm is a useful tool for patients ready for discharge but still requiring opioid analgesia. To our knowledge there have not been attempts to standardize opioid prescriptions for surgeries other than common outpatient surgeries such has umbilical and inguinal herniorrhaphy, or surgeries with standard pain profiles

Table 1
Algorithm performance.

	Correct	Over-estimate	Under-estimate
Overall n(%)	102 (84.3%)	15 (12.4%)	4 (3.3%)
Age (years)	6.6 (± 6.0)	10.7 (± 6.7)	14.5 (± 3.1)
Length of stay (days)	3.0 (± 1.7)	1.3 (± 0.7)	2.8 (± 1.5)
Satisfaction			
Very Satisfied	90 (88.2%)	12 (85.7%)	2(50%)
Satisfied	10 (9.8%)	2 (14.3%)	1 (25%)
Dissatisfied	0	0	1 (25%)
Unknown/ not recorded	2	1	0

Table 2
Non-opioid and opioid use.

	Baseline N = 205	Prospective N = 121	p
Acetaminophen prescribed, n (%)	134 (65.4%)	114 (95.8%)	<0.001
Ibuprofen prescribed, n (%)	77 (38.7%)	92 (86.0%)	<0.001
Opioid prescribed, n (%)	194 (94.6%)	28 (23.1%)	<0.001
Opioid amount (OME/kg)	6.17 (± 7.71)	0.21 (± 0.52)	<0.001
Laparoscopy	4.19 (± 5.03)	0.14 (± 0.49)	<0.001
Laparotomy	8.22 (± 10.94)	0.29 (± 0.65)	<0.001
Thoracoscopy	4.36 (± 2.78)	0.19 (± 0.39)	<0.001
Thoracotomy	6.41 (± 3.97)	0.20 (± 0.34)	<0.001
Readmissions/calls	18 (8.8%)	1 (0.8%)	0.002
Length of stay (days)			
Laparoscopy	1.5 (± 1.0)	1.3 (± 0.8)	0.307
Laparotomy	5.0 (± 1.7)	4.1 (± 1.2)	0.006
Thoracoscopy	1.3 (± 0.6)	1.6 (± 1.0)	0.204
Thoracotomy	3.4 (± 0.9)	3.4 (± 1.3)	0.996

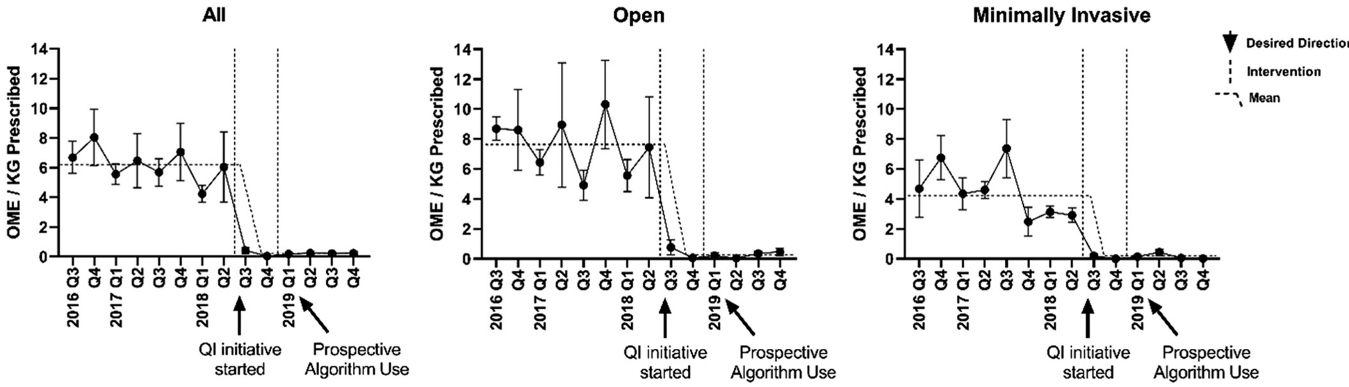

Fig. 2. Run chart depicting average opioid prescribed in oral morphine equivalents per kilogram (OME/kg) over time. Error bars depict standard error of the mean for each time point. Time points of quality improvement initiative and prospective algorithm use are marked by vertical dotted lines and text. The baseline mean and shift are depicted by horizontal dotted lines.

such as laparoscopic appendectomy. The size of the incision and the extent of the operation with associated visceral pain will widely vary between patients, even between patients with the same tumor types. This algorithm is intended to be broadly applied to basic surgical approaches with a varied post-operative course and allow a more personalized discharge analgesia plan. As this approach is used for more patients in a variety of settings and further refinements are made, the accuracy rate may improve further. The low proportion of patients for which the algorithm over-estimated the opioid needs without worsening readmissions seems indicative of a successful algorithm. The very small amount of excess opioid distributed to patients treated with this algorithm (one or two doses in our series) is a significant improvement from baseline and poses a much lower risk of overdoses, abuse, or diversion.

In our study, the factors noted to be associated with accurate prediction using the algorithm were younger age and longer hospital stay postoperatively. We could interpret the fact that the algorithm is less accurate in older patients as possibly attributable to psychosocial confounding factors which may be more prevalent than in the younger pediatric population [21]. As for the longer hospital stay, it is possible that, in the absence of postoperative complications, the use of opioids is reduced day by day, and therefore it is lower at the end of a longer admission and less prone to misestimation of opioid need at discharge.

We acknowledge that further refinements may be necessary. We made modifications to our prescribing when patients were still using inpatient opioid beyond the typical prescribing period. We hypothesize that older patients may have more complex pain requirements, and one should take age into account when estimating continued opioid needs. We also acknowledge that the goal is to ensure every patient has adequate pain control and avoid any readmissions for pain. However, it was surprising that the patient who returned for uncontrolled pain had not required any pain medicine in the hospital for >12 h prior to discharge. The only adjunct to pain control in that case was 0.25% bupivacaine injected at the port sites during surgery which would have dissipated prior to discharge. In our experience, it is extremely unusual for pain to return after such a period. We also acknowledge that opioid prescriptions were seen to decrease prior to routine algorithm use, likely due to our QI initiative. However, the amount of opioid prescribed has remained low, even after new providers have been added to the group (such as rotating surgical fellows).

We have previously discussed the unique patients and environment within a freestanding children's cancer hospital [7]. Our patients are typically discharged to hospital-provided housing with transportation readily available. This may impact how comfortable caregivers are leaving the hospital without opioids or a limited supply, knowing they have quick access to medical care should they need it. The follow-up appointments for our patients average 3 days from hospital discharge, which are likely shorter than most institutions. This makes recall of opioid usage easier for patients and parents. However, a phone call follow-up could also easily assess outpatient opioid usage for data collection at other institutions. We did not collect outpatient pain scores which may have added important information to adequacy of pain control. We elected to collect overall satisfaction with pain control and gain some information about pain's impact on function. We felt it was important to understand if pain limited daily activities. We were not able to compare our findings to historic controls since this information was not collected prior to our QI initiative.

Our institution also frequently utilizes regional anesthetics such as continuous epidural analgesia with epidural catheters. This likely impacted the amount of systemic opioids the patients used prior to discharge. It is typically our practice to turn off the epidural 24 h prior to discharge and ensure adequacy of oral analgesia. Recently, we have worked with anesthesia to turn off the epidural early (6:00 am) on the proposed day of discharge. This allows for 8 h of observation to determine if the patient will require opioid at discharge or not. Many of these patients are in the time period where the prescription is based on 8-h inpatient use. Regarding the use of adjuvant analgesics to supplement the standard acetaminophen/NSAID/opioid regimen for postoperative pain, in our current practice gabapentinoids (gabapentin, pregabalin) are not used for the type of surgeries included in this analysis; although, they are included as a standard approach in the pre and post-surgical pain management regimen for limb sparing and limb amputation surgeries.

While the cancer-specific surgeries are unique, the surgical approaches are not. We suggest that this algorithm could be applied in other pediatric settings. Collecting data on outpatient consumption following a broader group of surgical approaches will allow other centers to refine the algorithm further and hopefully apply this to other surgical approaches. This would also be a good area for machine learning to further pinpoint factors that contribute to pain such as age, operative factors, and co-morbidities. This would allow for an even more personalized approach.

4. Conclusion

Using an algorithm based on inpatient opioid use, outpatient opioid needs can be accurately predicted, thereby reducing excess opioid prescriptions without detriment to patient satisfaction or length of stay. Expansion of this study to other centers and operations will allow further refinement of the algorithm and personalized approach to post-operative pain control.

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