

Implementation of solutions to reduce opioid-induced oversedation and respiratory depression

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Purpose. The implementation of interventions to mitigate the causes of opioid-induced oversedation and respiratory depression (OSRD) is reported.

Summary. A single-site retrospective review of eligible rescue naloxone cases was conducted to identify the causes of opioid-induced OSRD in a hospital as well as to identify risk factors. A survey was used to assess potential opioid knowledge deficits among hospitalist prescribers. Based on the findings of the case reviews and results of the opioid knowledge assessments, a series of interventions to address noted deficiencies was implemented over the ensuing months, including enhanced monitoring for sedation, improved clinical decision support in the electronic medical record (EMR), and various adjustments to dosing for high-risk patients. The primary endpoint of our analysis was naloxone use for documented cases of opioid-induced OSRD to determine the effectiveness of the interventions. A mean of 16 OSRD events occurred per quarter before intervention implementation. An average of five risk factors (range, two to six) was found among OSRD cases, most commonly age of >60, obesity, and comorbidities of the kidneys and lungs. Deficiencies of clinical care were found in four inter-related domains: knowledge deficits, inadequate monitoring, failure to leverage the EMR, and cultural issues regarding pain assessments and sedation management.

Conclusion. Implementation of solution bundles that utilized an EMR to create meaningful clinical decision support and cultural changes related to pain goals and communication about sedation level at an acute care hospital resulted in a fivefold reduction in OSRD events that has been sustained for two years.

Keywords: analgesics, opioid; narcosis; narcotics; patient safety

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Patient harm due to opioid-induced oversedation and respiratory depression (OSRD) is a nationwide problem involving all opioid preparations and delivery routes. Estimates of life-threatening respiratory depression are imprecise and vary according to the population being studied, route of administration, and patients' risk factors. A frequency of 0.5% is commonly cited,¹ but this apparently low percentage translates into a high burden of serious events, considering the 51 million surgeries performed annually in the United States² and the high rate of opioid use

during nonsurgical hospitalizations. In one study of 1.14 million admissions, 51% of nonsurgical patients received opioids, with nearly a quarter of those patients receiving more than 100 mg/day of oral morphine equivalents.³ Other risk factors, including obesity, advanced age, sleep apnea, and comorbidities, are common among patients in U.S. hospitals,⁴ as is the use of nonopioid sedating medications, all of which contribute to OSRD.⁵ Opioid safety is further compromised by the variability of dose effect among individuals and the numerous agents and dosage forms,

which often require conversion as outpatients become inpatients.

Problem

OSRD occurred at an unacceptable frequency—more than five times per month—in our hospital. We sought to understand the full range of underlying causes of opioid-induced OSRD and to identify and implement multilevel solutions to reduce the rate of OSRD.

Background

Anne Arundel Medical Center is a 383-bed acute care hospital that serves a region of over 1 million people, with approximately 26,000 admissions and 7,900 inpatient surgeries each year. Inpatient care is predominantly provided by general medical hospitalists on both the medical and surgical floors. The intensive care unit is staffed by fellowship-trained intensivists only, but no trainees contributed to the care of the patients described herein. The hospital uses an electronic medical record (EMR) (Epic Systems, Verona, Wisconsin) for all order writing, documentation, vital sign recordation, and medication flow sheets.

Analysis and resolution

Identification and review of adverse opioid events. Our hospital's institutional review board (IRB) identified this project as a quality-improvement initiative and thus exempt from IRB review. With naloxone use as an indicator, all cases of potential OSRD in children and adults were identified from a pharmacy database. Naloxone use in the emergency department (ED) was excluded only if the OSRD episode was a result of opioid use before arrival at the ED. If naloxone use was due to an opioid received as therapy in our ED, it was counted among our cases. We also excluded naloxone use when given to hasten arousal from anesthesia in the operating room.

A multidisciplinary team of pharmacists, nurses, and physicians, drawn from existing harm-reduction committees, reviewed the medical

KEY POINTS

- Many patients in acute care hospitals have risk factors for opioid-induced oversedation and respiratory depression (OSRD).
- Underlying causes of OSRD can be classified as knowledge deficits, inadequate sedation monitoring, failure to leverage the electronic medical record (EMR) to guide dosing decisions, and cultural issues related to pain goals and sedation management.
- Solutions that utilize the EMR to create meaningful clinical decision support and lead to cultural changes related to pain goals and communication about sedation level can reduce the frequency of opioid-induced OSRD.

records of each patient receiving naloxone to confirm that the OSRD was likely due to opioids and not from other causes. Criteria for inclusion included an altered level of alertness from baseline as identified and documented in nursing or physician notes, a respiratory rate of <8 breaths/min, recent opioid use with or without other sedating medications, clinical response to naloxone, and the absence of other explanations (e.g., stroke, hypoglycemic coma) that appeared in the medical record. For each adverse opioid event, a primary pharmacist reviewer reconstructed the case and presented it to the review group, which included two physicians, two nurses, and two pharmacists.

In order to understand the underlying causes of OSRD events at our institution, the group analyzed each validated case, focusing on both individual and system or cultural errors. A dynamic system of underlying

causes was developed as cases were reviewed (Table 1). Patient risk factors were chosen from eight known patient-level risk factors⁵: age of >60 years, body mass index (BMI) of >30 kg/m², diagnosis of sleep apnea, active cigarette smoker, use of other sedating medications, opioid naive, comorbidities of the lungs, and comorbidities of the kidneys. Since the hospital did not routinely collect data from sleep apnea screening tools, such as the STOP-Bang probability scale,⁶ this score was not considered in the risk factor calculation. Diagnosed sleep apnea was included if entered in the “problem list” of the patient.

To further understand the areas of potential knowledge deficits among prescribers, a locally modified opioid knowledge assessment tool⁷ was administered to prescribing hospitalists, including physicians and physician assistants. Two additional questions assessing knowledge about cross-tolerance when converting between agents and the benefit of monitoring for sedation were added (Table 2). These data formed the basis of targeted education and the development of computerized decision support.

A total of 57 episodes of confirmed opioid-induced OSRD events were identified in the preintervention baseline year (March 1, 2013, through March 31, 2014). These 57 patients had a median of five patient risk factors (range, two to six); the most common risk factor was age of >60 years (found in 90% of cases).

Based on this review and case reconstructions, several underlying causes for opioid-induced OSRD were identified at our institution and categorized (Table 1). Some cases were associated with more than one underlying cause.

Deficits in knowledge about opioid prescribing and safety were common among 24 staff hospitalists surveyed. Table 2 lists the general topics assessed by the opioid knowledge assessment and the hospitalists' scores. Notable knowledge deficits were identified in the areas of definition of opioid toler-

Table 1. Underlying Causes of Opioid-Induced Oversedation and Respiratory Depression^a

Deficiency	Specific Causes
Knowledge deficits	<ul style="list-style-type: none"> • Danger of sustained-release opioids in opioid-naïve patients; lack of understanding of definition of <i>opioid naïve</i> • Too-rapid dosage escalation, including extended-release formulations • Multiple opioids used simultaneously • Sedation as a precursor for respiratory depression • Consideration for dosage reduction when converting from one opioid to another
Inadequate sedation monitoring	<ul style="list-style-type: none"> • Different scales in use; none developed specifically for opioids • No uniform policy and practice on frequency of assessments or action steps to be taken for sedation
Other practices	<ul style="list-style-type: none"> • Transferring sedated patients from postanesthesia care unit to general surgical floors • Opioid doses administered before transfer
EMR deficiencies	<ul style="list-style-type: none"> • No opioid conversion table easily available from within the EMR • No prescriber warnings about patient risk factors, use of long-acting opioids, and concomitant use of sedating medications • Information on pain scores, doses administered, and sedation levels located in multiple areas of EMR
Cultural issues	<ul style="list-style-type: none"> • Clinical culture stressed the elimination of pain or the achievement of a pain score below an arbitrary number • No culture or practice for consideration of sedation levels during multidisciplinary rounds

^aEMR = electronic medical record.**Table 2.** Opioid Knowledge Assessment Topics and Scores^a

Topic of Question	Numeric Score (% Correct Answers)	Numeric Score (% Incorrect Answers)
Definition of opioid tolerance	7 (29)	17 (71)
Indications for extended-release opiates	5 (21)	19 (79)
Equianalgesic conversion ratio between morphine and hydromorphone	20 (83)	4 (17)
Sleep apnea as a risk factor for opioid-induced respiratory depression	18 (75)	6 (25)
Role of benzodiazepines in contributing to oversedation after opioids	22 (92)	2 (8)
Patient risk factors (age and body mass index) for opioid-induced oversedation and respiratory depression	17 (71)	7 (29)
Pharmacokinetics of opioids used in dosage-escalation strategy	15 (63)	9 (38)
Sedation from opioids as a risk factor for subsequent respiratory depression	21 (88)	3 (13)
Dosage reduction when converting from one opioid to another due to incomplete cross-tolerance	11 (46)	13 (54)
Value of respiratory rate over pulse oximetry and apnea monitoring as an indicator of respiratory depression	13 (54)	11 (46)
Working knowledge of Pasero Opioid Sedation Scale ^b	19 (79)	5 (21)
Need for dosage reduction due to incomplete cross-tolerance	12 (50)	12 (50)
Sedation as the first sign of respiratory depression before abnormal vital signs	5 (21)	19 (79)

^aPercentages rounded to nearest whole number.^bAnswer is reported as percentage who answered yes.

ance, dosage adjustment strategies, and the value of sedation levels and respiratory rate when monitoring patients. Prescribers were also unfamiliar with the preferred sedation-monitoring tool.

We found that hydromorphone was commonly used in our ED for complaints of pain, six times more commonly than morphine. Some of these patients were admitted and subsequently given hydromorphone administered via patient-controlled analgesia (PCA) infusion pumps.

Interventions implemented.

Based on the findings of the case reviews and results of the opioid knowledge assessments, a series of interventions to address noted deficiencies was implemented over the ensuing months, including enhanced monitoring for sedation, improved clinical decision support in the EMR, and various adjustments to dosing for high-risk patients. The solutions used to address these deficiencies are summarized in Table 3.

Enhanced monitoring for sedation. Our institution lacked a standard approach for opioid sedation monitoring, including an interval of assessments and the steps to follow if patients were found to be oversedated. As noted in Table 2, there were prescriber knowledge deficits about the relationship between sedation and respiratory depression. To address these deficits, education efforts were prepared for both prescribers and nursing team members. We identified the Pasero Opioid Sedation Scale (POSS) as an evidence-based and easy to apply method of monitoring patients' sedation levels; this scale includes suggested action steps for nursing and medical staff.⁸ The tool was piloted on the hospital's joint and spine unit—the clinical unit with the most cases of OSRD at baseline—and then rolled out to all adult units with nonventilated patients. The POSS was incorporated into the EMR to facilitate documentation, assessment, and patient care actions by nursing. The rollout of the POSS was facilitated by mandatory

annual POSS education for all nurses via the online education software used at the medical center. All new nurse employees receive classroom education on pain management and POSS administration based on the new policies. The education is reinforced with the inclusion of the POSS in the nursing bedside shift report. Compliance with the POSS was tracked in each individual unit, with random audits of over 30 patients each. The compliance rates for POSS documentation were 88% for first opioid administration and 76% for subsequent doses within a few months of the rollout.

Clinical decision support. The EMR was leveraged to provide prescriber support, including linking a pharmacy and therapeutics committee–approved opioid equivalency table into every order for opioids. The table prominently displayed the recommended advisory that dosage reduction should be considered when switching drugs due to incomplete cross-tolerance and individual patient factors.⁹

To facilitate informed prescribing with opioids, an integrated documentation flow sheet was created for all clinicians within the EMR. It gathered together and displayed within a single-screen view any related information needed for safe prescribing and monitoring, such as pain scores, vital signs, sedation score, and analgesic doses given.

In addition, prescribing of preoperative long-acting opioids was removed from most electronic medical order sets. In the few in which it remained, the dose of preoperative extended-release oxycodone was reduced from 20 to 10 mg.

PCA. Beginning in August 2015, the EMR was also used to guide dosing for patients receiving PCA infusions. In the test environment, initial criteria for dose reduction included age of >60 years, BMI of >30 kg/m², creatinine clearance of <30 mL/min, a known diagnosis of emphysema or sleep apnea, or concurrent use of any central nervous system (CNS) depres-

sant (i.e., anxiolytics, hypnotics, or skeletal muscle relaxants); the presence of any of these criteria would have invoked reduced dosing for 90% of all patients using PCA. We therefore modified the criteria by increasing the age to ≥70 years, raising the BMI to ≥37 kg/m², and narrowing the list of potential CNS active drugs to include benzodiazepines only, since this class was most often associated with OSRD at our institution. This form of clinical decision support was built as an order set default to a lower dosing range. The alert for patients meeting any of the criteria would result in lower default demand doses (from 1.5 to 1.0 mg for morphine and from 0.3 to 0.2 mg for hydromorphone) and to a lower default four-hour lockout limit (from 30 to 24 mg for morphine and from 6 to 4.8 mg for hydromorphone). The reduced dose was modifiable by prescribers based on their clinical judgment and patient history. As basal rates of opioids are nearly five times more likely to cause respiratory depression than on-demand dosing,¹⁰ institutional PCA orders continued to avoid a basal rate.

Because hydromorphone was overrepresented in OSRD cases, we took a number of steps to encourage the use of morphine rather than hydromorphone and to make hydromorphone use safer. ED physicians indicated that they preferred hydromorphone 1- or 2-mg doses because the available dose of morphine in the automated drug-dispensing system was too often ineffective at a dose of 4 mg. Thus, a higher dose of morphine (8 mg) was added in addition to the 4-mg dose. We also lowered the default dose of hydromorphone in the pain order set from 1 to 0.5 mg. We implemented a “soft alert” for doses exceeding 1 mg of hydromorphone, which served to reinforce education about proper dosing to ED staff.

Measurable outcomes. The primary endpoint of our analysis was naloxone use for documented cases of opioid-induced OSRD. Figure 1 shows a sustained fourfold reduction

Table 3. Solutions Implemented, by Deficiency^a

Deficiency Addressed	Solution(s) Implemented
Inconsistent sedation assessments of patients receiving opioids: different scales in use, no uniform practice on frequency of assessment or action steps to be taken, hospital policies did not adequately address the optimum scale or the frequency of monitoring to be done	<ul style="list-style-type: none"> POSS introduced after trial on the joint and spine unit; rolled out to all adult care units as the standard evidence-based assessment tool Hospital policies on pain management revised to include use of POSS and standardize frequency of assessment
Poor communication among team members regarding level of sedation	<ul style="list-style-type: none"> Implemented new report within EMR to show pain scores, sedation score, medications given, and vital signs in a single location Introduced discussion of sedation score to the content of daily interprofessional rounds and bedside shift report
Clinical culture stressed the elimination of pain and/or the achievement of a pain score below an arbitrary number	<ul style="list-style-type: none"> Reeducated staff and rewrote hospital policies, indicating that goals of pain management should be individualized
Knowledge deficits among prescribers in the following areas: opioid conversions, patient-level risk factors, other sedating medications, risk of long-acting medications, danger of rapid escalation, incomplete cross-tolerance	<ul style="list-style-type: none"> Education delivered to hospitalists tailored to deficits identified by opioid knowledge assessment EMR live link to opioid conversion table from the opioid order page Clinical decision support/best-practice alert to fire when initiating opioids in patients with comorbid conditions or taking other sedating medications; advisory recommends lower starting doses and sedation monitoring Computerized decision support defaults to lower-dose opioid drip for high-risk patients based on computer detection of patient factors identified in chart
Underappreciation of high incidence of OSRD with hydromorphone (used frequently in ED and then converted to infusions on floors)	<ul style="list-style-type: none"> Reduced ED hydromorphone use by creating new pain order sets with default to morphine Added morphine 4 mg to automated drug-dispensing cabinet instead of hydromorphone
Underappreciation of risks of long-acting opioids in opioid-naïve patients; misunderstanding of definition of <i>opioid naïve</i>	<ul style="list-style-type: none"> Removed long-acting opioids from preoperative orthopedic order set Best-practice alert that defines <i>opioid naïve</i> when ordering long-acting opioids

^aPOSS = Pasero Opioid Sedation Scale, EMR = electronic medical record, OSRD = oversedation and respiratory depression, ED = emergency department.

in the number of validated naloxone interventions during the study period; these reductions have been sustained for two years. These improvements occurred despite a 41% increase in surgeries with a high risk of OSRD (thoracic, bariatric, and orthopedic),⁵ though total hospital patient-days declined by 3.5% over the study period. Overall opioid use decreased just 3% for the hospital.

The interventions to provide safer PCA dosing resulted in lower doses at initiation in 63% of all PCA orders. These EMR-generated clinical decision support recommendations were rarely overridden by medical staff. Over the course of these interventions, there was no change in overall patient satisfaction with regard to pain man-

agement, as measured by the Hospital Consumer Assessment of Healthcare Providers and Systems survey, a standard patient satisfaction tool.¹¹

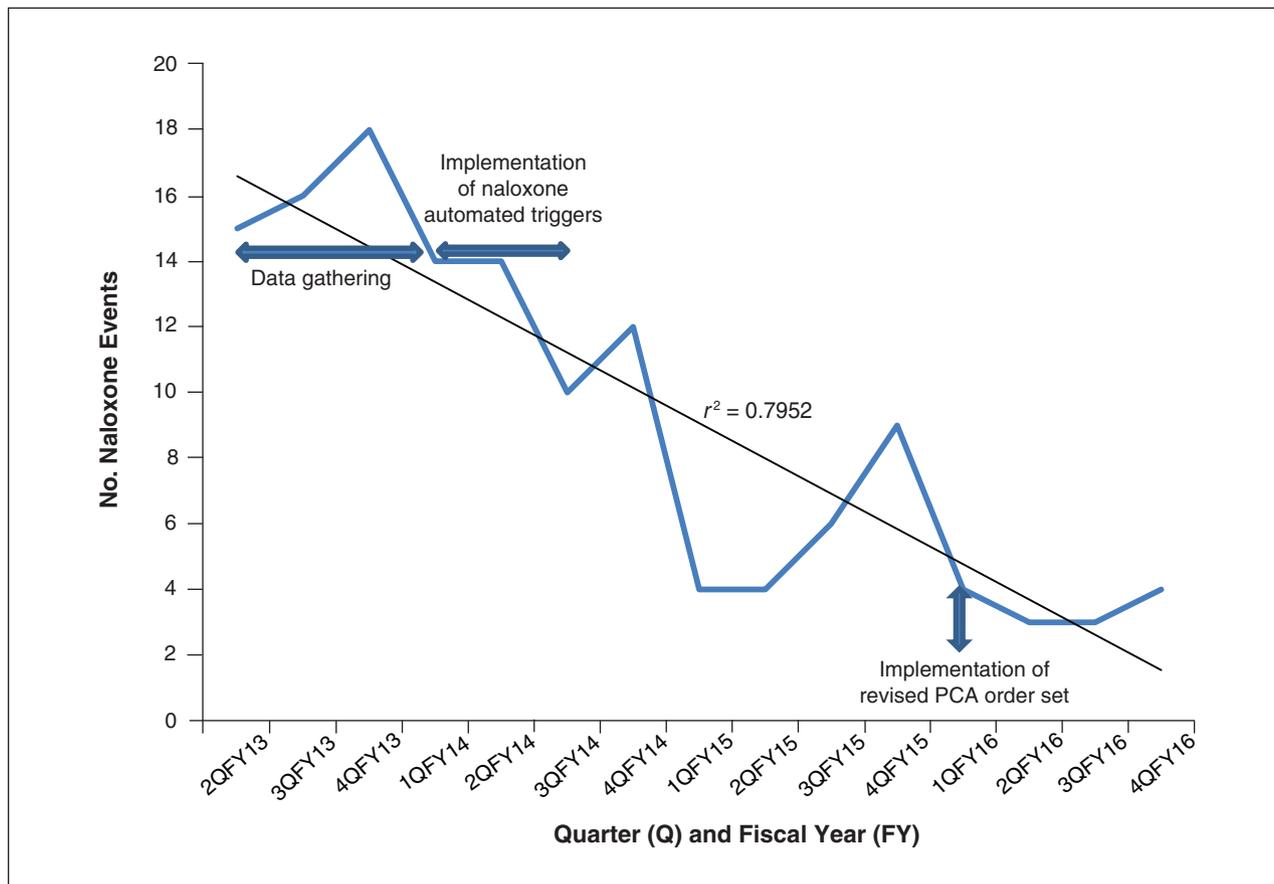
Discussion

The primary goal of this quality-improvement project was to understand the underlying causes of and intervene to eliminate opioid-induced OSRD at our hospital. Because deaths from opioid-induced OSRD are rare, we relied on the surrogate marker of validated naloxone use as an indicator of clinical OSRD. Naloxone administration is a useful proxy, as naloxone is routinely administered for OSRD and is easily tracked by pharmacy databases. However, naloxone use can be nonspecific; therefore, all instances of

its use were reviewed by experienced clinicians to verify that the patient actually had opioid-induced OSRD.

The improvements described in this article have been sustained for two years, and we attribute this success to institutional learning in four important areas: (1) the close relationship between sedation and subsequent respiratory depression with its attendant need for sedation monitoring, (2) enhanced caution about the transfer of sedated patients from the postanesthesia care unit, (3) the avoidance of extended-release opioids in opioid-naïve patients, and (4) the reappraisal of pain management goals by reducing the focus on a numeric pain score in isolation from other patient factors. All four concepts are emphasized in

Figure 1. Naloxone use for opioid oversedation and respiratory depression between 2013 and 2016. PCA = patient-controlled analgesia.



professional education, clinical decision support tools, and a culture that has moved toward the discussion of sedation levels concurrently with pain levels. We also sustain success by continuing to review all cases of naloxone use.

The POSS has been shown to generate consistent assessments and had high levels of user satisfaction in several studies.¹²⁻¹⁵ The tool was developed specifically for opioid sedation monitoring and incorporating specific action steps for nurses to follow when a certain sedation level is observed. The POSS also increased the amount of dialogue about sedation during interdisciplinary rounds and was included in shift-to-shift nursing handoffs.

Other institutions have reported on opioid OSRD events. Pawasauskas et al.⁴ performed a retrospective case-

control analysis of patients receiving opioids, regardless of whether they developed respiratory depression. Statistically significant differences between cases and controls were noted for age; current smoking; concurrent sedating medications; and renal, cardiac, and respiratory comorbidities but not opioid-naïve status. Patients who developed OSRD had a mean of 5.1 risk factors compared with controls, who had a mean of 3.3 risk factors ($p < 0.001$). Cases received 13% more morphine equivalents than non-OSRD controls, suggesting that overdosing may have played some role but not likely the principal role. We found a similar number of recognized risk factors in our study of OSRD patients. Many of our opioid-naïve patients received extended-release opioids, which may account for the difference

between our findings and those of Pawasauskas and colleagues.⁴ Meisel et al.¹⁶ reported a similar study focusing on postoperative patients. Some of the interventions they found helpful overlap our own improvements, including efforts to standardize pain assessments and monitoring, lower doses for high-risk patients, and require better handoffs of sedated patients.

This analysis had several limitations. Like many pre-post intervention studies in which solution bundles are implemented simultaneously, we cannot say which solution was most significant in achieving results. In addition, we used one particular EMR to introduce solutions that might not be transferable to other less comprehensive EMRs. The fact that nearly all hospital care, including postsurgical care, is rendered by hospitalists and hospi-

talist physician assistants allowed us to concentrate education efforts on a relatively small group of about 45 prescribers and not on a larger cadre of residents or on the entire medical staff of 1000 practitioners. In addition, data collection about patient satisfaction with pain management strategies was not limited to the approximately one half of our patients who received opioids and were thus affected by these changes.

Nevertheless, many of the institutional deficiencies found in this report have been described previously and are common in hospitals. For example, failure to monitor patients adequately was a factor in 29% of adverse opioid outcomes reported to the Joint Commission data base.⁵ In addition, a closed claim analysis of 92 postoperative opioid-induced respiratory depression-related lawsuits concluded that 97% were preventable with better monitoring and response.¹⁷

The role of sustained-release opioids used in orthopedic patients deserves special mention. Despite the fact that there are drug label precautions about use of sustained-release opioids in opioid-naïve patients, some surgeons incorporated these agents into preoperative order sets in a well-intentioned effort to facilitate early mobilization. But at least one randomized trial found a higher oversedation rate and no better pain control or reduction in total opioid use with preoperative long-acting opioids in joint arthroplasty patients.¹⁸ Indeed, a recent multisociety guideline noted no proven benefit from this practice.¹⁹

We noted that hydromorphone was overrepresented in episodes of OSRD and took the described steps to reduce hydromorphone use. A pattern of care at our hospital was to initiate this drug in the ED. It was thus frequently continued on the inpatient floors as a PCA. Other studies have suggested that currently recommended starting doses of hydromorphone or the recommended conversions are too high.^{15,20,21} A recent study found that lowering the standard dose of

hydromorphone via automatic substitution improved patient safety and did not reduce the adequacy of pain relief.²¹

Notably, the improvements described herein were achieved without the use of supplemental oximetry and capnography monitoring which some researchers have advocated.²²⁻²⁴ These techniques require both capital outlay and possibly increased labor expenses. In addition, the proliferation of alarms following expanded electronic monitoring has been implicated in patient safety incidents.²⁵ Recent multisociety professional guidelines do not recommend the use of oximetry or capnography outside of the operating room.¹⁹

Conclusion

Implementation of solution bundles that utilized an EMR to create meaningful clinical decision support and cultural changes related to pain goals and communication about sedation level at an acute care hospital resulted in a fivefold reduction in OSRD events that has been sustained for two years.

Disclosures

The authors have declared no potential conflicts of interest.

References

1. Dahan A, Aarts L, Smith TW. Incidence, reversal and prevention of opioid-induced respiratory depression. *Anesthesiology*. 2012; 112:226-38.
2. Centers for Disease Control and Prevention. Inpatient surgery. www.cdc.gov/nchs/fastats/inpatient-surgery.htm (accessed 2015 Dec 9).
3. Herzig SJ, Rothberg MB, Cheung M et al. Opioid utilization and opioid-related adverse events in nonsurgical patients in US hospitals. *J Hosp Med*. 2014; 9:73-81.
4. Pawasauskas J, Stevens B, Youssef R, Kelley M. Predictors of naloxone use for respiratory depression and oversedation in hospitalized adults. *Am J Health-Syst Pharm*. 2014; 71:746-50.
5. The safe use of opioids in hospitals. *Joint Commission Sentinel Event Alert*. 2012; 49:105.
6. Chung F, Subramanyam P, Liao P et al. High STOP-Bang score indicates a

- high probability of obstructive sleep apnea. *Br J Anaesth*. 2012; 108:768-75.
7. Pennsylvania Patient Safety Authority. Opioid knowledge self-assessment. <http://patientsafetyauthority.org/EducationalTools/PatientSafetyTools/opioids/Pages/assessment.aspx> (accessed 2016 Jun 28).
8. Pasero C. Assessment of sedation during opioid administration for pain management. *J Perianesth Nurs*. 2009; 24:186-90.
9. Fine PG, Portenoy RK, for the Ad Hoc Expert Panel on Evidence Review and Guidelines for Opioid Rotation. Establishing "best practices" for opioid rotation: conclusions of an expert panel. *J Pain Symptom Manage*. 2009; 38:418-25.
10. George JA, Lin EE, Hanna MN et al. The effect of intravenous opioid patient-controlled analgesia with and without background infusion on respiratory depression: a meta-analysis. *J Opioid Manage*. 2010; 6:47-54.
11. Giordano LA, Elliott MN, Goldstein E et al. Development, implementation, and public reporting of the HCAHPS survey. *Med Care Res Rev*. 2010; 67:27-37.
12. Smith A, Farrington M, Matthews G. Monitoring sedation in patients receiving opioids for pain management. *J Nurs Care Qual*. 2014; 29:345-53.
13. Nisbet AT, Mooney-Cotter F. Comparison of selected sedation scales for reporting opioid-induced sedation assessment. *Pain Manag Nurs*. 2009; 10:154-64.
14. Kobelt P, Burke K, Renker P. Evaluation of a standardized sedation assessment for opioid administration in the post anesthesia care unit. *Pain Manag Nurs*. 2014; 15:672-81.
15. Cronrath P, Lynch TW, Gilson LJ et al. PCA oversedation: application of healthcare failure mode effect analysis. *Nurs Econ*. 2011; 29:79-87.
16. Meisel S, Phelps P, Meisel M. Case study: reducing narcotic oversedation across an integrated health system. *Jt Comm J Qual Patient Saf*. 2007; 33:543-8.
17. Lee LA, Caplan RA, Stephens LS et al. Postoperative opioid-induced respiratory depression: a closed claims analysis. *Anesthesiology*. 2015; 122:659-65.
18. Musclow SL, Bowers T, Vo H et al. Long-acting morphine following hip or knee replacement: a randomized, double-blind, placebo-controlled trial. *Pain Res Manag*. 2012; 17:83-8.

19. Chou R, Gordon DB, de Leon-Casasola OA et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain*. 2016; 17:131-57.
20. Paparella S. Intravenous hydromorphone: can you manage the risk? *J Emerg Nurs*. 2011; 37:377-80.
21. Rickett A, Mateyoke G, Vallabh M et al. A pilot evaluation of hydromorphone dose substitution policy and the effects on patient safety and pain management. *J Pain Palliat Care Pharmacother*. 2015; 29:120-4.
22. Taenzer AH, Pyke JB, McGrath SP, Blike GT. Impact of pulse oximetry surveillance on rescue events and intensive care unit transfers: a before-and-after concurrence study. *Anesthesiology*. 2010; 112:282-7.
23. Abenstein JP, Narr BJ. An ounce of prevention may equate to a pound of cure: can early detection and intervention prevent adverse events? *Anesthesiology*. 2010; 112:272-3.
24. Kodali BS. Capnography outside the operating rooms. *Anesthesiology*. 2013; 118:192-201.
25. Ruskin KJ, Hueske-Kraus D. Alarm fatigue: impacts on patient safety. *Curr Opin Anaesthesiol*. 2015; 28:685-90.