

Improve safety with lessons learned from opioid-related events requiring naloxone

Vizient® Patient Safety Organization Safety Alert 2019

Background

Opioids—high-alert, frequently used medications—are one of the most common drugs involved in serious medication safety events reported to Vizient Patient Safety Organization (PSO). In 2012, The Joint Commission (TJC) published a sentinel event alert addressing opioid safety in the inpatient setting, stating that opioid analgesics rank among the drugs most frequently associated with adverse drug events.¹ TJC enhanced their pain assessment and management standards in 2017 to minimize harm associated with opioid use as well as ensure appropriate pain management, and retired the sentinel event alert in 2019 because opioid management is addressed in TJC standards, the survey process and the R3 reports.²

In a review of about 20 years of anesthesia closed claims data involving opioid induced respiratory depression (OIRD) cases, Lee and colleagues found that the majority of OIRD incidents occurred within 24 hours of surgery and were likely preventable with better monitoring. They indicated that ongoing sedation assessment to identify excessive sedation early was important in signaling impending respiratory depression. In addition, the study showed that OIRD results in devastating patient outcomes and substantial financial consequences for hospitals, with median litigation costs totaling \$216,750 per claim in 2012 dollars.

The recent national shortage of injectable opioids and small-volume parenteral, intravenous solutions required hospitals to evaluate and limit the use of intravenous opioid therapy.³ This national shortage of certain opioids and IV solutions created an opportunity for healthcare providers to carefully evaluate and make changes to their opioid use and practices. As a result of the need to reduce the use of intravenous opioids and patient controlled analgesia (PCA), experts say that an unintended consequence of the shortage has been safer opioid use.

The Vizient PSO staff reviewed opioid-related inpatient safety events in which naloxone was used to reverse serious adverse effects including OIRD and opioid-induced unintended advancing sedation (OIUAS). The Vizient PSO convened an advisory team (Appendix A) and shared the findings in our data to promote the safe use of opioids in hospitals. The advisory team discussed the results of the analysis of data, contributing factors, and current evidence related to opioid use. After a series of meetings, the advisory team members developed this paper to communicate the risks of opioid-related OIRD and OIUAS, and provide evidence-based recommendations.

Assessment

The Vizient PSO analyzed opioid-related patient safety event report data from January 2017 through May 2018. The Vizient PSO identified 72 safety events where naloxone appears to have been administered due to OIRD or OIUAS. In almost 80 percent of cases reviewed, the level of harm was categorized as requiring additional treatment, temporary or permanent harm or death. In 70 percent of reports, the patients had an OIRD risk factor (Appendix B), a prior history of OIRD or the patients were 70 years and older. Screening patients for risk factors and individualizing the plan of care based on the patient's risk is necessary to prevent OIRD and/or OIUAS.

High-risk opioid use, including intravenous (IV) and patient controlled analgesia (PCA)

TJC identified methadone, fentanyl, and IV hydromorphone as higher risk opioids.¹ These high-risk opioids were administered in more than 50 percent of the Vizient PSO reports reviewed. Over one-third of the reports involved IV opioids; the majority of which were PCA. A significant number of PCA events included both the use of a basal rate and a high-risk opioid. The factors that contributed to PCA-related OIRD and OIUAS events were pump programming errors, family and nurse PCA use by proxy, inadequate monitoring, excessive basal and demand doses prescribed, and failure to adjust the dose based on the patient's preexisting risk factors. Several events described OIRD or OIUAS after the patient received multiple opioids via several routes simultaneously; for example, oral, epidural or other IV opioids in addition to IV PCA.

Multiple opioids and concomitant sedative therapy

In 11 percent of events, "Opioid stacking"—a term often used to describe when several opioids are prescribed and administered within a short time—was noted as a contributing factor to OIRD or OIUAS. For example, one patient over the age of 55 with multiple comorbidities and posttraumatic injury was prescribed acetaminophen by mouth every 4 hours as needed for a pain score of 1 to 3, intravenous (IV) morphine every 6 hours as needed for a pain score of 4 to 6, or IV hydromorphone every 6 hours as needed for a pain score of 7 to 10. The patient deteriorated with agonal breathing and constricted pupils bilaterally the day after admission, however, responded positively to naloxone. Review of the record revealed that the patient had received multiple doses of different opioids within a 6-hour period for pain at various levels. In 2016, the American Society for Pain Management Nursing published a position statement opposing the prescribing of opioid analgesics for pain scale alone, because it does not take into account other essential elements of assessment that may contribute to problematic patient outcomes.⁶ Patient and family engagement in the assessment and reassessment process is critical in ensuring safety; therefore, patients and families need to understand that the nurse will awaken the patient at various intervals to assess vital signs, pain level, respiratory effort/quality and sedation level.¹⁶

When intravenous medications and oral opioid medications are given at the same time, it can lead to unexpected peaks and metabolite accumulation with potentially fatal consequences.¹⁶ One case highlights the challenges of managing acute pain for patients who are on chronic pain opioid therapy. In

this case, a patient who was on a fentanyl 100mcg transdermal patch and oral oxycodone 15-30mg every four hours as needed at home was admitted to the hospital. The patient was converted from the fentanyl patch to a hydromorphone PCA with a basal rate of 0.4mg per hour and a demand dose of 0.5mg every 15 minutes in the hospital. In addition to the PCA demands and basal rate, the patient received another 6mg of hydromorphone IV push within 12 hours for acute pain management. The patient was found with a respiratory rate of less than 8 per minute and somnolence. The patient's condition improved after multiple doses of naloxone. In this case, the PCA basal rate was 192 Morphine Milligram Equivalent (MME) and the patient was receiving 240 MME prior to admission. The issue most likely came from the 0.5mg every 15 minute demand dose, which makes the total dose substantially more than what was prescribed while out of the hospital. Complex conversion cases such as this require involvement of a pain management service or clinical pharmacist.

In another case, a patient had an outpatient interventional radiology procedure with general anesthesia. Post-procedure, the interventional radiologist asked a family member to give the patient an opioid pain medication brought from home while the patient was waiting to be admitted as inpatient. This case highlights the importance of the provider appropriately adjusting the pain medication order based on the other medication delivered and conducting a detailed medication reconciliation process before ordering medicine. There is also a risk that the home medication taken by the patient would not be documented in the electronic health record (EHR) or communicated to the inpatient nurse, physician or pharmacist before the patient transitions from interventional radiology to inpatient care.

In other cases, the patient received opioids with concomitant administration of sedating agents (e.g., benzodiazepines, antihistamines) and it did not appear that there had been adequate monitoring and dose adjustment.

Inadequate monitoring

In at least 15 percent of cases, there was infrequent and limited monitoring that resulted in delayed recognition of over-sedation. In one case, the pulse oximetry reading was within the appropriate range even though the patient displayed signs of sedation and lethargy. It is unknown if this patient was receiving supplemental oxygen or the patient's respiratory depth and rate was monitored. When the arterial blood gas was drawn, the carbon dioxide level was over 100mmHg, indicative of hypercapnia and respiratory depression. Pulse oximetry alone may not be the most accurate measure of a patient's ventilation status, particularly if the patient has supplemental oxygen.¹ Continuous capnography monitoring (end-tidal carbon dioxide) has been noted to be more effective to monitor ventilation status in patients with supplemental oxygen.^{1,4,7} Additional monitoring issues involved patients whose monitor alarms were turned off. This highlights the importance of central monitoring or nurse accountability for alarms and vigilance to avoid alarm fatigue.

Recommendations

Define standard work

Standard work should include all phases of the medication process, process and outcome measurement, observations, coaching staff and continually improving performance.

- Clinical leadership defines indications for opioid use, dose, frequency, route, monitoring criteria and order sets based on patient's OIRD and OIUAS risk level, perioperative phase and procedure, and medical conditions. Opioid sparing strategies should be incorporated into the plan of care.
- Prescriber individualizes orders based on the patient's medical condition, perioperative procedure and status, level of risk and response to opioids.
- Before opioid administration, prescriber and/or nurse screens for OIRD and OIUAS risk, documents findings in EHR, communicates findings to the care team and ensures the patient's orders are appropriate based on the patient's risk. It is imperative that any screening tool considers obstructive sleep apnea risk (Appendix B, D, and E).
- Health care team and information technology build alerts and documentation tools into the EHR and ordering system to aid providers in recognizing OIRD and OIUAS risk and completing standard work.
- Before ordering, prescriber verifies prior opioid use, dose, frequency, refills and renewals with a prescription drug monitoring program and/or primary prescriber. Before releasing an order, the pharmacist reviews this documentation and ensures that it is consistent with orders.
- Nurse ensures patient does not have access to home medications during hospitalization and follows hospital policy for securing the patient's medications and any other substances.
- Nurse explains the patient assessment and reassessment process to the patient and family and why it is important to wake the patient to ensure OIRD and OIUAS are not present.
- Before administering and at peak effect of an opioid, the nurse conducts and documents an iterative assessment for OIRD and OIUAS. If the patient demonstrates signs or symptoms of OIRD or OIUAS, the registered nurse has access to orders they may implement (Appendix C, D, F). Continuous electronic monitoring of respiratory status is available to all patients receiving systemic opioids, especially for the first 24 hours of initiating therapy, and continues if signs of respiratory insufficiency occur. Examples of devices that measure ventilation are 1) capnography, 2) pulse oximetry in combination with respiratory rate, and 3) minute ventilation. Pulse oximetry alone is not recommended in patients that require supplemental oxygen therapy. Multi-parameter measurement is superior to single parameter measurement.
- Nurse analyzes trends in respiratory and ventilation status for early detection of compromised respiratory status and contacts the provider to decrease doses of opioids or discontinue opioids as indicated.
- All monitors are equipped with alarms. Alerts are monitored at a central location or directly by the nurse in charge of the patient. Alarms are sufficiently discernable and set at thresholds to avoid alarm fatigue. An example for alarm settings in patients without significant respiratory disease that can

avoid alarm fatigue and decrease opioid related respiratory events using multi-parameter monitoring strategy include: etCO₂ mmHg high 60 and low 20 mmHg; RR high 38 and low 4 BPM; no breath 30 seconds; SpO₂ low 85 percent, MV <40 percent predicted for 2 minutes. If patient has a history of CO₂ retention, etCO₂ high may be adjusted up by 10 percent of high to a max of 66 mmHg.

- Multiple options of opioids via the same route should be avoided, but, if necessary, the prescriber must specify the interval between doses of all medications to avoid stacking. If the patient has multiple route options, the prescriber must clarify the indications for route. The intravenous route is only indicated if the patient is NPO, vomiting, or reports severe pain restricting function.
- An opioid dose range ordered should be adequate to permit appropriate and safe dose titration based on the patient's opioid naivety or tolerance. The dosing interval should be appropriate for the drug and route of administration, taking into account usual absorption and distribution characteristics, time to onset, time to peak effect, and duration of action. Limit opioid dose to no greater than 2-3 times the initial starting dose; for example, if the minimum dose is 1 tablet, do not go above 3 tablets as one dose without considering another alternative.
- If partial doses are administered upon initiation of therapy, wait until peak effect of the first dose has been reached before giving a subsequent dose. Avoid making a patient wait a full time interval after giving an additional partial dose within the allowed range.
- Consider implementing an EHR alert when a patient is requiring frequent doses of opioids, when a potential synergistic sedating medication is added, or when multiple formulations of opioids are used.
- Provide ongoing education pertaining to protocols, policy and procedures to guide all caregivers (registered nurses, pharmacists, licensed independent practitioners, and physician assistants) on appropriate implementation of interventions.
- Pharmacy concurrently reviews all patients receiving opioids for appropriateness and intervenes as indicated. This process includes conversion of IV orders to oral opioid when indicated with conversion algorithm approved by Medical Executive Committee and in accordance with state law restrictions.
- Naloxone is readily available on profile with opioids, overrides, and crash cart.
- After administration of a reversal agent, adequate staffing for iterative assessment, documentation of care and continuous electronic monitoring is in place as the half-life naloxone might be shorter than the opioid medication. Therefore, the patient may be at risk for re-sedation, and repeat naloxone dose may be needed.¹⁷

Quality assessment and improvement

- Establish an opioid stewardship team with strong executive sponsorship that includes frontline representation from each phase of the medication process, including a prescriber, registered nurse, pharmacist and the patient. This team's responsibility is to define standard work related to opioid use, collaborate with the education department to develop a staff education plan, measure performance and outcomes, coach staff and take actions to continuously improve opioid use and outcomes.

- Opioid stewardship team assigns responsibility to conduct an in-depth analysis of 100 percent of patients with unplanned naloxone use, unexpected transfer to critical care or unexpected cardiac or respiratory arrest with opioid administration suspected or possible as a contributing factor. This team will evaluate and discuss the event as soon after the event as possible and report conclusions, recommendations, actions and follow up. This team will provide the Quality Committee with update reports about the findings, conclusions, recommendations, actions taken, follow up planned and measures of success (implementation and effectiveness). This team will ask the following two questions in relation to every serious event:
 - 1) Was measurement sufficient to identify this risk in the environment before the event?
 - 2a) If yes, why did the organization fail to mitigate the risk before the event occurred?
 - 2b) If no, what changes to measurement are required?
- The team communicates lessons learned from measurements and actions taken to continuously improve opioid safety to all involved with opioid use.
- The Quality and/or patient safety manager reports all opioid safety events to the PSO for data aggregation and learning.
- Oversight team implements an opioid dashboard with the metrics outlined in Table 1, and reviews it monthly.

Table 1: Suggested volume, process and outcome metrics

	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec	T/E
Volume													
Number of IV opioid doses													
Number of PO opioid doses													
Number of days of PCA therapy													
Number of days of PCA therapy with basal rates													
Outcomes													
Numerator: the number of patients who received naloxone outside of the operating room either: (1) After 24 hours from hospital arrival; or (2) during the first 24 hours after hospital arrival with evidence of hospital opioid administration prior to the naloxone administration Denominator: all patients 18 years or older discharged from an inpatient hospital admission during the measurement period ¹⁸													
Number of doses naloxone administered for confirmed OIRD considered preventable													
Patient perception of communication about pain ranking (HCAHPS)													

Number of cardiac or respiratory arrests related to confirmed OIRD														
Number of unplanned transfers to critical care related to confirmed OIRD														
Process														
Number of opioid doses administered without pharmacy review														
Number of pharmacy intervention related to opioids														
Number of days of IV opioid therapy when patient could tolerate PO (exclude patients with one time orders)														
Percent of patients screened for OIRD or OIUAS risk before opioid administration														
Percent of reassessments completed within the required timeframe (sample)														
Percent of patients on opioid(s) meeting recommendations for continuous ventilation monitoring and it is not implemented (sample)														
Number of patients receiving more than one opioid at one time (sample)(after first 24 hours)														
Number of opioid naive patients receiving PCA basal rates with OIRD risk factor														
Number of patients that received prescription for more than 7 days opioids at discharge														
Number of patients discharged with opioid prescription and no opioid use for 48 hours prior to discharge														
Percent of patients receiving opioids with PDPM check documented (sample)														
Average Morphine MME per day														
Proportion of patients receiving opioids with more than one opioid order with duplicate indications														
Proportion of opioid-naive patients with long acting or extended release opioids														

Management of PCA use

Use a PCA checklist to guide current practice and minimize OIRD or OIUAS.

- Define indications for use of PCA.
- Require pain management or anesthesia oversight of any basal rate administration and limit use to those cases with complex pain management needs.
- Investigate use of PCA smart pumps with the following features:
 - Capnography monitoring technology with an automatic pump shut-off
 - Interface between the EHR and pump with capability to validate the syringe dose with the order
- See recommendations above for screening, assessment and monitoring.
- Avoid use of other opioids and minimize central nervous system depressants while the patient is using a PCA.
- Utilize standardize concentrations for PCAs and if more than one concentration, only one concentration is available outside of pharmacy.
- Two RNs complete an independent double-check prior to initiation of PCA, change of PCA setting and syringe change. The double-check includes the following elements:
 - Right patient (active identification – bar coding)
 - Completion of screening for OIRD and comprehensive assessment
 - Reassessment at peak effect (best performed with hourly rounding and the use of continuous monitoring of ventilation) (Appendix F)
 - Allergies to prescribed medication
 - Review of MAR for other medications that might place patient at OIRD risk
 - Appropriate drug, route, time, concentration and correct programming of loading dose, basal rate, patient controlled dose, lock-out period and other dose limits per the physician order
 - Review of total dose patient received since last review of settings.
 - Necessary dose adjustments needed for OIRD have been completed
 - IV line is attached to patient and tubing inserted correctly into pump
- Educate patients and family with written instructions and signage about PCA use before initiating a PCA. Emphasize that family and friends may not administer on-demand doses.¹¹

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Appendix A: Expert advisory team

Opioid best practice recommendations were developed by a Vizient PSO multidisciplinary task force.

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