Spotlight

Patient Safety Events Involving Opioid Dose Stacking
Source and Credits

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  o Commentary by: Hollie Porras, PharmD, BCPS and Cathy Lammers, MD

  o AHRQ WebM&M Editors in Chief: Patrick Romano, MD, MPH and Debra Bakerjian, PhD, APRN, RN
    o Spotlight Editors: Patricia Poole, PharmD and Debra Bakerjian, PhD, APRN, RN
    o Managing Editor: Meghan Weyrich, MPH
Objectives

At the conclusion of this educational activity, participants should be able to:

• Describe the role of standardized sedation assessments, such as the Pasero Opioid Sedation Scale (POSS), for predicting and preventing opioid-induced respiratory depression events
• Analyze how opioid dose stacking can result in fatal respiratory depression
• Identify patient monitoring tools with high prognostic value in determining respiratory depression events
• Compare the risk versus benefit profile of naloxone administration for suspected opioid overdose
• Summarize strategies that can help address the multifactorial nature of pain
PATIENT SAFETY EVENTS INVOLVING OPIOID DOSE STACKING

Two cases involving patients who experienced adverse events due to perioperative opioid stacking and the evidence-based strategies for optimal management of patients administered perioperative opioid therapy.
Case #1 Details (1)

- A 35-year-old male with a history of chronic opioid use, anxiety disorder, and major depression presented after a fall with a femoral fracture requiring stabilization.
- He underwent internal fixation without intraoperative complications and was admitted to a routine postoperative unit.
- Medication reconciliation was completed by the admitting team, confirming that he was opioid-tolerant.
- Upon admission, home doses of an antidepressant and lorazepam were continued.
Case #1 Details (2)

• The first evening after surgery, the patient called for pain medications multiple times.
  – Consequently, two oral hydromorphone doses were given early, and two supplemental doses were given intravenously.

• When the morning shift started, the new nursing assistant called the team to bedside as the patient was lethargic with shallow, slow breathing.
  – The rapid response team was called immediately.
  – The patient was given naloxone and safely intubated to help protect his airway and improve ventilation. An arterial blood gas was done, which revealed a high carbon dioxide (CO2) level.

• After correction of his respiratory deficit, he was successfully weaned off mechanical ventilation and extubated.
Case #2 Details (1)

- A 56-year-old female was sent to the Emergency Department (ED) from a skilled nursing facility due to a worsening wound from an amputation of the first metatarsal of right great toe at a different hospital.

- The patient had a past medical history of morbid obesity, hypertension, heart failure, chronic kidney disease (stage 3), diabetes, peripheral artery disease, and ischemic cardiomyopathy.
  - The patient had two procedures during the previous week - an arteriogram followed by balloon tamponade of the left femoral artery.

- Upon hospital admission, she was stabilized medically and sent to surgery for a trans-metatarsal foot amputation.
Post-operatively, her pain was difficult to control and she received multiple interventions and pain assessments in the PACU, including a popliteal block by the anesthesiologist.

She was transferred from the PACU to the inpatient floor that evening and started on a hydromorphone patient-controlled analgesia (PCA).

That night, the patient continued with high pain scores and received additional hydromorphone as well as doses of hydrocodone with acetaminophen several times.
Case #2 Details (3)

• When the nurse returned to the patient’s room after providing a supplemental dose of intravenous hydromorphone, the patient was found unresponsive, and a code was called.

• The code team attempted resuscitation for over one hour, but the patient expired less than nine hours after surgery.
  – The code team focused on treating her ischemic heart disease and did not administer naloxone.
PATIENT SAFETY EVENTS INVOLVING OPIOID DOSE STACKING

THE COMMENTARY

By Hollie Porras, PharmD, BCPS and Cathy Lammers, MD
A SYSTEMATIC APPROACH TO IMPROVING PATIENT SAFETY
The prevalence of opioid use has increased and consequently, fatal toxicity is also on the rise.

In 2012, the Joint Commission released the most common causes of sentinel events related to opioid administrations which included inadequate monitoring in a staggering 29% of cases.

However, without appropriate protocols, guidance, and monitoring resources in place, it can be challenging to provide adequate, yet safe, pain management.
A Systematic Approach to Improving Patient Safety (1)

• This commentary highlights several evidence-based strategies to optimal management of patients who are administered opioid therapy:
  – Standardized sedation assessment
  – Risk reduction strategies related to "dose stacking"
  – Advanced patient monitoring strategies
  – Naloxone administration during codes
  – Non-opioid pain management
IMPROVING PATIENT SAFETY: STANDARDIZED SEDATION ASSESSMENT
Standardized Sedation Assessment (1)

- Nurses are tasked with administering opioids and continuously monitoring patients for effective pain relief in addition to unwanted side effects; providing an adequate assessment of sedation is a critical step in providing this safe pain management.
- Historically, subjective patient data such as nonverbal behavior and self-reported pain scores, coupled with vital signs, have been utilized to determine if the patient is an appropriate candidate for further doses of opioids.
- In addition to vital signs and subjective data, validated sedation assessment tools can be used to provide more guidance for safe opioid administration or escalation of care.
The Pasero Opioid Sedation Scale (POSS) is an evidenced based, validated opioid assessment tool that can be used by nurses to identify undesired opioid-induced sedation and determine when or if a subsequent opioid dose is safe to administer.

<table>
<thead>
<tr>
<th>Description</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleeping, easy to arouse</td>
<td>Acceptable; no action necessary; may increase opioid dose if needed</td>
</tr>
<tr>
<td>Awake and alert</td>
<td>Acceptable; no action necessary; may increase opioid dose if needed</td>
</tr>
<tr>
<td>Slightly drowsy, easily aroused</td>
<td>Acceptable; no action necessary; may increase opioid dose if needed</td>
</tr>
<tr>
<td>Frequently drowsy, arousable, drifts off to sleep during conversation</td>
<td>Unacceptable; monitor respiratory status and sedation level closely until sedation level is stable at less than 3 and respiratory status is satisfactory; Notify provider to discuss a possible decrease opioid dose 25% to 50% or consider administering a non-sedating, opioid-sparing, nonopioid, such as acetaminophen or a NSAID, if not contraindicated.</td>
</tr>
<tr>
<td>Somnolent, minimal or no response to verbal and physical stimulation</td>
<td>Unacceptable; stop opioid; consider administering naloxone per orders; notify provider; monitor respiratory status and sedation level closely until sedation level is stable at less than 3 and respiratory status is satisfactory</td>
</tr>
</tbody>
</table>
Other standardized sedation assessments include the Richmond Agitation and Sedation Scale (RASS) and the Inova Health System Sedation Scale (ISS); however, POSS is a superior sedation scale for opioid administration and assessment.

Implementing POSS within an institution may be helpful in predicting and preventing opioid-related morbidity and mortality.
IMPROVING PATIENT SAFETY: OPIOID PHARMACOKINETICS AND “DOSE STACKING”
Opioid Pharmacokinetics and “Dose Stacking” (1)

- Additional factors to consider in the reassessment of a patient after opioid administration include the timing of the assessment, the pharmacokinetics and pharmacodynamics of the drug, and the route in which it was administered.
  - As a drug class, opioids are associated with wide interindividual variability in response and a narrow therapeutic index.
  - Opioids dosed intravenously have a quicker onset and peak, and shorter duration of action compared to those dosed orally. Inversely, opioids dosed orally have a more delayed onset and peak, and longer duration of action compared to those dosed intravenously.
- Taking these factors into consideration, if a subsequent opioid dose is administered prior to the onset of action of the previous dose, this can result in what is known as “dose stacking.”
Opioid Pharmacokinetics and “Dose Stacking” (2)

• Dose stacking can occur in a multitude of ways and is typically a consequence of patient-reported inadequate pain relief and repeated opioid dose administration without careful consideration of the onset or duration of action of the previous dose(s) administered.

• Dose stacking can also occur when a patient receives opioids via numerous sources or routes.
  – For example, administering opioids via patient-controlled analgesia (PCA) and simultaneously via intravenous push has historically led to fatal respiratory depression.
Opioid Pharmacokinetics and “Dose Stacking” (3)

- Risk reduction strategies pertaining to opioid dose stacking include incorporating institutional guidelines that outline, standardize, and consolidate the pharmacokinetic and pharmacodynamic variability between opioids.
- Another way to mitigate this risk is by standardizing opioid prescribing patterns, leveraging technology and establishing pain order sets.
  - Standardizing opioid prescribing patterns via order sets and institutional guidelines allows everyone on the care team to “speak the same language.”
  - Order sets also enable providers to order additional pain management safeguards, such as naloxone or capnography, automatically.
Opioid Pharmacokinetics and “Dose Stacking” (4)

Providing nurses with a table that notes when the medication reaches its “peak” provides clear guidance on optimal timing of patient reassessment and additional dose administration, which could further prevent this concept of dose stacking. Of note, sedation typically follows medication peak.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Onset</th>
<th>Peak*</th>
<th>Duration*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>IV: &lt; 1 min</td>
<td>IV: 1-3 mi</td>
<td>IV: 30-60 min</td>
</tr>
<tr>
<td></td>
<td>Transdermal: 12-24 h</td>
<td></td>
<td>Transdermal: 72-96 h</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>30-60 min</td>
<td>60-90 min</td>
<td>4-6 h</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>IV: 5-15 min</td>
<td>IV: 10-20 min</td>
<td>IV: 3-4 h</td>
</tr>
<tr>
<td></td>
<td>PO: 15-30 min</td>
<td>PO: 30-60 min</td>
<td>PO: 4-6 h</td>
</tr>
<tr>
<td>Morphine</td>
<td>IV: 5-10 min</td>
<td>IV: 15-30 min</td>
<td>Immediate release (IV, PO): 3-6 h</td>
</tr>
<tr>
<td></td>
<td>PO: 30-60 min</td>
<td>PO: ~60 min</td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Immediate release: 10-15 min</td>
<td>Immediate release: 30-60 min</td>
<td>Immediate release: 3-6 h</td>
</tr>
</tbody>
</table>
IMPROVING PATIENT SAFETY: ADVANCED PATIENT MONITORING STRATEGIES
Advanced Patient Monitoring Strategies (1)

- In addition to standardized pain management practices, more sophisticated types of patient monitoring should be considered, specifically for patients with coexisting disease known to increase risk of respiratory depression with opioids.
- Methods such as continuous oximetry, end-tidal carbon dioxide (ETCO2) monitoring, and acoustic respiratory monitoring should be utilized for patients identified to be at high risk of opioid-induced respiratory depression.
  - Together, ETCO2 monitoring coupled with continuous oximetry have high prognostic value in determining respiratory depression episodes and can aid in reducing the incidence and consequences of respiratory compromise in patients receiving opioid therapy.
IMPROVING PATIENT SAFETY: NALOXONE ADMINISTRATION DURING CODES
Naloxone Administration During Codes (1)

- Opioid toxicity deteriorates into cardiopulmonary arrest due to depression of respiratory drive and airway obstruction.
- In the event an opioid overdose is suspected, addressing the airway and ventilation is of the highest priority.
- Further steps in care include cardio-pulmonary resuscitation and naloxone administration as soon as possible.
Naloxone Administration During Codes (2)

- Naloxone is a potent opioid receptor antagonist and is indicated to treat opioid overdoses.
- When administered, naloxone rapidly displaces opioids from μ-receptors and consequently reverses the central nervous system and respiratory depressant effects associated with an opioid overdose.
- This reversal reestablishes respiratory drive and return of consciousness.
- Naloxone has an excellent safety profile; however, due to the short half-life, repeat doses of naloxone may be necessary to provide continued reversal.
IMPROVING PATIENT SAFETY:
THINKING BEYOND OPIOIDS
Thinking Beyond Opioids (1)

• Not all discomfort and pain respond to opioids and repeat opioid dosing in a narrow period of time may not relieve the patient’s pain and can dramatically shift the risk-to-benefit ratio.
• A patient whose pain is not responding to repeated dosing of opioids may need a change in strategy.
• Providing a multimodal, holistic strategy to treating pain can help address its multifactorial nature and provide personalized pain management.
  – Treatment teams should consider requesting a regional block from the Anesthesiology service and the addition of scheduled non-opioid adjunctive therapy.
  – Treatment modalities that incorporate non-pharmacologic therapy, ice/heat, elevation, and physical therapy can help ease the burden of post-operative pain.
Thinking Beyond Opioids (2)

• It is also important to note the experience and interpretation of pain varies significantly from person to person, and multiple biological and psychosocial factors contribute to these individual differences.

• Furthermore, it is crucial to consider patients’ psychological state, comorbidities, and social determinants of health such as social support system when deploying pain management strategies.
  – A behavioral health consult service may also offer vital assistance in providing adequate pain relief.
  – Intentional engagement from a family member, volunteer, or chaplain and the utilization of support animals may aid in the psychological distress that may be exacerbating pain.
  – Additional strategies that may be employed by nurses to aid in short-term pain relief include mindfulness, relaxation, and aromatherapy techniques.
TAKE HOME POINTS
Take-Home Points (1)

- Implementing standardized sedation assessments, such as POSS, aids nurses in the prediction and prevention of opioid-induced respiratory depression events.
- Opioid dose stacking can result in fatal respiratory depression.
- ETCO2 and continuous oximetry have high prognostic value in determining respiratory depression events.
- Naloxone has an excellent safety profile and is the mainstay treatment for suspected opioid overdose.
- Multimodal and holistic pain management techniques provide additional support in addressing the multifactorial nature of pain.
REFERENCES
References


