Identification of Patients at High Risk For Opioid-induced Respiratory Depression

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Conflicts of Interest:
Dr. Jungquist has received salary support from Medtronic, Inc. for her role as University at Buffalo site primary investigator for their PRODIGY study.
Dr. Jungquist was lead author for the 2019 Revisions to the ASPMN Monitoring for Advancing Sedation and Respiratory Depression Clinical Practice Guidelines for the Hospitalized Patient.

Thank you to our sponsors

Objectives

- Review significance of the problem
- Introduce recommendations for stratifying patient risk
- PRODIGY study
- Recommendations for integration into practice according to the ASPMN Monitoring Guidelines
Respiratory Compromise

• describes a deterioration in respiratory function in which there is a high likelihood of decompensation into respiratory failure or death

Looking to improve patient safety by early detection of patient deterioration by best practices for detecting respiratory compromise.

Incidence

• American Heart Association Get with the Guidelines – Resuscitation Data
  • 320 hospitals
  • 44,051 acute respiratory events in U.S. hospitals in 2012
  • 86% mortality in those that progressed to cardiac arrest characteristics associated with mortality were:
    • agonal breathing
    • septicemia
    • hypotension

• Looking to improve patient safety by early detection of patient deterioration by best practices for detecting respiratory compromise.
Significance of OIRD

Up to 4.2% of all hospitalized patients administered opioids for acute pain will experience some type of opioid related adverse events.

Postsurgical patients experiencing opioid-related adverse drug events have:
- 55% longer hospital stays
- 47% higher costs associated with their care
- 36% increased risk of 30-day readmission
- 3.4 times higher risk of inpatient mortality compared to those with no opioid-related adverse drug events

Opioid-related sentinel events cost the healthcare system $2.5 million per claim on average as well as contribute to nurse burnout.

(Davis et al., 2017; Fouladpour et al., 2016; Herzig, Rothberg, Cheung, Nagi, & Mercante, 2014; Kessler, Shah, Graudins, & Raju, 2012; Rosenfeld et al., 2016)

Respiratory Event: Time since last nursing assessment
Recommendations to address the problem

- American Society of Anesthesiologists Task Force on Acute Pain
- American Society of Enhanced Recovery
- American Society for Pain Management Nursing
- American Pain Society
- Society for Anesthesia and Sleep Medicine
- Anesthesia Patient Safety Foundation

Recommendation 1

The panel recommends that pain management strategies be individualized and aligned with peer-reviewed, published evidence-based guidelines and the joint commission current pain standards (strong recommendation, high-level evidence).
Recommendation 2

The panel recommends that clinicians recognize that all hospitalized patients receiving systemic (e.g., transdermal, IV, oral) or neuraxial opioids for acute pain management are at risk of opioid-induced unintended advancing sedation and opioid-induced respiratory depression. Some patients are at high-risk for opioid-induced adverse events (see Table 2) (strong recommendation, high level evidence).
Recommendation 3

The panel recommendations that all patients who will receive opioids undergo a comprehensive assessment of level of individual risk prior to initiation of opioid therapy. Ongoing re-assessment of risk that continues through the trajectory of clinical care is essential (strong recommendation, moderate level evidence).
Recommendation 4

The panel recommends that ongoing individualized patient-centric plans of care be based on the patient’s level of risk, which may change over the course of hospitalization, be developed, revised as needed, and communicated among all members of the patient care team (strong recommendation, moderate level evidence).

Recommendation 5

The panel recommends that clinicians identify patients at high-risk of opioid-induced unintended advancing sedation and opioid-induced respiratory depression by using evidence-based criteria which includes the use of validated assessment scales/instruments (strong recommendation, high level evidence).

https://www.drugabuse.gov/sites/default/files/OpioidRiskTool.pdf (ORT)
https://www.jopan.org/article/S1089-9472(15)00070-2/pdf (MOSS)
PRODIGY Risk Prediction Tool (under review)
STOP-BANG Questionnaire

Stratifying Risk

- STOP-BANG questionnaire
- Pre-op sleep studies or nocturnal oximetry study

(Chung et al., 2015; Adams, Bulas, & Spurlock, 2015)
**The PRediction of Opioid-induced respiratory Depression In patients monitored by capnoGraphY – PRODIGY Study**

- **Objective**: Develop a risk stratification score for Opioid induced Respiratory Depression
- **Design**: Multisite Observational
- **Measures**: Continuous $\text{SpO}_2$ + et$\text{CO}_2$ for patients receiving parenteral opioids for acute pain.

**Study Design**

- Enrolled 1,495 adult patients at 16 sites in US, EU, & Asia
- Patients were expected to receive parenteral opioid therapy on the GCF
- Analysis set included 1,335 enrolled patients who:
  - received opioid therapy on GCF
  - started continuous monitoring

**Measures of OIRD**

![Image of a study design and measures for OPIED (Opioid-induced Respiratory Depression)]
The PRODIGY study - Definition of an OIRD episode

OIRD episode defined as:
- RR ≤ 5 breaths for ≥ 3 continuous minutes
- SpO₂ ≤ 85% for ≥ 3 continuous minutes
- etCO₂ ≤ 15 or ≥ 60 mmHg for ≥ 3 continuous minutes
- apnea episode lasting >30 seconds
- or any respiratory opioid-related adverse event

Independent Clinical Event Committee adjudicated OIRD episodes

Predictor Variables Analysis

46 potential predictors assessed

PRODIGY Risk Score determined using all significant predictors from multivariate risk prediction model
### Participant Characteristics

<table>
<thead>
<tr>
<th>USA (n=769)</th>
<th>Europe (n=254)</th>
<th>Asia (n=312)</th>
<th>Total (n=1335)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA Physical Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA I</td>
<td>0.5%</td>
<td>13.8%</td>
<td>24.0%</td>
<td>8.7%</td>
</tr>
<tr>
<td>ASA II</td>
<td>35.8%</td>
<td>59.8%</td>
<td>66.0%</td>
<td>47.6%</td>
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<tr>
<td>ASA III</td>
<td>60.2%</td>
<td>26.0%</td>
<td>9.9%</td>
<td>41.6%</td>
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<tr>
<td>ASA IV</td>
<td>3.5%</td>
<td>0.4%</td>
<td>0.0%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Length of Surgery (hr)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2</td>
<td>37.7%</td>
<td>20.9%</td>
<td>27.9%</td>
<td>32.2%</td>
</tr>
<tr>
<td>2 - &lt;4</td>
<td>40.4%</td>
<td>49.2%</td>
<td>38.1%</td>
<td>41.6%</td>
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<tr>
<td>≥4</td>
<td>21.8%</td>
<td>29.9%</td>
<td>34.0%</td>
<td>26.2%</td>
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<tr>
<td>Opioid Naïve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>***</td>
<td>71.7%</td>
<td>88.2%</td>
<td>96.5%</td>
<td>80.6%</td>
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<tr>
<td>Multiple Opioids/Concurrent CNS/Sedating Medication</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>93.9%</td>
<td>86.6%</td>
<td>98.1%</td>
<td>93.5%</td>
<td>&lt;.001</td>
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<tr>
<td>Number of Distinct Opioids</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>One opioid</td>
<td>9.0%</td>
<td>20.5%</td>
<td>2.6%</td>
<td>9.7%</td>
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<tr>
<td>Opioid number ≥1 - &lt;4</td>
<td>58.6%</td>
<td>59.8%</td>
<td>88.8%</td>
<td>65.9%</td>
</tr>
<tr>
<td>Opioid number ≥4</td>
<td>32.4%</td>
<td>19.7%</td>
<td>8.7%</td>
<td>24.4%</td>
</tr>
</tbody>
</table>

### Predictors

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Patients with ≥1 RD episode (n = 614)</th>
<th>Patients without RD (n = 721)</th>
<th>OR</th>
<th>Significance (P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&lt;70 yrs)</td>
<td>24.3%</td>
<td>10.4%</td>
<td>4.12</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age (≥70 yrs)</td>
<td>5.5%</td>
<td>32.3%</td>
<td>4.70</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI</td>
<td>53.9%</td>
<td>33.7%</td>
<td>2.24</td>
<td>&lt;.001</td>
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<tr>
<td>Hypertension</td>
<td>30.7%</td>
<td>25.2%</td>
<td>1.31</td>
<td>.029</td>
</tr>
<tr>
<td>Diabetes - Type II</td>
<td>15.0%</td>
<td>25.4%</td>
<td>4.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Chronic Heart Failure</td>
<td>7.7%</td>
<td>4.7%</td>
<td>1.66</td>
<td>.025</td>
</tr>
<tr>
<td>Kidney Failure</td>
<td>5.4%</td>
<td>2.9%</td>
<td>1.89</td>
<td>.025</td>
</tr>
<tr>
<td>Number of distinct opioids</td>
<td>39.7%</td>
<td>77.1%</td>
<td>1.84</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Opioid number ≥1 - &lt;4</td>
<td>70.2%</td>
<td>62.3%</td>
<td>1.29</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

### PRODIGY Score Distribution

<table>
<thead>
<tr>
<th>PRODIGY Score Distribution</th>
<th>Low Risk</th>
<th>Intermediate Risk</th>
<th>High Risk</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>&lt;8 points</td>
<td>≥8 &amp; &lt;15 points</td>
<td>≥15 points</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>24%</td>
<td>42%</td>
<td>55%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Specificity</td>
<td>86</td>
<td>52</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>OR (P value)</td>
<td><strong>2.34; P &lt;.001</strong></td>
<td><strong>6.07; P &lt;.001</strong></td>
<td><strong>2.6; P &lt;.001</strong></td>
<td></td>
</tr>
</tbody>
</table>
PRODIGY Model Accuracy = 0.76

PRODIGY – Secondary Outcomes

Participants that scored ≥ 8 on the instrument:

- Higher incidence of adverse events

PRODIGY – Secondary Outcomes

Characterize the predictive values of individual parameters:

- end tidal CO$_2$
- SpO$_2$
- respiratory rate
- Integrated Pulmonary Index™ algorithm (etCO$_2$, SpO$_2$, RR, and HR)
Summary of PRODIGY findings

- RD episodes are common
- Clinical relevance of the RD episodes is not known, but in this study the participants who experienced these episodes had longer lengths of stay and more clinically relevant rapid response calls.
- Repetitive exposure to RD episodes may contribute to significant morbidity
- Current monitoring standards may not detect these events
- PRODIGY risk score: easy to implement tool for prediction of RD episodes
- Patients rated as high-risk by the PRODIGY score may benefit from proactive bedside interventions and need continuous cardiorespiratory monitoring.

Recommendation 6

The panel recommends that clinicians employ evidence-based pain management that incorporates opioid-sparing and multimodal analgesia therapies (strong recommendation, high level evidence).

Recommendation 7

The panel recommends that hospital policies and procedures reflect evidence-based and nationally published standards and ensure 1) effective communication among all members of the patient care team, 2) adequate and safe staffing ratios, and 3) purposeful hourly rounding by nursing staff (strong recommendation, weak to high levels of evidence).
**Recommendation 8**

The panel recommends that the nature, timing, frequency, and intensity of monitoring practices be based on ongoing nursing assessment and re-assessment of patient’s risks and response to pain therapies. Adaptations to the plan of care are driven by iterative assessments (strong recommendation, moderate level of evidence).

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**Recommendation 9**

The panel recommends evidence-based systematic nursing assessments for opioid-induced unintended advancing sedation and respiratory depression inclusive of 1) level of sedation, 2) respiratory rate and quality, and 3) oxygen saturation prior to initiation of opioid therapy, before administering an opioid dose, and at peak effect of opioid and/or other sedating medication co-administered within the therapeutic window of an opioid. Systematic nursing assessments should not be replaced with continuous electronic monitoring (strong recommendation, moderate level evidence).

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**Recommendation 10**

The panel recommends, that all patients deemed to be at risk for opioid-induced unintended advancing sedation and opioid-induced respiratory depression be evaluated for continuous electronic monitoring (see Table 2); and that the type of electronic monitoring be appropriate to the condition of the patient, presence of supplemental oxygen or positive airway pressure therapy, patient’s response to care, patient comfort and adherence to monitoring device, and the detection capability of the technology (strong recommendation, weak level evidence).
Monitoring Devices

Oximetry
- Pulse Oximetry

Ventilation
- Capnography
- Minute Ventilation
- Pulse Oximetry AND Respiratory Rate
- Transcutaneous Carbon Dioxide

Adverse event ending with Anoxic Brain Injury

Pulse Oximetry Over 36 Hours

Intermittent Oxygen Saturation Checks

What happens when we add supplemental O2?
Recommendation 11

The panel recommends the judicious use of naloxone based on patient evidence of life-threatening adverse events (strong recommendation, moderate level evidence).

Recommendation 12

The panel recommends clinician education on evidence-based and best practices for: 1) determining patient risks for opioid-induced unintended advancing sedation and respiratory depression; 2) best practices on assessing level of sedation and respiratory status; 3) use of trend monitoring as opposed to threshold monitoring when evaluating indicators for respiratory status; 4) appropriate use of positive airway pressure therapy; 5) early implementation of appropriate interventions when advancing sedation and respiratory depression are imminent; and 6) appropriately educating patients/family members who want to know how to participate in safety efforts. (strong recommendation, weak level evidence).
Recommendation 13
The panel recommends that hospital leadership support the development of practice and administrative policies and procedures that outline the implementation of strategies focusing on:
1) clinician, patient, and family awareness of and strategies to avoid the problem; 2) education of clinicians, patient, and family on risk assessment and adaptation of individualized monitoring procedures and policies; 3) proper training on the use of electronic monitoring systems with potential use of risk alerts within electronic health record systems. (strong recommendation, moderate level evidence).

The panel recommends the development of evidence-based policies and procedures that support clinicians, patients and family members education about the patient’s use of positive airway pressure devices to treat obstructive sleep apnea and obesity hypoventilation syndrome during hospitalization. (strong recommendation, weak level evidence).

Thank You!