RATING THE SEVERITY OF OPIOID-INDUCED ATAXIC BREATHING IN HEALTHY HUMANS

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OPIOID-INDUCED RESPIRATORY DEPRESSION

• 2015 Anesthesia Closed Claims Project database (1990-2009):
  • Majority of RD events (88%) occurred within 24 h of surgery
  • 97% were preventable with better monitoring and response

OPIOID-INDUCED RESPIRATORY DEPRESSION

**Fig. 1.** Time between last nursing check and discovery of opioid-induced respiratory depression (RD). Claims with unknown timing (n = 39) and not applicable (at home, n = 3) not shown.


OPIOID-INDUCED RESPIRATORY DEPRESSION

MONITORING STANDARDS

1. Respiratory Rate  
   (< 8-10 bpm)

2. Oximetry  
   (SpO₂ < 90-92%)

3. End-Tidal CO₂  
   (ETCO₂ > 50 mmHg)

4. Mental Status  
   (Sedated)
Respiratory Rate is Unreliable for Detecting Opioid-Induced RD

1. RR obtained by physical examination is notoriously inaccurate (e.g. poor technique, patient arousal).

2. Most technologies are not validated for detecting slow respiratory rates.

3. Automated methods are insensitive to respiratory patterns (e.g. apneas) resulting in inaccurate RR.

4. RR does not equate to adequate ventilation.

Comparison of seven different sensors for detecting low respiratory rates using a single breath detection algorithm in non-intubated, sedated volunteers.

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Respiratory Pattern versus Respiratory Rate

- Air Flow PTAF
- Air Flow Thermistor
- RIP Signals
- Chest Abdomen

Central Apnea
Paradoxical movement

Respiratory Rate ~12/min

60 sec
Variations of Biot's (ataxic) breathing patterns

Major obstacle for monitoring a patient for Biot’s (ataxic) breathing severity:

The need for manual offline analysis using a visual template

PRIMARY HYPOTHESIS

For healthy volunteers receiving steady state infusion pairs of an opioid and a hypnotic to model light sleep with opioid-induced ventilatory depression:

The ataxic breathing severity scores from three domain experts and a machine learning algorithm classifier will be in agreement.

METHODS

26 Consenting Healthy Volunteers
- Opioid naïve
- BMI 18-31,
- Age 18-41
Target Controlled Infusion Drug Schemes

METHODS

- Three domain experts scored the severity of ataxic breathing on a scale of 0-4 in accordance with a visual scoring template. A machine learning algorithm was trained on 50% of the data.

- Krippendorff’s alpha was used to rate agreement among all raters (machine and experts).

- Vanbelle’s Kappa was used to assess the agreement between the machine learning algorithm and the three experts
Ataxic Breathing Severity Score 0

Absolute change in Tidal Volume

Interbreath Interval at \( t = i \) (sec)

Interbreath Interval at \( t = i + 1 \) (sec)

Poincaré Plot

Ataxic Breathing Severity Score 1

Absolute change in Tidal Volume
Ataxic Breathing Severity Score 2

Air Flow Waveform

RIP Flow

PTAF

Poincaré Plot

Interbreath Interval at $t = i$ (sec)

Interbreath Interval at $t = i + 1$ (sec)

Absolute change in Tidal Volume

Ataxic Breathing Severity Score 3

Air Flow Waveform

RIP Flow

PTAF

Poincaré Plot

Interbreath Interval at $t = i$ (sec)

Interbreath Interval at $t = i + 1$ (sec)

Absolute change in Tidal Volume

Chest: Blue
Abdomen: Red
RESULTS

<table>
<thead>
<tr>
<th>Rater Statistic</th>
<th>Basic Classifier: RIP Band Mean (95% CI)</th>
<th>Basic Classifier: Intranasal Pressure Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krippendorff's Alpha</td>
<td>0.912 (0.852 - 0.949)</td>
<td>0.899 (0.819 - 0.941)</td>
</tr>
<tr>
<td>Vanbelle's Kappa</td>
<td>0.970 (0.951 - 0.983)</td>
<td>0.961 (0.921 - 0.979)</td>
</tr>
</tbody>
</table>
Example progression of ataxic breathing

[Graph showing data from an experimental study on ataxic breathing]
CONCLUSIONS

• A machine learning algorithm classified ataxic breathing severity in a manner consistent with a panel of domain experts.

• An ataxic breathing severity score may be helpful in conjunction with measures of respiratory rate and SpO2 to identify patients at risk for opioid-induced respiratory depression.

• Further work is needed to test the feasibility of this concept on clinical data.

THANK YOU

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