Narcolepsy in the Perioperative Setting: Is There Cause for Concern?

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• ABIM Sleep Medicine Exam Committee
  • No exam questions will be disclosed during this presentation
Objectives

• Consider the implications of narcolepsy and its therapy in the perioperative setting

• Review the patient with narcolepsy’s perioperative experience

• Review “recommendations” for the perioperative management of patients with narcolepsy
Narcolepsy in the Perioperative Setting

(Rahul Kakkar) (2016) (Me)

Society of Anesthesia and Sleep Medicine
Narcolepsy Perioperative Care Task Force

- Dennis Auckley (Co-chair)
- Rahul Kakkar (Co-chair)
- Frances Chung
- Yves Dauvilliers
- Bhargavi Gali
- Peter Gay
- Shelley Hershner
- Emmanuel Mignot
- Krishna Ramachandran
- Mandeep Singh
- Jean Wong
- Michael Thorpy
Narcolepsy and Perioperative Concerns

• While narcolepsy is relatively uncommon, perioperative providers are likely to see patients with narcolepsy
  • It is not expected that perioperative providers screen for or diagnose narcolepsy

• There has been concern raised about patients with narcolepsy undergoing anesthesia/sedation
Narcolepsy and Perioperative Concerns

- Potential problems for patients with narcolepsy undergoing anesthesia/sedation
  - Hypersomnolence -> prolonged emergence and postop hypersomnia
  - Increased perioperative cataplexy and sleep paralysis
  - Drug interactions with anesthetics, drug withdrawal effects
  - Impact on pain control
  - Autonomic dysfunction (affecting heart rate and blood pressure)
Narcolepsy and Perioperative Concerns: Questions

• Are narcolepsy and/or its therapy associated with increased perioperative risk for adverse events?

• What is the perspective of patients with narcolepsy undergoing surgery?

• What is the familiarity of perioperative providers with narcolepsy and its therapies?

• How should patients with narcolepsy be optimally managed in the perioperative setting?
Narcolepsy and Perioperative Concerns

- Case report (1977) of a patient with a history of sleep paralysis undergoing ovarian cyst removal;
  - During a previous admission, she had an episode of sleep paralysis for which she was given CPR.
  - During this admission, had an uneventful surgery
  - PostOp, experienced 3 episodes of sleep paralysis described as being found nonresponsive and glassy eyed with irregular breathing.
  - Was given physostigmine IV for each with response, and once responsive, described sleep paralysis episodes.

*Spector et al, Anesthesiology 1977*
Narcolepsy Perioperative Care

Step 1: Review the literature
Narcolepsy and Perioperative Care: Systematic Review

Hu and Singh et al, Anesth and Analg 2017
Narcolepsy and Perioperative Care: Systematic Review

Hu and Singh et al, Anesth and Analg 2017
Narcolepsy and Perioperative Care: Systematic Review

• 19 studies (n=49) for primary analysis
  • Mostly case reports, but 2 small case series / 1 series of 27
  • None of the reports were prospective or had control groups
  • Variety of medications used as stimulants (mostly methylphenidate and amphetamines)
    • 91% continued medications preoperatively
  • No patient used sodium oxybath for cataplexy (small number on SSRIs or TCAs)
  • Variety of surgeries were performed

Hu and Singh et al, Anesth and Analg 2017
Narcolepsy and Perioperative Care: Systematic Review

• **Background Data**
  • Age 47 +/- 14 yrs
  • Narcolepsy dx 27 +/- 14 yrs
  • % Male 61%
  • BMI 31 +/- 5 kg/m²
  • Other conditions HTN, COPD, high lipids, migraines, vascular disease

• **Anesthesia**
  • GA inhalational (78%), IV (22%)
  • Reversal 20%

*Hu and Singh et al, Anesth and Analg 2017*
Narcolepsy and Perioperative Care: Systematic Review

• **Complications**
  • **Intraoperative:**
    • HTN (1) and low blood pressure (1)
    • Slow heart rate (1)
    • Cataplexy (1) during LE procedure under RA
  
  • **Postoperative (31%):**
    • Pain (13)
    • Nausea/vomiting (3)
    • Fever (3)
    • Excessive sleepiness (2)
    • Sleep paralysis (1)
    • HTN (1)
    • EKG changes (1)
    • Desaturation (1)
    • Respiratory support (1)
    • Agitation (1)

_Hu and Singh et al, Anesth and Analg 2017_
Narcolepsy and Perioperative Care: Systematic Review

- OB: 2 studies \((n=486 \text{ deliveries})\) and 1 case report
  - Compared to Narcolepsy Type 2, Narcolepsy Type 1 had higher rates of:
    - Weight gain during pregnancy
    - Impaired glucose processing
    - Anemia
  - 5 episodes (1\%) of cataplexy were documented during deliveries
    - 1 report of status cataplecticus
    - 2 reports of emergency C-sections

*Hu and Singh et al, Anesth and Analg 2017*
Narcolepsy and Perioperative Care: Case-control Study

- Single institution retrospective 1:2 control study design
  - Matched by age, gender, type and year of surgery

- 76 patients with narcolepsy included
  - More likely to be stimulants (74% vs. 4%*)
  - More likely to be on antidepressants (46% vs. 28%*)
  - More likely to have sleep apnea (41% vs. 19%*)
  - No difference in other diseases, BMI or anesthetic age use
  - *P< 0.05

- Note, only 1 patient on sodium oxybate

Cavalcante et al, J Clin Anesthesia 2017
Narcolepsy and Perioperative Care: Case-control Study

- No difference in intraoperative complications

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Narcoleptic patients (n = 76)</th>
<th>Controls (n = 152)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase I recovery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of phase I recovery, min</td>
<td>101 (52)</td>
<td>99 (56)</td>
<td>0.77</td>
</tr>
<tr>
<td>Opioids, mg IV ME</td>
<td>5 (0–10)</td>
<td>5 (0–10)</td>
<td>0.85</td>
</tr>
<tr>
<td>Respiratory depression&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5 (6.6%)</td>
<td>12 (7.9%)</td>
<td>0.80</td>
</tr>
<tr>
<td>Intensive care unit or monitored unit admission&lt;sup&gt;c&lt;/sup&gt;</td>
<td>8 (10.5%)</td>
<td>11 (7.2%)</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>First 48 h after PACU discharge</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive care unit admission from ward&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1 (1.3%)</td>
<td>1 (0.7%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>ERT activation&lt;sup&gt;e&lt;/sup&gt;</td>
<td>5 (6.6%)</td>
<td>2 (1.3%)</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>30-d postoperative outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thromboembolic event</td>
<td>0</td>
<td>0</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td>1 (0.7%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>1 (0.7%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Hospital length of stay, d</td>
<td>3 (2–5)</td>
<td>3 (2–5)</td>
<td>0.57</td>
</tr>
</tbody>
</table>

- 5 ERT activations due to: low blood pressure (2), fast heart rate (1), severe infection (1), and respiratory depression (1)

*Cavalcante et al, J Clin Anesthesia 2017*
Narcolepsy and Perioperative Care: Case-control Study

- Single institution retrospective 1:3 control study design
- 25 OB patients with narcolepsy (59 pregnancies) vs. 75 OB controls (164 pregnancies) found narcolepsy:
  - More likely to have single pregnancies*
  - More likely to develop pregnancy-related diabetes*
  - No difference in complications during or after delivery
  - *Note, 6 patients on stimulants and none sodium oxybate

* P< 0.05

Calvo-Ferrandeiz et al, J Sleep Res 2017
Narcolepsy and Perioperative Care: Summary of Current Literature

- Data to date limited to retrospective cases/case series and mostly uncontrolled

- May be a signal for autonomic dysregulation that could impact perioperative outcomes

- Possibility of worsening of other narcolepsy symptoms / therapies impacting outcomes (i.e. *intraoperative awareness*, *delayed emergence*, *increased cataplexy*) is unclear

- Essentially no data on patients on sodium oxybate
Narcolepsy Perioperative Care

Step 2: Patient’s perspective
Narcolepsy and Perioperative Care: The Patient’s Perspective

- Data from retrospective cases may limit reported outcomes
- Patient perspectives and concerns are valid and important quality measures

Survey sent to:
1266 members of Narcolepsy Network and
6000 members of Facebook group of Narcolepsy Network

1162 respondents

1020 respondents had narcolepsy and underwent a procedure under sedation/general anesthesia

Hershner et al, in prep
Narcolepsy and Perioperative Care: The Patient’s Perspective

Hershner et al, in prep
Narcolepsy and Perioperative Care: The Patient’s Perspective

Preoperative Counseling

Hershner et al, in prep
Narcolepsy and Perioperative Care: The Patient’s Perspective

Patient-reported Outcomes

Hershner et al, in prep
Narcolepsy Perioperative Care

Step 3: Perioperative providers perspective
Narcolepsy and Perioperative Care: Periop Provider Comfort Level

?
Narcolepsy Perioperative Care

Step 4: Summary recommendations
Perioperative Management of Patients with Narcolepsy: Recommendations

• Preoperative counseling
  • Continue of medications preoperatively
  • Possible worsening of symptoms postoperatively
    • Driving avoidance

• Continue regular narcolepsy medications perioperatively
  • Controls symptoms
  • Prevents withdrawal
Perioperative Management of Patients with Narcolepsy: Recommendations

- Consider use of regional over general anesthesia when appropriate
  - Avoids drug-drug interactions
  - Limits intraoperative complications

- Consider depth of anesthesia monitoring such as BIS
  - May help to prevent awareness or delayed emergence
  - Can be useful if cataplexy occurs while under regional

- Consider use of IV anesthesia and shorter acting anesthetic agents whenever appropriate
Perioperative Management of Patients with Narcolepsy: Recommendations

• Avoid long-acting opioid medications, consider alternatives

• Postoperative monitoring for worsening narcolepsy symptoms
  • Consider Sleep Medicine consultation

• OB patients risk of increased cataplexy with delivery?
  • Consider Sleep Medicine consultation

• We have almost no knowledge about perioperative management of patients on sodium oxybate
  • Consider Sleep Medicine consultation
Perioperative Management of Patients with Narcolepsy: Recommendations

- Narcolepsy and OSA may coexist!
  - Up to 25% of patients with narcolepsy may have co-morbid OSA
    - Sansa et al, Sleep Med 2010
    - Frauscher et al, JCSM 2013

- Screening for OSA in patients with narcolepsy should be considered (preoperative clinic or otherwise)
Narcolepsy Perioperative Care

Step 5: Future directions
Narcolepsy and Perioperative Care: Future Directions

• Adverse events:
  • What are the medical risks, cardiovascular or otherwise, to the patient with narcolepsy that might be associated with anesthesia and surgery?
  
  • Do specific narcolepsy related medications have a greater association with adverse events?
Narcolepsy and Perioperative Care: Future Directions

• Outcomes:
  • What is the current understanding of perioperative providers regarding narcolepsy, its treatment, and risk for adverse outcomes?
  • What are the potential interactions of the clinical features of narcolepsy with anesthesia and the operative procedure, and are there differences between the phenotype of NT1 and NT2?
  • Can the clinical impact of the potential interaction of medications used to treat narcolepsy with anesthetic agents be better defined?
Narcolepsy and Perioperative Care: Future Directions

• Perioperative management
  • What is the appropriate management of narcolepsy medications during the pre / intra / post-operative periods?
  • Does anesthetic technique (regional vs. general) impact perioperative symptoms of narcolepsy patients?
  • What enhanced monitoring techniques should be used to better identify, and monitor patients with narcolepsy in the perioperative period?
Narcolepsy and Perioperative Care: Future Directions

• Perioperative management
  • How should the postoperative management be tailored, esp concerning possible prolonged emergence after general anesthesia?
  
  • When should narcolepsy medications be resumed if they were reduced in amount, or stopped, during the perioperative period?
    • What is the appropriate management of narcolepsy medications during the immediate postoperative period?
  
  • Is pain management adequate during the pre / intra / post-operative periods in patients with narcolepsy?
Thank you!!

Questions?