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

Dennis Auckley, MD
Director, Center for Sleep Medicine
MetroHealth Medical Center
Professor of Medicine
Case Western Reserve University

October 2018

Financial Disclosures

- UpToDate – written 2 sections
- ABIM Sleep Medicine Exam Committee
  - No exam questions will be disclosed during this presentation

Objectives

- Consider the implications of narcolepsy and it's 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

NARCOLEPSY NETWORK®

Supporting people with narcolepsy since 1986

(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 it's 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 it's 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 physiostigmine IV for each with response, and once responsive, described sleep paralysis episodes.

Spector et al, Anesthesiology 1977

Narcolepsy Perioperative Care

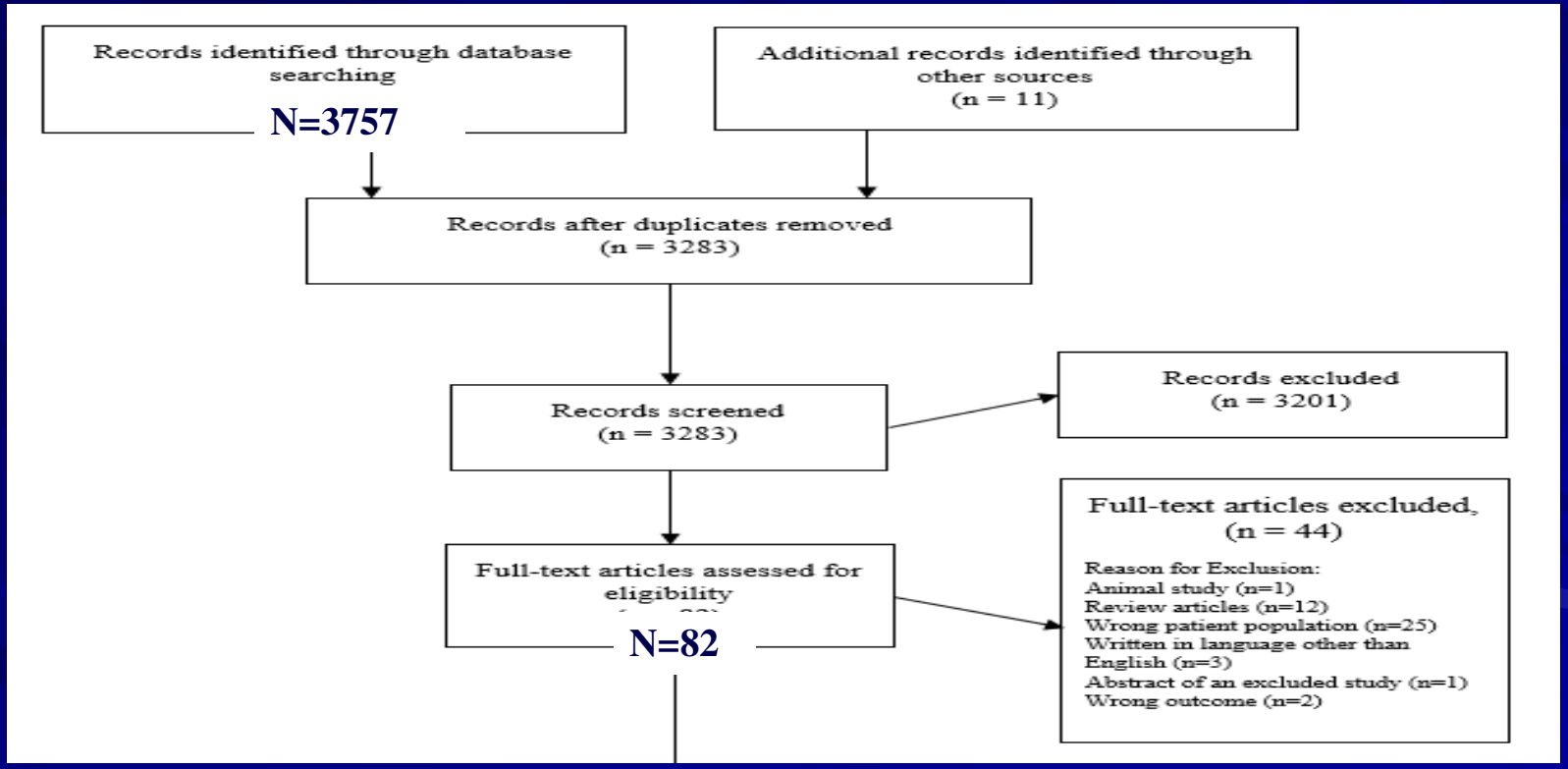
NARCOLEPSY NETWORK®

Supporting people with narcolepsy since 1986

+

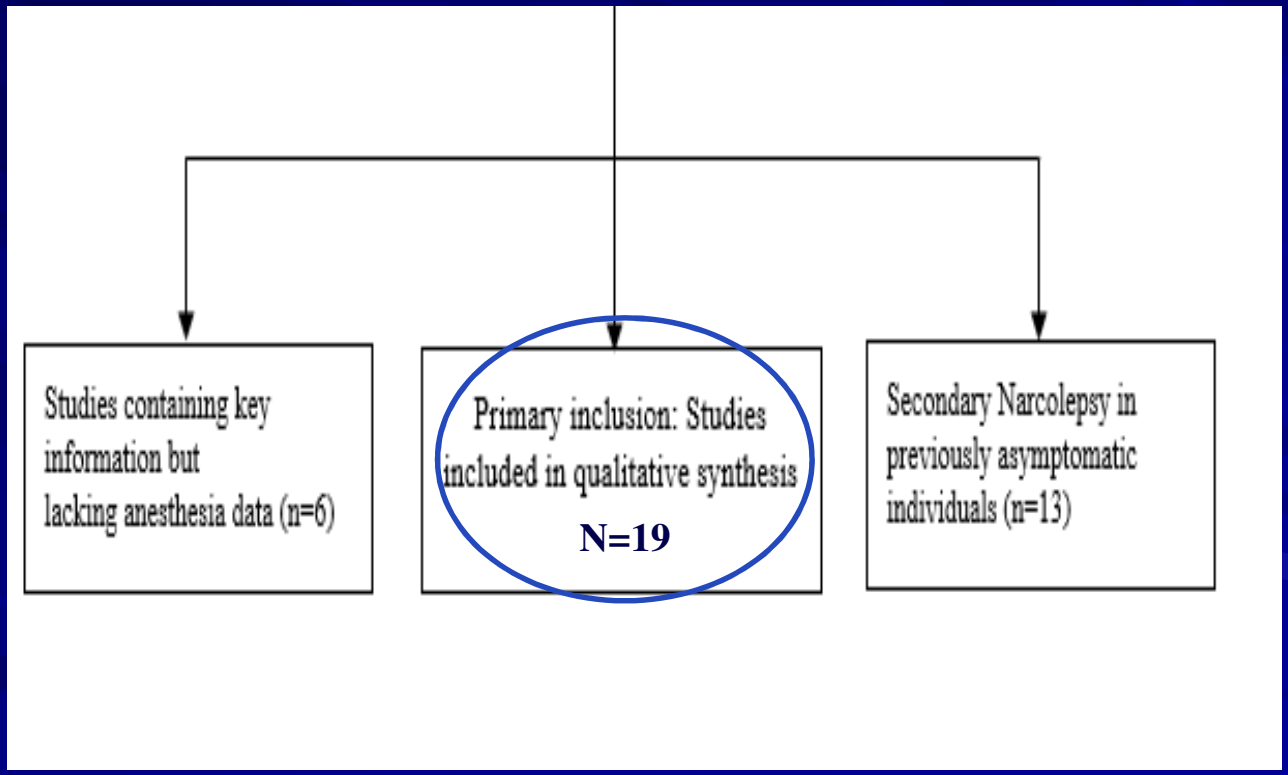
Step 1: Review the literature

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 oxybate 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/m^2
  - 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 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
  - *Note, only 1 patient on sodium oxybate*

* P< 0.05

Cavalcante et al, J Clin Anesthesia 2017

Narcolepsy and Perioperative Care: Case-control Study

- No difference in intraoperative complications

Outcomes for patients with and without narcolepsy.

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

- 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

NARCOLEPSY NETWORK®

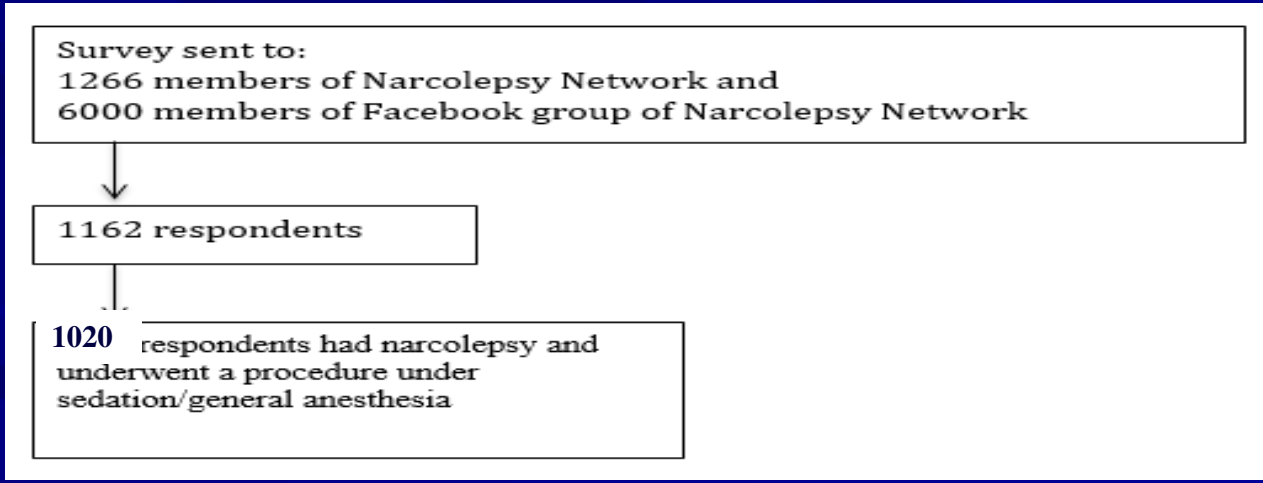
Supporting people with narcolepsy since 1986

+

Step 2: Patient's perspective

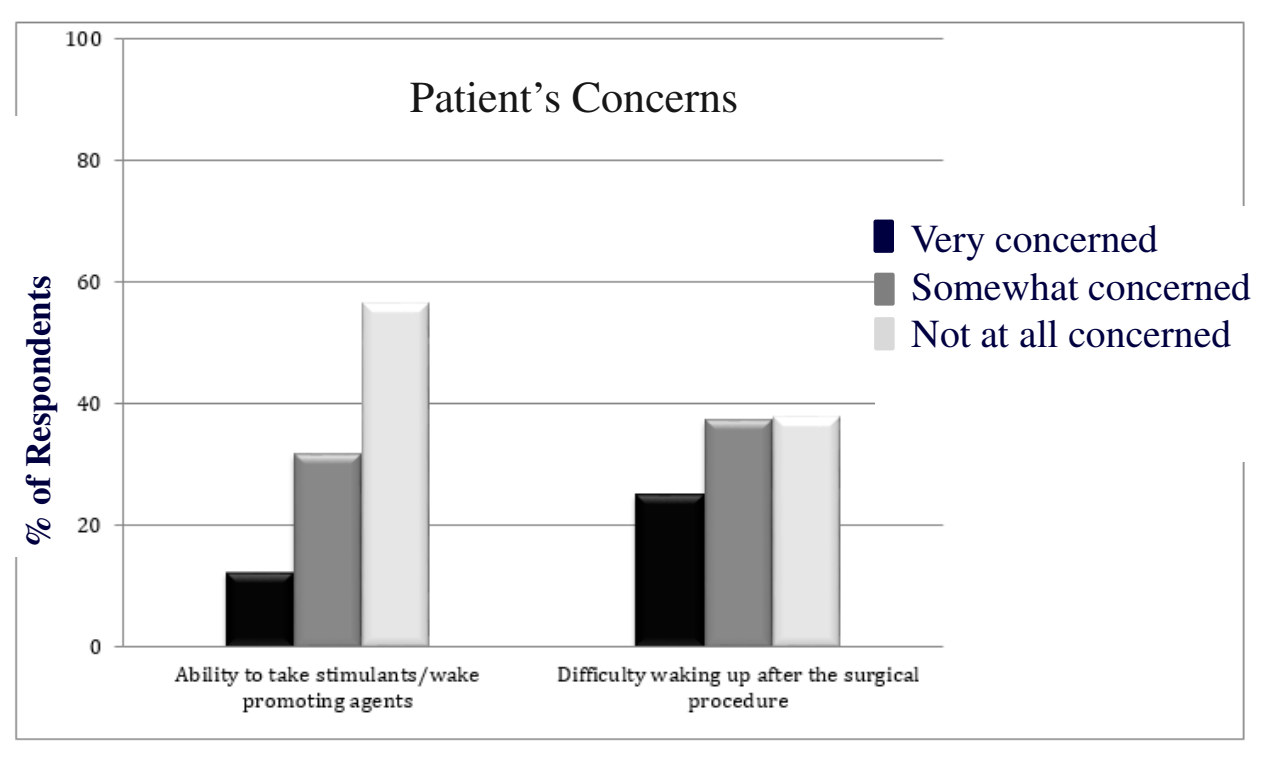
Narcolepsy and Perioperative Care: The Patient's Perspective

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



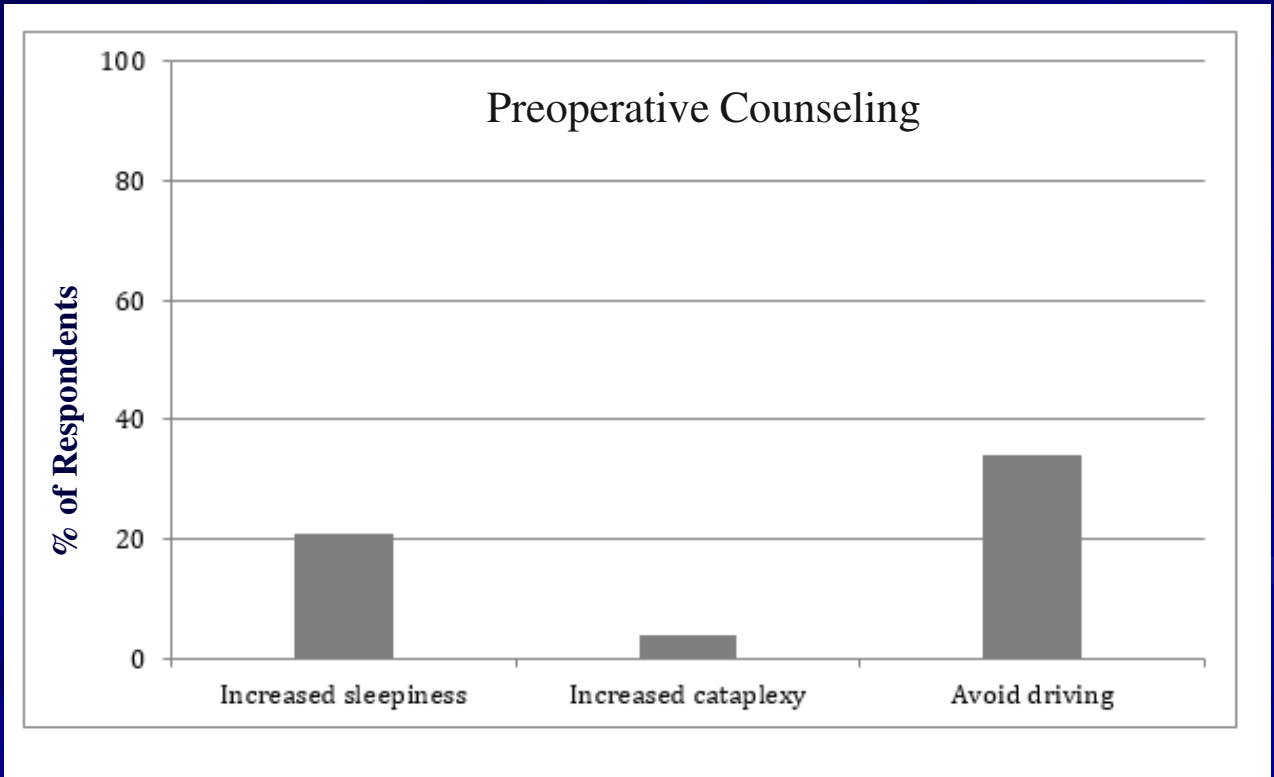
Hershner et al, in prep

Narcolepsy and Perioperative Care: The Patient's Perspective



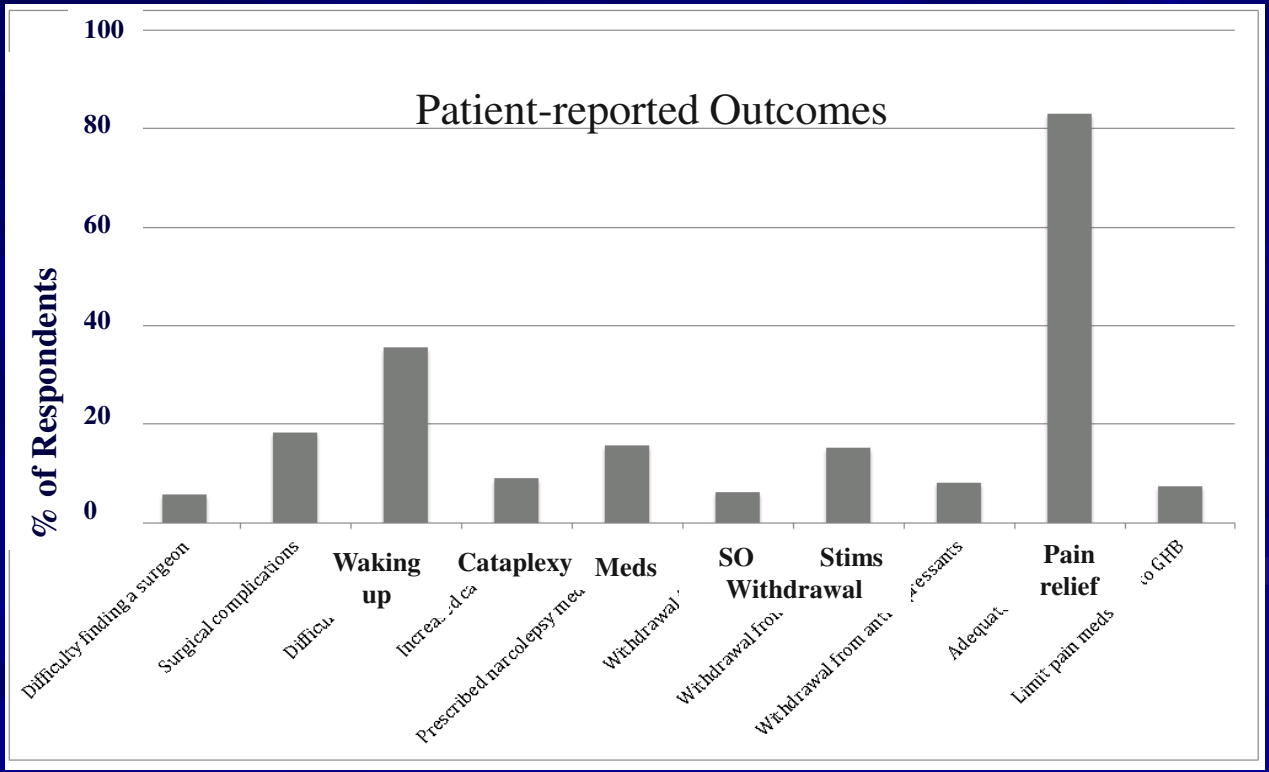
Hershner et al, in prep

Narcolepsy and Perioperative Care: The Patient's Perspective



Hershner et al, in prep

Narcolepsy and Perioperative Care: The Patient's Perspective



Hershner et al, in prep

Narcolepsy Perioperative Care

NARCOLEPSY NETWORK®

Supporting people with narcolepsy since 1986

+

Step 3: Perioperative providers perspective

Narcolepsy and Perioperative Care: Periop Provider Comfort Level

?

Narcolepsy Perioperative Care

NARCOLEPSY NETWORK®

Supporting people with narcolepsy since 1986

+

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

NARCOLEPSY NETWORK®

Supporting people with narcolepsy since 1986

+

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?

Narcolepsy Perioperative Care

NARCOLEPSY NETWORK®

Supporting people with narcolepsy since 1986

+

Thank you!!

Questions?