

Narcolepsy

Risk

- Prevalence approximately 1:2000
- Women and men equally affected
- Prevalence higher in Japan (1:600)

Perioperative Risks

- Potential for masking or mimicking periop complications
- Potential deleterious interactions between drugs for narcolepsy and drugs administered periop

Worry About

- There is little evidence that pts with narcolepsy actually have an increased periop risk.
- Theoretical concerns are:
 - Potential drug interactions with anesthetics leading to
 - Hemodynamic changes.
 - Altered anesthetic requirements.
 - Increased risk of serotonin syndrome.
 - Periop narcoleptic episodes mimicking or masking other anesthesia complications (e.g., delayed emergence or postop residual curarization).

Overview

- Chronic neurologic sleep disorder
- Onset usually in adolescence
- May take years to be diagnosed (polysomnography and multiple sleep latency test)
- Classic symptoms: Excessive daytime sleepiness, cataplexy, sleep paralysis, hypnagogic/hypnopompic hallucinations (nocturnal sleep disruption)
- Excessive daytime sleepiness:
 - Daytime sleep episodes occurring at inappropriate times
 - Difficult to avoid falling asleep
 - Frequently rationalized
 - Differential Dx: OSA, sleep deprivation
- Cataplexy:
 - Sudden decrease in muscle tone
 - Usually partial (e.g., affecting only facial or neck muscles)
 - May be complete, with fall risk; pts are fully conscious
 - Both partial/complete can be triggered by emotions (e.g., periop anxiety)
 - Can last up to 60 min

- Hallucinations:
 - Hypnagogic (during transition from waking to sleep) or hypnopompic (during transition from sleep to waking)
 - Often visual but may also be auditory, tactile, or multisensory
 - May be misdiagnosed as mental illness
- Sleep paralysis:
 - Inability to move during sleep onset or offset
 - Pt fully conscious
 - Breathing unaffected
 - May occur in conjunction with hallucinations
- Other symptoms:
 - Automatic behavior (performing routine tasks without conscious awareness)
 - Memory lapses
 - Secondary psychological symptoms (e.g., depression)

Etiology

- Multiple etiologies, at least partially genetic (HLA-DR and HLA-DQ).
- Decreased concentrations of neurotransmitter (hypocretin, also known as orexin) in lateral hypothalamus.
- Undetectable levels of hypocretin in CSF of most pts.
- Current theory favors an autoimmune process that attacks hypocretin-producing neurons (possibly triggered by upper airway infections).

Usual Treatment

- Modafinil:
 - Usually first line for sleep attacks, MOA unknown.
 - Low abuse potential, favorable side-effect profile.
 - Less effect on blood pressure compared with amphetamines.
 - Less rebound hypersomnolence upon withdrawal.
 - Armodafinil: R-enantiomer with longer half-life of 10–15 h.
 - Small studies suggest that modafinil may improve recovery from general anesthesia by making pts feel less fatigued or worn out and more alert; whether this also holds if modafinil if taken chronically needs to be determined.

- Amphetamines/methylphenidate:
 - Second line for sleep attacks.
 - Methamphetamine for pts with severe sleepiness.
 - Methylphenidate usually well tolerated; half-life of 3–4 h, but sustained release formulations available.
 - Emerging evidence suggests that amphetamines administered chronically for medical indications can/should be continued for elective surgery.
 - In case of hypotension, direct-acting vasopressors (phenylephrine or epinephrine) should be used, since response to indirect-acting vasopressors (ephedrine) will be attenuated secondary to catecholamine depletion.
- Sodium oxybate:
 - To treat nighttime insomnia and dysomnia, thus decreasing excessive daytime sleepiness and cataplexy.
 - Risk of respiratory depression (black-box warning).
 - May worsen OSA, especially in conjunction with sedative hypnotics or other CNS depressants.
 - Half-life 3–4 h.
- TCAs:
 - Imipramine, clomipramine, and protriptyline are used to treat cataplexy.
 - Unfavorable side-effect profile (e.g., anticholinergic, orthostatic hypotension, antihistaminergic, leading to sedation).
 - Increased risk of periop hypotension.
 - Potential of tachycardia/dysrhythmia with coadministration of ketamine, meperidine, and local anesthetics with epinephrine.
- SSRIs:
 - Fluoxetine and venlafaxine are less potent in treating cataplexy compared with TCA but have a favorable side-effect profile.
 - Theoretical concerns for serotonin syndrome: Mild: Tachycardia, myoclonus, restlessness, dilated pupils, anxiety, diaphoresis; Severe: Muscle rigidity, hyperthermia, multiorgan failure).
 - Periop drugs with potential SSRI interaction: Fentanyl, metoclopramide, 5-HT₃ antagonists, meperidine, linezolid, methylene blue.

Assessment Points

| System | Effect | Assessment by Hx | PE | Test |
|--------|--|---|----|---|
| CNS | Reduced concentration of neurotransmitter hypocretin in lateral hypothalamus May have altered anesthetic requirements | Excessive daytime sleepiness, cataplexy, hallucinations, sleep paralysis | | Polysomnography, multiple sleep latency test, reduced hypocretin concentration in CSF |
| HEENT | Increased risk of airway obstruction in pts on sodium oxybate | | | |
| CV | Side effects of medications: TCAs Amphetamines | Orthostatic hypotension Catecholamine depletion and profound hypotension | | BP change on standing |
| MS | Sleep paralysis, cataplexy | Ask about frequency and severity | | |

Key References: Leschziner G: Narcolepsy: a clinical review, *Pract Neurol* 14(5):323–331, 2014; Burrow B, Burkle C, Warner DO, et al.: Postoperative outcome of patients with narcolepsy. A retrospective analysis, *J Clin Anesth* 17(1):21–25, 2005.

Perioperative Implications

Preoperative Preparation

- Review medications and ask about the typical frequency and presentation of narcoleptic attacks (duration), cataplexy (partial vs. complete), sleep paralysis (duration).
- It is considered safe to continue medications for narcolepsy for elective surgery, even chronically used methamphetamine.
- Especially in outpatients on sodium oxybate, consider avoiding longer-acting sedatives such as midazolam.

Monitoring

- For potential change in anesthetic requirements, consider using an EEG monitor.
- For hemodynamic changes in pts on methamphetamine and/or TCAs, low threshold for placing arterial catheter.
- Use relaxometry to differentiate between residual curarization and cataplexy/sleep paralysis.
- Use direct-acting vasopressors (phenylephrine) to treat hypotension in pts on methamphetamine.
- Effect of direct-acting vasopressors may be enhanced in pts on TCAs.

Airway

- No special concerns

Induction and Maintenance

- Hemodynamic changes in pts on methamphetamine and/or TCAs (see Monitoring).
- Fentanyl, metoclopramide, and 5-HT₃ antagonists increase risk for serotonin syndrome in pts on SSRIs (clinical relevance unknown).

Extubation

- Cataplexy/sleep paralysis may mimic postop residual curarization.

Adjuvants

- Consider using local anesthetic without epinephrine for local infiltration/nerve blocks.

Postoperative Period

- Cataplexy/sleep paralysis may mimic postop residual curarization.
- Hallucinations may be misdiagnosed as postop/emergence delirium.
- Consider longer than usual PACU stay or ICU admission (overnight) for pts on sodium oxybate, depending on length of case, sedatives/hypnotics

administered intraop, and expected opioid requirements postop (increased risk for airway obstruction/respiratory depression and death).

- If shivering occurs in pts on SSRIs, meperidine may trigger serotonin syndrome.

Anticipated Problems/Concerns

- Retrospective study with 10 pts and 27 elective procedures under general anesthesia and endotracheal intubation showed no increase in periop complications; in this study only pts who received their

narcolepsy medication (five of them were on methamphetamine, none on modafinil or sodium oxybate) before the procedure were included.

- Although existing literature suggests that pts with narcolepsy do not have an increased risk for periop complications, clinical suspicion—especially for narcoleptic drug-anesthetic interaction and narcoleptic symptoms complicating the periop course—must be maintained.

Necrotizing Enterocolitis

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Risk

- Most common life-threatening intestinal surgical emergency in the newborn.
- Occurs predominantly in premature infants, with 75% in infants weighing <1500 g.
- Increasing incidence in term and near-term neonates as well.

Perioperative Risks

- CV instability, acidosis, shock, bowel ischemia, bacteremia, patent ductus arteriosus, polycythemia

Worry About

- Persistent metabolic acidosis and intestinal perforation are ominous signs.

Overview

- Presents commonly with generalized signs of sepsis, including glucose instability, hypothermia, apnea, feeding intolerance, and metabolic acidosis.
- The terminal ileum is most commonly involved, followed by the distal small bowel and ascending colon. Bowel ischemia may lead to gangrene of the bowel with perforation as well as peritonitis, CV and respiratory collapse, shock, and death.
- Multisystem failure commonly involves the respiratory, CV, renal, and hepatic systems. Abnormal elevated inflammatory mediators, such as TNF, IL-6, and PAF, are associated.

- In severe cases, the abdominal wall may be erythematous, signifying intestinal perforation and peritonitis.
- Pneumatosis intestinalis is evident as a linear collection of air and hydrogen gas in the wall of a dilated loop of bowel; it may extend into the portal venous circulation.

Etiology

- Associated with bowel ischemia, enteral feeds, infection, and prematurity. Clearest link is with prematurity, leading to the theory that an underlying developmental immaturity of bowel is potentially the initiating problem leading to this life-threatening condition.

Assessment Points

| System | Effect | Assessment by Hx | PE | Test |
|--------|---|---|--|---|
| CV | Shock PDA | Pulm edema, RDS, shock | Murmur BP/HR | ABG, BP UO |
| RESP | RDS | Apnea or tachypnea | | ABG CXR |
| ID | Sepsis | Bacteremia Peritonitis | Abdominal wall cellulitis, peritonitis | Blood and peritoneal fluid cultures |
| GI | Peritonitis, bloody stools, malabsorption | Large feeding residuals, bilious emesis | Residuals, guaiac stools | Lytes, bowel sounds, KUB examination Temperature instability |
| RENAL | Prerenal failure | | UO, BP | BUN, Cr |
| HEME | DIC Polycythemia | Bleeding | | Hct, plt count, fibrinogen PT/PTT |

Key Reference: Henry MC, Moss RL: Necrotizing enterocolitis, *Annu Rev Med* 60:111–124, 2009.

Perioperative Implications**Preoperative Preparation**

- Most neonates can be treated medically with fluid resuscitation, antibiotics, ventilatory support, and hyperalimentation.
- Surgery is indicated for pneumoperitoneum from intestinal wall perforation, intestinal gangrene (detected by abdominal paracentesis), and the presence of portal vein gas. Other indications include clinical deterioration, abdominal wall erythema, and an unresolved ileus.
- Discontinue enteral feeds and insert NG tube connected to suction for intestinal decompression.
- Therapeutic goals include normalization of vital signs and ensuring adequate oxygenation and ventilation (e.g., tracheal intubation, mechanical ventilation, adequate perfusion).

- Ensure vigorous fluid resuscitation to keep up with third-space losses from peritonitis and sepsis.
- Correct metabolic acidosis (achieved through fluid resuscitation).
- Inotropic agents such as dopamine and dobutamine may be required to optimize cardiac output.
- Correct coagulopathy with FFP, plts, and packed RBCs.
- Administer broad-spectrum antibiotics, with anaerobic coverage highly considered as well.

Monitoring

- Routine plus glucose and lytes

Induction/Maintenance

- Potent anesthetic agents are poorly tolerated.
- A carefully titrated narcotic and muscle relaxant technique is satisfactory.
- N₂O is usually avoided because of its potential for causing bowel distention.

- Fluid resuscitation (lactated Ringer solution, 5% albumin, and sometimes packed RBCs) is actively carried out during surgical procedures.

Postoperative Period

- Closely monitor in NICU for ongoing fluid requirements as third-space loss continues.
- Prolonged TPN is often required.
- Stricture formation leading to partial or total bowel obstruction is a common complication in both medically and surgically treated neonates.
- Short-bowel syndrome can occur, leading to long-term complications.

Anticipated Problems/Concerns

- Hypovolemia and bowel ischemia
- Acidosis, shock, and death