Clinician's guide to hospitalization and anesthesia for people with idiopathic hypersomnia and narcolepsy types 1 and 2

Hypersomnia sleep disorders are chronic neurologic conditions defined by excessive daytime sleepiness and several other debilitating symptoms. Person(s) with hypersomnias (PWH), such as idiopathic hypersomnia or narcolepsy type 1 or 2, may face unique challenges when hospitalized or having anesthesia (including during dental procedures and colonoscopies).

PWH and healthcare teams need to pay special attention to managing hypersomnia symptoms before, during, and after anesthesia or hospitalization. This guide helps with preparation, expectations, and understanding how hypersomnias impact care.

Special consideration is needed because PWH:

- Often require a specific sleep schedule and medicines taken at precise times to best manage symptoms. A procedure or hospitalization may significantly disrupt sleep and medicine schedules and lead to severe sleepiness and/or cognitive dysfunction that could mimic or cause delirium.
- Often have symptoms that will raise concerns, or be confused with an adverse response to medicines or a worsening condition, if healthcare staff are not prepared. If sleep and hypersomnia medicine schedules are not maintained, symptoms are likely to get much worse.
- May respond differently to anesthesia and be slower to awaken from anesthesia (delayed emergence).
- Have a higher risk of sleep apnea.
- May need to wait more than the usual 24 hours after anesthesia before safely driving or operating heavy machinery.

Special considerations for medicines:

- Hypersomnia medicines often have significant interactions with other medicines.
- Sedating medicines (such as opioids, benzodiazepines, and anesthetics) can also worsen hypersomnia symptoms.
- Many hypersomnia medicines may not be available in the hospital pharmacy, have unusual dosing schedules, or are scheduled substances. Existing processes for securing and dosing medicines may need accommodations.

Recognize hypersomnia symptoms

Healthcare teams will need to recognize hypersomnia symptoms and respond quickly if they're worsening. Symptoms may include:

- Excessive daytime sleepiness
- Brain fog, causing difficulty thinking or following directions
- Extended nighttime sleep (9 to 12 or more hours)
- Daytime sleep needs (required naps which may be hours long)
- Significant difficulty awakening from sleep, with severe and/or prolonged sleep inertia (sleep drunkenness)
- Automatic behaviors, in which PWH behave in ways that seem normal, but later forget what they said or did
- Autonomic symptoms, such as orthostatic hypotension, overactive bowel or bladder, and difficulties with temperature regulation
- Disrupted nighttime sleep
- Cataplexy, a sudden temporary muscle weakness triggered by strong emotions (such as laughing), during which the person remains fully conscious and aware
- Sleep paralysis
- Sleep-related hallucinations
- Sudden sleep attacks, including microsleeps

Plan accommodations

- Allow PWH to meet their sleep needs whenever possible. Schedule tests or surgeries at times of day that will least disrupt their normal sleep pattern. As much as possible, create optimal sleep conditions during scheduled sleep times.
- Maintain dosing schedules whenever possible. Delaying or stopping medicines can lead to rapid worsening of symptoms.
- Plan for times that medicines can't be taken by mouth, such as after GI surgery. Are there any reasonable substitutions?
- Prepare to safely store and dispense medicines that may not be available at the hospital or facility.
- Two hypersomnia medicines, flumazenil and oxybates, have unusual dosing schedules and other considerations.

Special accommodations for flumazenil

Compounded flumazenil creams or lozenges are used to increase wakefulness in PWH. Hospital pharmacies are unlikely to have enough flumazenil for hypersomnia treatment, so PWH will need to bring it from home. Accommodations are needed to store and precisely dispense it.

Special accommodations for oxybates

Oxybates must be stopped the night before and the night after anesthesia and carefully timed with opioids to avoid dangerous interactions. For hospitalizations of a few days or less, stopping oxybates may be appropriate. For longer hospitalizations, accommodations will be needed. **Immediate-release oxybates (such as Xyrem and Xywav)** have a half-life less than 1 hour and are considered cleared from the body within 5 hours. Our medical advisory board (MAB) recommends not taking opioids within 6 hours of an oxybate dose. **Extended-release oxybates (such as Lumryz)** have a time to elimination of 9 hours – similar to that for 2 doses of immediate-release oxybates. Our MAB recommends not taking opioids within 9 hours of an oxybate dose.

Oxybate access

In the U.S., oxybates are dispensed only by certified pharmacies, shipping directly to PWH using special security measures. They must be signed for by an adult age 21 or over with a valid ID. They cannot be shipped to any business address, such as a hotel or school, or any facility with a DEA number, including most hospitals and pharmacies. They can be shipped to FedEx holding locations (where pick up requires the tracking number) or most residential addresses. (Apartment complexes or dorms require a locked mail room if the delivery can't be made directly to the apartment.) When the collaborative decision is made by a PWH and their sleep and hospital doctors to continue oxybate

treatment during a hospitalization, PWH will have to bring the oxybates from home or arrange approved delivery. For planned hospitalizations, early refills may be possible.

Oxybate security accommodations

Security at the hospital or facility is important, as oxybates are scheduled medicines and very expensive. Accommodations are needed to meet the precise dosing schedule while following safety and security procedures. Whenever possible, store oxybates in the PWH's locker and have staff monitor the PWH's mixing and taking their own doses. Since oxybates are very expensive and difficult to replace, it's critical not to waste any.

Oxybate dosing accommodations

Oxybates are liquid or powder forms of GHB (gamma-hydroxybutyrate) that PWH mix with water and take in 1 to 3 doses. Some PWH take a single dose at bedtime. Most PWH take 2 doses, the first at bedtime and the second 2.5 to 4 hours later, immediately upon awakening. Some PWH need a third dose. These doses may vary, and precise measurement and timing of doses is critical. Taking a dose that is too high or early can cause dangerous side effects. Taking a dose that is too small or late can lead to significantly reduced efficacy.

Follow the home regimen as closely as possible:

- Caloric consumption must stop 2 hours before the first dose
- PWH mix all doses at bedtime and keep them at the bedside
- Some PWH need alarms to wake up for subsequent doses
- It is critical that the subsequent doses are available to take immediately after waking
- If an early morning appointment is planned, the dosing schedule for the night before may need to be adjusted

Oxybates are heavily sedating. PWH may be very difficult to awaken, especially soon after each dose. If awakened while oxybates are in effect, the PWH will likely experience extreme discomfort such as severe nausea, dizziness, and disorientation.

How to manage sedating medicines in PWH

- Opioids are sedating for most people, but they may have the opposite effect on PWH, decreasing sedation. Ask PWH about their experiences with these medicines.
- If the PWH is known to be sensitive to sedating medicines or will be taking them for the first time, they will need closer-than-usual monitoring.
- Consider alternatives to limit the use of sedating medicines. When you must choose between pain control and hypersomnia symptom control, ask PWH which is their highest priority.

Customize anesthesia plans for PWH

- Schedule procedures for a time of day that least disrupts the PWH's normal sleep schedule.
- If the PWH has had complications with anesthesia or this is their first procedure with anesthesia, use closer-than-usual monitoring for alertness or oversedation. Complications may include delayed awakening, cardiovascular from medicine interactions, and awareness during anesthesia. PWH may need higher or lower doses of anesthesia due to oversensitivity to sedating medicines or their history of treatment with scheduled medicines.
- If the PWH has had anesthesia complications, review the records. Provide details to the perioperative team including the anesthesiologist and surgeon, so they can understand the anesthetic considerations and consider mitigating steps.
- Inform the healthcare team that PWH may be more groggy, disoriented, and unresponsive than typical patients, and it can be difficult to determine if these symptoms are due to their hypersomnia or a complication.
  - Have flumazenil, which can improve wakefulness in some PWH (Trotti, 2016), and the PWH's prescribed stimulants available to treat delayed emergence.
  - If there is any reason to suspect that oxybates may not have been held around the time of anesthesia, diclofenac or other NSAIDs may help limit passage of oxybates into the brain (Rodriguez-Cruz, 2021).
- If delayed emergence or other complications are likely, consider using sedation, nerve blocks, or shorter-acting anesthetics.
- Consider regular- and long-acting nerve blocks and "multi-modal analgesia" (multiple different techniques or types of medicines for pain control) to minimize the need for opioids during and after the procedure.
- Carefully review sleep studies to ensure any sleep-related breathing problems are treated appropriately. For example, sleep apnea has been independently associated with adverse outcomes following anesthesia.
- Decide how long PWH should wait (which may need to be longer than the usual 24 hours) and if they will need their hypersomnia medicines adjusted before driving or operating heavy machinery.
- If anesthesia complications happen, make sure PWH get a copy of their anesthesia records.

For more information, including references and resources, see our web page for doctors at www.hypersomniafoundation.org/professionals/anesthesia.

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Disclaimer

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