

BENZODIAZEPINE OVERDOSE

(Last updated 12/08/2019; Reviewers: Amelia Barwise, MBBCh, BAO; Chanyan Huang, MD)

PRESENTING COMPLAINT: Confusion, slurred speech,coma

FINDINGS

- **A** Check Airway
- **B** Respiratory depression rare unless co-ingestion
- **C** BP, HR normal
- **D** Variable altered (V,P,U,D)*
- **E** ataxia, nystagmus, hallucinations, hypotonia, weakness
- **Lpc** Glucose, acetaminophen, ethanol and salicylate levels, electrolytes
- **Upc** Hyperechoic focus consistent with ingested pills within the stomach

***V** (verbal), **P** (pain), **U** (unconsciousness), **D** (delirious)

Upc (point of care ultrasound) **Lpc** (point of care labs)

OTHER HISTORY

- Other symptoms: “Coma with normal vital signs”(may resemble ethanol overdose), altered (most commonly depressed) mental status, blurred vision, hallucinations, weakness, paradoxical agitation
- Predisposing conditions: Suicidal ideation, iatrogenic/accidental overdose, liver failure
- Most intentional overdoses involve ethanol as a co-ingestant

DIFFERENTIAL DIAGNOSIS

Hypo/hyponatremia, hypoglycemia, head injury, stroke or intracranial bleed, meningitis and encephalitis, head trauma, carbon monoxide poisoning, alcohol ingestion or overdose of other drugs including antidepressants, neuroleptics, antihistamines, barbiturates, and sedative- hypnotics, opiates and recreational street drugs

OTHER INVESTIGATIONS

Lab findings:

- Benzodiazepines not detected in standard urine screening tests for drugs of abuse. However, the most common BZD urine test identifies metabolites of 1,4-benzodiazepines, such as oxazepam, after three hours of ingestion This test may not detect clonazepam, lorazepam, midazolam, or alprazolam.
 - Check fingerstick glucose, serum electrolytes, BUN, creatinine clearance

- Check for other drugs including acetaminophen, salicylates, opiates, etc and ethanol levels (blood or urine).
- ECG: for cardiac arrhythmias and QT interval from other substances.
- Pregnancy test: in women of childbearing age.
- ABG: if respiratory depression is present, consider carbon monoxide levels
- Imaging:
 - Chest x-ray if respiratory depression
 - CT head if trauma is suspected or unclear cause of drowsiness

THERAPEUTIC INTERVENTIONS

- ABCs
- Supportive Care
- Airway protection as needed, including intubation
- Respiratory monitoring: end tidal CO₂ can be useful for monitoring patients at risk for hypoventilation
- Activated charcoal is NOT recommended
- Medications: Flumazenil (Romazicon) is a specific antidote for BZDs, however its risks usually outweigh any possible benefit. In long-term BZD users, flumazenil may precipitate withdrawal and seizures
 - In adults, 0.2 mg given intravenously (IV) over 30 seconds. Repeated doses of 0.2 mg, to a maximum dose of 1 mg may be given. If re sedation occurs, repeat the regimen to a maximum of 3 mg in 1 hour
 - In children, the initial dose is 0.01 mg/kg given IV over 15 seconds (maximum dose 0.2 mg). The initial dose may be followed at one or more minute intervals with up to four repeat doses of 0.005 to 0.01 mg/kg (maximum 0.2 mg) per dose. The maximum dose should NOT exceed 1 mg total or 0.05 mg/kg; the lower dose is preferred
 - Consult poison control if Flumazenil infusion is contemplated

ONGOING TREATMENT

- Follow-Up with Poison Control, if concern about poisoning from other sources/Psychiatry if suicidal attempt
- Labs and imaging to rule out co-existent cause
- Admit to ICU for monitoring if needed
- If no concerns and patient can ambulate safely consider discharge
- Manage Complications:

- Withdrawal from benzodiazepines can cause tremors, anxiety, perceptual disturbances, dysphoria, psychosis, seizures and can be life threatening (more likely in chronic users).
- Aspiration secondary to poor airway control may require antibiotics

CAUTION

- Complications:
 - Propylene glycol toxicity is rare but can occur in patients receiving large or continuous infusions of parenteral benzodiazepines (lorazepam)
 - Symptoms include skin and soft tissue necrosis (from extravasation), hemolysis, cardiac dysrhythmias, hypotension, lactic acidosis, seizure, coma, and multisystem organ failure

REFERENCES & ACKNOWLEDGMENTS

Acknowledgement: *Sandhya Samavedam, MBBS*

– Marraffa JM, Cohen V, Howland MA. Antidotes for toxicological emergencies: a practical review. *Am J Health Syst Pharm.* Feb 1 2012;69(3):199-212

– The Flumazenil in Benzodiazepine Intoxication Multicenter Study Group. Treatment of benzodiazepine overdose with flumazenil. *Clin Ther.* Nov-Dec 1992;14(6):978-95

– Buckley NA, Dawson AH, Whyte IM, O'Connell DL. Relative toxicity of benzodiazepines in overdose. *BMJ* 1995; 310:219.

– Mowry JB, Spyker DA, et al. 2012 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 30th Annual Report. *Clin Toxicol (Phila).* Dec 2013;51(10):949-1229

– Pavuluri, MN, Janicak, PG, et al. *Principles and Practice of Psychopharmacotherapy* ((2010).5th ed.). Philadelphia, PA: Wolters Kluwer Health / Lippincott Williams & Wilkins. p. 535. ISBN 978-1-60547-565-3

–UptoDate https://www.uptodate.com/contents/benzodiazepine-poisoning-and-withdrawal?search=BENZODIAZEPINE%20OVERDOSE&source=search_result&selectedTitle=1~29&usage_type=default&display_rank=1