

Novel Approaches in the Management of Severe Alcohol Withdrawal

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Disclosure

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Objectives

- Given a patient case, develop a patient-specific medication regimen for alcohol withdrawal management.
- Discuss concepts and recent literature related to use of adjunctive agents.
- Compare and contrast the role of barbiturates with benzodiazepines in alcohol withdrawal management.

What is Severe Alcohol Withdrawal?

- A: Alcohol withdrawal that occurs in an ICU
- B: Alcohol withdrawal that is associated with severe hemodynamic alterations
- C: Alcohol withdrawal that is associated with hallucinations
- D: Alcohol withdrawal that is associated with delirium

Alcohol withdrawal in the ICU

- Often happens in conjunction with critical illness from other causes
 - Trauma
 - Infection
 - Elective surgery
- Assessment of withdrawal can be challenging in this population
 - Ability to communicate
 - Confounding comorbidities (delirium, pain, hemodynamic alterations)
- *Just because a patient is withdrawing from alcohol while admitted to the ICU **does not** mean the withdrawal is severe*

Case:

- JS is a 45 year old male struck by a car crossing the street currently with a blood alcohol level of 120 mg/dL. JS is admitted to the trauma ICU with multiple fractures and a right sided pneumothorax. JS is currently displaying lateral nystagmus and slurred speech. The nurse asks if the patient should be placed on a CIWA-based protocol for benzodiazepine administration at this point in time. You answer:
 - A. Yes – JS is withdrawing and needs symptom-triggered therapy
 - B. No – Symptom-triggered therapy is not indicated in the ICU
 - C. No – The patient is still intoxicated
 - D. Yes – To minimize the risk of developing severe alcohol withdrawal

Alcohol withdrawal vs intoxication

- Just because a patient is agitated doesn't mean they are in withdrawal
- Be cautious not to medicate patients who are still intoxicated
- Benzodiazepine administration may promote respiratory compromise in the alcohol-intoxicated patient

Assessing risk of withdrawal in the ICU

How likely is our patient to withdraw from
alcohol?

Back to JS

- Upon questioning, JS endorses that he drinks alcohol 6 days per week, and usually consumes a 6 pack of beer per occasion.
- Which of the following would be a good screening tool to assess his risk for withdrawal?
 - A: Clinical Institute for Withdrawal from Alcohol score (CIWA)
 - B: AUDIT-C questionnaire
 - C: AST/ALT ratio
 - D: Blood alcohol level of 120 mg/dL on admission

Screening for Alcohol Dependence

- Validated screening tools- most widely used
 - CAGE
 - AUDIT-C
- All ports of entry to institution
 - Emergency Department (ED)
 - Pre-op
 - Transfer from outside hospital (OSH)

AUDIT and CAGE

- Alcohol use disorders identification test (AUDIT)
 - 10-question survey that includes 3 about the quantity and frequency of current drinking, and 7 related to drinking history
 - AUDIT-C that uses the first three AUDIT questions
 - Positive AUDIT-C; Men > 4; Women > 3
- Cut down, annoyed, guilty, and eye opener questionnaire (CAGE)
 - Focuses on signs of impaired control, use of alcohol despite consequences, and dependence
 - Limitation is its inability to differentiate between current and former alcohol abuse
 - Positive: Yes to two or more questions

AUDIT-C - Patient JS

Questions	Points				
	0	1	2	3	4
How often did you have a drink containing alcohol in the past year?	Never	< monthly	2-4 times/month	2-3 times per week	> 4 times per week
How many drinks did you have on a typical drinking day in the past year?	0 to 2	3 to 4	5 to 6	7 to 9	> 10
How often did you have 6 or more drinks on one occasion in the past year?	Never	< monthly	monthly	weekly	daily
Positive AUDIT-C; Men > 4; Women > 3					

- JS drinks 6 times per week – 4 points
- JS drinks 6 beers per day – 2 points
- JS drinks 6 beers per occasion daily – 4 points
- AUDIT-C score for JS = 10 (positive)

Risk Assessment

High Risk

- In active withdrawal
- Delirious
- History of alcohol withdrawal
- **History of seizures**
- **History of Delirium Tremens (DTs)**

Low Risk

- Screen positive only
- No symptoms
- Communicative
- No history of seizures
- No history of withdrawal

Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

- Potentially a useful tool to assess the risk of a patient developing severe alcohol withdrawal
- Based on yes/no answers to 10 questions/Items
 - A yes answer equals one point
 - A score ≥ 4 has a 100% sensitivity and specificity in a small pilot study to detect complicated alcohol withdrawal in medically ill patients

PAWSS

1. Have you consumed any amount of alcohol within 30 days?
2. Have you ever experienced previous episodes of alcohol withdrawal?
3. Have you ever experienced alcohol withdrawal seizures?
4. Have you ever experienced delirium tremens or DT's?
5. Have you ever undergone alcohol rehabilitation treatment?
6. Have you ever experienced blackouts?
7. Have you combined alcohol with downers (benzodiazepines) in the past 90 days?
8. Have you combined alcohol with any other substance of abuse during the last 90 days?
9. Was the patient's blood alcohol (BAL) on presentation >200?
10. Is there evidence of increased autonomic activity (HR>120, tremor, sweating)?

Patient Interaction Required

- Screening tools require honest patient interaction
- Biomarker predictors of withdrawal are lacking
 - Mean corpuscular volume, AST/ALT, Gamma-Glutamyl Transferase
 - Carbohydrate deficient transferrin
 - Phosphatidylethanol

Alone or in combination may predict exposure, not withdrawal
Patient symptoms, history, medication requirement paint the picture

JS Begins to worsen...

24 hours into the ICU stay, JS becomes agitated with associated HR to 120, BP to 160/95, with tremors and sweating. He remains on nasal cannula at 2L/min, and is currently CAM negative. Which of the following tools would be best to quantify the severity of his withdrawal?

- A: PAWSS
- B. CIWA-Ar
- C. RASS score
- D. CAM-ICU

Monitoring of Withdrawal Symptoms

- **CIWA (A, Ar, AD)**

- Most widely cited
- Implementation of Ar associated with improved outcomes
- Not validated in the following patients
 - ICU patients
 - Delirious patients/history of alcohol withdrawal seizures
 - Non-communicative patients (for any number of reasons)

- **MINDS (Minnesota Detoxification Scale)**

- Limited published data
- Targeted for ICU patients
- Not validated

Reoux JP et al. *Am J Addict.* 2006; 15(1):85-93.

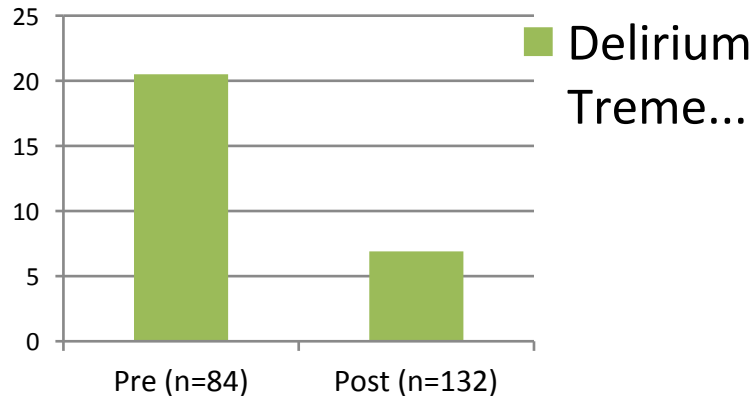
Sullivan JT et al. *J Clin Psychopharmacol.* 1991; 11(5):291-5.

Jaeger TM et al. *Mayo Clin Proc.* 2001; 76(7):695-701.

Stanley KM et al. *Pharmacotherapy.* 2003; 23(7):843-54.

Decarolis DD et al. *Pharmacotherapy.* 2007; 27(4):510-8.

CIWA in General Medicine Patients



Significant patient characteristics/metrics/outcomes

Variable	Pre	Post	<i>p</i> value
Treated with benzo†	74 (88.1)	108 (81.8)	NS
Duration therapy, hrs*	55.5 ± 54.5	44.9 ± 49.6	NS
Benzo equivalents, mg *	20.1 ± 20.7	20.1 ± 29.7	NS
Seizure†	0	0	NS

*Data presented in median

†Data presented as n (%)

Single center, before-after analysis of 216 general medicine patients admitted at risk for alcohol withdrawal pre (n=84) and post (n=132) implementation of a CIWA-based alcohol withdrawal guideline at St Mary's Hospital, Rochester MN between January 1, 1995, and December 31, 1998.

MINDS

Symptom	Score
Pulse (High)	0-2
Diastolic blood pressure (High)	0-2
Tremor	0-6
Sweating	0-6
Hallucinations	0-3
Agitation (RASS score)	0-9
Orientation	0-6
Delusions	0 or 6
Seizures	0 or 6

Dosing (lorazepam) based on MINDS score

Scores broken into tertiles:

- >20
- 15-19
- <15

Pharmacotherapy - “typical” alcohol withdrawal

- Gamma Aminobutyric Acid (GABA) receptor agonists
 - Benzodiazepines
 - Barbiturates (Phenobarbital)
- Adrenergic symptoms
 - Clonidine
 - Dexmedetomidine
- Delirium/Hallucinations
 - Antipsychotic agents

A note on symptoms... Utilize targeted therapy

- CNS excitation: Anxiety, restlessness, bothered by light/sounds – treated with GABA receptor agonists
- Adrenergic hyperactivity: N/V, tremor, sweating, hypertension, tachycardia – treated with sympatholysis (clonidine/dexmedetomidine)
- Delirium: Haloperidol

JS was evaluated and found to have a CIWA score of 16. Which of the following interventions would be most appropriate at this time?

- A: Symptom-triggered lorazepam for CIWA >10
- B: Dexmedetomidine 0.4 mcg/kg/hr
- C: Fixed dose lorazepam 2mg IV q4 hours
- D: Propofol, initiated at 30 mcg/kg/min

Benzodiazepines

- The foundation of therapy in most ICU literature
- No single agent preferred
- Caution with benzodiazepine intoxication!
 - Watch for: Nystagmus, slurred speech
- Symptom-triggered therapy (CIWA-Ar) in **appropriate patients**

Don't forget the thiamine!

- Thiamine is a co-factor in carbohydrate metabolism
- Thiamine deficiency (both intake and storage) often seen in alcoholics, can result in significant CNS deficits
 - Amnesia, confabulation
 - Nystagmus, ataxia
- All patients treated for alcohol withdrawal should be given 100 mg IV daily of thiamine for 3-7 days for prevention
- Treatment dose: 500mg IV three times daily

Case 2

EV, 35 yo M, dropped off to the ED symptoms consistent with alcohol withdrawal. He is somewhat interactive, endorses AUD, AUDIT/ CAGE/ PAWSS. CIWA scores ranging 18-24. He receives vitamins and lorazepam 4 mg IV x 1 with minimal improvement. Team is looking for recommendations for treatment of AWS (NPO), you recommend:

- A. Continue lorazepam (2-8mg IV q 2 hours prn withdrawal)
- B. Phenobarbital (10mg/kg IBW x 1 or 130 mg IV every 8 hours prn)
- C. Dexmedetomidine (0.4-1.2 mcg/kg/hr titrated prn withdrawal)
- D. Haloperidol (2.5-10mg IV q 4 hours prn withdrawal)
- E. Diazepam or phenobarbital prn w/d + haloperidol prn hallucination

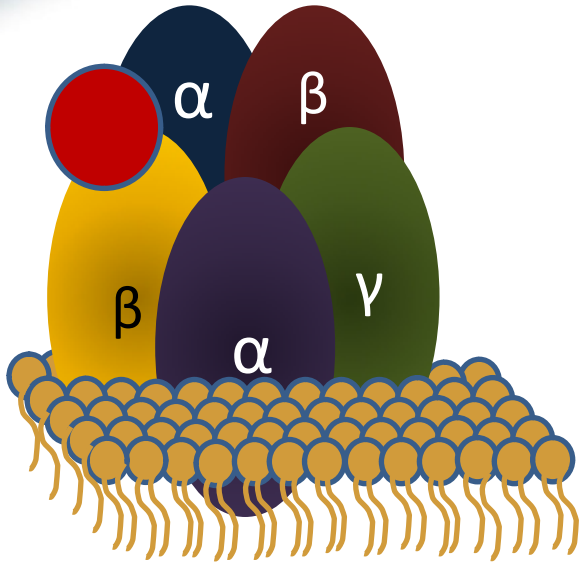
Pharmacotherapy

- Gamma Aminobutyric Acid (GABA) receptor agonists
 - Benzodiazepines (intermittent dosing vs continuous infusion)
 - Barbiturates (Phenobarbital)
 - Propofol (Severe and Intubated patients)
- Adrenergic symptoms
 - Clonidine/Dexmedetomidine
- Delirium/Hallucinations
 - Antipsychotic agents
- Refractory withdrawal
 - Dexmedetomidine
 - Propofol
 - Ketamine
- Other adjunctive agents with specific rationale: Baclofen, Valproate, Gabapentin

Discussion

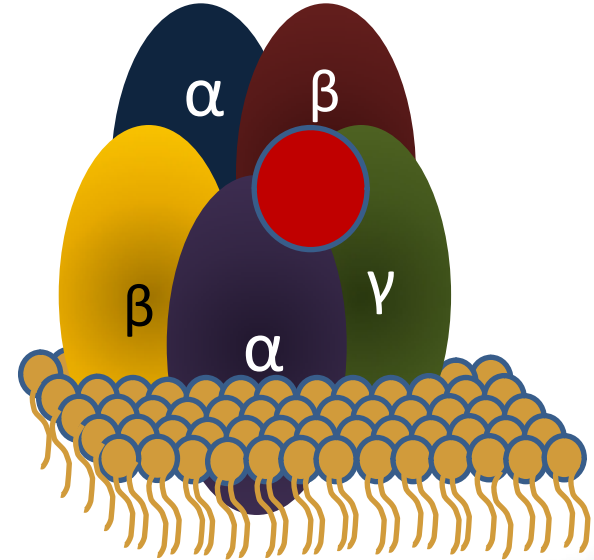
- Risk for severe withdrawal: High
- Symptom triggered therapy common
 - Driven by non-inferior/better outcomes with less medication exposure
 - Benzodiazepine based therapies
- Targeting GABA with benzodiazepines considered backbone
 - Effective and Safe

Barbiturate Binding



Endogenous GABA Independent at high doses

Benzodiazepine Binding



Endogenous GABA Dependent

Weight-based Phenobarbital for EtOH Withdrawal in the ED

- Prospective, randomized, blinded, placebo controlled
- 102 patients, 51 received 10mg/kg IV phenobarbital load
- All patients CIWA guided institutional protocol
- Phenobarbital patients required less ICU admission (8% vs 25%), less lorazepam infusions (4% vs 31%), less lorazepam overall, and trend towards less ICU and Hosp LOS
- *A good way to “hide” GABA agonists in the ED*

Patient 2 Progression

EV is put on symptom driven lorazepam, becomes less interactive. Proxy now provides history: previous ICU admissions for etoh w/d, twice requiring prolonged intubation, ? seizure. CIWA ranging 18 – 24, received lorazepam 26mg in the ED over 2 hours, CIWA now 10 but intermittently agitated and hallucinating when he arrives in the MICU. You would recommend:

- A. Switch to continuous infusion of lorazepam
- B. Continue lorazepam prn and add phenobarbital
- C. Continue lorazepam prn and add dexmedetomidine
- D. Continue lorazepam prn and add haloperidol prn
- E. Continue lorazepam prn, add phenobarbital and haloperidol prn
- F. Continue lorazepam prn, add phenobarbital, haloperidol prn and dexmedetomidine

Benzodiazepines

- The foundation of therapy in most ICU literature
- No single benzodiazepine preferred
 - Caution high-dose intravenous lorazepam/diazepam due to propylene glycol toxicity – monitor osmolar gap
- Caution with continuous infusion!
 - Benzodiazepine intoxication, resistance with low endogenous GABA?
- Symptom-triggered therapy (CIWA-Ar or MINDS) in appropriate patients

Awissi DK et al. *Intensive Care Med.* 2013; 39:16-30.

Schuckit MA. *NEJM.* 2014; 317:2109-13.

Wilson KC et al. *CHEST.* 2005; 128:1674-81.

Multi-modal Approach

- Don't forget: multimodal approach with a GABA agonist backbone and symptom triggered (including clonidine) have:
 - Resulted in positive outcomes
 - Meta-analyses – adjunctive medications decrease symptoms
 - Adjunctive agents are univariate predictors of lower mortality with DT (in some studies)
- Prospective, randomized, double-blind trial
- Compared an infusion-titrated with a symptom-oriented bolus-adjusted (i.e., multi-modal) approach to symptom management

Symptom Triggered (Multimodal) Therapy: ICU

Significant patient characteristics/metrics/outcomes

Variable	Multimodal (n = 23)	Infusion-titrated (n = 21)	<i>p</i> value
Flunitrazepam, mg*	69.7	162	<i>P</i> < 0.01
Clonidine, mg*	1.2	61	<i>P</i> < 0.01
Haloperidol (mg)	180	1713	<i>P</i> < 0.01
Maximum Ramsay Sedation Scale (SAS)	4	5	<i>P</i> < 0.01
Pneumonia†	9 (39)	15 (71)	<i>P</i> < 0.01
Duration of withdrawal (days)	2	6	<i>P</i> < 0.01
Duration of Ventilation (days)*	6	12	<i>P</i> < 0.01
ICU LOS (days)*	8	14	<i>P</i> < 0.01

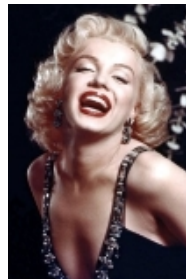
*Data presented as median †Data presented as n (%)

Titration of CIWA-Ar <10 or Ramsay 2-4 scale, HR and BP parameters.

Spies CD et al. *Intensive Care Med.* 2003; 29(12):2230-8.

Phenobarbital

- Some studies suggest phenobarbital may have a role in “benzodiazepine-resistant” alcohol withdrawal
- Has a long half-life (up to 4 days) in healthy adults
 - Provides an auto-taper, but once it’s in it’s in
- Caution use in:
 - Patients with a history of hypersensitivity to antiepileptics
 - Drug-drug interactions



Phenobarbital Escalation Protocol

- Retrospective evaluation of a combination of phenobarbital (escalating doses) and diazepam versus diazepam alone
 - Phenobarbital dose escalation (doses given if significant agitation within 1 hour of receiving last dose)
 - 65 mg ➡ 130 mg ➡ 260 mg
 - Protocol called for diazepam 200mg before initiation of IV phenobarbital with titration to SAS of 3-4.
 - Adjunctive propofol and haloperidol allowed in both groups.
- Patients: Admitted for alcohol withdrawal

Addition of Phenobarbital to Benzodiazepines in ICU

$p < 0.001$

Significant patient characteristics/metrics/outcomes

Variable	Benzo alone (n = 54)	Benzo+ Barb (n = 41)	P Value
Haloperidol use†	2 (4)	0	NR
Phenobarbital use†	9 (17)	24 (58)	$p < 0.01$
Intubation requirement†	26 (47.3)	9 (21.9)	$p < 0.01$
Days intubated	6.4 ± 1.6	3.1 ± 1.3	$p = 0.01$
Nosocomial Pneumonia intubated (%)	55.5	12.5	$p = 0.02$
*Data presented as mean ± SD †Data presented as n (%)			

No protocol (Cl/barb/prop) vs protocol
Caution not to over interpret findings

Duby et al

- Examined a protocolized treatment of alcohol withdrawal compared with non-protocolized management (pre-post design)
- Used RASS to titrate therapy
- Utilized escalating doses of diazepam (max dose 120 mg) followed by addition of phenobarbital 60-120-240 mg (every 30 min)

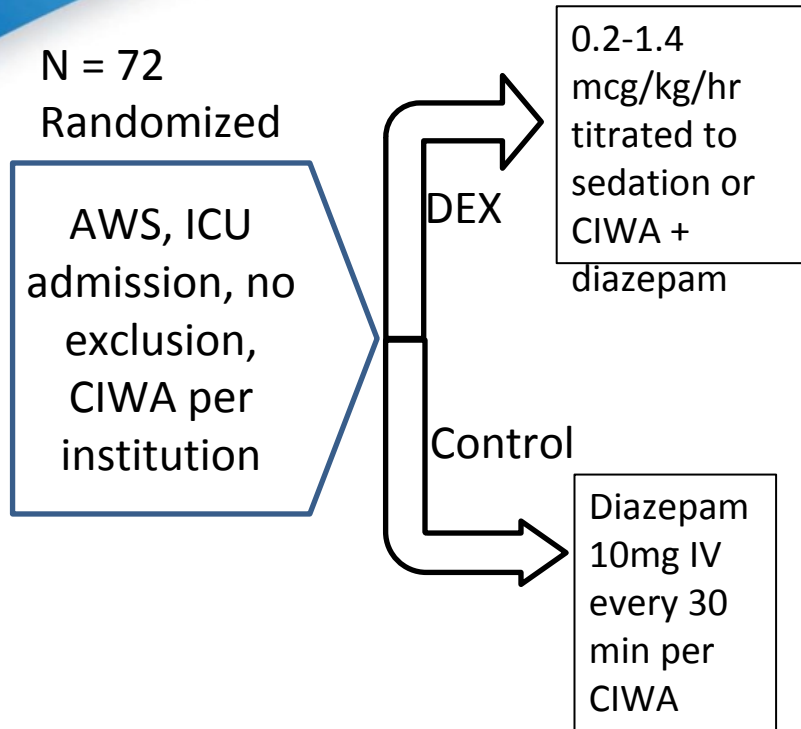
Benzodiazepine + Phenobarbital

- Due to trial design, significant differences between baseline characteristics of the two groups
 - Older age in the non-protocolized group
 - Higher severity of illness in the non-protocolized group

Variable	Non-Protocolized	Protocol	p value
ICU Length of Stay	9.6 days	5.2 days	0.0004
Intubation	22%	5%	<0.001
Ventilation duration	5.6 days	1.3 days	<0.001
Mean Benzodiazepine dose	320 mg	90 mg	0.0002
Mean Phenobarbital dose	50 mg	90 mg	0.04

AGAIN: Caution not to over interpret findings

Addition of DEX to BZD for AWS in the ICU



Outcomes

- 24 hour diazepam requirements → 20 vs 40 mg -less cumulative exposure
- ✓ ICU LOS → 50 vs 70 hrs
- ✓ Need for intubation → No difference
- ✓ Sedation quality → Sedation quality, communication, haloperidol requirements, all favorable
- ✓ Ability to communicate →
- ✓ Haloperidol requirements →

Trend of lower ICU/Hosp LOS exploratory

DEX: Benzodiazepine Sparing Agent

Other evidence:

- Only prospective, DB-RCT: decreased acute lorazepam requirements (-48 mg in 24 hours) but not prolonged requirements
- Retrospective, semi-matched: decreased acute lorazepam requirements (-11.6 mg in 12 hours)
- Case series and cohorts: decreased lorazepam requirements after initiation
 - Publication bias and natural progression of decreasing benzodiazepine requirements over time
 - Caution not to over interpret findings
 - With benzodiazepines, adjunctive DEX not associated with more seizures

Mueller SW, Crit Care Med 2014;42:1131-1139

VanderWeide LA, J Intensive Care Med 2016;31(3):198-204

Rayner S, Ann Intensive Care 2012;2:12

Lizotte RJ, Clin Pharmacol 2014;6:171-177

Crispo AL, Pharmacotherapy 2014;29:298-302

GABA Then Treat Symptoms

- Gamma Aminobutyric Acid (GABA) receptor agonists
 - Benzodiazepines (intermittent dosing vs continuous infusion)
 - Barbiturates (Phenobarbital)
 - Propofol (Severe and Intubated patients)
- Adrenergic symptoms
 - Clonidine/Dexmedetomidine
- Delirium/Hallucinations
 - Antipsychotic agents
- Refractory withdrawal
 - Dexmedetomidine
 - Propofol
 - Ketamine
 - Other adjunctive agents with rationale: Baclofen, Valproate, Gabapentin...

“you buy the tube”

Just not enough data yet

You Recommend a Multimodal Approach

- Escalated to phenobarbital q8 hours, lorazepam per CIWA, haloperidol prn hallucination and clonidine prn hyperadrenergic sx
- Then the weekend hits and it's October
 - Wisconsin Badgers are looking OK
 - Brewers almost made the playoffs
 - Packers are doing what they do, win
 - You left confident in your plan
- Monday morning...

Case Progression

Haloperidol held due to qtc concerns, initiated on lorazepam infusion (worsening hallucinations), clonidine to dexmedetomidine (delirium), phenobarbital continued and finally was intubated and started on propofol. It is day 9, EV's symptoms (sedation) are reasonably controlled and his breathing mechanics are suitable for extubation and is receiving the following medications. How would you de-escalate therapy to facilitate extubation?

- A. Lorazepam infusion 5mg/hr, discontinue
- B. Lorazepam 5mg/hr → 1mg/hr, d/c propofol 35mcg/kg/min prior to extubation
- C. Phenobarbital 130mg IV every 8 hours, discontinue
- D. Dexmedetomidine 0.5mcg/kg/hr, discontinue
- E. Discontinue propofol now, lorazepam 5mg/hr → 1mg/hr tomorrow

Caution with CIWA-Ar Use!

- Single-center, retrospective analysis of alcohol withdrawal (n=124)
- Symptom triggered appropriateness defined as:
 - Intact verbal communication (not delirious)
 - Medical record documented recent heavy alcohol consumption in the week before hospital admission and a history of alcohol dependence or abuse
- 60 (48%) met both criteria for symptom triggered therapy
- 64 (51%) **did not** meet both criteria for symptom triggered therapy
 - 20 (31%) met no criteria
 - 35 (55%) had not been drinking heavily
 - **9 (14%) did not have intact communication**

What can we use?

- CIWA-Ar in ICU: excluded or did not mention intubated patients
- MINDS (Minnesota Detoxification Scale): reasonable alternative
- Sedation Agitation Scale (SAS): Used to titrate pharmacotherapy
 - A score ≥ 5 triggered intervention, with a goal of 3-4 in the treatment trial (Gold et al)
 - A score of 4 was targeted in the prevention study (Weinberg)
- Richmond Agitation Sedation Scale (RASS) may be considered if your institution does not use SAS
- CIWA-Ar needs an interactive patient

Gold JA et al. *Crit Care Med*. 2007 Mar; 35(3):724-30.

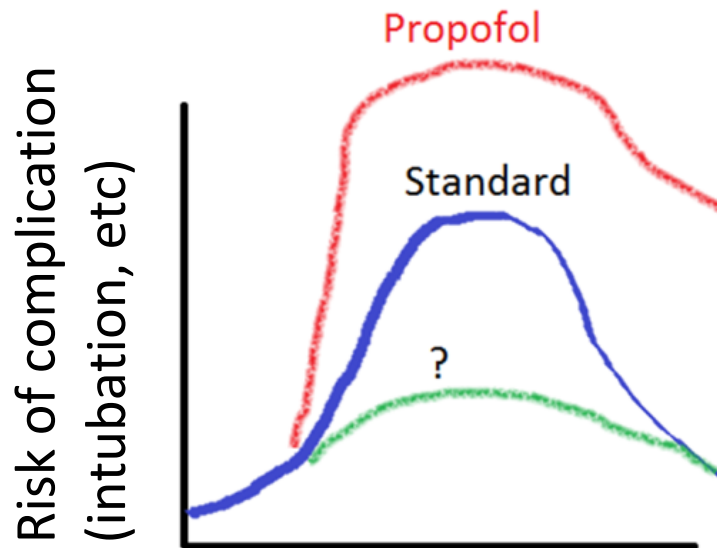
Weinberg JA et al. *J Trauma*. 2008; 64:99-104.

Discussion

- Data for sedation de-escalation is lacking
 - Case reports and case series
- Use pharmacologic principles as rationale to attain goals
 - Make hypothesis, implement, monitor, be at bedside to adjust
 - Must D/C propofol, should minimize lorazepam prior to extubation
 - Continuous infusion benzo's associated with prolonged intubation vs propofol, propofol associated with prolonged intubation vs dexmedetomidine in retrospective case series
 - Easy to over interpret reports, minimize and remove complication

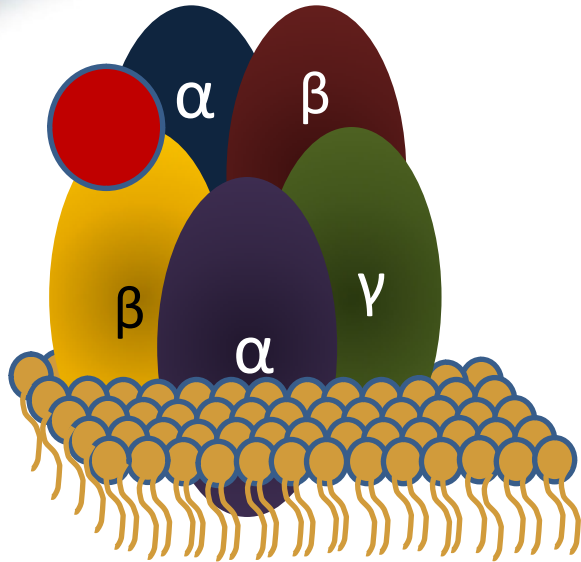
Maybe We Can Do Better Next Time

- Can we better predict who will have severe withdrawal and prevent it?
 - Early intervention in target populations, better studies, baclofen?
- Once withdrawing, can we curtail progression?
 - Minimize disease, risky medications, treat symptoms



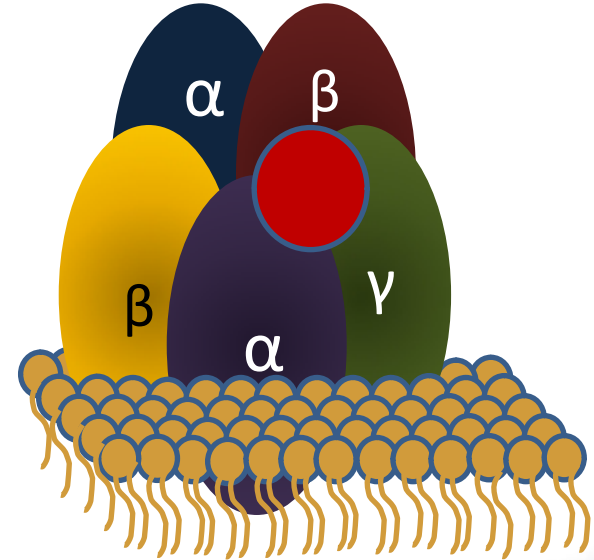
What about phenobarbital-based therapy in the ICU?

Barbiturate Binding



Endogenous GABA Independent at high doses

Benzodiazepine Binding



Endogenous GABA Dependent

Phenobarbital vs Symptom-triggered benzodiazepine therapy

- Before/after quasi-experimental study
- Patients: Admitted to the medical ICU with complicated alcohol withdrawal
- Interventions:
 - Symptom-based benzodiazepine therapy
 - Phenobarbital loading dose/taper
- Patients were matched by demographics and pre-ICU benzodiazepine administration

BIDMC Critical Care Guideline for Phenobarbital Use in Alcohol Withdrawal

Loading Dose (Day 1) of Phenobarbital (IV)

10 mg/kg IV over 30 minutes
If response inadequate after 1-6 hours, may give an additional 2.5 or 5 mg/kg IV rescue dose (maximum cumulative loading dose is 15 mg/kg)

All doses are based on Ideal Body Weight unless the patient weighs less than IBW, at which time actual weight should be used.

Ideal Body Weight (IBW) (In kg)
Male: $50 + 2.3(\text{Inches} - 5 \text{ feet})$
Female: $45 + 2.3(\text{Inches} - 5 \text{ feet})$

Loading dose may be given IM in patients with no IV

Consider Symptom-Oriented therapy if symptomatic after loading dose(s):

- Clonidine for adrenergic hyperactivity (Nausea, vomiting, tremor, sweating, hypertension, tachycardia). If severe, may consider dexmedetomidine
- Haloperidol for perceptual disturbances/disturbed thinking ("alcoholic hallucinosis")

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- Clonidine for adrenergic hyperactivity (Nausea, vomiting, tremor, sweating, hypertension, tachycardia). If severe, may consider dexmedetomidine
- Haloperidol for perceptual disturbances/disturbed thinking ("alcoholic hallucinosis")

Maintenance dose (MD) is given orally every 5-8 hours after loading dose is given. MD = $(0.096 \text{ L/kg/day}) \times \text{IBW}$. See Appendix 1 for specific dosing.

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Contraindications: Acute intermittent porphyria, active/previous history of rash with antiepileptic drugs

protocol for details surrounding discharging patients early/AMA cases

NO BENZODIAZEPINES allowed

Results

	Benzodiazepine (n=125)	Phenobarbital (n=125)	P value
Median amount of lorazepam received pre-ICU admission (mg)	25	25	
Duration of alcohol withdrawal (hr)	30	10	<0.0001
ICU Length of Stay (hr)	45	37	0.007
Mechanical Ventilation	25 (20%)	15 (12%)	0.04
Post-admission seizure	5 (4%)	4 (3.2%)	0.58
In-hospital death	3 (2.5%)	2 (1.6%)	0.49

Key Takeaways

- Key Takeaway #1
 - Exercise caution when considering treatment in a currently intoxicated patient
- Key Takeaway #2
 - Proper risk assessment and symptom monitoring is critical to properly managing alcohol withdrawal in the Intensive Care Unit
- Key Takeaway #3
 - Symptom-oriented therapy should be implemented to avoid excessive GABA agent administration