

Alcohol Withdrawal & Alcohol Use Disorder From Acute Withdrawal to Long-term Treatment

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The importance of alcohol withdrawal

- Mild syndrome to medical emergency
- Clinical spectrum:
 - anxiety
 - tremor
 - autonomic hyperactivity
 - hallucination
 - seizure
 - delirium tremens

Goals of treatment

- Prophylaxis/treatment of:
- seizure
- delirium
- autonomic hyperactivity
- morbidity , mortality
- Patient entrance to AUD treatment

Detox ≠ Treatment of AUD

Neurobiology of Withdrawal

- **Chronic alcohol exposure**
- ↑ GABAergic inhibition
- ↓ NMDA/glutamatergic activity
- **Abrupt reduction/cessation**
- ↓ GABAergic inhibition
- ↑ glutamatergic/NMDA activity
- ↑ sympathetic activity

- SO:
- **CNS hyperexcitability**
- → tremor
- anxiety
- insomnia
- autonomic hyperactivity
- seizure
- delirium

Kindling

- Recurrent Withdrawal:
- Increased CNS excitability
- Increased severity of next withdrawals
- Increased risk of seizure
- increased risk of severe withdrawal
- So :
- **Number of past withdrawal is important.**

Timeline

6–24 h

- Anxiety
- Tremor
- Insomnia
- Nausea/vomiting
- Sweating
- Tachycardia

Timeline

- **12-48h**
- Withdrawal seizures
- Alcohol hallucinosis
- **48–96 h**
- Delirium tremens
- Overlap
- Timeline is not definitive

Clinical Spectrum

Severity	CIWA-Ar
Mild	<10
Moderate	10–18
Severe	≥19

- **CIWA-Ar = severity measure**

Not:

- **complete risk assessment**
- Seizure & delirium = high-risk patient

History

- The last dose
- How much
- Since when?
- The pattern?
- Decreased measure?
- past withdrawal?
- Past seizure?
- Past DT?
- Past detox
- Benzodiazepine? or other substances?
- Liver dx, epilepsy, malnutrition, other medical problems?

Risk Factors for Severe Withdrawal

- Previous DT
- Previous withdrawal seizure
- Multiple previous withdrawals
- Heavy/prolonged alcohol use
- Concomitant sedative-hypnotic withdrawal
- Significant medical comorbidity
- Electrolyte abnormalities
- Malnutrition
- Older age
- Poor social support
- **Risk ≠ Current Severity**

- **Positive BAL $\neq$ No Withdrawal**
- Alcohol in blood :
- **Not R/O Withdrawal.**
- In dependent patient:
- **Rapid decline in alcohol concentration**
- Can precipitate withdrawal
- So :
- **Clinical trajectory is more important than a single BAL.**

Initial Assessment

:

- BP, HR, RR
- Temperature
- O₂ saturation
- Mental status, Level of consciousness
- Tremor
- Agitation
- Hallucinations
- Autonomic instability
- Neurologic examination
- Searching other agitation/delirium causes.

Laboratory Assessment

- CBC
- Glucose
- Na, K, Mg, Phosphate
- BUN/Cr
- LFT
- ECG If indicated
- Ethanol level
- Toxicology

CIWA & Risk Stratification

- **CIWA-Ar**
- withdrawal severity assessment
- monitoring
- medication titration
- **More suitable if The patient :**
- is awake and alert
- Can communicate
- Is not delirious .

when CIWA-Ar is not suitable?

- Delirium
- Intubation
- Severe cognitive impairment
- Severe psychosis
- Not able to communicate
- Severe sedation
- In this case:
- **Clinical assessment > CIWA-Ar**

Risk Assessment

- **1. How much is the patient symptomatic**
- → CIWA / clinical assessment
- **2. risk of severe withdrawal**
- → history + risk factors
- e.g. **CIWA = 7**
- But :
- **Previous DT + previous seizure + multiple detoxes**
- → the pt is not low-risk

Indications of admission

- Heavy drinking
- Past seizure history
- Past DT history
- concurrent benzodiazepine withdrawal
- significant physical/psychiatric comorbidity
- cognitive impairment
- No social support
- frail or multiple comorbidities

– **First-line Treatment**

- **Benzodiazepines**
- In moderate-severe withdrawal :
- **Benzodiazepines = First-line**
- goals:
- CNS hyperexcitability control
- prevention of seizures
- prevention/treatment of DT
- autonomic hyperactivity control

Which Benzodiazepine?

- **Preferred in many patients**
- Diazepam
- Chlordiazepoxide
- **advantages:**
- Long half-life
- smoother withdrawal control
- Decreased fluctuation of drug level
- **But choosing should be based on:**
- liver function, age, respiratory status, other sedatives, setting

- In significant hepatic dysfunction:
- **Do not forget accumulation of active metabolites.**
- **More suitable choices:**
- Lorazepam
- Oxazepam
- Less dependence on glucuronidation & hepatic oxidative metabolism.

1. Symptom-triggered Regimen

- **Based on patients signs and symptoms**
- **advantages:**
- Decrease unnecessary benzodiazepine exposure
- More accurate titration possibility
- Less duration
- **indications:**
- Regular monitoring
- Trained staff
- Specific protocol
- Hospitalized patient

Fixed-dose Regimen

- If symptom-triggered monitoring is not indicated
- Specially in community detox.
- gradual reduction
- 7-10 days

Front-loading

- In severe/high-risk withdrawal
- **Goals:**
- rapid control
- prevention of progression
- prevention of seizure/DT
- **Diazepam 10 mg PO q1h**
- or
- **Diazepam 20 mg PO q2h**
- For patients at severe withdrawal risk.

Practical Treatment by Severity

- **Mild**
- Supportive care
- monitoring
- Pharmacotherapy in some patients
- **Moderate**
- Benzodiazepine first-line
- symptom-triggered or fixed-dose
- **Severe**
- Benzodiazepine
- consideration of front-loading
- close monitoring
- **Seizure / DT**
- **Immediate escalation**

Adequate control of withdrawal

- Decrease agitation
- decrease tremor
- Autonomic hyperactivity CONTROL
- prevention of seizure/DT
- **Without :**
- excessive sedation
- respiratory depression
- aspiration

Under-treatment

- Persistent tachycardia
- Hypertension
- Tremor
- Agitation
- Hallucination
- Seizure

Over-treatment

- Somnolence
- Respiratory depression
- Aspiration
- Loss of airway protection
- **Clinical reassessment is essential.**

Alcohol Withdrawal Seizure

- generalized tonic-clonic
- 1st 6-48 h
- **Increase Risk of severe/complicated withdrawal.**
- treatment:
- **Benzodiazepine**
- Quick-acting like lorazepam

Questions After a Withdrawal Seizure

- **True withdrawal seizure ?**
- **evaluate:**
- hypoglycemia
- electrolyte disturbance
- head trauma
- epilepsy
- intoxication
- other withdrawal syndromes
- CNS pathology

What NOT to Do

- **Phenytoin**
- Not effective for alcohol withdrawal seizure.
- **Antipsychotic monotherapy:**
- Inappropriate .
- Why?
- Decrease seizure threshold
- phenytoin not suitable for alcohol-withdrawal seizure

– Delirium Tremens

- 3 important symptoms:
- **Delirium**
- **Autonomic hyperactivity**
- **Agitation / hallucination**
- **symptoms:**
- Inattention, Disorientation, Altered consciousness, Tremor
- Tachycardia, Hypertension, Sweating, Fever, Hallucination

Hallucinososis vs DT

- **Alcohol hallucinososis**
- hallucination
- relatively preserved sensorium
- May be intact.
- **DT**
- impaired attention
- altered awareness
- disorientation
- autonomic instability
- **Distinction matters.**

DT: Treatment

- **Benzodiazepine-based treatment**
- Goals:
 - control agitation
 - control autonomic hyperactivity
 - prevent seizure
 - maintain safety
- In severe cases:
- **ICU / high-level monitoring**
- oral lorazepam : first-line
- If PO tx is not a choice: parenteral lorazepam or haloperidol.

Autonomic Hyperactivity

- Tachycardia
- Hypertension
- Sweating
- Tremor
- Fever
- Adjuncts:
 - beta-blocker
 - alpha-2 agonist
- **They don't treat seizure and withdrawal**
- **Adjunct ≠ substitute for benzodiazepine**

Refractory Withdrawal

- Uncontrollable with benzodiazepine:
- Diagnosis reevaluation .
- Evaluate other intoxication/withdrawal.
- Evaluate Infection/metabolic causes.
- Evaluate Liver/renal dysfunction.
- increase monitoring.
- **Severe refractory withdrawal**
- → ICU-level management

Phenobarbital indications

- refractory withdrawal
- benzodiazepine contraindication/intolerance
- adjunct
- alternative.
- **Risks :**
- respiratory depression
- oversedation

Gabapentin / Carbamazepine / Valproate

- In some patients:
- mild withdrawal
- Or adjunct
- **Severe withdrawal**
- → benzodiazepine remains first-line.
- **Valproate Contraindications/cautions:**
- significant liver disease
- women of childbearing potential

Wernicke / Nutrition

- **High risk patients:**
- malnutrition
- chronic heavy drinking
- acute withdrawal
- decompensated liver disease
- Thiamine
- **prophylactic example:**
- **Thiamine 100 mg IV/IM daily × 3–5 days**
- severe malnutrition †malabsorption suspected Wernicke:
- **Parenteral treatment preferred.**

Wernicke Encephalopathy

- **classic:**
- Confusion
- Oculomotor abnormalities
- Ataxia
- but:
- **Triad often complete**
- So in high risk patient:
- **Low threshold for treatment**

Glucose & Thiamine

- Thiamine before glucose
- But never delay glucose in severe hypoglycemia

Electrolytes & Nutrition

- K
- Mg
- Phosphate
- Correction :
- dehydration
- electrolyte abnormalities
- nutritional deficiencies
- In severe malnutrition:
- **Consider Refeeding syndrome**

Differential of Agitation

- **Is this withdrawal?**
- Or
- Delirium?
- Sepsis?
- Hypoglycemia?
- Hypoxia?
- Electrolyte disturbance?
- Hepatic encephalopathy?
- Medication toxicity?
- Other substance intoxication?
- Other withdrawal?
- Primary psychiatric illness?
- **First rule out the dangerous medical causes.**

Psychopharmacology in the Medically Ill

- **1. Liver?** Metabolism, accumulation, hepatotoxicity
- **2. Kidney?** Clearance, dose adjustment
- **3. Respiratory status?** additive CNS/respiratory depression
- **4. Drug interactions?** Pharmacokinetic, pharmacodynamic
- **5. Polypharmacy?** Sedation, QT, anticholinergic burden

Alcohol Withdrawal in medically ill

- **1. WHAT is happening?**
- Withdrawal or medical delirium?
- **2. WHAT can I safely give?**
- liver
- kidney
- respiratory status
- age
- polypharmacy
- **3. WHERE should I treat?**
- Ward?
- Monitored bed?
- ICU?

– Delirium: Diagnostic Trap

- Hallucination due to alcohol
- Or :
- **Alcohol withdrawal hallucinosis**
- assess:
- Attention
- Awareness
- Orientation
- Fluctuation
- Autonomic signs
- Timing of last alcohol
- Medical precipitants
- **Delirium is a syndrome, not a diagnosis of exclusion.**

Suicide / Psychiatric Risk

- AUD is associated with risk of:
- Suicidality
- Impulsivity
- Depression
- Trauma-related symptoms
- Interpersonal dysfunction
- So after stabilization:
- **Suicide risk assessment**

Pain + Alcohol + Opioids

- Consider interactions of
- **Alcohol**
- **Opioids**
- **Sedative medications**
- → increased risk of:
- CNS depression
- respiratory depression
- overdose
- candidates for naltrexone:
- opioid exposure

After Withdrawal management

- – **Detox ≠ Treatment**
- After stabilization:
- → AUD treatment
- Part of a complete tx not an option

AUD Maintenance Pharmacotherapy

- **Naltrexone**
- **50 mg PO once daily**
- **Acamprosate**
- **666 mg PO TID**
- **= 1998 mg/day**
- **Disulfiram**
- **250 mg/day**
- Range:
- **125–500 mg/day**

Naltrexone

- **50 mg/day**
- Before start:
- Opioid use?
- Opioid dependence?
- Need for opioid analgesia?
- Liver disease?
- LFT
- goal:
- Decrease heavy drinking
- decrease relapse
- decrease reinforcing effects of alcohol

Acamprosate

- **666 mg TID**
- **= 1998 mg/day**
- Goal: abstinence persistence
- **Renal function**

Disulfiram

- **250 mg/day**
- Range:
- **125–500 mg/day**
- More appropriate for:
- motivated patient
- Goal: abstinence persistence
- patient selection
- Before prescription:
- Liver function
- contraindications
- informed consent
- **Alcohol + Disulfiram**
- → potentially severe reaction

Maintenance

- **Naltrexone**
- if:
- the goal is decreasing heavy drinking
- opioid use : no
- liver status : ok
- **Acamprosate**
- if:
- abstinence is the goal
- detox has been done
- renal function : ok
- **Disulfiram**
- if:
- highly motivated
- Goal: abstinence
- Patients prefer/ other choices are not suitable

The End.