Alcohol Withdrawal: A primer for RAAM Clinicians

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MENTORING, EDUCATION, AND CLINICAL TOOLS FOR ADDICTION
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Conflict of Interest

- Received honorarium from Indivior and Master Clinician for speaking engagements on the topic of treatment options for opioid use disorder.

Bias Mitigation

- Opioid use disorder treatment options will not be discussed.
- Discussion the off-label use of gabapentin for alcohol withdrawal.

Learning objectives

- Describe the clinical features of alcohol withdrawal
- List the main complications of alcohol withdrawal
- Discuss the medical treatment of withdrawal
- Outline a protocol for elective treatment of withdrawal as a therapeutic intervention

Physiology of alcohol withdrawal

- Alcohol suppresses the NMDA system (neuroexcitatory) and enhances GABA
- Chronic heavy alcohol use causes compensatory increase in number and sensitivity of NMDA receptors and decrease in GABA receptors
- If alcohol abruptly discontinued, the upregulated NMDA system causes autonomic hyperactivity:
  - Tremor, sweating, seizures, DTs etc.

Clinical features

- Severity of withdrawal associated with amount consumed
- Withdrawal uncommon in people drinking less than six drinks per day
- Individuals show predictable pattern of withdrawal
  - People with previous withdrawal seizures are at high risk for recurrence

Clinical features (2)

- Begins 6–12 hours after last drink
- Acute withdrawal usually resolves within 2–3 days, may last up to 7 days
- **Most reliable signs: Tremor and sweating**
  - If tremor not present, review the diagnosis
  - Postural and intention, not resting
  - Can elicit by having patient hold arms outstretched and hands raised
  - Severity of tremor diminishes as withdrawal resolves
- Other signs: Tachycardia, hypertension, hyperthermia
- Symptoms: Anxiety, nausea, headache

Symptom-triggered treatment

- Give high dose of benzodiazepines when severe symptoms present; don't give benzos if minimal symptoms
- Severity of symptoms measured by a standardized scale – CIWA-Ar (Clinical Institute Withdrawal Assessment) scale, or objective scales eg SHOT, BAWS
- Compared to scheduled treatment, symptom-triggered treatment relieves withdrawal more rapidly and completely than scheduled treatment, therefore:
  - Shortens length of stay in the ED, prevents complications (e.g., seizures, DTs)
  - Prevents over-medicating and over-sedation

Symptom triggered treatment (2)

- Regardless of protocol used, **the patient should only be discharged when they are in no or minimal withdrawal**
- If they are still in withdrawal, they will almost inevitably relapse to alcohol use
- Recurrent episodes of withdrawal actually worsen withdrawal severity – “kindling”
  - Embers catch faster than dry wood

Withdrawal severity scales

- **CIWA scale** (see next slide)
- 10 items
- Scale is measured every 1-2 hours
- A score of 10 or more indicates the need for treatment
- Treatment is completed when score is less than 8 on two consecutive occasions
- CIWA is the most studied and used withdrawal severity scale

Limitations of the CIWA

- Most of the ten items are subjective (nausea, headache) and non-specific
  - False positives in patients who are anxious, in psychosis, have essential tremor, cerebellar disease, delirium not related to alcohol, febrile illness, or seeking medications
  - False negatives if language barriers, cognitive delay, dementia, impaired consciousness, education level
  - Time consuming (5+ minutes); not feasible to administer hourly in a busy ED

CIWA-Ar scale (1)

Nausea/vomiting: "Do you feel sick to your stomach? Have you vomited?"		
0 No nausea or vomiting 1	2 3 4 Intermittent nausea with dry heaves	5 6 7 constant nausea, frequent dry heaves and vomiting
Tremor: Arms extended and fingers spread apart		
0 No tremor 1 Tremor not visible but can be felt fingertip to fingertip	2 3 4 Moderate with patient's arms extended	5 6 7 Severe, even with arms not extended
Paroxysmal sweats		
0 No sweat visible 1 Barely perceptible sweating, palms moist	2 3 4 Beads of sweat obvious on forehead	5 6 7 Drenching sweats
Anxiety: "Do you feel nervous?"		
0 No anxiety, at ease 1 Mildly anxious	2 3 4 Moderately anxious, or guarded, so anxiety is inferred	5 6 7 Equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions
Headache, fullness in head: "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or light-headedness. Otherwise, rate severity.		
0 Not present 1 Very mild	2 Mild 3 Moderate 4 Moderately severe	5 Severe 6 Very severe 7 Extremely severe

CIWA-Ar scale (2)

Agitation		
0 Normal activity 1 Somewhat more than normal activity	2 3 4 Moderately fidgety and restless	5 6 7 Paces back and forth during most of the interview, or constantly thrashes about
Tactile disturbances: "Have you had any itching, pins and needles sensations, any burning or numbness, or do you feel bugs crawling on your skin?"		
0 None 1 Very mild itching, pins and needles, burning, or numbness	2 Mild itching, pins and needles, burning, or numbness 3 Moderate itching, pins and needles, burning, or numbness 4 Moderately severe hallucinations	5 Severe hallucinations 6 Extremely severe hallucinations 7 Continuous hallucinations
Auditory disturbances: "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?"		
0 Not present 1 Very mild harshness or ability to frighten	2 Mild harshness or ability to frighten 3 Moderate harshness or ability to frighten 4 Moderately severe hallucinations	5 Severe hallucinations 6 Extremely severe hallucinations 7 Continuous hallucinations
Visual disturbances: "Does the light appear to be too bright? Is its colour different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?"		
0 Not present 1 Very mild sensitivity	2 Mild sensitivity 3 Moderate sensitivity 4 Moderately severe sensitivity	5 Severe hallucinations 6 Extremely severe hallucinations 7 Continuous hallucinations
Orientation and clouding of sensorium: "What day is this? Where are you? Who am I?"		
0 Oriented and can do serial additions 1 Cannot do serial additions or is uncertain about date	2 Disoriented for date by no more than 2 calendar days	3 Disoriented for place by more than 2 calendar days 4 Disoriented for place and/or person

Objective scales: SHOT and BAWS

- SHOT: Sweating, Hallucinations, Orientation, Tremor
- BAWS: Sweating, Hallucinations, Orientation, Tremor, Agitation
- **Advantages**:
- No subjective symptoms so fewer false positives
- Takes 1 minute to complete, vs 5 minutes for CIWA, so greater compliance with q1H measurements in the ED
- Better at identifying delirium and other causes of altered consciousness
- Disadvantage: Less research on validity and reliability
- But preliminary research has found strong correlation with CIWA scores

SHOT scale

Sweating	0 – No visible sweating 1 – Palms moderately moist 2 – Visible beads of sweat on forehead
Hallucinations "Are you feeling, seeing, or hearing anything that is disturbing to you? Are you seeing or hearing things you know are not there?"	0 – No hallucinations 1 – Tactile hallucinations only 2 – Visual and/or auditory hallucinations
Orientation "What is the date, month, and year? Where are you? Who am I?"	0 – Oriented 1 – Disoriented to date by one month or more 2 – Disoriented to place or person
Tremor Extend arms and reach for object. Walk across hall (optional).	0 – No tremor 1 – Minimally visible tremor 2 – Mild tremor 3 – Moderate tremor 4 – Severe tremor

Brief Alcohol Withdrawal Scale

	0 None	1 Mild	2 Moderate	3 Severe	Score
Tremor	No tremor	Not visible but can be felt	Moderate, with arms extended	At rest, without arms extended	
Diaphoresis/Swats	No sweats	Mild, barely visible	Beads of sweat	Drenching sweats	
Agitation	Alert and calm (RASS = 0)	Restless, anxious, apprehensive, movements not aggressive (RASS = 1)	Agitated, frequent non-purposeful movement (RASS = 2)	Very agitated or combative, violent (RASS = 3 or 4)	
Confusion/Orientation	Oriented to person, place, time	Disoriented to time (e.g. by more than 2 days or wrong month or wrong year) or to place (e.g. name of building, city, state) but not both	Disoriented to time and place	Disoriented to person	
Hallucinations (visual, auditory, tactile)	None	Mild (vague report, reality testing intact)	Moderate (more defined hallucinations)	Severe (obviously responding to internal stimuli, poor reality testing)	
				Total	

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Diazepam treatment

- High doses are safe: patients who are highly tolerant to alcohol are also highly tolerant to benzodiazepines
- Diazepam is preferred because it is metabolized to active metabolites, so has a duration of action of up to 5 days
- Once withdrawal is resolved, prolonged action of diazepam prevents rebound withdrawal
- Dose: 10-20 mg diazepam PO q 1-2 H when CIWA-Ar ≥10 or SHOT ≥2
- Treatment completed when CIWA-Ar < 8 or SHOT < 2 on two consecutive measurements, with minimal tremor

Lorazepam treatment

- Lorazepam does not have active metabolites, so is safer in patients at high risk for diazepam toxicity:
- Elderly
- Cirrhosis with liver dysfunction
- Respiratory impairment
- On high doses of potent opioids
- Dose 2–4 mg q 1-2H for CIWA =>10, SHOT =>2
- **Note**: Patients given lorazepam should be reassessed within 24 hours because their withdrawal symptoms could return

Lorazepam in liver or respiratory failure

- Benzodiazepines can trigger encephalopathy in patients with decompensated liver disease, and respiratory arrest in patients with respiratory failure
  - Decompensated liver disease: Ascites, encephalopathy, varices, low albumin, high bilirubin
- Therefore with these patients, use small doses of lorazepam (0.5 mg) for moderate to severe withdrawal
- If patient in mild withdrawal (eg CIWA 10-12), safer just to observe
- Probably safer to admit these patients

Complications of alcohol withdrawal

Prevention in a non-hospital setting

Withdrawal Timeline

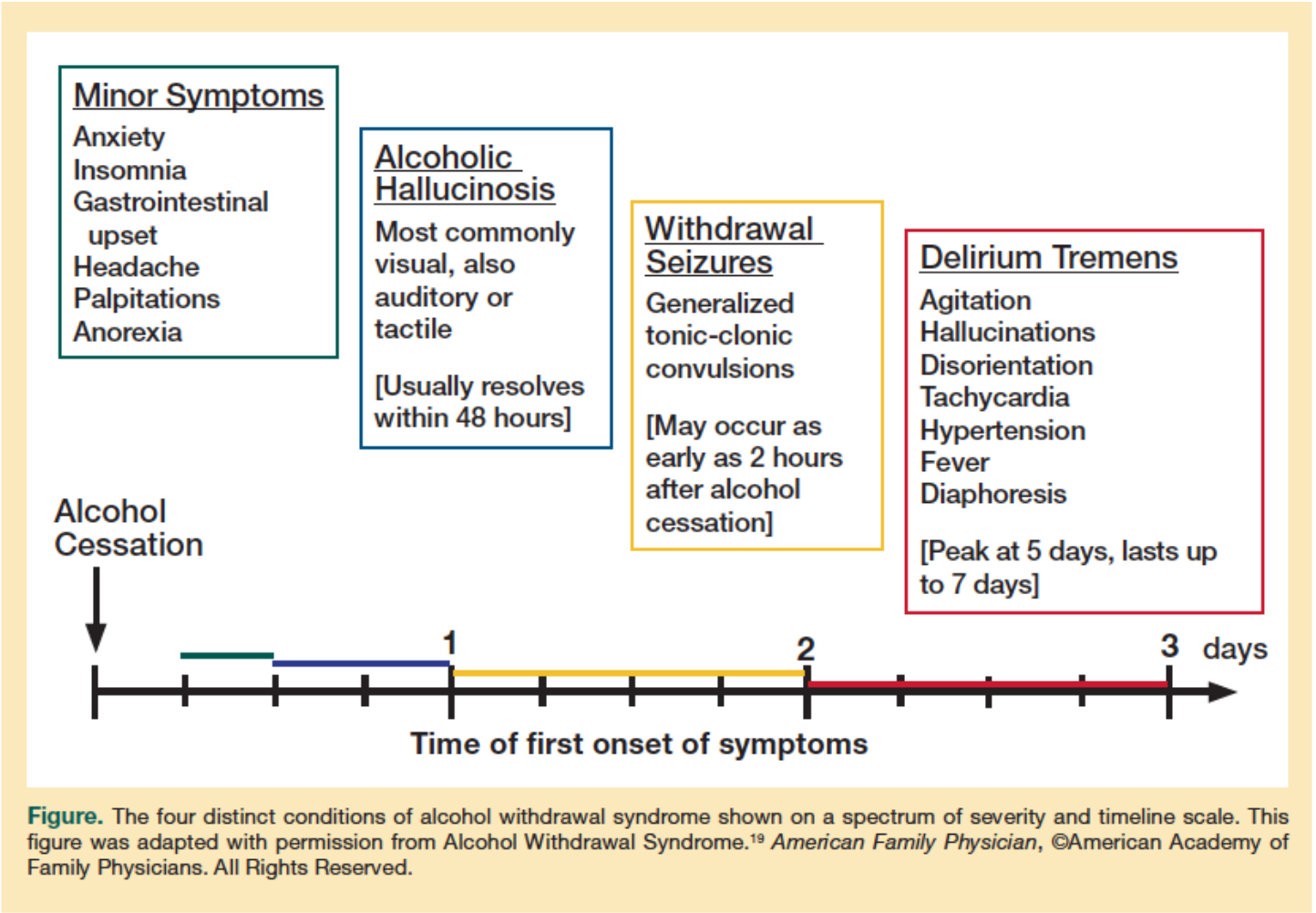
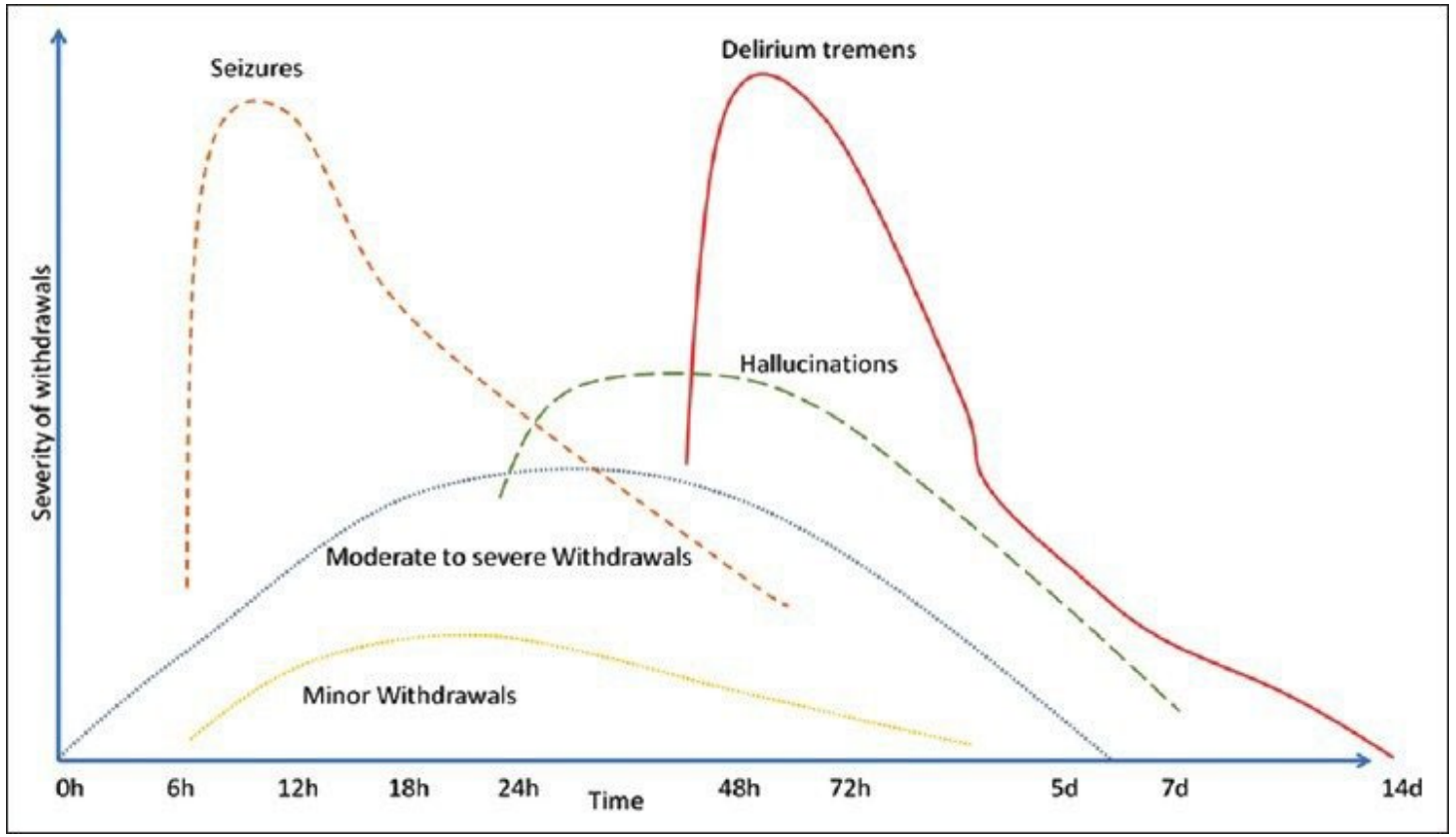


Figure. The four distinct conditions of alcohol withdrawal syndrome shown on a spectrum of severity and timeline scale. This figure was adapted with permission from Alcohol Withdrawal Syndrome.[19] *American Family Physician*, ©American Academy of Family Physicians. All Rights Reserved.

https://www.alltreatment.com/alcohol-withdrawal-timeline/

Withdrawal Timeline



https://www.researchgate.net/figure/Graph-depicting-the-time-course-of-alcohol-withdrawal-symptoms-based-on-clinical_fig2_263860038

Alcoholic Hallucinosis

- Hallucinations
  - Predominantly visual
    - Think of differentials if auditory
  - NO clouding of sensorium like with DTs
    - Distressing, as they are aware it's a hallucination
- Vitals usually normal
- Develop within 12-24h
- Typically resolved within 48h (earliest point DTs develop)

Withdrawal seizures - features

- Risk increases with amount consumed
- Patients who have had seizures in the past are at high risk of recurrence
- An estimated 10-15% of patients with severe alcohol use disorder have had at least one withdrawal seizure
- Typically occurs 12-72 hours after the last drink
- Usually but not always preceded by autonomic hyperactivity – tremor and sweating
- Grand mal, non focal, brief

Prevention of withdrawal seizures

- Benzodiazepine loading in patients who have a history of withdrawal seizures
- Diazepam 20 mg q1H x 3, or
- Lorazepam 4 mg q1H x 3
- Diazepam or lorazepam is administered even if the CIWA or SHOT scores are low
- Continue with symptom-triggered treatment if patient has withdrawal symptoms after three loading doses
- No evidence that anticonvulsant medications are effective in preventing withdrawal seizures

Withdrawal delirium – features

- Also known as “Delirium tremens”
- Risk factors:
  - Very heavy alcohol consumption
  - Medical illness eg pancreatitis, pneumonia
  - Inadequate treatment of early withdrawal symptoms
  - Past history of DT’s
- Starts day 3-5 after last drink

Clinical features (2)

- Patient is confused and disoriented
- Tachycardia, hypertension, low-grade fever, agitation, diaphoresis, hallucinations (predominantly visual)
- May be ‘living in a dream’, eg ‘I’m in my apartment, it’s 1974, and you are a policeman’
- Not always easy to diagnose:
  - Patient may have learned by repeated questioning to state the correct date and location
  - Ask, ‘why are you here? Who am I? What am I doing here’?
- “Sundowning’: Patient may be agitated and confused at night, and calm and oriented in the morning

“Pre-DTS”

- Severe withdrawal symptoms: Diaphoresis, tremor
  - Hypertension, tachycardia
  - Agitation
  - Sometimes fever
- Symptoms getting worse despite symptom-triggered benzodiazepine treatment

Management of pre-DTs

- Accelerated benzodiazepine treatment, eg:
- Lorazepam 4 mg q 30 minutes x four, repeat as needed
- Don’t need to do CIWA after each dose
- Send to hospital if not responding to accelerated bzd treatment
- In hospital, pre-DTs can be managed with phenobarbital
- If not effective, ICU admission

Prevention of Arrhythmias

- Sudden death can occur in severe withdrawal and DTs
- Likely cause: Ventricular arrhythmias triggered by prolonged QT interval
- If possible, baseline ECG in all patients requiring benzodiazepine treatment
- Aggressive benzodiazepine treatment can prevent arrhythmais
  - QT interval normalizes as withdrawal resolves
- Correct low Mg and other electrolyte imbalances (if possible)
- Send patients to ED if sustained tachycardia or irregular pulse

Wernicke's Encephalopathy

- Confusion, ataxia, ocular abnormalities
  - Slow, unsteady gait
  - Double vision, nystagmus, paralysis of oscular muscles
- Difficult to diagnose in a patient who is intoxicated or in withdrawal
- Risk factors: Poor diet, liver disease, poor absorption (e.g. gastric bypass)
- Can result in Wernicke-Korsakoff Syndrome
  - Chronic deficits of memory impairment
    - Usually short-term memory loss

Wernicke’s Encephalopathy Prevention

- Thiamine
  - 300mg IM/IV daily for 3-5 days
  - Or 100mg PO three times daily for 3-5 days if IM/IV is not available
  - Then 100mg PO once daily for 2-3 weeks

Elective treatment of withdrawal

Elective withdrawal treatment: Rationale

- Therapeutic intervention for patients who are unable to reduce drinking because of ongoing withdrawal symptoms
- Patient should be committed to abstinence and there should be a treatment plan in place
- Admitting patients simply because they have withdrawal symptoms is likely to be futile

Effectiveness of elective withdrawal treatment

- Retrospective study of 73 patients admitted electively to WCH short stay unit for management of alcohol withdrawal
- Patients had all received counselling and anti-craving medications at the WCH SUS clinic
- All patients were heavy drinkers and had daily withdrawal symptoms that made it difficult for them to reduce drinking
- (Wyman et al, unpublished, 2022)

Baseline data

Mean age	45.6 years
Mean number drinks/day	11.8
Mean CIWA score on admission	18..1
Mean diazepam equivalent dose	82.3

Three month follow up

Change In drinking	
Abstinent	15 (20%)
Reduced	20 (27%)
No change/increase	3 (4%)
Lost to follow up	35 (48%)

Three month follow up (2)

Change in well being	
Improved	28 (38%)
No change	7 (10%)
Worsened	3 (4%)
Lost to follow up	35 (48%)

Limitations

- Chart review study, so:
- No standardized instruments for measuring alcohol consumption
- Large loss to follow up
- No control group

Elective withdrawal treatment: Settings

- Withdrawal Management Service (if it has the capacity to administer symptom-triggered treatment)
- General hospital (if RAAM clinician has admitting privileges)
- RAAM clinic (preferably open at least 8 hours)

Indications for elective admission

1. Daily withdrawal symptoms that make it difficult for patients to maintain abstinence
2. Committed to abstinence (or markedly reduced drinking)
3. Committed to a treatment plan involving medications, counselling and follow up
4. Withdrawal symptoms unlikely to resolve without medical treatment
5. Home withdrawal management unlikely to be successful

Precautions/exclusion

- At high risk for benzodiazepine toxicity
  - Eg decompensated liver disease, respiratory impairment, on high doses of potent opioids, frail elderly
- History of severe, prolonged withdrawal or serious complications of withdrawal in the past that have required hospitalization and intensive medical support – eg withdrawal delirium, arrhythmias.
  - A history of withdrawal seizures is not disqualifying; seizures can be prevented through the benzodiazepine loading protocol).

Profile of patient who might benefit

- Drinks at least six drinks per day
- Starts drinking at a set time of day eg morning or afternoon
- Reports anxiety plus physical signs of withdrawal (tremor when reaching for coffee cup)
- May not recognize that this indicates withdrawal
- Inability to stop drinking for more than 1-2 days because of anxiety, tremor, vomiting
- Has been in ED or hospital before for medical treatment of withdrawal

Protocol

- Advise the patient to have the last drink the night before and attend the RAAM clinic, WMS or hospital in the morning
- Patient should be in early, mild withdrawal; if not, admission should be rescheduled
- Breathalyzer can be of assistance
- Apply symptom triggered protocol using SHOT or CIWA
- Give thiamine 100 mg IM or 300 mg PO
- If blood work is an option, do CBC, LFT

Transfer to ED if…

- Withdrawal symptoms getting significantly worse despite 80-100 mg or more of diazepam dispensed every 1-2 hours
- Worsening withdrawal is indicated by rising CIWA score (above 20) **and** increasingly severe tremor, sweating +/- tachycardia and hypertension.
  - This could indicate benzodiazepine resistance, requiring hospital admission and possibly phenobarb.
- Signs of impending DTs: Confusion, disorientation, hallucinations, delusions, severe autonomic hyperactivity (tremor, sweating)

Transfer to ED (2)

- Severe hypertension (>180/120),or tachycardia (> 120)
- Profuse sweating, frequent vomiting (concern re electrolyte imbalances, dehydration)
- Drowsiness (due to benzodiazepine toxicity, opioid toxicity, encephalopathy)
- Hypoxia (due to benzodiazepine toxicity, COPD etc) (SpO2 < 90%)

Discharge

- Discharge when CIWA is < 8 or SHOT < 2 on two consecutive occasions
- Patient should be comfortable with minimal or no tremor
- Ideally, patient would be accompanied home by partner or friend – shouldn't drive home
- Thiamine 100 mg OD x 1 month
  - 300 mg PO OD x 1 month especially if patient has cirrhosis or is malnourished

Discharge (2)

- Arrange follow up, preferably within a week
- Explain that alcohol is no longer needed to relieve withdrawal symptoms
- Arrange counselling if not already done
- Prescribe anti-craving medications if not already done

Mild withdrawal symptoms on discharge

- Sometimes, patient is still in mild withdrawal when RAAM clinic is about to close
- May prescribe diazepam 10 mg tid with tapering doses over the next few days
- Arrange follow up (in person or phone) in next 1-2 days
- OR gabapentin – see next slide

Gabapentin post-discharge

- Note: Use of gabapentin for alcohol withdrawal is off-label
- Relieves acute and subacute withdrawal symptoms
- Preferred over benzodiazepines:
  - Can maintain gabapentin as an anti-craving medication, whereas benzodiazepines should be discontinued after a few days
  - Less sedating than diazepam
  - Sometimes also effective for comorbid anxiety disorders, insomnia, pain, cannabis cravings
- Start with 300 mg bid; increase by 300 mg every 1-2 days
- Maintenance dose is 900-1800 mg per day in divided doses

Acamprosate post discharge

- Acamprosate relieves subacute withdrawal symptoms (insomnia, dysphoria, cravings)
- Many patients who experience acute withdrawal will also have subacute withdrawal
- Best for patients who have abstinence as a goal
- Dose 666 mg tid (333 mg in renal insufficiency)
- LU code 531

Thank you!

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