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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

HOW DO I ADDRESS EMERGING ANXIETY DURING SUBSTANCE USE RECOVERY?

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SPEAKER DISCLOSURES

- ✓ No conflicts of interest

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OBJECTIVES

1. Discuss characteristics between a substance induced anxiety disorder and a primary anxiety disorder.

2. Talk through different treatment options for anxiety symptoms.

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54YO M WITH ALCOHOL USE DISORDER

- A 54yo M with a history of Bipolar II and daily cannabis and alcohol use initially presented asking for help to stop drinking. This was triggered by his teenage daughter no longer wanting to stay with him because he was yelling at her and acting “erratically” while drinking. Patient has struggled with heavy drinking off and on for years and used to be able to stop when his daughter came over, but over the past 6 months he has not been able to do that. He has also been using cannabis daily for years, and finds it causes sleep problems and can make him feel restless at times. He would like to stop both substances.

54YO M WITH ALCOHOL USE DISORDER

- Upon further evaluation he reports stopping drinking about 3 days ago. He is having some mild withdrawal symptoms. He is started on Gabapentin 300mg/300mg/600mg for alcohol withdrawal which is completed without incident over the next week.
- He now presents stating that his anxiety is starting to become intolerable.

54YO M WITH AUD NOW POST DETOX WITH INCREASING ANXIETY.

What is your working diagnosis?

A. Alcohol withdrawal
B. Generalized anxiety disorder
C. Adjustment disorder with anxious features
D. PTSD
E. Protracted alcohol withdrawal
F. Other

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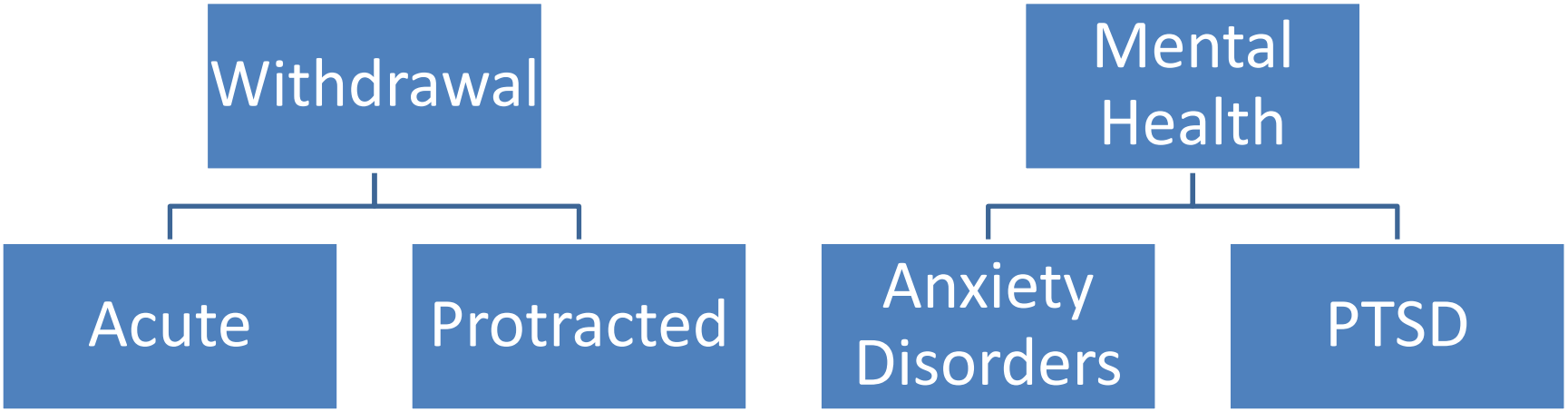
DIFFERENTIAL DIAGNOSIS OF ANXIETY AFTER ACUTE SUBSTANCE WITHDRAWAL



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ACUTE WITHDRAWAL AND ANXIETY

Substance	Onset	Duration	Symptoms
Alcohol	6-24hr	2-3 days (mild)	anxiety, agitation, restlessness, insomnia, tremor, diaphoresis, palpitations, headache (Consider CIWA)
Opioids	Within hours (can vary)	Days to weeks	Dysphoric mood/anxiety, N/V, muscle aches, lacrimation/rhinorrhea (Consider COWS)
Cannabis	24-72hr	1-2 weeks	Anxiety, irritability, sleep problems, restlessness, abdominal pain, tremors, diaphoresis
Stimulants	Hours to days	2 weeks	Dysphoric mood, fatigue, poor concentration, insomnia

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PROTRACTED WITHDRAWAL AND ANXIETY

- Not clearly defined set of symptoms that are common to acute withdrawal but persist beyond typical acute withdrawal timeframe.

Substance	Onset	Duration	Symptoms
Alcohol	After acute withdrawal	Often months	Anxiety, dysphoria, irritability, fatigue, insomnia, poor concentration, unexplained physical complaints
Opioids			Anxiety, dysphoria, elevated reward thresholds, lower pain thresholds, cravings.
Cannabis			Not clear-likely similar to acute withdrawal
Stimulants			Decreased effort for preferred reward (rats); Dysphoric mood, poor concentration (anecdotal)

Caputo, F et al, 2020; Koob, G 2020; Hart EE, et al, 2018

SUBSTANCE USE AND ANXIETY DISORDERS

Substance	Epidemiology	Diagnostic Considerations
Alcohol	Nearly 50% of those with GAD have had AUD. SAD has unique relationship with AUD-increased severity. Relapse risk.	GAD-Difficult to distinguish, presents after development of AUD. Anxiety during prolonged abstinence? **Expert opinion key symptom: worsening symptoms over time.** SAD-easier to distinguish as it precedes the onset of AUD. **Key symptom: fear of performance or social situations.** Panic-still occurring during abstinence?

Hartwell K.J. et al 5th Ed ASAM Addiction Med; Schellekens, AFA, et al 2015; Schneier, FR, et al, 2010

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CAN I USE THE GAD-7 TO HELP ID ANXIETY DISORDERS IN PATIENTS WITH SUDS?

- You can...
  - Limitations
    - Small sample: N-103
    - Setting: addiction treatment center
    - Mostly Male (77%)
    - Mostly White (93%)
    - Mix of substance problems: alcohol, opioids, stimulants
- Results
  - GAD7 ≥ 9, sens-80% and spec-86% for any anxiety disorder.

Practice Tip: recommend to use GAD7 in a repeated fashion to screen for anxiety disorder in SUDs

Degadillo, J et al, 2011; Degadillo, J et al, 2012

WHAT ABOUT PTSD?

- Should be assessed
  - High prevalence: 11-41%

- Less abstinence is typically required because of the unique symptoms of PTSD
  - Trauma history
  - Intrusive symptoms: recurrent thoughts, etc

Hartwell K.J. et al 5th Ed ASAM Addiction Med; van Dam D et al, 2010

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WHAT ABOUT PTSD?

How to screen?

- PC-PTSD
  - Cut-off of 2
    - Sens-0.86, Spec-0.57
  - Similar limitations
    - Small sample for validation
    - Mostly white men (Dutch setting)
    - https://www.ptsd.va.gov/professional/assessment/screens/pc-ptsd.asp

In the past month, have you …

1. had nightmares about the event(s) or thought about the event(s) when you did not want to?	YES	NO
2. tried hard not to think about the event(s) or went out of your way to avoid situations that reminded you of the event(s)?	YES	NO
3. been constantly on guard, watchful, or easily startled?	YES	NO
4. felt numb or detached from people, activities, or your surroundings?	YES	NO
5. felt guilty or unable to stop blaming yourself of others for the event(s) or any problems the events may have caused?	YES	NO
Total score is sum of "YES" responses in items 1-5.	**TOTAL SCORE**	

Practice Tip: recommend to use PC-PTSD to screen for PTSD in SUDs

Hartwell K.J. et al 5th Ed ASAM Addiction Med; van Dam D et al, 2010

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54YO M WITH ALCOHOL USE DISORDER

- 10 days after his last drink he presents to the ED because his anxiety was so intense. He denies relapsing on any drugs or alcohol. Anxiety has impacted his ability to attend the IOP. In the ED he was given Lorazepam and found it immediately helpful. He pleads with me to start a trial of Lorazepam. Tearful and frustrated. "I am an adult!" He is still taking his Gabapentin, Quetiapine and Lithium.

54YO M WITH AUD NOW POST DETOX WITH INCREASING ANXIETY.

What would you do next?

A. Start Sertraline
B. Start Hydroxyzine prn
C. Get a baseline GAD7 and follow him in 1 week
D. Increase his Gabapentin
E. Continue Lorazepam
F. Call the Provider Consultation Line (and ask for Rick)

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THE 3 PHASES OF ALCOHOL WITHDRAWAL SYNDROME

1. Acute phase
2. Early abstinence phase
   - Immediately after acute phase
   - Improves over 3-6 weeks
   - Anxiety, low mood, disrupted sleep

3. Protracted abstinence phase
   - Poorly defined
   - Up to 75% of people could experience it
   - Some case reports describe this lasting 2+ years (sleep abnormalities up to 3years)

Common Symptoms

- anxiety, hostility, irritability, depression, mood instability, fatigue, insomnia, difficulties concentrating and thinking, reduced interest in sex, anhedonia, and unexplained physical complaints especially of pain

Caputo, F et al, 2020

TREATING EARLY AND PROTRACTED ALCOHOL WITHDRAWAL SYMPTOMS

- Setting
  - N=33
  - 78% Male, 48% White, 18% Native American, 30% Latino, 3% African American
  - 20% days abstinent
  - Excluded mental health problems
  - Needed to be “cue reactive”
- Intervention
  - Gabapentin 300mg/300mg/600mg vs Placebo

Mason, BJ et al, 2008

TREATING EARLY AND PROTRACTED ALCOHOL WITHDRAWAL SYMPTOMS

- Results

Outcome	*Gaba*	*Placebo*	*G–P*	t	P	n
Alcohol craving questionnaire	40.2	33.0	7.2	1.08	NS	22
Beck depression inventory	7.4	9.3	–1.9	0.63	NS	27
Pittsburgh sleep quality index						
Quality	0.00	0.81	–0.81	4.60	<0.001	29
Latency	0.50	1.00	–0.50	2.05	<0.06	29
Duration	1.15	1.24	–0.11	0.29	NS	29
Efficiency	0.38	1.19	–0.81	2.02	<0.06	29
Disturbance	1.12	1.05	0.08	0.41	NS	29
Use of sleep meds	0.25	0.43	–0.18	0.51	NS	29
Daytime dysfunction	0.63	0.75	–0.13	0.56	NS	28
Global index	4.13	6.50	–2.38	2.01	<0.05	28

Larger values imply greater dysfunction across all measures. NS = not significant.

Mason, BJ et al, 2008

MED TREATMENT OF PROTRACTED ALCOHOL WITHDRAWAL

- Gabapentin-can be used to treat acute withdrawal and then continued for as long as the patient finds it helpful.

- Hypothetically there may be role for Acamprosate and Gabapentin
  - Acamprosate-NMDA antagonist

Caputo, F et al, 2020

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54YO M WITH ALCOHOL USE DISORDER

- 3 weeks later he is endorsing a return in his anxiety lasting all day. He is afraid of being alone and has difficulty calming down. He then tried taking Gabapentin 600mg/600mg/600mg/600mg, but did not find it helpful. (He is still taking Quetiapine and Lithium.) GAD7: 19/21

54YO M WITH AUD WITH PERSISTENT AND WORSENING ANXIETY, DESPITE GABAPENTIN INCREASE.

What would you do next?

A. Start Sertraline or some other SSRI
B. Start Hydroxyzine prn
C. Start Clonazepam 0.5mg BID
D. Refer to therapy
E. Call the Provider Consultation Line (and ask for Rick)
F. Other

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MHD PHARMACOTHERAPY IN AUDS

ANXIETY

- CBT
- Antidepressants/anxiolytics are modestly effective
    - Sertraline + CBT
    - Buspirone + CBT relapse prevention

****Treating anxiety did not always impact SUD treatment****

Wolitzky-Taylor, K, Ries, R, et al, 2011

DISULFIRAM + LORAZEPAM?

- *Methods*: 41 with DSM-IV alcohol dependence who also met syndromal criteria for anxiety disorder with or without co-occurring major depressive syndrome.
  - Open Label pilot

- Intervention: lorazepam (starting dose 0.5 mg three times daily) + disulfiram (starting dose 500 mg three times weekly).
  - Participants received 16 weeks of monitored pharmacotherapy with manualized medical management.

Borgenschutz, MP, et al 2018

DISULFIRAM + LORAZEPAM?

- *Results*:
  - Adherence to treatment decreased steadily with time (85.4% at 4 weeks, 36.6% at 16 weeks).
  - Participants showed significant increases in percent abstinent days during treatment and at 24 weeks follow-up.
  - Large reductions in anxiety, depression, and craving were observed during treatment, and improvement remained significant at 24 weeks.
  - Duration of adherence with disulfiram strongly predicted abstinence at 16 weeks.
  - There was no evidence of misuse of lorazepam or dose escalation during the study.

- *Conclusion*: Lorazepam can be safely used for short-term treatment of anxiety in combination with disulfiram treatment of alcohol use disorder. However, it is not clear that making lorazepam dispensing contingent on adherence to disulfiram enhances retention in disulfiram treatment.

Borgenschutz, MP, et al 2018

TAKEAWAYS

- Comorbid anxiety disorders can negatively impact SUD outcomes.
- Identifying anxiety disorders can be challenging, but it is doable.
- Protracted withdrawal symptoms need to be considered.
- Anxiety specific treatments are helpful, but may not always make a difference in SUD outcomes.

54YO M WITH ALCOHOL USE DISORDER CASE UPDATE

- Fast forward 8 weeks. Has tried Sertraline, an increase in his Quetiapine, Gabapentin dose adjustments, Propranonol-all developed intolerable side effects.
- Had a lapse on non-alcoholic beer (0.05ABV) for a week, but is now sober and going to IOP, AA, and an individual therapist.
- Eventually anxiety continued to be a significant problem and I agreed to start a trial of Clonazepam. Upon furhter dose titrtion he has found 0.25mg QID. He has also started Naltrexone and has stopped Gabapentin. He continues to take his Lithium and Quetiapine for his Bipolar disorder.
- Relationship with daughter is going well.

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QUESTIONS

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