ACCEPT

Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics

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Session Date: Friday, February 17, 2023

Didactic Topic and Presenter:
Outpatient Benzodiazepine Withdrawal Management

Ritu Bhatnagar, MD MPH FASAM DFAPA
University of Wisconsin School of Medicine and Public Health
Content Experts:
Ritu Bhatnagar, MD; CRC; Sheila M. Weix, MSN, RN, CARN, Joesph Galey, CPS

- 12:15 PM: Attendance text-in – Introductions
- 12:25 PM: Case Presentation and Discussion
  - Presenter: Jayme Christoffersen Cebi, DO - *University of Wisconsin Hospitals and Clinics, Department of Psychiatry*
- 1 PM: Didactic Presentation
  - Presenter: Ritu Bhatnagar, MD MPH FASAM DFAPA - *University of Wisconsin School of Medicine and Public Health*
- 1:15 PM End of Session

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Interprofessional Continuing Education Partnership
UNIVERSITY OF WISCONSIN-MADISON
School of Medicine and Public Health
School of Nursing
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Project ECHO
University of Wisconsin

ECHO ACCEPT
Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics
2022-2024
Outpatient Benzodiazepine Withdrawal Management
2/17/2023
Didactic Presenter: Ritu Bhatnagar, MD MPH FASAM DFAPA
Case Presenter: Jayme Christoffersen-Cebi, DO

Provided by the University of Wisconsin–Madison Interprofessional Continuing Education Partnership (ICEP)

Intended Audience:

Nurses, Nurse Practitioners, Pharmacists, Physicians, Physician Assistants, Pharmacy Technicians, Psychologists, Social Workers, Patient/Caregivers, Students

Objectives:

As a result of this educational regularly scheduled series, learners as members of the healthcare team will be able to:

1. Describe need for benzodiazepine withdrawal.
2. Explain challenges encountered by patients during benzodiazepine withdrawal.
3. Identify options for managing symptoms of benzodiazepine withdrawal for prescribers.

implications

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Name	Role	Financial Relationship Disclosures	Discussion of Unlabeled/Unapproved uses of drugs/devices in presentation?	COI completion date
Randall Brown	RSS Chair	Usona Institute (Grant / Contract), multi-disciplinary association for psychedelic studies (Grant / Contract)	Yes	1/30/2023
Nada Rashid	RSS Coordinator	No relevant financial relationships to disclose	No	1/31/2023
Kathleen Maher	RSS Coordinator	No relevant financial relationships to disclose	No	1/30/2023
Ritu Bhatnagar	Planner	No relevant financial relationships to disclose	Yes	1/29/2023
Paul Hutson	Planner	No relevant financial relationships to disclose	Yes	1/28/2023
Susan Mindock	Planner	No relevant financial relationships to disclose	No	1/31/2023
Sheila Weix	Planner	No relevant financial relationships to disclose	No	2/3/2023
Kellene Eagen	Planner	No relevant financial relationships to disclose	No	1/27/2023
Joseph Galey	Planner	No relevant financial relationships to disclose	Yes	1/27/2023
Ritu Bhatnagar	Presenter	No relevant financial relationships to disclose	Yes	2/5/2023

Jayme Christoffersen-Cebi	Presenter	No relevant financial relationships to disclose	No	2/15/2023

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Case Presentation

Jayme Christoffersen Cebi, DO
University of Wisconsin Hospitals and Clinics
Department of Psychiatry

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Project ECHO University of Wisconsin

Case Introduction

- 43 y/o F with a significant history of PTSD, and anxiety and benzodiazepine dependance who presented for medication management of her mental health diagnoses.

- Primary question for discussion: What is the ethical/safest way to discontinue prescribing benzodiazepines for a patient with escalating use who fails to recognize a problem with their benzodiazepine abuse and who has had numerous trials of other psychotropic medications but fails due to side effects/lack of effectiveness?

Medical & Behavioral Health Diagnosis:	Current Medications:
• Irritable Bowel Syndrome • Fatty Liver • Traumatic Brain Injury • Migraine headache • Seizure disorder (NES) • Anxiety disorder • Nondependent Alcohol Abuse • Post Traumatic Stress Disorder • Attention Deficit Hyperactivity • Fibromyalgia • Chronic Back Pain • Intracranial Hemorrhage • Circadian Rhythm disorder	• Albuterol Inhaler • Carisoprodol 250mg TID • Clonazepam 2.5mg BID • Diphenhydramine 100mg TID • Lidocaine 5% patch once daily • Linzess 2290 MCG cap one time daily • Omeprazole 40mg one time daily • Ondansetron 4mg q 8 hours • Propanolol 20mg

Substance Use

- History: Began using benzodiazepines at 6 years old, was given grandmother's Valium
- Consequences of Substance Use:
  - Social/occupational/educational: Unemployed, married to her best friend to obtain insurance benefits and live in his apartment. Has degree in psychology did not pursue. DUI arrest in 2020
  - Physical (including evidence of tolerance/withdrawal): Participates in frantic seeking behaviors for refills of benzodiazepines. Begins to experience withdrawal symptoms within 8 hours of last dose. Has a pattern of early refills on her benzodiazepine prescriptions. Has seen multiple physicians in an attempt to gain additional/supplemental prescriptions
- Past treatments: Each psychiatrist she has seen attempts to taper.

Social History:	Family History:
• Social Factors/History: Mother with bipolar disorder/schizophrenia. Parents were emotionally, sexually and verbally abusive and neglectful she was placed in her grandparents home as a toddler. Grandmother began giving her Valium when she was 6 years old to help with her anxiety. • Education/Literacy: College educated with a Bachelors in psychology. • Income source: Currently on disability due to seizure disorder	• Mother with Bipolar disorder and "mild" schizophrenia. • Brother with schizophrenia and ADHD • Brother attempted suicide • Aunt completed suicide

Patient strengths & protective factors:	Risk factors:
• Previously had positive outlets for coping • Positive self image • Resiliency • Spirituality	• Limited social support • History of Chronic Substance Abuse • Not recognizing the substance abuse as a problem • History of trauma • LGBTQ+ • Currently limited coping skills • Lack of structured activities

Labs

- 2019- Alcohol posivite 0.1
- 2019- Urine Drug Screen positive for benzodiazepines
- 2018- Urine Drug Screen positive for benzodiazepines

Patient Goals & Motivations for Treatment

- This patient does not recognize she has a benzodiazepine use disorder she believes the medication is the only thing that will help her mental health
- Goals for treatment are to decrease/abolish nightmares/flashbacks and to continue to use benzodiazepines

Proposed Diagnoses

- Benzodiazepine Use Disorder
- Post Traumatic Stress Disorder
- Panic Disorder

Proposed Treatment Plan

- Initiate treatment with a SSRI, likely duloxetine or desvenlafaxine
- Taper clonazepam 0.5 mg in 2 week increments with a goal to 0

Discussion:

- Primary question: What is the ethical/safest way to discontinue prescribing benzodiazepines for a patient with escalating use who fails to recognize a problem with their benzodiazepine abuse and who has had numerous trials of other psychotropic medications but fails due to side effects/lack of effectiveness?

DSM-5 Substance Use Disorder ("Addiction")

- Tolerance
- Withdrawal

} **Physical Dependence ≠ Use Disorder**

- Larger amts/longer periods than intended
- Persistent desire/failed attempts to quit/control use
- Much time obtaining/using/recovering
- Important activities sacrificed
- Continued use despite known adverse effects
- Failure to fulfill major obligations
- Recurrent hazardous use
- Craving
- Ongoing use despite interpersonal problems

2-3 = mild
4-5 = moderate
≥ 6 = severe

By initialing here _____ you have acknowledged that Project ECHO case consultations do not create or otherwise establish a provider-patient relationship between any ECHO clinician and any patient whose case is being presented in a teleECHO clinic.

Outpatient Benzodiazepine Withdrawal Management

Ritu Bhatnagar, MD MPH FASAM DFAPA

February 17, 2023

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Objectives

At the conclusion of this presentation, the attendee will be able to:

1. Describe need for benzodiazepine withdrawal (BZD w/d)
2. Explain challenges encountered by pts during BZD w/d
3. Identify options for managing symptoms of BZD w/d for prescribers

Overview

- Circumstances where BZD taper is needed
- Difficulties for person undergoing taper
- Difficulties for prescriber guiding this person
- (and how to manage the last 2)

Scope of problem

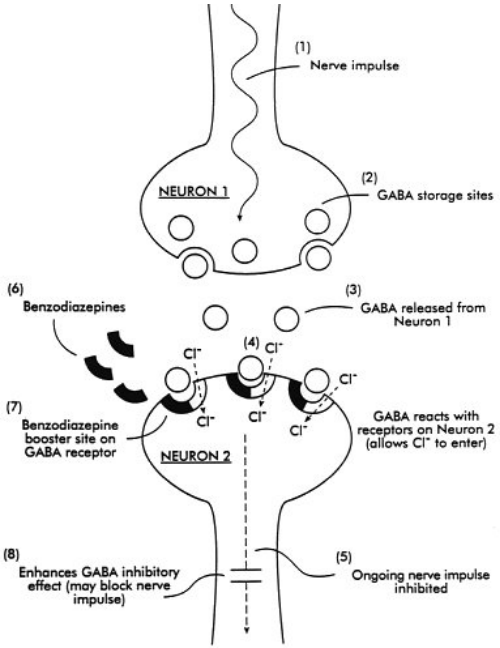
- A 2019 study found that the number of **BZD prescriptions in the U.S. increased by about 50 percent** between 2005 to 2015
  - most of the prescriptions from Family Practice Providers.
- Fatality increases with current wave of opioid epidemic with polysubstance impact on respiratory depression
  - Overdoses with BZD increased most in women 30-64 y.o. b/w 1996 to 2017 (CDC)

Agarwal S et al, 2019. Patterns in Outpatient Benzodiazepine Prescribing in the United States. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2722576

Acute and chronic effects of BZD

- Acute: GABA-A agonism
- Increase GABA in the brain, bind to receptors, promote calm
  - CNS depression
- Chronic: neuro-adaptation occurs
  - down regulation of GABA receptors
  - d/t exogenous supply of GABA from BZD

Ashton manual https://benzo.org.uk/manual/



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Dangers of sudden cessation

- Longer than 4 weeks, likely to note some w/d
- Similar to alcohol effects in brain
- GABA receptors down regulated
- No GABA = unopposed glutamate
- Brain (and person) in sympathetic overloaded state
- Increased anxiety → confusion/ paranoia/ psychosis
- Seizures
- ? Death

Why taper BZD?

- Person wants to taper
  - Not like dependence/ reliance on medical system for refills
  - Side effects/ increasing tolerance over time
- Prescriber wants to taper
  - Safety concern with alcohol/ opioids/ meds
  - Falls/ dementia
  - Driving impairment
  - Increased mortality with long term use
  - Misuse
  - Diversion

Brett J et al, 2015. Management of Benzodiazepine Misuse and Diversion. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4657308/

Who initiates?

- Careful review of medications and their need annually
- Monitor closely
- Always check PDMP/ use patterns
- Ensure buy-in before proceeding with taper: MI
  - Without this, lack of honest interactions/ “firing”
  - Takes time
  - Consider additional supports available – therapy/ family

Duration of symptoms

- Varies extensively
- BZD concentrations in the blood have been measured and shown to reach undetectable levels in 3-4 weeks after cessation

Ashton manual https://benzo.org.uk/manual/

Protracted withdrawal

Symptoms	Usual Course
Anxiety	- Gradually diminishing over a year
Depression	- May last a few months; responds to antidepressant drugs
Insomnia	- Gradually diminishing over 6-12 months
Sensory symptoms: tinnitus, tingling, numbness, deep or burning pain in limbs, feeling of inner trembling or vibration, strange skin sensations	- Gradually receding but may last at least a year and occasionally several years
Motor symptoms: muscle pain, weakness, painful cramps, tremor, jerks, spasms, shaking attacks	- Gradually receding but may last at least a year and occasionally several years
Poor memory and cognition	- Gradually receding but may last at least a year and occasionally several years
Gastrointestinal symptoms	- Gradually improving but may last a year and occasionally several years

Ashton manual https://benzo.org.uk/manual/bzcha03.htm#t3

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Challenges and what to do

Increased anxiety
Tremors, sweating
Increased HR
Agoraphobia
Muscle tension
Hypertension
Loss of appetite/ nausea
Diarrhea
Tingling in hands/feet
Depression
Difficulty focusing
Sleep disturbance

Slow taper

Valproic acid *
Clonidine *
Hydroxyzine *
Trazodone *
Gabapentin *
Baclofen? *
Tizanidine? *
SSRIs
Low inflammatory foods *

(* off-label, symptom relief driven approaches to minimize sympathetic overload, stabilize cellular and physical distress)

Tapering strategies

- Convert short acting BZD (like alprazolam) to long acting BZD (like clonazepam)
- Dose converter: https://clincalc.com/Benzodiazepine/
- Taper by 5-10% every 1-2 weeks as tolerated.
- Adjunctive medications important/ useful
  - Seizure precautions with short-term Valproic acid
  - Sx driven approaches
- More frequent visits/ shorter duration of refills
  - Engage family members to help with dispensing meds
- Increase/ add therapy support
- Check PDMP

Flumazenil

- GABA-A antagonist
- Low dose flumazenil for BZD detox:
- low-dose subcutaneous flumazenil infusions (4 mg/24 h for approx. 8 days)
- Abstinence at 3 mos. b/w 46 and 61%
- For high dose BZD use (>30 mg diazepam eq)
- Speaks to challenges of remaining BZD free

(MacDonald et all, 2022. Outcomes of patients treated with low-dose flumazenil for benzodiazepine detoxification: A description of 26 participants. https://doi.org/10.1016/j.drugalcdep.2022.109517)

Ways to increase GABA without BZD?

- Exercise – cardio, anyone?
- Yoga
- Meditation/ mindfulness (free online resources abound: Headspace, Calm, insight, Healthy Minds App, mindfulrp.com)
- EFT / acupressure/ acupuncture/ somatic therapies
- Supplements like Magnesium, B6, Zinc can help with adaptogenic support
- Reduce environmental stresses

Caveats

- Not all supplements are equal (or equally safe!)
- Lavender oil (fair evidence)
- GABA foods? (unclear bioavailability)
  [https://www.ororecovery.com/ways-to-increase-gaba-naturally-for-anxiety-without-benzos/]
- Phenibut, or beta-phenyl-gamma-aminobutyric acid Hcl, = designer GABA analogue
  - Abusable, can lead to dependence
  - Available online easily

Conclusions

- BZD tapering as outpt is possible
- Discuss/ agree to rationale before tapering
- Monitor closely
- Support sxs as they emerge
  - be patient with process
- Engage other modalities
- Consider other options for anxiety management to avoid needing to taper in the future!

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- Tolerance
- Withdrawal

} **Physical Dependence ≠ Use Disorder**

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