ACCEPT

Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics

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Session Date: Friday, August 16, 2024

Didactic Topic and Presenter:
Medications for Alcohol Use Disorder: Review of FDA approved and off-label MAUD

Randy Brown, MD, PhD
Content Experts: Sheila Weix and Joe Galey

- 12:15 PM: Attendance text-in – Introductions
- 12:25 PM: Case and Didactic
    - Presenter: Randy Brown, MD, PhD
- 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
School of Pharmacy

Project ECHO
University of Wisconsin

ECHO ACCEPT
Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics
2024-2025
Medications for Alcohol Use Disorder: Review of FDA approved and off-label MAUD
8/16/2024

Didactic and Case Presenter: Randy Brown, MD, PhD

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) Discuss the neurobiological effects of alcohol and implications for pharmacotherapy
2) Describe the mode of action and approach to patient selection for FDA-approved AUD medications
3) Discuss literature regarding non-FDA approved MAUDs

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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	1/29/2024
Nada Rashid	RSS Coordinator	No relevant financial relationships to disclose	No	2/5/2024
Kathleen Maher	RSS Coordinator	No relevant financial relationships to disclose	No	2/6/2024
Ritu Bhatnagar	Planner	No relevant financial relationships to disclose	Yes	2/8/2024
Paul Hutson	Planner	No relevant financial relationships to disclose	Yes	1/29/2024
Susan Mindock	Planner	No relevant financial relationships to disclose	No	1/29/2024
Sheila Weix	Planner	No relevant financial relationships to disclose	No	2/9/2024
Kellene Eagen	Planner	No relevant financial relationships to disclose	No	1/29/2024
Joseph Galey	Planner	No relevant financial relationships to disclose	No	2/13/2024
David Leinweber	Planner	No relevant financial relationships to disclose	Yes	1/20/2024
Randall Brown	Presenter	No relevant financial relationships to disclose	Yes	8/8/2024

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Case Presentation

Randy Brown
UW Health

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For this educational activity there are no reported conflicts of interest

Project ECHO University of Wisconsin

Case Introduction

- 42 yo M w/ hepatic steatosis, AUD

- Primary question for discussion:
- Pharmacotherapy in setting of alcohol-associated liver disease

Medical & Behavioral Health Diagnosis:	Current Medications:
• Hepatic steatosis (CT demonstrated) • Tobacco use disorder • Major depressive disorder	• Bupropion 150mg BID • Trazodone 50-100mg QHS

Substance Use

- History: 750mL whiskey consumption daily for past 10+ yr. Longest period of abstinence ~4 wk after OWI #2/classes. Several ED reports in last yr due to falls/intoxication, but no significant injury requiring hospitalization/intervention. ↑ LFT, hep steatosis noted on ED eval and pt referred to ALD clinic. Abstinent x ~24 hr. Experiencing anx/tremor.
  - No Sz/DT hx
- Past treatments:
  - Nova residential in 2000's
  - OWI classes
  - No prior pharmacoTx

Social History:	Family History:
• Social Factors/History: Roommate drinks heavily • Education/Literacy: HS grad • Income source: part-time at recycling center	• No known AODA • Mother w/ MDD

Patient strengths & protective factors:	Risk factors:
• Family supportive • Employment • Motivated by health & legal (3rd OWI recently)	• Living situation • Ongoing craving • Withdrawal Sx • Frequent waking • Legal outcome uncertain

Labs

Lab	Value	NI
AST U/L	90*	17–59
ALT U/L	33	0–49
T bili mg/dL	0.6	0.2–1.3
Albumin g/dL	4.5	3.5–5
INR	0.9	0.9–1.1
Hgb g/dL	13.3*	13.6–17.2
MCV fL	89	80–97
Plt K/uL	117*	150–450

Patient Goals & Motivations for Treatment

- Abstinence
  - Motivated by health concerns (falls, liver dz)
  - Legal – 3rd OWI. Court pending.
  - Return to work

Proposed Diagnoses

- ALD—hep steatosis
- AUD, severe
- Mild alcohol w/d
- MDD
  - Insomnia due to MDD vs. w/d

Discussion:

- Primary question: Medication(s) selection?

Proposed Treatment Plan

- SUD tx intake pending
- Peer recovery coach
- Gabapentin

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.

Medications for Alcohol Use Disorder (MAUD)

Randall Brown MD, PhD, DFASAM

Project ECHO ACCEPT

August 19, 2024

Introduction

20+% lifetime prevalence of AUD in US

30+% of patients in hospital & primary care settings engage in current risky or problem alcohol use

MAUD is severely under-offered/utilized

McPheeters M 2023. JAMA.

Alcohol & Neurobio

Acute effects

↑ GABA (inhibitory transmitter)

↓ glutamate (excitatory transmitter)

Endogenous opioids → rewarding effects/craving

Chronic, heavy consumption

↓ GABA

↑ Glutamate

Unopposed CNS excitation & ↑dopaminergic transmission with abrupt cessation (alcohol withdrawal/craving)

Medications for Alcohol Use Disorders (MAUD)

- **Naltrexone**
  - Oral (Revia)
  - Monthly injectable (Vivitrol)
- **Acamprosate (Campral)**
- **Disulfiram (Antabuse)**
- **Other non-FDA-approved (but evidence-based) stuff**

Ayyala D 2022. Hepatology.
Jonas DE 2014. JAMA.

MAUD: Naltrexone

Mode of action = μ-opioid antagonism	Contraindications	Cautions
• Blunted positive reinforcement • Reduction of μ-mediated positive expectancies	• Opioid dependent/opioid analgesia • Acute hepatitis • Hypersensitivity	• Pregnancy/breastfeeding, inadequate data, but unlikely teratogenic • Active liver dz (AST, ALT > 3-5x normal)

Naltrexone Initiation

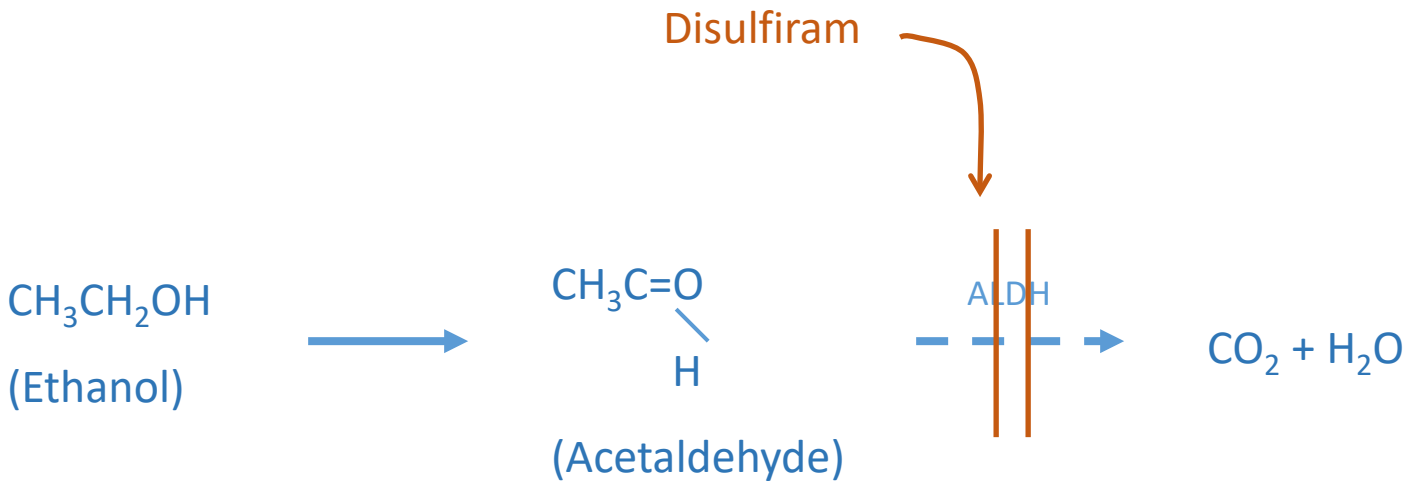
- Initial LFTs, urine drug screen (UDS)?
  - No need to delay Rx for LFT result if no clinical evidence of liver disease
- Oral Dose
  - Typical = 50mg daily
  - At-risk (< 3 days abstinence, young age)
    - 12.5-25mg daily x 1 week
    - Titrate up to 50mg daily
  - Sinclair Method
- Injection
  - 380mg IM monthly
  - Room temp ~30 min prior to injection

MAUD: Acamprosate

Mechanism of action	Contraindications	Cautions	Dosing
• Poorly characterized • Indirect fx on GABA and glutamate receptors ("modulation") • Better for maintaining than initiating abstinence or use reduction	• Hypersensitivity • Severe renal dysfunction (Cl_{Cr} < 30 mL/min)	• Pregnancy/breastfeeding – unlikely teratogenic, inadequate data • Moderate renal dysfunction (Cl_{Cr} 30-60 mL/min) • Age > 65	• Initial: 333mg TID for 3-5 days • Maintenance: 666mg TID = FDA-approved; some fx at 999mg BID

Jonas DE 2014. JAMA.
Rosner S 2010. Coch Database Syst Rev.

MAUD: Disulfiram



Disulfiram-alcohol reaction → Poor adherence

No effect in blinded RCTs

(Skinner MD 2014. PLoS ONE)

MAUD: Disulfiram

Contraindications

Severe myocardial dz

Hypersensitivity (disulfiram, nickel, sulfur)

Pregnancy

Cautions

LFTs > 3 x upper normal

Recent alcohol exposure

Age > 60

Disulfiram Initiation

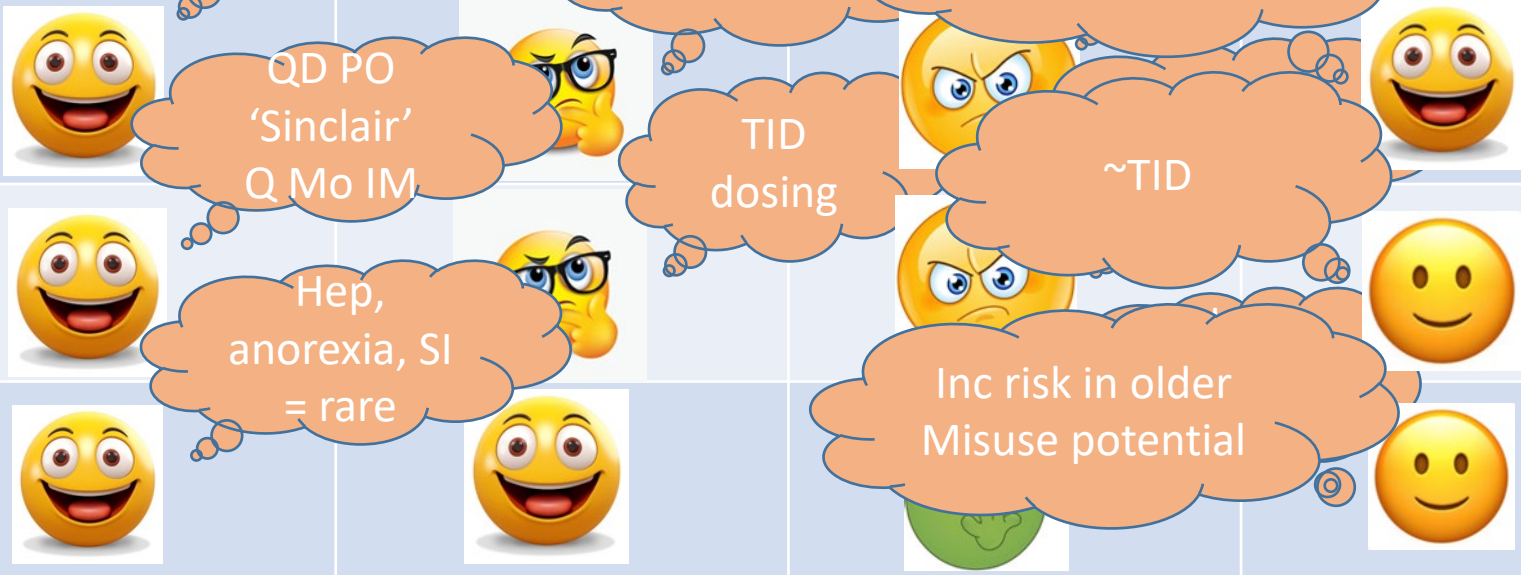
- 12+ hours abstinence and/or BAC = 0
- Baseline LFTs, urine HCG
- ECG if clinically indicated
- Dosing
  - 250mg/day up to 500mg/day
  - Supervised dosing preferred

Disulfiram Adverse Effects

- Common
  - Dermatitis, metallic taste, disulfiram-alcohol reaction
- Less common
  - Hepatitis, peripheral neuropathy, optic neuritis, psychosis, headache, drowsiness, sexual dysfunction
- Multiple drug interactions (TCAs, warfarin, metronidazole. . .)

FDA-approved Pharmacotherapies + Gabapentin: Summary & Pt selection

	Nalt	prosate	Disulfiram	Gabapentin*
Effectiveness	Fam Hx Craving Mu blockade	Maintain abstinence	Post-acute w/d Craving	
Convenience	QD PO 'Sinclair' Q Mo IM	TID dosing	~TID	
Toxicity	Hep, anorexia, SI = rare		Inc risk in older Misuse potential	



Non-FDA Approved

- Gabapentin + naltrexone (Anton RF 2021. JAMA Int Med; Anton 2011. Am J Psych)
- Topiramate (Blodgett JC 2014. ACER; Johnson B 2007 JAMA)
- Ondansetron (Johnson B 2024. Eur J Int Med; Dawes M 2005 Addict Beh.)
- Prazosin (Raskind 2023. ACER; Andrade 2021. J Clin Psych; Fox H 2012 Alc: Clin Exp Res)
- Baclofen? (Duan F 2023. J Psych Res; Garbutt 2010 Alc: Clin Exp Res & 2021 Neuropsychopharm)
- GLP-1 antagonists (Shen MR 2024. J Add Med)
  - Peeps are excited, but human studies are mixed w/ pos results mainly in individuals w/ obesity + AUD

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