Management of Alcohol Use Disorder

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Background on chemical dependencies: occur because of changes in neurotransmitters; changes may also be related to environment or culture

Depressant drugs: benzodiazepines (BZDs); barbiturates; many prescription sleep medications; alcohol (most popular for recreational use to attain euphoric effects); data on alcohol relate to most other depressants as well

Patient monitoring: imbibing >3 standard drinks per day negatively affects health; regardless of whether patients meet criteria for alcohol use disorder (AUD), those who consume these quantities require attention

AUD in Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition; DSM-5): recurrence of events related to alcohol that interfere with life functioning and despite which person continues to use alcohol; dependence criteria — needing greater quantities of alcohol to achieve effects (ie, tolerance); withdrawal (occurs only in minority of individuals with alcohol dependence); using more alcohol than intended; inability to control usage

Origins of AUD or heavy drinking: result from complex series of occurrences, and thus require complex treatment; personal variables — genetic makeup (not all individuals have equal risks for AUD); reinforcers of use (eg, heavy pattern of use, using increasing amounts as body adapts); societal factors — alcohol easily available, and peers frequently encourage its use; society, availability, and cost all have major effect on development of heavy drinking and AUD; demography — women have lower risk for use of alcohol, heavy drinking, and AUD; however, women who develop AUD show impairment comparable to (or greater than) that in men

Course of substance use disorder (SUD): fluctuates over time; study (Schuckit et al, 2014) — included 1600 participants who were predominantly white-collar college students; among participants in study, as well as among more indigent patients at speaker’s VA treatment center, courses fluctuate (eg, patients cut back and enter phase of controlled drinking [lasting days to months], but eventually develop problems due to vulnerability to AUD); spontaneous remission — occurs in ≥20% of patients (even with severe impairment); not necessarily related to Alcoholics Anonymous attendance or treatment; occurs unpredictably, but often coincides with major crisis (commonly related to health)

Ramifications: because of fluctuating course of SUDs and incidence of spontaneous remission, virtually any intervention may appear to show efficacy over short term; thus, speaker emphasizes importance of paying attention to double-blind controlled trials of treatments rather than relying on personal clinical judgment without data

Treatment

Role of medications: important and helpful, but must not be relied upon alone; they constitute only part of treatment, and may not be most important part

Identification: since physician cannot immediately identify patients with AUD, consider all patients to be at risk for heavy drinking and AUD; speaker asks about, eg, relationships, job, accidents, then asks patients what other people in their lives complain about regarding them, and then assesses whether those patterns of problems might relate to alcohol or substance use patterns; avoid stereotypes and screen everyone (physicians may expect to see AUD in, eg, indigent patients, but AUD more likely among affluent patients)

Questionnaires: many available, ranging from 1 to 30 questions; those with more questions provide more knowledge about patient and may do more to help patients determine whether they have problem; Alcohol Use Disorders Identification Test (AUDIT) — preferred by speaker; 10 questions; first 3 questions focus on drinking frequency, typical daily quantity, drinking ≥6 drinks, while remaining questions relate to DSM criteria (eg, uncontrolled use, failing in roles) and nondiagnostic problems frequently seen in individuals who drink too heavily (guilt regarding drinking, “blackouts”); items rated from 0 (nonexistent) to 4 (highly problematic); patients with scores of 7 to 8 likely to face problems, and patients with scores of ≥20 probably meet criteria for AUD; AUDIT-C — shortened version; asks about frequency of drinking, usual number of drinks, and frequency of ingesting ≥6 drinks during single occasion; scores of ≥2 in women and ≥4 in men indicate possible problems; specificity — these scales do not diagnose AUD, but indicate high likelihood

Gamma-glutamyl transferase (GGT) level: useful blood test in patients with suspected AUD; levels of ≤50 IU/L may be normal in patients with liver disease, but most individuals do not have GGT levels >35 IU/L; GGT of 35 to 50 IU/L (or higher) has 70% chance of being caused by heavy drinking (even if patient does not meet criteria for AUD)

Motivational interviewing and brief intervention: tools used by physicians to encourage patient’s involvement and

Educational Objectives

The goal of this program is to improve the recognition and treatment of heavy drinking and alcohol use disorder (AUD). After hearing and assimilating this program, the clinician will be better able to:

1. Identify problematic drinking and AUD in patients who deny or remain unaware of their issues.
2. Apply tools such as brief interventions and motivational interviewing to help patients recognize their issues with alcohol and develop the desire to change.
3. Determine whether patients require detoxification in order to safely wean themselves from a chemical dependency.
4. Provide evidence-based therapy to help patients abstain from or reduce their alcohol consumption.
5. Reduce the side effects of withdrawal and a patient’s likelihood of resuming drinking through the use of targeted medications.

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adherence during treatment; they help patients realize they may have problems, wrestle with their problems, look at various options, and decide (under physician’s guidance) whether they should stop or cut back on drinking

**Detoxification**: necessary with patients using or withdrawing from depressants; patients who take high doses of agents for sufficient periods (varies based on age, sex, and physical condition) before discontinuing develop rebound syndrome with symptoms opposite to acute effects of depressants

**Withdrawal from alcohol and other short-acting depressants**: varies based on course of disorder; since alcohol has short half-life, patients enter withdrawal as soon as blood alcohol drops below usual levels, and symptoms typically appear within 8-10 hr; intensity of symptoms typically peaks on day 2 and diminishes by day 5; after acute withdrawal, lingering symptoms (affecting, eg, pulse, respiration, galvanic skin response, pupil response) may remain for 3 to 6 months; in contrast, patients who use long-acting agents may not start withdrawal for 4 to 5 days, and withdrawal tends to last several weeks; benefits of medications (eg, acamprosate) probably relate to 3 to 6 mo period of protracted symptoms

**Initial steps of detoxification from depressants**: replace brain depressants responsible for withdrawal with different depressants to improve comfort during first 5 days of weaning; any depressant may be used (eg, alcohol, BZDs); anticonvulsants have higher costs, less relevant data, and greater dangers compared to BZDs; BZDs — gold standard of treatment for alcohol withdrawal

**Outcomes**: patients with alcohol dependence or AUD who show willingness to enter and stay in treatment program often have positive outcomes; even among destitute patients at speaker’s VA clinic, 52% remained abstinent at 1 yr (after staying for ≥3 wk of 4-wk inpatient program; verified by informants and blood and urine testing); with more generalized populations, 1-yr abstinence rates should reach 65% to 75%; 1 yr abstinence predicts 5-yr abstinence (individuals who have abstained or severely cut back drinking at 1 yr have ≥70% chance of remaining in long-term abstinence for 5 yr)

**Core of treatment**: increasing motivation for change; helping patients rebuild lives in different way; help patients recognize signs they have returned to old habits or heavy drinking, and deal with those risks when they develop

**Cognitive behavioral therapy (CBT)**: core of treatment for, eg, smoking cessation, alcohol problems, excessive drinking, and AUD; goals — changing how patients think about disorders and their responsibility for disorders; identifying triggers associated with drinking, and learning to handle and cope with those triggers; changing behaviors, peer groups, and handling of stress

**Medications**

**Disulfiram (Antabuse)**: inhibits enzyme (acetaldehyde dehydrogenase [ALDH]) in mitochondria responsible for metabolism of alcohol, leading to build-up of acetaldehyde; ingesting alcohol in context of disulfiram causes vomiting, nausea, headaches, fainting, and potentially death (extremely rare); side effects — liver reactions; depression; mood changes; literature review (Jørgensen et al, 2011) — included 11 studies, some of which monitored whether patients ingested ≥250 mg (not sufficient to totally inhibit ALDH); when adherence monitored and supervised, disulfiram had benefits slightly superior to placebo; cost — relatively inexpensive (≈$154 per month); conclusions — considered by speaker as third-level medication (due to difficulties constructing double-blind trials, side effects, dangers of alcohol-disulfiram reactions, and uncertainty regarding efficacy)

**Naltrexone**: available in 50 mg oral dose or 380 mg extended-release injection (Vivitol); effects on reward and dopaminergic systems may affect alcohol intake (since opioids have relationship to alcohol and drinking); mechanism relates to μ-opioid receptors; some data indicate decreases in cravings and severity of relapse; costs — injection may cost ≤$1300 per month, whereas oral treatment costs ≤$100 per month; Asp40 allele of OPRM1 gene — genetic variation associated with increased response to naltrexone

**Acamprosate**: dosed as 666 mg tid (due to poor absorption); affects protracted alcohol withdrawal (state marked by insufficient γ-aminobutyric acid [GABA] functioning and excessive functioning in stimulatory N-methyl-D-aspartate [NMDA] glutamate receptors); said to increase probability of remaining abstinent; cost ≤$230 per month

**Comparison by meta-analysis (Maisel et al, 2012)**: included 45 double-blind, controlled trials with naltrexone and 16 with acamprosate (total of ≥5000 participants); when assessing whether patients returned to drinking, acamprosate more likely to have acceptable effect size (0.4); naltrexone showed some benefit when researchers assessed whether patient could cut back on drinking after returning from abstinence; data on cravings remain inconclusive, but greater quantity of data support naltrexone’s effects on cravings over possible effects of acamprosate

**Speaker’s conclusion**: when combined with CBT, each medication increases probability of having significant effects by ≥15%

**Nalmefene**: μ-opioid receptor antagonist (similar to naltrexone), with additional effects at δ-opioid and κ-opioid receptors; study (Mann et al, 2012) — included 604 participants from ≥8 treatment programs; assessed whether nalmefene helped patients cut back on drinking (if they refused to abstain); after 6 mo, nalmefene reduced heavy drinking by 11 days per month, compared to 9 days with placebo (significant); not available in United States

**Ondansetron (Zofran)**: serotonin agonist (studies using animal models have associated low serotonin activity with slightly higher amounts of drinking); study (Johnson et al, 2013) — 283 alcohol-dependent individuals received low dose (on per-kilogram basis) of ondansetron or placebo for 11 wk; overall, no effects observed; however, in patients with long version of allele associated with less rapid transport of serotonin out from synapse, ondansetron decreased alcohol consumption by 4 to 5 drinks per day (compared to 3 drinks with placebo or patients who had different version of serotonin transporter allele), and increased number of days abstinent to 23% (vs 12-13% with remaining participants); cost — ≤$110 per month; speaker’s conclusion — not recommended due to side effects, questionable efficacy, and necessity of genotyping

**Selective serotonin reuptake inhibitors (SSRIs)**: although antidepressants in general lack benefit, some SSRIs (eg, sertraline [Zoloft]) may have efficacy; study (Kranzler et al, 2012) — SSRIs decreased drinking only in patients with long variant of serotonin transporter allele (reduced drinking days to 15% vs 30% with placebo) and drinks per day by significant margin; cost — ≤$400 per month

**GABA-boosting agents**: topiramate — study (Johnson et al, 2007) found that although topiramate was inferior to placebo at reducing heavy drinking days, it was superior at increasing days spent abstinent; issues with topiramate — side effects; high costs (≈$600 per month); not recommended, but may hold future promise; gabapentin — in small study (Anton et al, 2011; 50 participants), patients treated with gabapentin plus naltrexone showed greater benefit than those treated with naltrexone alone; side effects of gabapentin — significant and include blood dyscrasias (rare, but potentially fatal); not recommended by speaker; baclofen — inexpensive, but studies show highly mixed outcomes

**Varenicline (Chantix)**: barely superior to placebo

**Prazosin (Minipress)**: α-adrenergic antagonist; may eventually be shown superior to placebo, but further data required
Questions and Answers

Protracted alcohol withdrawal: includes sleeping problems and autonomic nervous system hyperactivity; improves week by week, but patients feel unwell; acamprosate probably helps by moderating NMDA overactivity, making patients feel less unwell and thus less likely to drink

Severe depressive episodes: triggered by alcohol in ≈40% of alcoholics; episodes resembling MDD typically lift above level of DSM diagnosis within 1 wk to 1 mo

Atypical antipsychotics: in study by Litten et al (2011), despite efforts to produce high-quality data and control for variables, quetiapine and placebo had equal benefits; speaker does not see promise in using antipsychotics for AUD

β-blockers: not recommended for alcohol withdrawal because adrenal blockade can mask signs of impending seizures or delirium tremens (occur in 3%-5% of withdrawals)

Bupropion: may hold promise for particular subgroups (similar to SSRI); warrants further research

BZDs for alcoholism: speaker advocates conservative approach because of difficulties with weaning and lack of evidence supporting other GABA-boosting agents; excellent for treatment of withdrawal; further data required

Short-acting vs long-acting BZDs: failure to take short-acting agents every 4 hr can lead to seizures, and adjusting to levels of short-acting BZDs can complicate brain’s existing issues with GABA during alcohol withdrawal; speaker recommends long-acting BZDs (except with extremely severe liver disease or persisting periods of neurocognitive impairment predating withdrawal)

Study by Ouimet et al (2013): 5- to 10-minute interventions significantly decreased recidivism and overall drinking among individuals convicted of driving while intoxicated; speaker recommends brief interventions and motivational interviewing at any stage of alcohol or substance problems

Patients unwilling or unable to enter treatment: speaker recommends having them select Alcoholics Anonymous group with members similar to their own background (or helping them find one)

Acknowledgments

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Review Educational Objectives on page 1 5 minutes
Take pretest 10 minutes
Listen to audio program 60 minutes
Review written summary and suggested readings 35 minutes
Take posttest 10 minutes
1. Compared to men, women have a _______ risk for heavy drinking and developing alcohol use disorder (AUD), and women who develop AUD show levels of impairment that are _______ those in men.
   (A) Lower; lower than
   (B) Lower; comparable to (or higher) than
   (C) Higher; lower than
   (D) Higher; comparable to (or higher) than

2. What percentage of patients with a substance use disorder spontaneously enter remission, often as a result of a life crisis?
   (A) ≈35%
   (B) ≈20%
   (C) ≈10%
   (D) ≈5%

3. Testing the level of gamma-glutamyl transferase (GGT) in the blood can be useful in assessing possible AUD; in _______ of patients with a GGT level of 35 to 50 IU/L (or higher), the increased level is associated with heavy drinking.
   (A) ≈45%
   (B) ≈55%
   (C) ≈70%
   (D) ≈90%

4. The symptoms of acute alcohol withdrawal typically peak between _______ after stopping consumption:
   (A) 96 hr and 1 wk
   (B) 48 and 96 hr
   (C) 24 and 48 hr
   (D) 8 and 24 hr

5. After acute alcohol withdrawal ends, a variety of symptoms, such as increased pulse and respiratory rates, may linger for 3 mo to 6 mo.
   (A) True
   (B) False

6. Which type of medications is considered the gold standard for treatment of acute alcohol withdrawal?
   (A) BZDs
   (B) Anticonvulsants
   (C) γ-Aminobutyric acid boosting agents
   (D) Antipsychotics

7. Which of the following elements is generally considered the core of treatment for AUD?
   (A) Motivational interviewing or brief intervention
   (B) Cognitive behavioral therapy
   (C) Medication to reduce withdrawal symptoms
   (D) Medication to prevent or mitigate relapse

8. Patients with AUD who test positive for the Asp40 allele of the OPRM1 gene have greater responses to _______ than patients who do not.
   (A) Naltrexone
   (B) Acamprosate
   (C) Ondansetron
   (D) Topiramate

9. Which of these medications consistently shows the greatest effect sizes in preventing patients from resuming alcohol consumption?
   (A) Disulfiram
   (B) Naltrexone
   (C) Acamprosate
   (D) Nalmefene

10. Unless a patient has severe liver disease or a history of persistent neurocognitive impairment, long-acting BZDs are preferred over short-acting BZDs for the treatment of alcohol withdrawal.
    (A) True
    (B) False

Answers to Audio Digest Psychiatry Volume 43, Issue 18: 1-A, 2-C, 3-D, 4-A, 5-C, 6-B, 7-B, 8-C, 9-D, 10-B