CLINICAL VIGNETTE

Diagnosis and Treatment of Alcohol Use Disorder

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Case 1

A 55-year-old female with depression and alcohol use disorder quit drinking at the start of her 10-day inpatient detoxification program and was subsequently started on extended release naltrexone injections one month after she completed the program. Two weeks following her first injection, she experienced joint pain, fatigue, dizziness, weakness, significant weight gain, and worsening insomnia and depression. She subsequently elected to discontinue the injections. The patient presented again at 470 days of sobriety with the desire to try oral naltrexone to prevent relapse in the setting of her worsening depression and subsequent craving to drink. She was started on oral naltrexone 50mg daily and has been taking it consistently, in addition to attending Alcoholics Anonymous (AA) meetings. She has not experienced any significant side effects from the oral naltrexone and months later proudly reported no alcohol consumption for 540 days, with no desire to return to drinking.

Case 2

A 56-year-old male with psoriasis, psoriatic arthritis, and alcohol use disorder for over ten years with an associated DUI. He first attempted abstinence through self-referral to AA 9 years ago. He continued to experience relapses every two to three months over the last ten years. His alcohol use contributed to his separation from his wife and dismissal from his job two years ago. He has participated in five inpatient detoxification programs and one intensive outpatient program over the last six years. He tried disulfiram (Antabuse) and oral naltrexone (Revia) two years ago, but quickly relapsed. Extended release intramuscular naltrexone (Vivitrol) was the most helpful treatment during this time at preventing his cravings and prolonging his sobriety. Due to lapsing insurance and Vivitrol's high out of pocket cost ($800-$1500), he was unable to afford the Vivitrol injections. He used oral naltrexone, with at least two more associated relapses, until nine months ago when, in the midst of a divorce, he presented to clinic requesting a Vivitrol injection, while continuing to take his oral naltrexone. Over the last nine months, due to the stress from his divorce and not seeing his family, he has relapsed at least five times. He has not been regularly involved in AA. However, he has continued to actively seek out the Vivitrol injections and they have helped him to continue his new job despite continued drinking by reducing the number of heavy drinking days.

Discussion

Epidemiology

Alcohol use disorder is a prevalent, costly, and devastating medical condition, affecting 16 million people in the United States, and contributing to $294.0 billion cost annually and 88,000 deaths per year related to alcohol misuse.[1] National Institute on Alcohol Abuse and Alcoholism (NIAAA) 2015 data show 28% of adults in the United States exceed the threshold for risky use of alcohol, and the third National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-III) estimated that 29.1% of adults meet criteria for an alcohol use disorder in their lifetime.[1,2] Despite the significant prevalence of AUD, in a recent national epidemiologic survey only 7.7% of people with AUD within the last 12 months and 19.8% of people with a lifetime diagnosis of AUD sought treatment or help for AUD, with only 3.6% seeking help from health care practitioners.[2]

Clinical Presentation

Given the small percentage of AUD patients that actively seek care from physicians, it is important to recognize the various presentations of risky alcohol use and AUD, and routinely screen for alcohol misuse. As with our patient in Case 2, AUD commonly manifests in the primary care setting as social or behavioral problems rather than the overt admission to alcohol abuse, acute intoxication, or withdrawal.[3] Important warning signs include motor vehicle accidents, failure to meet obligations at work or school, falls, injuries, unsafe sex, interpersonal difficulties including divorce, and legal problems.[3] There are also a variety of medical manifestations of AUD, including hypertension, arrhythmias such as atrial fibrillation, cardiomyopathy (known in the UK as "Holiday Heart"), stroke, seizures, peptic ulcers, gastroesophageal reflux, sleep apnea, obesity, pancreatitis, cirrhosis, vitamin deficiencies and associated manifestations, and hypogonadism with associated sexual dysfunction and osteoporosis.[3] Anxiety, mood disorders, and other substance-use disorders are also common psychiatric presentations.[3]

Clinical Diagnosis

In the Diagnostic and Statistical Manual of Mental Disorders V (DSM-V), AUD replaced the DSM-IV terms alcohol abuse and alcohol dependence, and is diagnosed when a patient meets any two of the 11 DSM-V criteria during the same 12-month period

(Table 1).[4,5] In order to identify high risk drinkers who have an increased likelihood of experiencing alcohol-related problems, the NIAAA guidelines recommend screening men who consume more than 4 standard drinks per day (or more than 14 drinks per week) and women who consume more than 3 standard drinks per day (or more than 7 per week).[1] A standard drink is defined as 12 ounces of 5% beer, 5 ounces of 12% wine, 1.5 ounces of 40% distilled spirits, and 8-9 ounces of 7% malt liquor.[1] It is important to note that many beers, wine, and mixed drinks easily exceed these limits in percentages, volume consumed, or combination of multiple liquors. For example, a typical margarita contains 1.7 drinks, and many beers contain 6-9% alcohol.[6] Binge drinking is considered drinking that elevates blood alcohol concentration (BAC) levels to 0.08 g/dL, which is typically 4 drinks for women and 5 drinks for men over about 2 hours.[1]

Treatment

Given the variable, chronic, and relapsing nature of AUD, there is no standard treatment regimen and it is important to tailor the treatment to the needs of the patient. While literature has demonstrated that psychosocial therapy and pharmacotherapy are each helpful in reducing alcohol intake and associated adverse effects, a randomized controlled trial found no difference in outcomes between medical therapy alone compared to medical therapy combined with psychosocial therapy.[7] The variation in effectiveness of the different AUD therapies is likely due to differing patient characteristics, belief systems, and the degree of social support or stress outside of the psychosocial interventions.[8] The effectiveness of different treatment modalities for a patient may also change over time as patient characteristics and external stressors evolve. For example, with our Case 1 patient, psychosocial support through AA attendance was initially adequate for preventing her relapse, but the onset of depressive symptoms necessitated a change in management to oral naltrexone. Our Case 2 patient, on the other hand, has suffered significant social and financial stress secondary to his AUD and reduction in heavy drinking through a combination of oral and injectable naltrexone has helped him maintain his job and stability.

Traditionally, the goal of AUD treatment has been complete abstinence from alcohol use. However, in select patients, such as that in Case 2, reduction of heavy drinking has been shown to be an appropriate goal.[9] A review of seven large multisite studies demonstrated that in the year following treatment for alcoholism, although only one third of AUD patients remained abstinent or used alcohol moderately without negative outcomes while the other two thirds still engaged in periods of heavy drinking, those with continued heavy drinking reduced overall consumption and alcohol-related problems by more than half.[10]

Psychosocial therapy alone may be appropriate in select patients and, due to the wide spread availability of these interventions, it is often recommended as initial treatment for AUD. Cognitive-behavioral therapy, brief interventions, motivational enhancement therapy, and 12-step facilitation help patients to develop skills for preventing relapse and coping with triggers, address psychosocial issues that contribute to alcohol consumption, and offer social support.[11] Intensive outpatient programs (IOPs) and residential treatments are other options to aid in sobriety maintenance and coping skills development. While for some patients, like the one in Case 1, psychosocial therapy may be sufficient or beneficial, such therapy may not improve outcomes in severe AUD as evidenced by the Case 2 patient. Most commonly, a trial of Alcoholics Anonymous (AA) meetings is followed by a referral to an IOP. If participation in an IOP fails to curb drinking, the next step is typically an inpatient stay. Referral and consultation with addiction medicine or addiction psychiatry is helpful in these situations.

Medications are often reserved for moderate to severe or chronic relapsing AUD, although it may also be appropriate for patients who are highly motivated not to relapse for the purposes of keeping their jobs or relationships.[3] Pharmacotherapy plays an important role in complementing psychosocial therapy by countering alcohol-induced alterations in brain chemistry. The US Food and Drug Administration (FDA) has approved several medications for AUD treatment, including disulfiram, acamprosate, oral naltrexone, and extended-release injectable naltrexone.[11] The selection of a pharmacotherapy regimen must take into account a patient's co-occurring disorders. For patients without specific co-morbidities dictating treatment, the 2018 American Psychiatry Association guidelines recommend offering either naltrexone or acamprosate first as pharmacologic treatment for moderate to severe AUD, and then considering disulfiram, topiramate, or gabapentin next in patients who do not respond to those initial two agents.[12] Disulfiram inhibits acetaldehyde dehydrogenase, which increases alcohol's adverse effects and provides a strong deterrent. However, its associated hepatotoxicity, potential for psychosis, and low adherence rate, reduce its effectiveness.[11] Acamprosate inhibits glutamate receptors and modulates NMDA receptors, and has been shown to increase the duration and rate of abstinence, although there is conflicting data regarding its efficacy depending upon study population and age.[11] Antiepileptics, including topiramate and gabapentin, modulate GABA and glutamate receptor stimulation and attenuate or inhibit alcohol withdrawal symptoms.[11,13] More recently, gabapentin has been shown to be more effective in curbing alcohol withdrawal and reducing cravings and relapse when compared to using benzodiazepines with withdrawal symptoms during early sobriety.[14]

Interestingly, increasing data has supported the use of opioid antagonists, including both oral and extended-release injectable naltrexone, as adjuvant treatment, particularly in the reduction of heavy drinking. These drugs block alcohol-induced release of endorphins, enhance the sedative effects of alcohol, and reduce cravings for alcohol.[11] Use of oral naltrexone 50 mg daily has been associated with a reduction of the risk of heavy drinking by 17% and drinking days by 4%, and extended-release injectable naltrexone has been shown to reduce heavy drinking days by 25%.[15,16] Oral naltrexone is limited in efficacy

by low plasma trough levels which likely contribute to the need for 85% adherence to achieve therapeutic effect, as well as adverse events, such as nausea and headache, associated with high peak levels.[17] Extended-release injectable naltrexone was designed to provide a more steady release and constant level of the drug at a low enough concentration to avoid adverse effects.[17] Extended-release injectable naltrexone also has been shown to be effective in patients who are not abstinent prior to treatment, whereas most studies involving oral naltrexone have required abstinence prior to medication initiation.[16] Although this effect is likely a selection bias, this makes extended release naltrexone an ideal medication in patients like that in Case 2 who cannot sufficiently adhere to the oral naltrexone regimen and relapse frequently. Although reportedly better tolerated than oral naltrexone, at least 10% of patients using extended-release injectable naltrexone still experience adverse effects, like our Case 1 patient experienced, with the most common side effects being nausea, headache, and fatigue.[16] Transaminitis, injection site reactions, and pneumonitis are other less common side effects.[11,16] However, the primary challenge is often cost and insurance coverage.

Regardless of the selected treatment method, regular follow up is recommended for AUD patients, especially those with moderate to severe AUD. Although there remains significant opportunity for improvement in AUD treatment, close physician-patient relationships and appropriate modification of management can help provide patients with the best outcome possible and helps them meet their personal and professional goals.

Table 1: Criteria for Alcohol Abuse, Alcohol Dependence, and Alcohol Use Disorder

DSM-IV Alcohol Abuse Criteria[5]

A maladaptive pattern of alcohol use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12- month period:

1. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to alcohol use; alcohol-related absences, suspensions, or expulsions from school; neglect of children or household)
2. Recurrent alcohol use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by alcohol use)
3. Recurrent alcohol-related legal problems (e.g., arrests for alcohol-related disorderly conduct)
4. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the alcohol (e.g., arguments with spouse about consequences of intoxication, physical fights)

The symptoms must never have met the criteria for alcohol dependence.

DSM-IV Alcohol Dependence Criteria[5]

A maladaptive pattern of alcohol use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

1. Tolerance, as defined by either of the following:
   a) A need for markedly increased amounts of alcohol to achieve intoxication or desired effect
   b) Markedly diminished effect with continued use of the same amount of alcohol
2. Withdrawal, as manifested by either of the following:
   a) The characteristic withdrawal syndrome for alcohol
   b) The same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
3. Alcohol is often taken in larger amounts or over a longer period than was intended
4. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use
5. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects
6. Important social, occupational, or recreational activities are given up or reduced because of alcohol use
7. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol

DSM-V Alcohol Use Disorder Criteria[4]

Patient must meet any two of the 11 criteria during the same 12-month period, with mild AUD defined as 2-3 symptoms, moderate as 4-5 symptoms, and severe as 6 or more symptoms:

In the past year, have you:

1. Had times when you ended up drinking more, or longer, than you intended?
2. More than once wanted to cut down or stop drinking, or tried to, but couldn't?
3. Spent a lot of time drinking? Or being sick or getting over other aftereffects?
4. Wanted a drink so badly you couldn’t think of anything else?
5. Found that drinking—or being sick from drinking—often interfered with taking care of your home or family? Or caused job troubles? Or school problems?
6. Continued to drink even though it was causing trouble with your family or friends?
7. Given up or cut back on activities that were important or interesting to you, or gave you pleasure, in order to drink?
8. More than once gotten into situations while or after drinking that increased your chances of getting hurt (such as driving, swimming, using machinery, walking in a dangerous area, or having unsafe sex)?
9. Continued to drink even though it was making you feel depressed or anxious or adding to another health problem? Or after having had a memory blackout?

10. Had to drink much more than you once did to get the effect you want? Or found that your usual number of drinks had much less effect than before?
11. Found that when the effects of alcohol were wearing off, you had withdrawal symptoms, such as trouble sleeping, shakiness, restlessness, nausea, sweating, a racing heart, or a seizure? Or sensed things that were not there? (DSM-V 2013)

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