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PHARMACOTHERAPY FOR ALCOHOL ADDICTION IN A PATIENT WITH ALCOHOLIC CIRRHOSIS AND MASSIVE UPPER GASTROINTESTINAL BLEED: A CASE STUDY

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Abstract

Alcohol use causes a substantial burden of morbidity and mortality worldwide. The pharmacologic treatment of alcohol dependence has been increasingly studied and proven to improve outcomes in individuals with alcohol use disorder. However, the treatment of alcohol use disorder is often challenging in the context of patients with hepatic impairment as many medications to treat alcohol use disorder are hepatically metabolised or may cause liver toxicity in some instances. We present a case history of an individual with significant medical complications from alcohol use disorder and explore the dilemma faced in prescribing pharmacologic treatment of alcohol use disorder in patients with significant liver dysfunction.

Keywords

alcoholism; drug therapy; liver cirrhosis; alcohol-related disorder; addiction treatment

INTRODUCTION

The burden of morbidity and mortality due to alcohol is substantial; the World Health Organization reports that 5.9% of global deaths in 2012 were attributable to alcohol [1]. In this context, the pharmacologic treatment of alcohol use disorder has been increasingly studied and validated over the past few decades given the beneficial health effects on reducing or abstaining from consumption of alcohol. However, prescribing of medications to treat this disorder remains low. In the USA, figures from 2007 estimate that only 720 000 prescriptions were filled for medications to treat alcohol use disorder despite nearly 8.5 million Americans with this disorder [2].

This issue may be partially explained by the fact that the pharmacologic treatment of alcohol use disorder is complicated by the progression of disease to severe liver impairment, which

poses a treatment dilemma as many medications to treat alcohol use disorder are hepatically metabolised or may cause liver toxicity themselves. However, there are strategies for the treatment of alcohol use disorder even in patients with decompensated cirrhosis. This is of critical importance given that complete abstinence from alcohol is associated with 60% 5-year survival compared with 30% in patients who continue to drink alcohol [3].

To illustrate these issues, we present a case history of an individual with alcohol use disorder, a long-standing history of medical complications and no history of evidence-based treatment for her severe alcohol use disorder. The discussion considers the dilemma faced in prescribing pharmacologic treatment of alcohol use disorder in patients with significant liver dysfunction.

CASE HISTORY

A 55-year-old female was admitted to the Intensive Care Unit (ICU) at St. Paul's Hospital in Vancouver, British Columbia, due to a massive upper gastrointestinal (GI) bleed secondary to esophageal varices in the context of alcoholic cirrhosis. On presentation, the patient was haemodynamically unstable with a blood pressure of 60/40 mmHg and a heart rate of 120 beats per minute. Initial laboratory investigations revealed a haemoglobin of 5.2 g/dL with a lactate of 22 mmol/L and international normalized ratio of 1.6. Her liver enzymes were markedly elevated with alanine aminotransferase and aspartate aminotransferase measuring 5794 U/L and 14 804 U/L, respectively.

The patient was intubated and resuscitated with vasopressors, blood transfusions, intravenous (IV) fluids as well as treated with IV pantoprazole and octreotide. An esophagogastroduodenoscopy was emergently performed, which showed bleeding esophageal varices that were subsequently banded. Her ICU course was complicated by multi-organ failure, including shock liver and acute kidney injury requiring dialysis. She was also treated for alcohol withdrawal using midazolam infusion and, subsequently, dexmedetomidine and propofol. She was extubated 8 days after admission and transferred to an inpatient medicine unit where she was seen by the hospital's Addiction Medicine Consult Team.

Review of this patient's medical history demonstrated that the patient had a longstanding history of alcohol use beginning at age 18, and she predominantly engaged in binge-drinking behaviour 1–2 times per month; her binges lasted 2–3 days at a time, and she would consume three-quarters of a 26 ounce bottle of vodka, equivalent to 13 standard drinks, per drinking day. She experienced mild alcohol withdrawal symptoms of tremor but denied seizures or delirium tremens. She reported numerous social consequences of her drinking behaviour, such as financial problems, loss of multiple jobs, a legal charge for driving under the influence of alcohol, a motor vehicle collision and significant relationship losses. Her medical consequences were also significant and included blackouts; fractures of her kneecap, nose and ankle while intoxicated; alcoholic cirrhosis with esophageal varices and portal hypertension; and a previous upper GI bleed in 2013. Her medical history also included depression, osteoporosis, endometriosis, knee surgery for a fractured left kneecap,

breast cancer surgery with lumpectomy and radiation in 2012 and total thyroidectomy in 2014.

According to the patient's online medical records, from March 2012 through to this admission in late 2014, the patient had 23 recorded interactions with medical specialists, including multiple gastroenterologists and a total of five upper endoscopies, anaesthesia, surgical oncology, endocrinology, radiation oncology, orthopedic surgery, general internal medicine, and a physician certified in addiction medicine. The majority of the documentation from these visits recorded her alcohol use and two noted the patient's interest in abstaining from alcohol. However, illustrative of the known lack of regular prescribing of treatments for alcohol use disorder, none documented a discussion related to pharmacologic therapy to help her reduce alcohol consumption. Similarly, there is no record of a prescription for an anti-craving or anti-relapse medication being provided despite being often prescribed medication to treat the sequelae of her alcoholism, such as beta-blockers for her esophageal varices and thiamine for nutritional support.

DISCUSSION

The present case highlights many missed opportunities for treatment of alcohol use disorder in a patient who developed numerous medical and social consequences of her drinking with repeated life-threatening events (i.e. upper GI bleeding) caused by her alcohol use. Past research has described the gaps in care for individuals with drug and alcohol addiction. For instance, a recent audit of health care among US adults found that, in the case of alcohol addiction, the percentage of recommended care received was approximately 10% [4]. This patient has had significant interaction with the medical system, including being seen by several gastroenterologists and an addiction certified physician for her alcohol-related liver disease, and no mention of pharmacotherapy was recorded in any consultation. During this admission, she reported having been offered pharmacotherapy treatment for alcohol use only once with disulfiram many years prior.

This case study provides the opportunity to review the current medications approved for alcohol use disorder, including naltrexone, disulfiram and acamprosate and off-label prescription of other medications with less evidence of effect but possible benefit for this population, such as gabapentin, baclofen and topiramate. Particularly, this case exemplifies the dilemma faced in prescribing pharmacologic treatment of alcohol use disorder in patients with significant liver dysfunction.

Naltrexone is an opioid antagonist thought to block endogenous opioids triggered by alcohol use. The COMBINE trial showed a statistically significant decrease in total number of drinking days and heavy drinking days with a number needed to treat of 9 for preventing return to heavy drinking [5]. Commonly, acute hepatitis or liver failure are listed as contraindications for naltrexone. However, the evidence for proposed hepatotoxicity is limited, and it should likely still be considered for patients with alcohol use disorder and liver disease as long as liver function is monitored carefully [6,7]. Naltrexone's proven efficacy in reducing alcohol consumption, a significant hepatotoxin in itself, warrants judicious use in patients with severe alcoholism and liver dysfunction. Naltrexone can be

initiated with actively drinking patients, and a recent meta-analysis estimated the number needed to treat (NNT) to see abstinence with the use of naltrexone was 8, and the NNT to achieve no heavy drinking was 5 [2].

Acamprosate is also approved for treatment of alcohol use disorder and is believed to be most useful for maintaining abstinence and less effective at reducing cravings or relapse to heavy drinking if any drinking occurs [8]. It is not recommended in actively drinking patients but can be used in those with liver disease regardless of its severity, making it highly useful in those who have severe hepatic complications of their alcoholism and whose goal is complete abstinence. A recent meta-analysis estimated that acamprosate has a number needed to treat of 12 for preventing one person from returning to drinking of any severity [9].

Gabapentin, commonly used as an anticonvulsant and analgesic, is increasingly being used to treat alcohol use disorder. Although it has not been compared head-to-head to naltrexone or acamprosate in adequately powered clinical trials, it has been shown to have a significant linear dose effect in increasing the rates of complete abstinence and no heavy drinking compared with placebo [2]. As it is not hepatically metabolised, it can also be used in patients with significant liver impairment.

There are several other medications used in the treatment of alcohol addiction. Disulfuram, one of the oldest medications approved for alcohol use disorder, is less commonly prescribed now because of limited efficacy and known hepatotoxicity [9,10]. Although not compared head-to-head with either naltrexone or acamprosate, there is also now increasing interest and evidence emerging for the use of baclofen and topiramate in the treatment of alcohol addiction, neither of which is contraindicated in those with severe liver disease [11–13].

After 12 days in the ICU, the patient was transferred to the inpatient medical service and discharged from hospital just over 1 month after her admission. She was offered treatment with gabapentin given its safety profile in hepatic impairment. Additionally, her pattern of binge drinking lends itself well to the effect of gabapentin on reducing heavy drinking. Ultimately, it is noteworthy that the patient declined pharmacotherapy as she had been abstinent since her month-long admission and felt confident in her ability to maintain this without medication in the wake of her life-threatening upper GI bleed.

CONCLUSIONS

This case has provided the opportunity to review the use of pharmacotherapy in patients with severe alcoholic liver disease. This case also highlights the lack of prescribing of pharmacotherapy for the treatment of alcohol use disorder despite strong evidence of its efficacy. As described above, a range of options are available with meta-analyses of randomised clinical trials demonstrating that the number needed to treat for acamprosate and naltrexone are much lower than the NNT for many commonly prescribed medications. As in the case of this patient, the lack of prescribing is likely due to a combination of factors, including poor physician awareness of pharmacological options for alcohol use disorder as

well as patient preferences. However, severe liver dysfunction is not a barrier to pharmacotherapeutic treatment of alcohol use disorder. With increased physician and patient awareness of these medications, greater numbers of patients can be prevented from progressing towards the life-threatening and extremely resource-intensive complications associated with untreated alcohol use disorder. As is commonplace in current guidelines for cigarette smoking cessation, taking every opportunity to offer evidence-based treatments for addiction-related disorders can eventually result in prevention of severe morbidity and mortality [14,15].

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