Review Article

Review on Alcohol Withdrawal Complication and Clinical Management

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ABSTRACT

Alcoholism is the most common forms of substance abuse and dependence in world-wide. In many countries, it is a widespread, age-old problem. Alcohol withdrawal syn-drome (AWS) is the symptoms that occur when a heavy drinker suddenly stops or significantly reduces their alcohol intake. In patients with a history of alcohol abuse, AWS manifests itself with symptoms of autonomic hyperactivity, tremors, hallucinations, agitation, anxiety, and seizures. Progression of AWS, called delirium tremens (DT), is associated with increased mortality. The Clinical Institute Withdrawal Assessment-Alcohol, revised (CIWA-Ar) is an assessment tool. It is used to quantify the severity of alcohol withdrawal syndrome (AWS) and to provide information on benzodiazepine treatment for alcohol withdrawal. The most common method of treating alcohol withdrawal is CIWA-Ar protocol. Traditionally, AWS is treated with benzodiazepines which have a well-established record for reducing symptoms of withdrawal and provide adequate control of both seizures and DT.

Keywords: Alcohol withdrawal, complications, delirium tremens, clinical management.

INTRODUCTION

According to the World Health Organization, alcoholism or alcohol use disorder refers to any form of alcohol consumption that results in health and other problems. Alcohol is a central nervous system depressant. Alcoholism is the most common forms of substance abuse and dependence in worldwide. In many countries, it is a widespread, age-old problem. In the USA alone, over 27% of the population aged 12 and above are considered risky drinkers [1]. Alcohol use is a global health problem, and leading causes of death and disability. About 8 million alcohol-dependent peoples are present in the United States, and approximately 500,000 episodes of withdrawal severe enough to require pharmacologic treatment occur each year, between 2 and 7 percent of patients with heavy alcohol use admitted for general medical care will develop severe alcohol withdrawal. More amount of alcohol consumption can also lead to major health problems. This study mainly focused into Alcohol Withdrawal Syndrome (AWS) also known as discontinuation syndrome[2]. The dose of benzodiazepine required per day is calculated according to the average daily alcohol intake. An estimate of the amount of alcohol consumption is given by the following formula: Alcohol (in g) = Volume of liquor (ml) × 0.008 × (%) ethanol content in the liquor (w/v). The percentage of alcohol in various liquors is: Beer (standard) – 3-4%, Beer (strong) – 8-11%, Wines – 5-13%, Fortified wines – 14-20%, Spirits/Indian Made Foreign Liquor like (rum/whiskey/gin/ vodka/brandy) – 40%, arrack – 33%. One standard drink contains about 10 g of absolute alcohol or ethanol[3]. Six to 12 hours after the cessation, withdrawal symptoms such as shaking, headache, sweating, anxiety, nausea, or vomiting can occur. Other comparable symptoms may also occur in this period. 12 to 24 hours after the ingestion of the last drink, other conditions may develop such as confusion, hallucinations (with awareness of reality), tremor, agitation, and similar ailments. At 24 to 48 hours following the last alcohol consumption, where have a possibility to develop seizures. Sometimes these Seizures carry the risk of death for the alcoholic. The improvement of patient condition will be normal within 48 hr, even though some kind of withdrawal symptoms which continue its severity and lead delirium tremens, which is characterized as hallucinations, severe confusion, seizures, high blood pressure, and fever[4-5].

Management

Alcohol withdrawal is a common condition and the patient may present with the mild symptoms like tremor and agitation or more severe symptoms like withdrawal seizures and delirium tremens[6]. The Clinical Institute Withdrawal Assessment-Alcohol, revised (CIWA-Ar) is an assessment tool. It is used to quantify the severity of alcohol withdrawal syndrome (AWS) and to provide information on benzodiazepine treatment for alcohol withdrawal. The most common method of treating alcohol withdrawal is CIWA-Ar protocol. Although various types of rating scales are used for the assessment of alcohol withdrawal[7]. Common medications include benzodiazepines to help treat symptom like anxiety, insomnia and seizures. Also take antiseizure medications and anti-psychotics along with other drugs.

Detoxification

Detoxification is a process of gradually deprive a person from a substance which produce addiction in a safe and

effective manner by gradually reducing the dependence producing substance or by substituting the substance with a cross-tolerant pharmacological agent and reducing it[8]. This process minimizes the withdrawal symptoms, prevents complications and speed up the process of abstinence from the substance[3]. Detox alone isn't treatment; the alcohol detox is the first step in treating alcoholism. During this stage, alcohol is completely removed from your body. The alcohol detox phase can involve withdrawal symptoms ranging from mild to life-threatening. The duration of alcohol detoxification is different for each person.

General Supportive Care

Supportive care, including intravenous (IV) fluids, nutritional supplementation, and frequent clinical reassessment including vital signs, is important[9].

Sedation should be provided to calm the patient as early as possible. Fluid and electrolyte imbalances must be appropriately corrected[3]. Adequate nutrition must be ensured with care to prevent aspiration in over-sedated patient. Supportive care does not care hallucination or seizure. It can be completed by detoxification using social support alone. Some patient with mild withdrawal symptoms may benefit from supportive care alone. Heavy alcohol uses also reduce body of vital electrolytes and vitamins, such as folate, magnesium, and thiamine. So, treatments may also include electrolyte corrections and multivitamin fluids[10].

Benzodiazepines

Benzodiazepines are most commonly used treatment for AWS and it can be administrated using a front-loading, fixed-dose, or symptom triggered approach. Chlordiazepoxide or diazepam are the long acting benzodiazepines these are commonly used and it provide a smoother withdrawal effect than the shorter acting benzodiazepines, but here no data to support superiority of one benzodiazepine over another. Patients like elderly or those having with significant liver disease may have the problems like excessive accumulation and reduced clearance level of long acting benzodiazepines. Lorazepam and oxazepam may preferred to these patients[6]. The oral route is preferred if the patient can take oral medication. If the patient is too excited or disoriented, the intravenous route can be used. We do not advocate the use of IM administration since the absorption of the drug can be erratic and unpredictable. If IV access is temporarily unavailable, you can use IM Lorazepam[11]. Table 1 provides the equivalence of the approximate dose with plasma half-lives.

Table 1: Equivalence of the approximate dose with plasma half-lives[12].

Drug name	Approximate dose equivalent in mg	Elimination half-life (hours)
Lorazepam	0.75-1	10 to 20
Diazepam	5	20 to 80
Chlordiazepoxide	25	5 to 30
Oxazepam	15	5 to 20

Anticonvulsants

Anticonvulsants also known as antiepileptic drugs or as antiseizure drugs are a diverse group of pharmacological agents used in the treatment of epileptic seizures. Antiepileptic medications work in different ways to prevent seizures, either by decreasing excitation or enhancing inhibition. Specifically, they act by either: Altering electrical activity in neurons by affecting ion (sodium, potassium, calcium, chloride) channels in the cell membrane[13]. Benzodiazepine anticonvulsants are most commonly used for AWS. In the case of outpatient management of alcoholism Gabapentin is potentially efficacious treatment for reducing the risk of relapse. The benefits of Gabapentin are easy use, rapid titration, good tolerability and efficacy in AWS patients. Carbamazepine and Gabapentin are the most suitable treatment for the AWS.

Topiramate appears to have a powerful effect on reducing harmful drinking in alcoholics. A retrospective analysis of over 700 patients comparing CBZ with valproate (VPA) revealed that VPA offers some advantages over CBZ, such as favourable tolerability and shorter treatment duration[14]. The mechanism of action of valproic acid in neuropsychiatric disorders is not fully understood. The anticonvulsants such as Gabapentin and Pregabalin are used in AWS due to its GABAergic properties and inhibitory effect on voltage-gated calcium channels. The Gabapentin may be effective the mild to moderate AWS but not severe symptoms. Because of its limited abuse potential, decreased sedation effect compared to benzodiazepine-based detoxification and relatively safe when combined with alcohol. Gabapentin is a potentially efficacious treatment for reducing the risk of relapse to harmful drinking patterns in outpatient management of alcoholism[15].

Antipsychotic agents

A cluster analysis of alcohol withdrawal symptoms by Driessen *et al*.[16] showed that hallucinosis is a severe form of alcohol withdrawal. It is often associated with Delirium Tramon's. In most cases of AWS, the hallucinations last about one week, but may last up to one month in some patients after which the antipsychotic can be stopped. However, it is a condition that may cause apparent failure of the loading dose regimen and recommend a fixed dose strategy to cover the period of alcoholic hallucinosis. In this

problem may be given low doses of antipsychotics like chlorpromazine 100-200 mg/day or risperidone 1-3 mg/day to control severe agitation due to hallucinations[3].

Gamma-Hydroxybutyrate (GHB)

Gamma-hydroxybutyrate or GHB is a metabolite of GABA, to which it is structurally similar. GHB is naturally present in the human brain and is involved in the regulation of sleep cycles, temperature regulation, cerebral glucose metabolism and blood flow, memory, and emotional control[17]. Regarding its use in the treatment of AWS, GHB has the interesting characteristic of being a weak agonist of GABAB-receptors and the fact that exogenous GHB is converted to GABA which results in an indirect activation of GABAA-receptors. Consequently, GHB partly mimics the actions of alcohol in the brain and may therefore act as a substitute drug[18].

α2-Agonists

The symptoms of AWS are partly the product of noradrenergic overdrive. One of the prime receptors for noradrenergic transmission in the brain is the α2-receptor. Normally this receptor inhibits the firing of the presynaptic norepinephrine neuron, but during AWS its sensitivity is impaired which results in augmented noradrenergic transmission[19].

It is believed that alpha-2 agonists reduce sympathetic oversteer and the autonomic symptoms associated with alcohol withdrawal syndrome. These drugs (mainly clonidine) have been studied in the treatment of alcohol withdrawal syndrome[20-21].

Treatment For Wernicke-Korsakoff Syndrome

There are no logical metabolic indications or explanations for the acute precipitation of Wernicke with 1 dose of glucose IV in an emergency environment[22]. Metabolically, thiamine is incorporated into the cell at a rate less than glucose, thereby minimizing, if necessary, pre-treatment with thiamine[23]. Therefore, parenteral thiamine (100 mg intramuscularly or intravenously) may be administered before or after 1 dose of glucose IV. The oldest literature advocated the intramuscular use of thiamine on the IV route. The concern was the precipitation of anaphylactoid reactions[24]. The literature now supports the thesis that the dilution vector for thiamine, clorbutanol, is the cause of most of these anaphylactoid reactions[25]. By using aqueous forms of thiamine, these side effects have been significantly reduced. However, there are still some cases of thiamine IV reactions, even in the purest form[26]. A study conducted by Wrenn and co-workers on 1000 patients showed that doses of up to 500 mg can be safely tolerated[27].

COMPLICATIONS

Delirium Tremens

Delirium tremens is a severe form of alcohol withdrawal, usually starts one to four days after the last drink in persons who have been drinking excessively for years[28]. Signs of DT's include extreme hyperactivity of the autonomic nervous system, along with hallucinations. It involves sudden and severe mental or nervous system changes. It can cause increase heart rate dangerously or can cause blood pressure to increase dramatically. Also, it can cause severe dehydration. Symptoms can include confusion, disorientation, nervous or angry behaviour, stupor or loss of consciousness, irrational beliefs, soaking sweats and sleep disturbances. It occurs most often in people who have a history of alcohol withdrawal and It is especially common in those who drink 4 to 5 pints (1.8 to 2.4 litres) of wine, 7 to 8 pints (3.3 to 3.8 litres) of beer, or 1 pint (1/2 litre) of "hard" alcohol every day for several months. It also commonly affects people who have used alcohol for more than 10 years. Women experiencing DT's less frequently than men. Death may occur in up to 5 percent of patients with DT's. If patients receiving adequate medication and medical support, the risk of death can reduce[29].

Alcoholic Hallucinosis

Alcoholic hallucinosis is a rare complication of chronic alcohol abuse. It is a pathological mental condition characterized by an acute onset of predominant auditory hallucinations that occur during or after a period of heavy alcohol consumption[30].

This symptom usually begins within 12 to 24 hours after the last alcohol drink, and may last as long as 2 days once it begins. It is common for people who are withdrawing from alcohol to see multiple small, similar, moving objects. Sometimes the vision is perceived to be crawling insects or falling coins.

Tremors

Tremor is one of the symptoms that greatly disturbs patients because it can limit their daily activities. The most common action tremor which occurs occasionally in everyone is enhanced physiological tremor[31].

Alcohol Withdrawal Seizures

The Seizures can also be directly caused by alcohol, even without withdrawal. Seizures may occur as soon as a few hours after your last drink (the cessation) or 1 to 2 days later. More than 90 percent of alcohol withdrawal seizures occur within 48 hours after the patient stops drinking (cessation). Fewer than 3 percent of such seizures may occur 5 to 20 days after the last drink (cessation) (Victor and Brausch 1967). Clinical data suggest that the likelihood of having withdrawal seizures, as well as the severity of those seizures, increases with the number of past withdrawals. The correlation between the number of alcohol detoxifications and the development of alcohol withdrawal complications, including seizures, has been ascribed to cumulative long-term changes in brain excitability (i.e., the "kindling" hypothesis)[29-32]. The clinical diagnosis of an alcohol - related seizure can only be made by obtaining a drinking history that indicates (of) alcohol overuse prior to the seizure. A good drinking history

includes both the quantity and frequency of alcohol intake and changes in drinking pattern (changes), at least during the previous 5 days (drinking history), as well as the time of the last alcohol intake[33].

Wernicke-Korsakoff Syndrome

Wernicke's encephalopathy is an acute neuropsychiatric emergency due to thiamine deficiency[34]. It occurs mainly, but not exclusively, in malnourished alcohol dependent patients or as a result of malnutrition due to other causes. Wernicke encephalopathy is easily reversible with sufficient doses of parenteral thiamine, preferably within the first 48-72 hours after onset of symptoms [34-35]. If Wernicke's encephalopathy is not treated with adequate doses of thiamine, Korsakoff syndrome may die or progress by as much as 20%. Autopsy studies report a prevalence of Wernicke's encephalopathy between 0.4% and 2.8%, with Australia having the highest prevalence (1.1-2.8%) in the Western world; In patients with alcohol consumption disorders, the prevalence increases to 12.5%[36].

CONCLUSION

Alcohol Withdrawal Syndrome results in people who are dependent on alcohol and either stop drinking, or reduce the alcohol consumption. This results from a shift in the neurotransmitter levels in the brain, from GABA inhibition to glutaminergic stimulation. The symptoms are generally mild to moderate and resolve within a few days. However, severe forms of AWS may be associated with generalized seizures, hallucinations and delirium tremens, which can be fatal. AWS are best monitored regular scale-based assessments such as CIWA-Ar. Treatment of exposed patients AW has been varied at times controversial.

Although clinicians generally agree on the need for a severe AW large pharmacological intervention, various medicines have been used. Benzodiazepines are the mainstay of management of alcohol withdrawal states. Therapeutic studies show that early intervention in primary care is feasible and effective, and that a variety of behavioural and pharmacological interventions are available to treat alcohol withdrawal.

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