



Management of Alcohol Dependence in General Hospital Inpatient Setting: An Update

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ABSTRACT

Increasing prevalence of alcohol use disorders in India is likely to translate into general hospital inpatients catering more to patients with alcohol dependence. This review provides a background of the management of patients with alcohol use disorders in the inpatient setting, updated with the recent findings. The review discusses the diagnostic criteria usually used for the diagnosis of alcohol dependence. This is followed by discussion of overall management principles and assessment perspectives. The management of the initial detoxification phase and the subsequent maintenance phase are discussed, both in terms of pharmacological management and non-pharmacological approaches.

Keywords: Alcohol dependence, abuse, general hospital, management, complications.

INTRODUCTION

Alcohol dependence is a chronic relapsing and remitting disorder that is associated with considerable medical morbidity and societal costs.^{1,2} The occurrence of the disorder has been suggested to be increasing in the Indian population over time as reflected by cross-sectional surveys reporting the prevalence rates.³ Indian studies have reported that up to 37% of the population may be using alcohol, with hazardous use being present in about 15% of the population and dependence/abuse being present in about 2% of the population. Gradually increasing production and sale indices over time indicate that the problem of alcohol use and consequent harm is likely to gradually increase in the time to come.⁴

Given the growing burden of alcohol use, the occurrence of alcohol dependence is likely to increase further, resulting in the increase in medical complications associated with it. Alcohol affects various organ systems of the body including the gastrointestinal and hepatic system, cardiovascular system, nervous system, endocrine and reproductive system.⁵⁻⁸ A brief list of the disorders related to alcohol use is provided in table 1. Apart from the mentioned medical complications, patients with alcohol dependence also seek surgical referral and opinion when they encounter accident while being under intoxication, which may require neurosurgical, orthopaedic, and general surgical intervention.

Thus, hospitals are likely to cater to more and more patients with alcohol use, either those whose medical problems have genesis in alcohol use, or those who have unrelated medical/surgical disorder but have alcohol use problem concurrently. This review takes a look at the criteria for diagnosis of various alcohol disorders, overview of management, assessment of patient, initial detoxification treatment, and further treatment for

prophylaxis. The newer approaches of treatment of alcohol dependence along with the genetic testing are discussed further, along with the future research needs.

Table 1: Alcohol related medical complications

Organ systems and disorders
Gastrointestinal and hepatic
Gastritis
Peptic ulcer
Fatty liver
Liver cirrhosis
Pancreatitis
Gastroesophageal varices
Mallory Weiss tears
Cardiovascular
Increased blood pressure
Coronary artery disease
Atrial and ventricular arrhythmias
Cardiomyopathy
Neurological
Peripheral neuropathy
Cerebellar ataxia
Wernicke's encephalopathy
Korsakoff's psychosis
Dementia
Hematological
Macrocytic anaemia (due to vitamin B12 deficiency)
Microcytic anaemia (due to nutritional iron deficiency or blood loss)
Impaired leukocyte functioning
Reproductive
Impaired erectile functioning
Hypogonadism
Fetal alcohol syndrome
Others
Myopathy
Decreased bone density
Decreased vasopressin secretion
Decreased T ₃ and T ₄



Criteria for diagnosing alcohol related disorders

Though use of alcohol is common in the general population, not all alcohol users would fulfil criteria for alcohol dependence and harmful use. Not all patients who use alcohol need treatment, but those who have a greater severity of alcohol use reflected by a diagnosable alcohol use disorder probably would benefit with management of this condition. The criteria for dependence and harmful use are depicted in table 2.⁹ As evidenced in the table 2, alcohol dependence is a more severe diagnosis than harmful use.

Apart from the above, alcohol intoxication and alcohol withdrawal state often present for treatment in general hospital setting. Alcohol intoxication typically occurs after heavy alcohol intake and includes features of disinhibition, argumentativeness, aggression, lability of mood, impaired attention, impaired judgement, interference with personal functioning, unsteady gait, slurred speech, nystagmus, decreased level of consciousness, flushing face and conjunctival injection. Alcohol withdrawal presents with tremor of the outstretched hands, tongue or eyelids, sweating, nausea, retching or vomiting, tachycardia or hypertension, psychomotor agitation, headache, insomnia, and transient visual, tactile or auditory hallucinations or illusions. In severe withdrawal states, patients may present with seizures and delirium.

Table 2: Criteria for alcohol dependence and alcohol harmful use.

Alcohol Dependence Syndrome

A cluster of physiological, behavioural, and cognitive phenomena in which the use of a substance (alcohol) takes on a much higher priority for a given individual than other behaviours that once had greater value. For a diagnosis of dependence, three or more of the criteria mentioned below should be present together in the last year

- a strong desire or sense of compulsion to take the substance
- difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use
- a physiological withdrawal state when substance use has ceased or been reduced
- evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses
- progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects
- persisting with substance use despite clear evidence of overtly harmful consequences when the user was potentially or actually aware of the of the harm

Alcohol harmful use

A pattern of psychoactive substance use that causes damage to health. The damage may be physical (as in cases of hepatitis) or mental (episodes of depressive disorder secondary to heavy consumption of alcohol).

Management overview

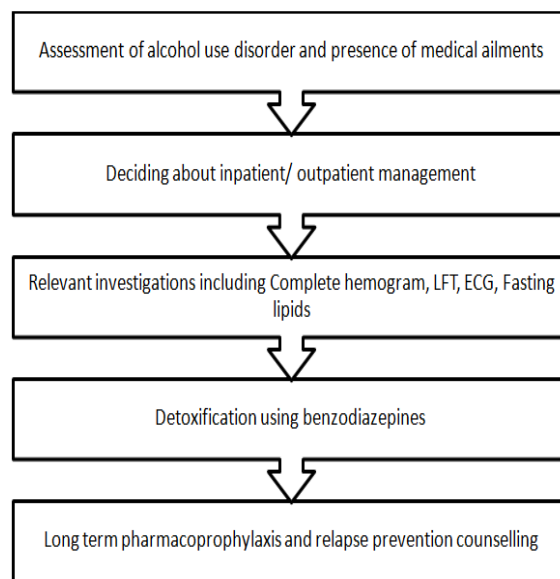


Figure 1: Overview of management of patients with alcohol use disorders

Comprehensive management of patients with alcohol use disorders needs to take into consideration a variety of factors including the extent of alcohol use problems, presence of associated psychiatric disorders and medical problems, psycho-social support available to the patient, motivation of the patient. The general outline of treatment of patients with alcohol use disorders is depicted in figure 1. The plan for admission of the patient is based upon the presence and acuity of the medical problems, extent and pattern of alcohol use, history of having seizures or altered sensorium (delirium) during the withdrawal from alcohol, presence of psychiatric disorders requiring close observation including violent behaviour and suicidality, presence of social supports, and patient and therapist preference.

Patients with alcohol dependence usually have poor motivation for treatment. Hence encounter in the medical/ surgical setting gives an opportunity to start engagement for treatment of alcohol use disorder and enhance motivation.¹⁰ Motivation enhancement therapy (MET) involves a non-confrontational approach to the patient wherein the therapist attempts towards generate insight into problems related to alcohol use. The basic theme of such a therapy is to discuss the extent of alcohol use, the advantages of drinking alcohol and the problems if any to the patient due to alcohol use. The therapy utilizes techniques of developing discrepancy, augmenting ambivalence, rolling with resistance, expressing empathy and supporting self-efficacy, summarized as acronym DARES.

The objective of treatment should be clarified and discussed with the patient and/or the family members. The family members offer an important support and resource in the treatment process and their role needs to be acknowledged in the Indian context. Alcohol

dependence typically has a remitting and relapsing course, and patients need to be forewarned of a relapse which can occur despite adequate treatment. The patient need to be kept in the treatment loop and treated as early as possible after return to drinking.

Assessment and management of complications

Assessment of patients with alcohol use disorders encompasses history taking, examination and appropriate investigations. The history of alcohol use disorders should attempt to establish features of alcohol dependence, the frequency and pattern of drinking in recent past (intermittent, binge or regular), the quantity of alcohol used on a daily basis, the abstinence attempts in the past and the reasons of relapse, and the time from last intake of alcohol. The history of alcohol related complications should also be assessed to look for problems in the domains of physical health, psychological health, social and occupational functioning, and any legal issues (e.g. drunken driving). History of concurrent medical illnesses like hypertension, diabetes mellitus and other disorders need to be ascertained and recorded. Patients with alcohol dependence may also have other substance use disorders, especially nicotine dependence (both smoked and smokeless tobacco) which needs to be recorded.

Physical examination in patients with alcohol dependence needs to be customized according to the findings of the history. Blood pressure and pulse rate may give an indication of withdrawal state, as well complications like dehydration and hypovolemia due to gastric bleed. Abdominal examination with a focus on the liver abnormalities may ascertain hepatomegaly, presence of ascitis, and spider naevi. Neurological and cardiovascular examinations may also reveal abnormalities in patients with alcohol dependence. An effort needs to be made to look for signs of withdrawal like tremor, diaphoresis, increased blood pressure and pulse rate in patients who have recently stopped alcohol intake. Consciousness and orientation also need to be assessed for patients with alcohol dependence as these may be altered in states of delirium.

The investigations that are helpful in patients with alcohol dependence include hemogram with peripheral smear, liver function tests including bilirubin, SGOT, SGPT, alkaline phosphatase, and serum proteins. An ECG would be helpful to discern arrhythmias, while ultrasound of the liver can help to detect fatty liver, cirrhosis of the liver and ascitis. Gamma-glutamyl transferase (GGT) is a sensitive and specific marker to help detect recent consumption of alcohol.

Detoxification treatment

The term detoxification usually refers to the process of ridding the body of substances in a controlled and safe manner. Detoxification from alcohol can usually be conducted with benzodiazepines and multivitamins.¹¹ Benzodiazepines are given to reduce the withdrawal

symptoms like tremors, anxiety, and insomnia. They also reduce the probability of withdrawal seizures and delirium. Long acting benzodiazepines like diazepam and chlordiazepoxide are preferred as they minimize the need for frequent dosing, and effectively control withdrawal symptoms over a longer period of time. However, in cases of liver failure, lorazepam, oxazepam, and temazepam are preferred benzodiazepines as these are not metabolized by the liver.

The doses of benzodiazepines are determined on the basis of the amount of alcohol being consumed by the patient and the severity of withdrawal symptoms. Concurrent abuse of other sedative-hypnotics necessitates the use of higher doses. The benzodiazepines are initiated at higher doses, for example, chlordiazepoxide (50-200 mg per day), diazepam (20–60 mg per day), lorazepam (4–8 mg per day), and oxazepam (60–180 mg per day). The medications are tapered off approximately over a week's time. Dose can be reduced by 10–15 percent per day.

Another regimen that can be followed is the one recommended by Clinical Institute of Withdrawal Assessment (CIWA). The withdrawal symptoms are charted and management decisions regarding medication dosages are made in accordance to CIWA scale. Loading of benzodiazepines can be done with long-acting benzodiazepines. Repeated doses of benzodiazepines (e.g. 10 mg diazepam) can be given till the patient is in light sedation. This would yield the daily requisite dose which can be given in divided daily doses and then tapered off.

Multivitamins are given as alcohol dependent patients are deficient in many vitamins. Thiamine supplementation is especially warranted in the immediate period of detoxification as thiamine deficiency is associated with emergence of Wernicke's encephalopathy and Korsakoff's amnesic state. Thiamine can be given orally and parenterally (after sensitivity testing) in doses of 100-200mg/ day.

Proton pump inhibitors like pantoprazole may be used in the initial period when patient is undergoing detoxification. Patients may have gastritis due to alcohol use which would reduce with these medications. Apart from the above medications, other regimens may be used for the treatment of alcohol dependence during the withdrawal phase. This includes use of gabapentin to relieve withdrawal symptoms, and carbamazepine and valproate to prevent the occurrence of seizures.

The detoxification of alcohol dependent patient in the general hospital inpatient setting needs adequate support and care from the nursing personnel. Development of delirium needs to be watched for cautiously. Patient may require sedation with injectable antipsychotics if they become agitated. Attention needs to be paid towards oral nutrition, and hydration should be maintained and input-output charted if oral intake cannot be ensured.



Long term treatment

Since patients with alcohol dependence have high rates of relapse, they benefit with long term treatment, both with pharmacological and non-pharmacological approaches. It is imperative to keep the patient engaged in the treatment process to improve the outcomes. The pharmacological agents for alcohol dependence include:

1. **Disulfiram:** It is a deterrent agent. The usual daily dose is 250 mg per day (500 mg per day in some cases). It is started only after informed consent from the patient and the family members. This medication is preferred for patients who are motivated, can control their craving and have good social supports for supervision of the treatment. The side effects of disulfiram are fatigue, dermatitis, impotence, peripheral neuropathy, optic neuritis, a variety of mental changes, and hepatic damage. When alcohol is taken over disulfiram, a Disulfiram-Ethanol reaction (DER) is precipitated which includes tachycardia, flushing, palpitations, throbbing headache, vomiting, and in severe cases hypotension, coma and death. A person abstains from alcohol fearing the precipitation of DER.
2. **Baclofen:** It is an anticraving agent. The usual daily dose is 30 to 60 mg per day, and sometimes upto 80 mg per day. It can be given safely in patients with liver dysfunction. The commonest side effects include back pain, constipation, diarrhea, dizziness, drowsiness, fatigue, headache, increased salivation, muscle weakness, nausea, and vomiting.
3. **Naltrexone:** It is an anticraving agent which is given in a daily dose of 50mg. The drug is metabolized through the liver and can lead to increase in levels of transaminases. The common side effects include nausea, abdominal pain, constipation, dizziness, headache, anxiety, and fatigue.
4. **Acamprosate:** It is an anticraving agent. Dose for patients weighing more than 60 kg is 333mg 2 tablets thrice a day, and for weight less than 60 kg 333mg 2 tablets twice a day. The drug is excreted through the kidneys and does not involve hepatic metabolism. The common side effects include diarrhoea, flatulence, nausea, abdominal pain, headache, back pain, infection, flu syndrome, chills, somnolence, decreased libido, amnesia, confusion, depression and anxiety.
5. **Topiramate:** It is an anticraving agent. The prescribed dose is 100 to 400 mg per day. It is preferred in patients with comorbid seizure disorder or mood disturbances. The most common dose-related adverse effects are fatigue, nervousness, poor concentration, anxiety, mood problems, confusion, metallic taste, depression, anorexia, weight loss, and tremor. In some patients renal calculus can be precipitated.

The psychotherapeutic technique that has shown good evidence for patients with alcohol dependence is Relapse Prevention Counseling (RPC). RPC comprises of counseling measures aimed at reducing the chances of relapse. RPC is carried out in many sessions and is modified according to the individual characteristics of the patient. It consists of the helping patients identify their high-risk relapse factors and develop strategies to deal with them and to check the attitudinal, emotional, cognitive, and behavioural changes prior to the re-initiation of alcohol intake. It aims to help patients understand and deal with alcohol related cues and cravings and to deal with social pressures to use substances. Attempt is made to curtail the negative emotional states of being hungry, angry, and lonely or tired (HALT), which often predispose to a relapse. The RPC also envisages for strategies for quick return to treatment in case of a lapse or relapse.

Other therapies like family therapy and marital therapy are likely to be effective in the treatment of patients with alcohol use disorders. Often the genesis of alcohol use in the family context lays in the interaction with the significant others. A co-dependent relationship with a substance using family member may help in perpetuating the substance taking behaviour.¹² Family and marital therapies may help in curtailing such influences and affording help indirectly to the patient with substance use disorder.

Newer approaches and Genetic testing

Drug development for any disease including substance use disorders is a long drawn process. Of the molecules showing promise in the preclinical stage, only a fraction are finally approved for clinical use, that too after an extended period of time in which the Phase I, II and III trials are conducted and regulatory approvals are obtained. The process is slower for medications of the central nervous system.¹³ Yet, preclinical models for alcohol dependence may serve as useful markers for ascertaining the potential of newer compounds. The bridge from promise to actual clinical practice can be traversed by expediting clinical trials and conducting well powered clinical trials with superior effect size demonstrations that can make the newer drugs in development lucrative for use.¹⁴

Another approach that holds promise is the development of personalized medicine for patients with alcohol use disorders. All patients with substance use disorder do not respond similarly with the same interventions. Hence, genetic testing for finding indicators for response to particular medication may be able to customize the treatment to the patient's profile. It has been seen that certain polymorphisms of serotonin receptors respond to ondansetron, while others do not.¹⁵ Variations in μ -opioid receptors changes the response of patients to naltrexone.¹⁶ As of now, usage of pharmacogenomic testing is being explored in the treatment of cancer, epilepsy and bipolar disorder.¹⁷ Similar use of



personalized medicine for patients with alcohol dependence may be useful in improving the outcomes. Certain genes are found to increase the risk of dependence in substance use disorders and certain genes are found to have a protective effect against dependence like ADH1B and ALDH2¹⁸. Codependence with other substances like nicotine and cannabis is also quite common and certain genes are found to be associated with it like GABRA2 gene¹⁹. Some genetic traits are found to exert effects on alcohol susceptibility like genetic variations in liver enzymes, variations in neurotransmitters like dopamine and endorphin, variations in withdrawal response and odour sensitivity to alcohol.

Nature vs Nurture

Gene environment interaction is complex in the contribution to alcohol dependence and its interplay plays the role in dependence. Genetic testing and its advances lead to greater exploration of genetic detail, whereas environmental factors are widened from family, peers, etc to society. Genes also play a role in the personality attributes of the person which further adds as a factor determining dependence. Both the factors also play a role in comorbid conditions like depression, suicidality, antisociality, etc.

CONCLUSIONS AND FUTURE DIRECTIONS

To conclude, alcohol use disorder is a commonly encountered condition in the general hospital setting and is associated with many physical complications. The effective and safe treatment of alcohol use disorder in the general hospital setting needs to consider multiple factors. Judicious use of investigations may be required for finding out abnormalities, especially pertaining to the hepatic system. The treatment of patients with alcohol use disorders can be broadly divided into initial detoxification stage and subsequent long-term maintenance phase. Adequate doses of benzodiazepines may be required in the initial period, followed by the use of pharmacoprophylactic agents on the long term. Since relapses are common occurrence for these patients, an inclusive approach aimed at retaining the patient in the treatment net may be beneficial.

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