Management of Alcohol Use Disorder in Patients With Alcoholic Liver Disease

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Alcohol use disorder (AUD) is a common condition that develops on the background of heavy alcohol use and is characterised by the loss of control over alcohol use and a compulsion to use alcohol, often despite negative consequences. AUD is a leading cause for the resumption of alcohol use in patients with alcoholic liver disease (ALD) after treatment. Hence it is essential to screen all patients with ALD for the presence of AUD. Screening tools such as alcohol use disorders identification test (AUDIT) and AUDIT-C are used, following which the diagnosis and severity of AUD are determined using DSM-5 criteria. The management of AUD in patients with ALD is best carried out using an integrated approach involving psychiatrists and gastroenterologists/hepatologists. The treatment most often involves a combination of pharmacotherapy and psychosocial interventions which try to achieve and maintain abstinence. Although, there is limited evidence, Baclofen is the first line pharmacological agent for long-term management of AUD in patients with ALD. Intensive psychological interventions such as motivation enhancement therapy and cognitive behavioural therapy are also seen to be beneficial. Treatment retention and follow-up are vital and can positively influence outcomes. (J Clin Exp Hepatol 2022;12:1514–1526)

Alcohol use is among the leading risk factors for deaths and disability-adjusted life years (DALYs) globally,[1] accounting for 38.8 deaths and 1759 DALYs per 100,000 persons, respectively.[2] Digestive diseases, including alcoholic liver disease (ALD), make up a substantial proportion, resulting in 8.3 deaths and 307 DALYs per 100,000 people.[3] The continued use of alcohol after the onset of ALD is associated with severe consequences, including mortality[4] and is often due to the presence of alcohol use disorder (AUD). This is of particular importance in patients with ALD who have received liver transplants, where the resumption of alcohol use is a major concern.[5–7]

AUD is a chronic relapsing illness that develops in the background of heavy alcohol use. It is characterised by a compulsion to take alcohol, often despite negative consequences, loss of control over alcohol use and the emergence of a negative physical and emotional state in the absence of alcohol. It is known to be accompanied by changes in key brain areas which can persist even after cessation of use, and may result in excessive salience to alcohol-related cues, changes in the motivational properties of natural rewards, an altered and exaggerated response to stress and difficulties with executive control and self-regulation.[8] AUD is extremely common with prevalence for a lifetime diagnosis ranging between 0.7% and 22.7 %in different populations.[9] Despite this, it is usually under-diagnosed and under-treated, with only about one in six patients with AUD receiving treatment.[10]

Despite advances in medical and surgical management, the cessation of alcohol use is the mainstay of treatment and is critical in patients with ALD.[11] A recent large study among US veterans found that about one-third of patients with a diagnosis of cirrhosis had AUD, and only about 14% received any AUD treatment. However, among those receiving treatment, there was a significant reduction in hepatic decompensation and all-cause mortality.[12] Therefore, the recognition and treatment of AUD is integral to successful outcomes in patients with ALD.

In this review, we present a step-wise approach to screening, diagnosis, and treatment (pharmacological and psychosocial) of patients with AUD and ALD.

Keywords: alcohol use disorder, alcoholic liver disease, diagnosis, pharmacotherapy, psychotherapy
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Abbreviations: AA: Alcoholics Anonymous; ALD: Alcoholic Liver Disease; AMPA: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; AUD: Alcohol Use Disorder; AUDIT: Alcohol Use Disorder Identification Test; AUDIT – C: Alcohol Use Disorder Identification Test – Consumption; CBT: Cognitive Behavioural Therapy; CDT: Carbohydrate Deficient Transferrin; CIWA – Ar: Clinical Institute Withdrawal Assessment for Alcohol Revised; DALY: Disability Adjusted Life Years; EtG: Ethyl glucuronide; EtS: Ethyl Sulphate; FAEE: Fatty acid ethyl ester; FDA: Food and Drug Administration; GABA: Gamma-Aminobutyric acid; GGT: Gamma glutamyl transferase; HCV: Hepatitis C Virus; HE: Hepatic Encephalopathy; LT: Liver Transplantation; MCV: Mean corpuscular volume; MET: Motivation Enhancement Therapy; MI: Motivational Interviewing; NMDA: N-Methyl-D-aspartate; PEth: Phosphatidylethanol; RCT: Randomised control trial; SMS: Short Message Service

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SCREENING FOR AUD

Screening for the presence of AUD is essential in all patients presenting with liver disease and a history of alcohol use. This is because patients who die due to ALD often have a history of prior hospitalisations for alcohol-related problems, which represent potential opportunities for intervention.[13]

There are many tools available to screen problematic patterns of alcohol use (Table 1). These have been tested extensively in medical settings and have also been utilised in the background of ALD.[14]

The alcohol use disorders identification test (AUDIT) is a 10-item screening tool developed by the World Health Organisation and is recommended for use in medical settings. It has been translated into several languages and validated in different parts of the world. A score of more than 8 suggests hazardous or harmful alcohol use, while a score greater than 20 suggests dependent alcohol use.[15]

The AUDIT-C is a brief version consisting of the first three items of AUDIT that focus on alcohol consumption and may be used by clinicians in busy settings. A score of 3 or more for women and 4 or more for men is indicative of harmful alcohol use.[16]

The four-item CAGE questionnaire (Cutting down, Annoyance by criticism, Guilty feeling and Eye-opener) has also been used to identify alcohol dependence, with a score of more than 2 being indicative.[17]

AUD screening can be done in outpatient, inpatient and emergency room settings and across the spectrum of ALD severity, although challenges may be encountered in the setting of advanced liver disease.[18]

EVALUATION AND DIAGNOSIS OF AUD

Following the application of screening instruments, if the clinician suspects that the patient may have AUD, then a diagnostic evaluation must be carried out. Table 2 lists information that should be obtained as part of the diagnostic evaluation for AUD.

The diagnosis of AUD can be established using DSM-5 criteria, where AUD is defined as a maladaptive behaviour with an impaired ability to stop or control alcohol use despite adverse social, occupational or health consequences characterised by 2 or more of the features described in Table 3 in the past 12 months. It is classified as mild (2–3 criteria), moderate (4–5 criteria) and severe (>6).[19]

The diagnosis of AUD is made clinically based on information available from patients, family, friends and medical records. Underreporting of alcohol use often poses challenges in making a diagnosis and establishing severity.[20] This may be due to a number of reasons, including not being motivated to quit alcohol, stigma and shame surrounding AUD diagnosis, fear of adverse social or occupational consequences related to AUD diagnosis (loss of job or welfare benefits) or secondary to cognitive dysfunction as a sequel of chronic alcohol use.

In this context, the use of objective biochemical measures of recent alcohol consumption can supplement clin-

Table 1 Scales to Assess Alcohol Use Disorder.

Scale	Purpose	Brief description	Cut off	Inference
AUDIT	Screening	A clinician administered 10-item screening tool evaluating hazardous use, harmful use and dependence symptoms	Score of 8 or more indicates harmful use	8 to 15—Simple advise 16 -19—Brief counselling and monitoring >20—Diagnostic evaluation for alcohol dependence
AUDIT – C	Screening	Brief screening instrument with 3 questions	A score of 4 or more is considered positive in men and 3 or more in women	Positive score indicates hazardous drinking or active alcohol use disorder
CAGE	Screening	Brief screening questionnaire with 4 questions	A score of 2 or more indicates positive	2 indicates need for further evaluation
CIWA-Ar	Assess withdrawal	A 10-item clinician administered tool to evaluate withdrawal and initiation of treatment	A score of 8 or above indicates withdrawal	<8—No pharmacotherapy 8 to 15—Symptomatic treatment >15—Symptomatic- and benzodiazepine-based treatment at hospital or community setting

Abbreviations: AUDIT, alcohol use disorder identification test; AUDIT – C: alcohol use disorder identification test – consumption; CIWA – Ar, clinical institute withdrawal assessment for alcohol revised.

Table 2 Diagnostic Evaluation.

(1) Age and circumstance of initiation—How did it start? What were the first few experiences?
(2) Progression from occasional to regular use—At what age did the substance use become regular?
(3) Changes experienced in effects of alcohol over time (Tolerance)
(4) Presence of impaired control over alcohol use (Loss of control)
(5) Presence of craving
(6) Details of withdrawal symptoms (When first experienced? Severity and complicated withdrawals)
(7) Effects of intoxicated behaviour
(8) Complications associated with drug use (a) Physical (b) Psychological (c) Financial (d) Occupational (e) Family-related (f) Social (g) Legal
(9) Periods of abstinence from the substance (a) Number of abstinence attempts and reasons for the same (b) Any treatment sought and its nature and duration (c) Functioning during abstinence period (d) Any other substance use during abstinence from one substance (e) Reasons for relapse to substance use after abstinence
(10) Maintaining factors for use—What led to continuing use?
(11) Current (Past 1 month) pattern of consumption—Average use, Last use
(12) Reasons for seeking treatment
(13) Past medical or psychiatric history, if any
(14) Family history
(15) Personal history
(16) Premorbid temperament
(17) High-risk behaviours (driving under influence, high-risk sexual behaviour)
(18) Other behavioural addictions (gambling, racing, excessive use of the internet)

Table 3 DSM-5 Criteria.

Alcohol use disorder is a problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:
1. Alcohol is often taken in larger amounts over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.
3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol or recover from its effects.
4. Craving, or a strong desire or urge to use alcohol.
5. Recurrent alcohol use resulting in a failure to fulfil major role obligations at work, school or home.
6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
7. Important social, occupational or recreational activities are given up or reduced because of alcohol use.
8. Recurrent alcohol use in situations in which it is physically hazardous.
9. Alcohol use is continued despite knowledge pf having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.
10. Tolerance, as defined by either of the following: a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effects. b. A markedly diminished effect with continued use of the same amount of alcohol.
11. Withdrawal, as manifested by either of the following: a. The characteristic withdrawal syndrome for alcohol noted b. Alcohol is taken to relieve or avoid withdrawal symptoms.

ical history and examination findings (Table 4). These are broadly classified as indirect and direct state markers.

The indirect state markers include gamma glutamyl transferase, mean corpuscular volume and carbohydrate deficient transferrin and are the most commonly used measures in clinical practice. Gamma glutamyl transferase and mean corpuscular volume are of little value in measuring alcohol consumption in patients with liver disease as their values are deranged as a consequence of the disease process. Carbohydrate deficient transferrin has been used to monitor alcohol use in patients with ALD and demonstrates low sensitivity but high specificity.[21] There are also some concerns of its accuracy in the background of severe liver disease.[22]

The direct state markers include ethyl glucuronide, ethyl sulphate, phosphatidylethanol and fatty acid ethyl ester. They are detectable in serum over hours, urine up to 7 days, whole blood up to 2 weeks and in hair for months. A recent systematic review evaluating the diagnostic accuracy of alcohol biomarkers in patients with ALD concluded that urinary and scalp ethyl glucuronide are the most well-validated, while phosphatidylethanol is promising, albeit tested less in the ALD setting.[21]

However, it is extremely important for clinicians to note that these objective measures need to be employed with the intent to build rapport with patients by attempting to normalise discussions surrounding ongoing alcohol use rather than as evidence with which to confront patients.

Once the diagnosis of AUD is established, screening for co-occurring mental health conditions must be done, given their high prevalence in this population.[9] Further, it is also important to evaluate whether the patient has presented in

Table 4 Biomarkers Related to Alcohol.

Biomarker	Sample	Indicator	Time Frame	Comments
Liver function tests	Blood	Ratio of 2 or more indicative of alcohol related liver disease	3–7 days	Inexpensive and widely available
AST/ALT ratio		Early indicator of liver disease and chronic heavy alcohol use	2 weeks	
GGT				
Carbohydrate deficient transferrin (CDT)	Blood	Heavy alcohol use	2–3 weeks	Low sensitivity in patients with alcoholic liver disease
Ethyl glucuronide (EtG) and Ethyl sulphate (EtS)	Hair	Long-term consumption of alcohol	Several months	No influence of gender, age or ethnicity
	Urine		3–5 days	
	Blood		48 h	
Fatty acid ethyl ester (FAEE)	Hair	Recent heavy alcohol use	1 month	Increases validity of EtG
Phosphatidylethanol (PETh)	Blood	Correlates with amounts of alcohol consumed and is not affected in	2–4 weeks	Correlates with amount of alcohol consumed
Direct alcohol measurement	Blood	Ratio of 2 or more indicative of alcohol related liver disease	3–7 days	
		Early indicator of liver disease and chronic heavy alcohol use	2 weeks	

an acute withdrawal state. This can be assessed using the Clinical Institute Withdrawal Assessment for Alcohol Revised (CIWA–Ar) Scale[23] which can be used to decide the mode and schedule of treatment. It is a 10-item, clinician rated instrument and a score of >8 suggests the need for pharmacotherapy (Table 1). The assessment and diagnosis of alcohol withdrawal are discussed in another article in this issue.

The clinical assessment should be concluded with the provision of feedback regarding the initial evaluation, including diagnosis. This should be followed by a discussion regarding goals of treatment (Abstinence vs Controlled Drinking), although in most cases with ALD, depending on the extent of organ damage, abstinence would be the sole option as it significantly improves the survival rate of patients with ALD.[24] This process should be collaborative and respect the autonomy of the patient to make choices about treatment.

TREATMENT OF AUD

The treatment of AUD is broadly divided into two stages, acute and long-term treatment. The focus of acute treatment is the management of alcohol withdrawal, nutritional deficiencies and co-occurring medical illnesses, whilst also engaging with the patient and building motivation to change. The treatment of acute alcohol withdrawal and nutritional deficiencies is discussed in another article in this issue. The focus of long-term treatment is preventing relapse, addressing co-occurring psychological and social issues and retention in treatment. Treatment in both stages is a combination of pharmacological and psychosocial interventions.

A recent study evaluated the cost effectiveness of treatments for AUD in patients with alcohol-related cirrhosis and found that compared to a do-nothing scenario, pharmacotherapy (particularly Naltrexone and Acamprosate) and counselling were found to be cost-saving from a healthcare perspective, which means that they provide more benefits with less costs than no intervention.[25] This underlines the importance of providing interventions for AUD in patients with ALD. Figures 1 and 2 summarise the approach to be used in management of AUD in patients with ALD, in general and based on the stage of disease.

PHARMACOLOGICAL INTERVENTIONS FOR AUD

Following the management of acute alcohol withdrawal, most treatment guidelines recommend pharmacotherapy to reduce the possibility of relapse in patients with moderate to severe AUD.[26] Currently, there are 3 FDA approved drugs available for treatment of AUD–Disulfiram, Naltrexone and Acamprosate. In addition, other drugs, such as Baclofen, Nalmefene, Topiramate, Gabapentin,

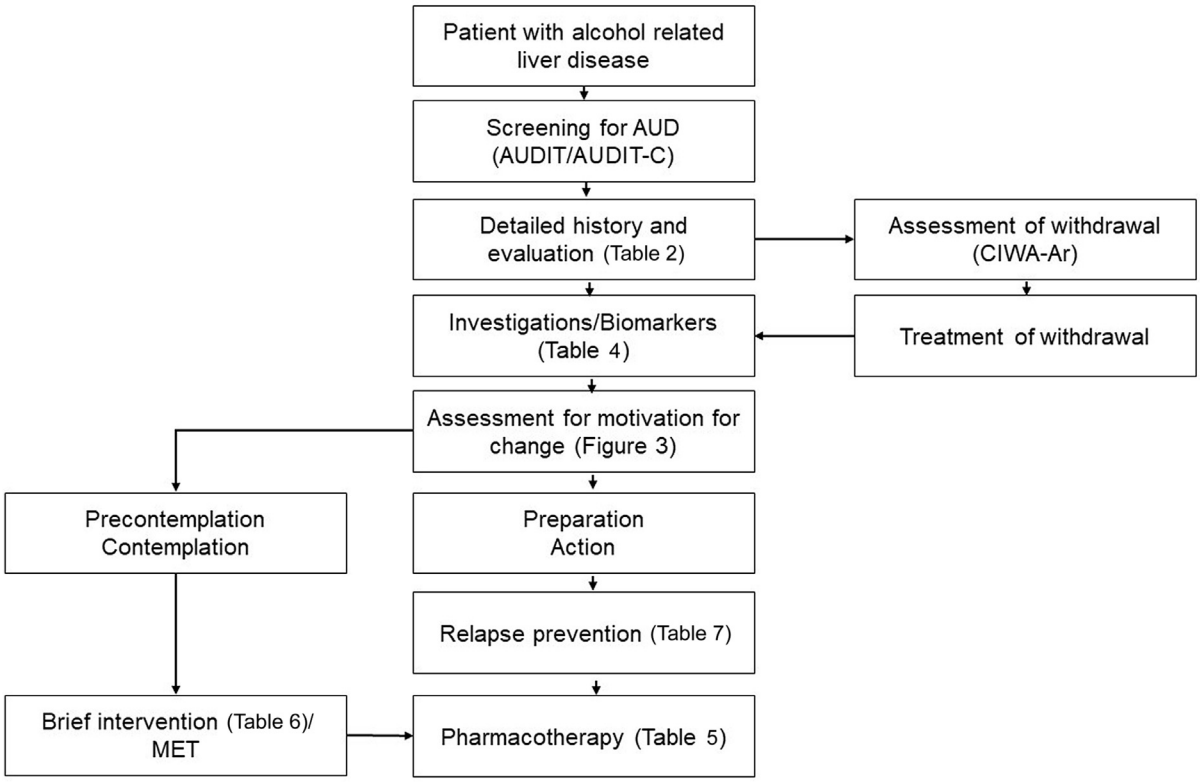

Figure 1 Approach to a case of AUD with ALD. Abbreviations: AUD, alcohol use disorder; AUDIT, alcohol use disorder identification test; AUDIT – C, alcohol use disorder identification test – consumption; CIWA – Ar, clinical institute withdrawal assessment for alcohol revised; MET, motivation enhancement therapy.

Pregabalin, Ondansetron and Varenicline, have been studied and are used off label for treatment of AUD.[26]

The literature on the use of these medications in the background of ALD is limited[27] and will be reviewed in this section and is summarised in Table 5.

Baclofen is a gamma-aminobutyric acid (GABA)-B receptor agonist that is approved in France for the treatment of patients with AUD following failure of other available medical treatments.[28] It has predominant renal metabolism, is safe in the setting of liver disease and till date is the only agent that has demonstrated efficacy in patients with AUD and ALD. A seminal double blind RCT in patients with AUD and liver cirrhosis found a higher proportion of patients on baclofen achieved and maintained abstinence than placebo and the medication was well-tolerated.[29] Two subsequent randomized control trial (RCTs) demonstrated that baclofen promoted abstinence in patients with and without ALD[30] and in patients with alcohol dependence and HCV associated liver cirrhosis.[31] A prospective cohort study in 219 patients with ALD attending a joint liver and alcohol treatment centre found that treatment with baclofen led to improvements in measures related to alcohol use at the end of one year and that adherence to medications was good.[32] Another prospective study in 65 patients with ALD recruited over 3 years, suggested that baclofen treatment was well-tolerated and led to reductions in alcohol use, significant improvement in biological markers and liver function tests.[33] Hence, in keeping with the recommendations made in the Cagliari statement, an expert consensus group with members from backgrounds, including addiction medicine, hepatology and gastroenterology, baclofen currently forms first line treatment for AUD in ALD[34] and can be prescribed safely even in advanced stage liver disease.[35]

Acamprosate is an N-Methyl-d-aspartate (NMDA) receptor agonist and has been extensively studied in treatment of AUD, particularly in primary care settings where it has better effectiveness and acceptability than naltrexone.[36] It is of particular interest in patients with liver disease owing to its lack of hepatic metabolism and theoretically should be safe in patients with ALD. A recent retrospective review comparing the safety of acamprosate and baclofen in patients with AUD and alcoholic cirrhosis (Child Pugh B and C) suggested lower chances of admission in those treated with Acamprosate.[37] There is also an ongoing Phase 2 trial to evaluate the safety of Acamprosate in patients with ALD in USA.[38] There are some concerns regarding the precipitation of hepatic encephalopathy (HE) in individuals

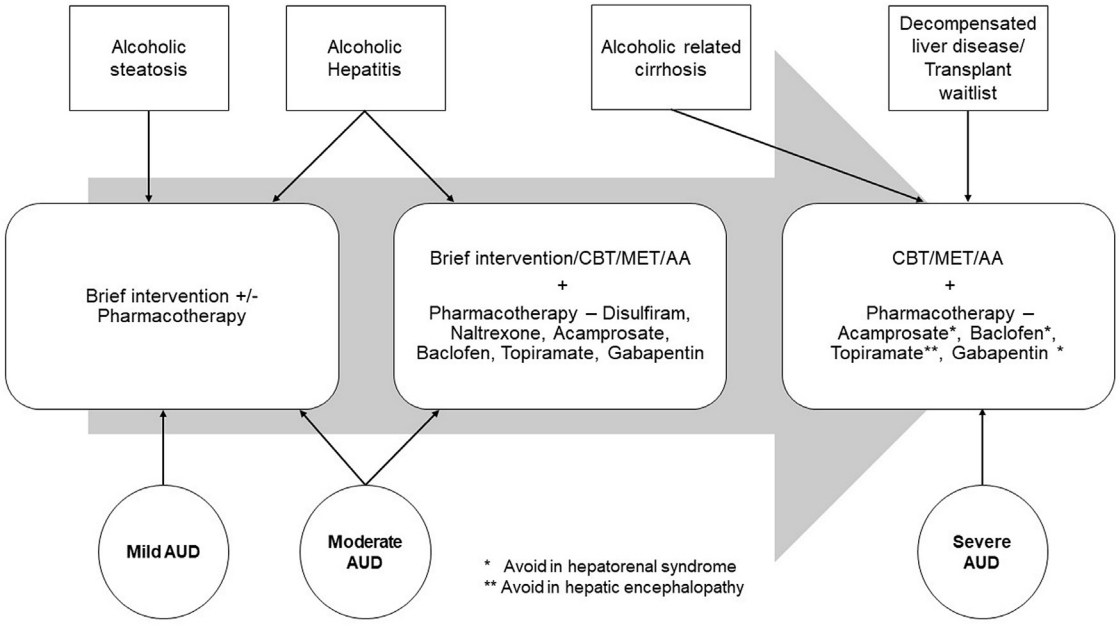

Figure 2 Staging of AUD and ALD and treatment. AUD, alcohol use disorder; CBT, cognitive behavioural therapy; MET, motivation enhancement therapy.

with ALD due to glutamate receptor antagonism,[39] though an early study noted no increased risk of HE after an acute administration of acamprosate in individuals with alcoholic cirrhosis.[40]

Topiramate is an anticonvulsant used in patients with AUD. It antagonises the glutamate activity at α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor and facilitates GABA action. It has been found to have a beneficial effect in terms of reduction in drinking in RCTs and meta-analyses.[41–43] While there are no specific trials in patients with AUD with ALD, it is recommended in hepatic dysfunction owing to its predominant renal excretion and improvement in liver function was reported after treatment with topiramate.[44]

Gabapentin and pregabalin are anticonvulsants which act on voltage gated calcium channels and secondarily influence GABA activity. They have been used in the treatment of AUD,[26] particularly with significant alcohol withdrawal symptoms,[45] although their efficacy remains questionable. They may be useful in patients with ALD considering they are hepatic sparing and undergo renal metabolism. There are currently no studies available in patients with AUD and ALD. However, they are found to be useful in management of pain in cirrhosis[46] and alcohol related neuropathy[47] and are also being evaluated for ALD-associated itching.[48]

Naltrexone is a μ, κ and δ opioid receptor antagonist.[49] It reduces craving and rewarding effects of alcohol, whilst increasing alcohol-induced sedation and negative mood states.[50] Its proposed mechanism of action is the suppression of ethanol-evoked increases in mesolimbic dopaminergic and opioidergic activity.[51] It is effective in reducing the number of heavy drinking days and returning to drinking.[41] Naltrexone is metabolised in the liver and received an FDA black box warning due to concerns about elevation in liver enzymes, particularly when prescribed at doses of 100 mg and above.[52] Although a number of subsequent studies suggest that there is no evidence of hepatotoxicity in clinical practice,[53–55] it is prudent to exercise caution when prescribing Naltrexone in patients with ALD. This includes regular monitoring of serum transaminases in patients with early liver disease and preferably avoiding the drug in the setting of advanced liver disease. An ongoing RCT to evaluate safety and efficacy of Naltrexone in patients with ALD in India is likely to offer further insights.[56] Naltrexone is also available as a long-acting injectable formulation at a dose of 380 mg once monthly. Although it lacks first pass metabolism and has lesser propensity to cause hepatic dysfunction, it is contraindicated in advanced liver disease.[57]

Nalmefene is another opioid receptor antagonist at delta and mu and partial agonist at kappa receptors which is approved for the reduction of heavy drinking in Europe and Japan in individuals with high levels of alcohol use.[58] It is suggested to be less hepatotoxic than naltrexone.[59] Although there are no specific studies in patients with AUD and ALD, there is a case series on improvement of hepatic functioning in patients with alcohol related cirrhosis with reduction in alcohol use.[60]

Disulfiram is a deterrent agent that causes the irreversible blocking of the enzyme aldehyde dehydrogenase, thereby eliciting a severe, unpleasant and potentially life-threatening physiological reaction in the presence of alcohol due to the accumulation of acetaldehyde. It is

Table 5 Pharmacological Intervention in AUD With ALD.

Drug	Mechanism of action	Dosage	Adverse effects	APA recommendation	Role in AUD with ALD
Baclofen	GABA-B receptor agonist	10–30 mg three times a day, oral	Fatigue, sleepiness, and dry mouth	NA	First-line agent for use in ALD No concerns of hepatotoxicity
Acamprosate	NMDA receptor antagonist	666 mg three times a day, oral	Diarrhoea	First line	No concerns of hepatotoxicity Caution in patients with hepatorenal syndrome
Topiramate	GABA action augmentation, glutamate antagonism	Initially 25 mg daily, titrated up to 150 mg twice a day, oral	Paraesthesia, altered taste, anorexia, difficulty concentrating	Second line	Can be used in AUD with ALD but caution in cases with hepatic encephalopathy and hepatorenal syndrome
Gabapentin	Modulates GABA activity through action at presynaptic calcium channels	300–600 mg three times a day, oral	Fatigue, headache, insomnia	Second-line	No concerns of hepatotoxicity
Naltrexone	Mu opioid receptor antagonist	50 mg daily oral, 380 mg monthly, IM	Diarrhoea, nausea, somnolence	First-line	Concerns of hepatotoxicity
Nalmefene	Mu and delta opioid receptor antagonist	10–20 mg	Insomnia, dizziness and headache	NA	Possible hepatotoxicity

contraindicated in liver disease owing to its potential to cause hepatotoxicity.[61]

Ondansetron is a 5-HT3 receptor antagonist that has been used as off-label treatment for AUD.[62] It is safe for use in patients with ALD, although no studies have evaluated efficacy in this population.[63] Metadoxine, which has been used for treatment of both ALD and non-alcoholic fatty liver disease, has demonstrated a decrease in drinking and improvement in liver parameters in a retrospective study and may merit further study.[64]

In summary, pharmacotherapy should be considered wherever possible in patients with AUD and ALD. However, caution must be exercised while prescribing any form of pharmacotherapy in patients with complications such as HE and hepatorenal syndrome where concerns surrounding worsening cognitive function often preclude their use. Baclofen is the first-line agent with evidence of both safety and efficacy. Acamprosate, Topiramate and Gabapentin are agents which are safe, though efficacy needs to be established. Naltrexone and Nalmefene, despite initial concerns surrounding hepatotoxicity appear to be safe at least at doses typically prescribed but require systematic evaluation for safety and efficacy in patients with ALD.

PSYCHOSOCIAL INTERVENTIONS FOR AUD

Psychosocial interventions are considered the mainstay in the treatment of AUD and can be provided either alone or in combination with pharmacotherapy. There are various psychosocial interventions used in treatment of AUD, including brief interventions, motivation enhancement therapy and relapse prevention therapy.

Brief interventions for alcohol use can be delivered by a health care professional in any setting in a time of 5–10 min. The FRAMES model (Table 6) is a commonly used brief intervention framework which focuses on providing personalised feedback to the patient regarding assessments, encouraging responsibility for change, advising the patient to change, providing a menu of options available to facilitate change and doing so empathetically so as to enhance the patient's self-efficacy. This approach is found to be helpful in individuals with hazardous or harmful alcohol use in both high and low resource settings.[65,66] Studies evaluating brief interventions in patients with ALD are scarce and have shown mixed results[67] and larger studies maybe required to establish efficacy.[68] Nonetheless, an effort should be made by clinicians to provide these easily delivered interventions wherever possible.

Motivational interviewing is a broad term for a non-directive, non-judgemental approach focusing on collaboration to evoke change. It utilises open ended questions, affirmation, reflective listening and summary reflections to elicit change talk.[69] Motivation enhancement therapy (MET) is a specific form of treatment where the

Table 6 Principles of brief intervention—FRAMES.

1. Feedback of personal risk
After clinical assessment and investigations, clearly inform the patient about his pattern of substance use and existing or potential harmful effects. For e.g.:
"Your drinking is going to worsen your stomach pain".
"Your blood tests suggest damage to your liver due to alcohol use".
2. Responsibility
Inform your patient that decision about making a change in substance use is their responsibility and choice solely. For e.g.: "Now it is up to you to take a decision on drinking".
3. Advice
As a doctor, give clear advice to reduce drinking and other drug use.
Ask your patient to make a balance sheet. Ask about the advantages and disadvantages of using the substance.
Help the patient see that the disadvantages of using are much more than the advantages of using and the advantages of stopping are greater than the disadvantages of stopping.
Clarify any worries or doubts the patient may have about stopping.
Clear advice regarding the substance needs to be provided For e.g.: "the best way you can reduce your risk of liver disease is to cut down or stop using".
4. Menu of alternative choices
Suggest patient a menu of alternative options available to cut down the drinking. - Identifying a high-risk situation and avoiding them. - Planning ahead to limit drinking or use of substance. - Learning to cope with everyday problems that encourage drinking or use of substance. - Finding alternate sources of enjoyment. - Dealing with stress, anxiety and mood symptoms.
5. Express empathy
Do not belittle or criticise. Do not refer to the person as an addict/alcoholic directly or to family members while discussing with others.
Acknowledge that substance dependence is a problem that can be difficult to overcome but can be with some effort and help.
6. Self-efficacy
Encourage patient to be optimistic and to bring about the changes in drinking/substance use behaviour.

therapist evokes strategies for change, based on the patient's current level of motivation (Figure 3).[70] The emphasis of MET is upon helping the patient to develop discrepancy between their intent and behaviour with a view to reduce the ambivalence to change. This is achieved using an empathetic approach, which avoids argumentation and where the patient's own resources to effect a change (self-efficacy) are encouraged. A number of meta-analyses have shown some benefit in terms of reducing binge drinking and quantity and frequency of drinking, but these effects appear small and inconsistent, a fact that may be related to inaccurate delivery of the interventions.[71] A small study using an MET-based intervention in patients with AUD awaiting liver transplantation (LT) found that while proportions of relapse were similar to a treatment as usual group, the quantity and frequency of drinking reduced in the active group.[72]

Relapse prevention therapy, is a type of cognitive behavioural therapy (CBT) that focuses on identifying and coping high-risk situations, enhancing self-efficacy, managing craving and lapses, eliminating myths and cognitive restructuring (Table 7). A recent study integrating principles of motivational interviewing and CBT was found to be acceptable in patients with ALD and led to improved quality of life.[73]

A systematic review assessing the efficacy of psychosocial interventions in induction and maintenance of abstinence among patients with AUD and chronic liver disease found that integrated therapy incorporating MET and CBT along with comprehensive medical care helped to achieve abstinence. It also seemed to help with treatment retention.[74]

In addition to the psychosocial interventions described above, self-help groups such as alcoholics anonymous, based on twelve steps are also often utilised by patients with AUD. These typically include meetings lasting for 60–90 min with intent to increase psychological well-being, enhance ability to cope with stress and adapt to a sober lifestyle. A recent Cochrane review found higher abstinence rates among patients attending alcoholics anonymous/twelve-step facilitation programs than CBT and MET both in the short- and long-term over 24 and 36 months.[75]

Finally, a number of patients with AUD and ALD have significant medical morbidity, making it difficult to visit hospitals frequently for counselling sessions. Hence, the role of digital interventions merits further exploration for this population. A Cochrane review evaluating digital interventions for hazardous and harmful alcohol use found that it may help to lower alcohol consumption.[76] A pilot study in 15 pre liver transplant patients with AUD found high satisfaction with an SMS-based intervention and differences in urine positivity for alcohol compared to a control group, receiving standard care.[77]

In summary, psychosocial interventions are an integral component of treatment of AUD in patients with ALD. Psychosocial interventions should ideally be conducted over a long-term and incorporate elements of MET and CBT for relapse prevention. Leveraging digital technology may also enhance treatment adherence. An integrated multidisciplinary approach, where a psychiatrist and psychologist/psychiatric nurse are part of the treating team in the liver clinic is associated with better AUD outcomes in terms of alcohol abstinence irrespective of the severity of illness of AUD or ALD.[78–80]

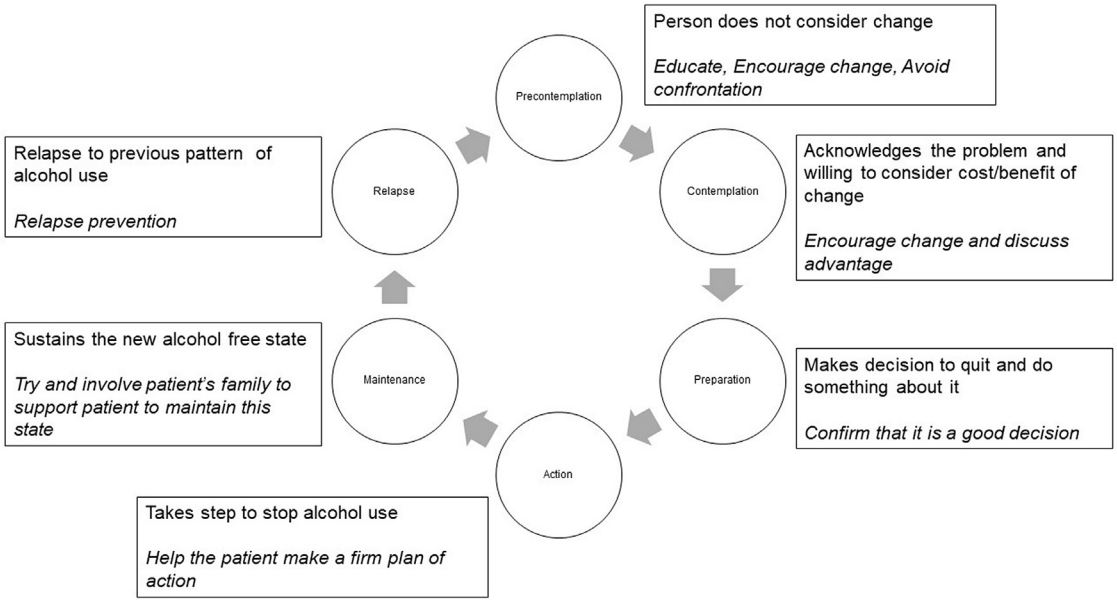

Figure 3 Psychosocial interventions based on motivation to change alcohol use.

Table 7 Relapse Prevention Strategies.

1. Managing high-risk situations
2. Managing craving
3. Learning drink/drug refusal skills
4. Dealing with faulty cognitions
5. Managing negative moods
6. Addressing self-harm
7. Anger management
8. Managing temperamental issues
9. Having a balanced lifestyle

LIVER TRANSPLANTATION IN PATIENTS WITH AUD

The use of LT for patients with AUD remains a debated topic. This is due to concerns related to the resumption of alcohol use leading to graft dysfunction and loss. A meta-analysis showed that the relapse rate annually was 4.7% for any alcohol use and 2.9% for heavy alcohol use, with an overall relapse rate of 26.3% over the median follow-up period of 6 years. There were also significantly higher odds of graft steatosis, steatohepatitis, hepatitis and cirrhosis in relapsers.[81] This was in line with a large study on the natural course of recurrent alcohol-related cirrhosis after LT.[82] This has led to policies in most transplant centres which mandate a period of abstinence from alcohol, ranging between 3 and 6 months. The empirical data related to the utility of pre-transplant abstinence are unclear,[83] although a recent study showed that relapse rates were slightly higher in patients undergoing early transplantation for severe alcoholic hepatitis than standard transplantation.[84] A number of other factors, such as the presence of psychiatric co-morbidity, poor social support and smoking are also known to be associated with risk of relapse to alcohol use following LT.[85–87] This is important because a number of these factors can be addressed using appropriate interventions. There are no studies that have investigated the utility of pharmacological or psychosocial interventions for AUD specifically in patients who have undergone LT. However, it is clear that an integrated care approach delivered by a multidisciplinary team consisting of surgeons, hepatologists, psychiatrists and psychologists, in both the pre- and post-transplant period is associated with better survival.[88,89] A recent review describes the issues of AUD in the setting of LT.[90]

CONCLUSION

The early identification of AUD in patients with liver disease through screening, followed by diagnosis will improve outcomes in patients with ALD. Treatment for AUD should be instituted in all diagnosed patients, with a combination of pharmacotherapy and psychotherapy, which enhances motivation to change and addresses factors that lead to relapse. The approach should be collaborative and should focus on retention of patients in treatment. The goal of treatment should be to achieve total abstinence, but with an awareness that this may not occur in many patients immediately. Failure to achieve abstinence should not be a reason to withhold treatment for AUD at any stage. A collaborative approach involving multiple

specialities, including addiction medicine professionals at every stage of ALD treatment should be considered and would be an important step to reduce ALD-related morbidity and mortality.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

PM, PKC and JM – Conceptualisation, DS and JM - Writing – Original draft preparation, PM and PKC – Supervision, PM and PKC – Writing – Reviewing and Editing

CONFLICTS OF INTEREST

There are no conflicts of interest to be declared by any of the authors.

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