Alcohol abuse in the critically ill patient

Marc Moss, Ellen Lyda Burnham

Alcohol abuse and dependence disorders are common in the 10% of hospitalised patients who need admission to the intensive care unit (ICU), but these disorders are often undiagnosed. The systemic effects from the excessive use of alcohol increase susceptibility to, or directly cause various important disorders in the critically ill. Early recognition of alcohol abuse and dependence is necessary and should prompt consideration of several alcohol-specific diagnoses that have important prognostic and therapeutic implications for these patients. We discuss the use of screening tests to improve the identification of alcohol abuse and dependence disorders, the epidemiology and pathogenesis of important alcohol-related disorders, differences in the presentation of several common alcohol-related diagnoses in the ICU, and important alcohol-specific therapies.

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Divison of Pulmonary Sciences and Critical Care Medicine, University of Colorado at Denver and Health Sciences Center, Denver, CO 80262, USA (M Moss MD, E L Burnham MD)

Correspondence to:
Dr Marc Moss
Marc.Moss@uchsc.edu

See Online for webpanel 1

Alcohol is one of the most commonly used drugs worldwide, and when used excessively it has deleterious effects on almost every organ system. A history of alcohol abuse is common in the 10% of patients in hospital admitted to an intensive care unit (ICU).[1] In some hospitals in the USA, alcohol abuse is responsible for up to 40% of all ICU admissions, and is associated with a doubling in hospital mortality.[2–4] Because of its systemic activity, alcohol increases susceptibility to or directly causes various common disorders seen in the critically ill (figure 1). Prompt recognition of alcohol abuse has important diagnostic, prognostic, and therapeutic implications. Failure to identify specific alcohol-related disorders can delay the initiation of readily available therapies and increase the morbidity and mortality in these ICU patients.

Definitions of alcohol dependence and abuse

A wide spectrum of unhealthy alcohol use can be seen in the critically ill patient.[5] The two most severe forms of alcohol use disorder are alcohol dependence (alcoholism) and alcohol abuse (harmful use). The most devastating type is alcohol dependence characterised by alcohol craving, the inability to stop drinking, the development of withdrawal symptoms after stopping drinking (physical dependence), and tolerance. Alcohol abuse or harmful use is defined as a pattern of drinking that leads to clinically significant physical or psychological harm within a 12 month period. Some studies use questionnaires that identify at-risk or risky alcohol use, defined by an excessive average daily or weekly consumption of alcohol (panel 1).[6]

Identifying the problem

To properly care for these critically ill patients, a history of unhealthy alcohol use needs to be identified. Unfortunately, screening for alcohol use is not routinely done. However, the American College of Surgeons Committee on Trauma now mandates routine screening for alcohol abuse for all level one and two trauma centres.[7] There are many screening methods available that assist in identification of individuals with unhealthy alcohol use. One validated screening questionnaire that accurately detects alcohol abuse or dependence is the alcohol use disorders identification test (AUDIT), a ten question survey that includes three about the quantity and frequency of current drinking, and seven related to drinking history.[8] In critically ill patients, there are sex differences in the AUDIT threshold for detection of alcohol use disorders (webpanel 1).[9] Another instrument that can be used is the CAGE (an acronym derived from the important themes of each question—cut down, annoyed, guilty, and eye opener) questionnaire, which focuses on signs of impaired control, use of alcohol despite consequences, and dependence. It is a well respected, validated predictor of lifetime alcohol dependence.[10] However, one limitation of the CAGE questionnaire is its inability to differentiate between current and former alcohol abuse.

Though screening questionnaires accurately identify patients with alcohol abuse and dependence, they have been criticised because they take a long time to do thoroughly.[11] Therefore, shorter questionnaires have been advocated, including the AUDIT-C that uses the first three AUDIT questions.[12] The US National Institute on Alcohol Abuse and Alcoholism has recommended the use of a single screening question that determines the quantity and frequency of heavy drinking days.[13] This one question accurately identifies the presence of current alcohol use disorders or recent hazardous

Search strategy and selection criteria

We searched the Cochrane Library and MEDLINE from 1966 until 2006 for published work relevant to this subject. We entered the search terms "alcohol-related disorders", "alcohol-induced disorders", "alcoholism", "alcohol drinking", "alcoholic intoxication", and the words "alcohol use disorder", "alcohol dependence", "excessive alcohol use", "alcohol abuse", "alcohol ingestion", and "alcoholic". These search terms were then grouped together, identifying over 100 000 articles. We then entered 32 search terms and individually cross-matched them with the alcohol-related articles. We mainly selected publications from the past 10 years, but did not exclude commonly referenced or highly regarded older publications. We also searched the reference lists of these articles and selected additional articles that we judged to be relevant. Pertinent review articles and book chapters were also included.

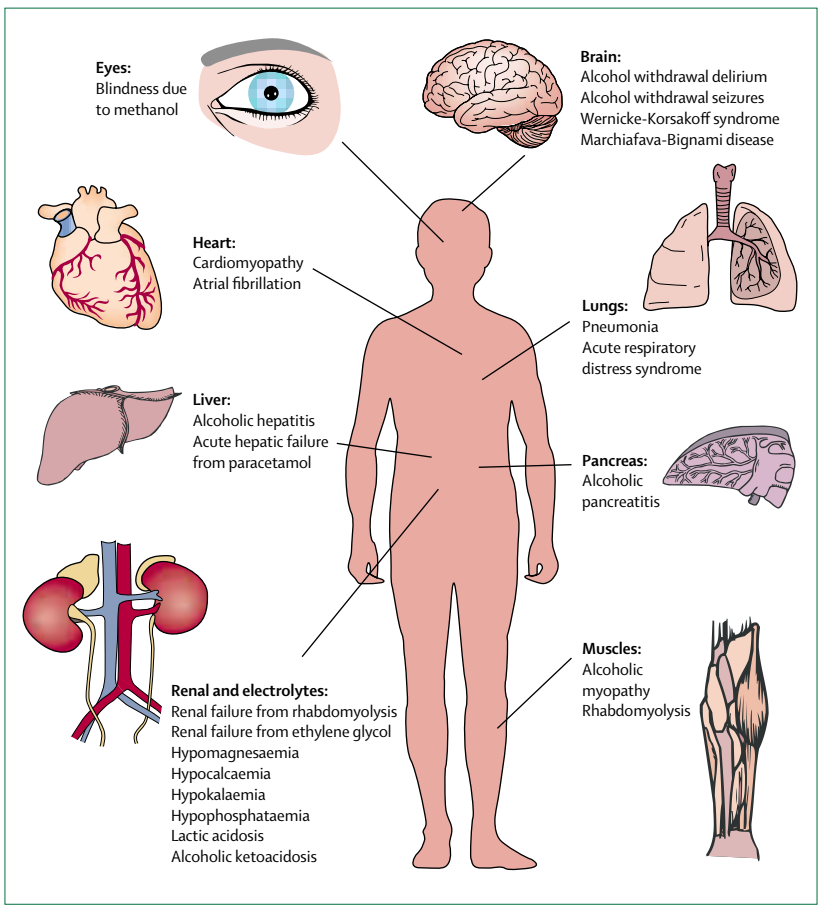

Figure 1: **Disorders that can occur in critically ill patients as a result of alcohol abuse or dependence**

drinking problems in emergency patients, but it has not been validated for ICU patients.[14]

ICU patients cannot always communicate effectively because of the use of endotracheal tubes and sedative agents, so they may be unable to answer even simple questionnaires. In such a situation, other screening tests for alcohol abuse or dependence would be necessary. Some of the screening instruments, including the AUDIT, have been validated when answered by a proxy.[3,15] The greatest degree of agreement occurs when the proxy is in frequent contact with the patient, is a spouse or partner, or is confident about their information.[16] Blood alcohol concentrations might be helpful, since 55–75% of critically ill trauma patients with a positive value will meet criteria for an alcohol use disorder.[17] However, the test would not be helpful in the up to 45% of trauma patients with a risky alcohol history who have a negative value on admission.[17] Conventional blood tests such as liver function tests, or mean corpuscular volume have limited sensitivity and specificity in detection of excessive drinking.[18] Use of results from a γ glutamyltransferase assay, in combination with the CAGE questionnaire improves the detection of alcohol abuse in some patient populations.[19] Other biological markers, including carbohydrate deficient transferrin concentrations, can identify alcohol dependence in trauma patients, especially when measured before aggressive volume resuscitation.[20]

Panel 1: Classifications of unhealthy alcohol use in the USA[6]

- The maximum drinking limit for healthy men aged up to 65 years is no more than four drinks in a day, and no more than 14 drinks in a week. For women and healthy men aged over 65 years, the maximum drinking limit is no more than three drinks a day, and no more than 7 drinks in a week.
- Risky use is consuming more than the recommended amount of alcohol.
- Problem drinking is a classification of unhealthy alcohol use, in which people have alcohol-related consequences but do not meet formal criteria for alcohol abuse or dependence
- Alcohol abuse and dependence are often grouped together and termed alcohol use disorders

Initial management

Early identification of alcohol-related laboratory abnormalities or vitamin deficiencies is important in the management of the critically ill patient. The following laboratory tests should be considered on admission for the critically ill patient with alcohol abuse or dependence: renal and electrolyte profile; liver function tests; amylase, lipase, and creatine phosphokinase tests; complete blood count; coagulation studies; urinalysis; urine toxicology screen; and blood alcohol concentration.

In the western world, alcohol abuse is the most common cause of thiamine deficiency. Thiamine is a water-soluble vitamin (B1) that participates in carbohydrate metabolism.[21] Thiamine deficiency can lead to the development of Wernicke's encephalopathy, an acute neuropsychiatric disorder characterised by ocular motor-disorders, ataxia, and altered mental status,but this classic triad of symptoms occurs in only 10% of patients. Disease onset can be acute or chronic, making diagnosis difficult.[22] Thiamine deficiency can also cause Korsakoff's psychosis, which is characterised by antegrade and retrograde amnesia, disorientation, and confabulation (ie, invented memories). These two disorders are usually combined and termed Wernicke-Korsakoff syndrome because of their close relationship.[23] The prevalence of this syndrome is eight to ten times higher in people with alcohol dependence than in the general population.[24] A metabolic stressor, such as critical illness, in conjunction with a carbohydrate load, typically precedes its development. In view of the difficulties in diagnosing Wernicke-Korsakoff syndrome, thiamine should be given to all patients at risk for or with signs of the syndrome. Thiamine has poor enteral absorption in alcohol-dependent individuals, so should be given parenterally in high risk patients at a dose of 100–250 mg

infused over 30 min, once a day for several days.[22] However, there have been rare case reports of anaphylaxis after parenterally-dosed thiamine.[25] Additionally, patients with any history of unhealthy alcohol use who are treated with intravenous glucose should simultaneously receive intravenous thiamine to prevent precipitating Wernicke-Korsakoff syndrome.[22]

Up to 25% of patients with an alcohol use disorder will have a metabolic acidosis on hospital admission (panel 2).[26] Metabolic acidosis can be caused by non-alcohol-related disorders, such as sepsis or salicylate overdose, but there are types of metabolic acidosis that are specifically related to alcohol ingestion, including alcoholic ketoacidosis, lactic acidosis, and acidosis caused by the ingestion of other toxic substances. Patients with alcoholic ketoacidosis will present with nausea, vomiting, and abdominal pain, and often have a high anion gap acidosis (panel 2).[27] On examination, patients have tachypnoea, tachycardia, and abdominal tenderness without abdominal distension or rebound tenderness. The acidosis is mainly caused by starvation with glycogen depletion, a raised NADH:NAD ratio related to alcohol metabolism by alcohol dehydrogenase, and volume depletion resulting in ketogenesis.[28] Treatment for alcoholic ketoacidosis should include giving of intravenous volume and glucose. Glucose infusion is imperative to prevent ketogenesis, stimulate insulin production and secretion, promote oxidation of NADH, and to replenish glycogen stores.[24] Patients with alcohol abuse or dependence can also develop lactic acidosis, as a direct effect of alcohol, or after seizures.[29] Additionally, 61% of patients with alcoholic ketoacidosis have raised lactate concentrations, usually as a result of concomitant disorders such as pancreatitis, severe hepatitis, or rhabdomyolysis.[27] Thiamine deficiency can also directly cause lactic acidosis because of the impairment of pyruvate dehydrogenase and the accumulation of pyruvate that is subsequently converted to lactate.[30] In these patients, the acidosis can be quickly reversed by administration of parenteral thiamine. Patients with an unexplained anion gap acidosis should be questioned about the ingestion of other toxic alcohols.

Although the diagnostic accuracy of the serum osmolar gap has been questioned, its measurement might be helpful as a screening test for ethylene glycol or methanol consumption (panel 2).[31] Other disorders that can cause an increased osmolar gap in the critically ill patient with alcohol abuse include alcoholic ketoacidosis (resulting from accumulation of acetone) and the continuous infusion of lorazepam (resulting from use of propylene glycol as a solvent in the lorazepam).[32,33] If the osmolar gap is increased or there is a positive history of a toxic ingestion, ethylene glycol and methanol concentrations should be tested. Treatment with fomepizole should be initiated, especially if blood pH is less than 7·3 and serum bicarbonate concentration is less than 20 mmol/L.[34,35] Fomepizole, an inhibitor of alcohol dehydrogenase, alters the toxicokinetics of ethylene glycol and methanol by prolongation of their elimination, and reduction of the formation of the toxic substances glycolate and formate. Patients with methanol ingestion should receive an extended course of fomepizole because methanol has a longer elimination half life than does ethanol. If fomepizole

***Panel 2:* Useful formulas that can assist in caring for the critically ill patient with alcohol abuse or dependence disorder**

Anion gap (mmol/L)=
$Na^+ - (Cl^- + HCO_3^-)$
Range: 8–16 mmol/L
Raised in
- Ketoacidosis
- Uraemic acidosis
- Drug ingestion of
  - Aspirin
  - Methanol
  - Ethylene glycol
- Lactic acidosis

Osmolal gap (mmol/kg)=
Measured serum osmolality–Calculated osmolality
Range: –14 to +10
Where calculated osmolality is
1·86×Na (mmol/L)+glucose (mmol/L)+BUN (mmol/L)
+ethanol (mmol/L)
Raised by
- Methyl alcohol
- Acetone
- Ethylene glycol
- Mannitol
- Other low molecular weight hydrocarbons

Hepatic discriminant function=
4·6×(protime–control protime)×(bilirubin [mmol/L]/17·1)
Value greater than or equal to 32 suggests that patient could benefit from corticosteroid treatment.

Ranson's criteria for acute pancreatitis
Admission
Age >55 years; LDH >350 IU/L
WBC >16 g/L; AST >250 IU/L
Glucose >11 mmol/L
Initial 48 h
Hct fall >10% ; PaO_2 <60 mm Hg
Ca^{++} <2 mmol/L; Base deficit >4 mmol/L
BUN rise >1·8 mmol/L of urea
Fluid sequestration >6L
Negative prognosis
Associated with the presence of one or more criteria. WBC count and serum glucose might be more useful for prediction of major systemic complications and/or mortality in alcoholic pancreatitis.

BUN=blood urea nitrogen. WBC=white blood cell. LDH=lactate dehydrogenase. AST=aspartate aminotransferase. Hct=haematocrit.

is not available, an intravenous infusion of ethanol can be initiated because ethanol will also competitively inhibit alcohol dehydrogenase. In patients with severe ethylene glycol or methanol poisoning, haemodialysis should also be considered.[34,35]

Alcohol abuse is a common cause of hypomagnesaemia, resulting from poor diet and increased urinary and fecal loss.[36,37] Magnesium replacement therapy should be routinely considered in these patients, remembering that serum concentration does not necessarily correlate with total body depletion.[37] Parenteral magnesium should be administered in patients with symptomatic, moderate-to-severe magnesium deficiency (concentrations below 0·75 mmol/L). In cases of seizures or acute arrhythmia, 4–8 mmol should be administered intravenously over 5–10 min, followed by 25 mmol per day, with the goal of keeping the plasma magnesium concentration above 0·4 mmol/L.[38] Lower doses of magnesium replacement therapy should be used in patients with renal failure. Magnesium deficiency can lead to decreased parathyroid hormone secretion, resulting in hypocalcaemia. In patients in whom both these electrolytes are low, calcium replacement is often unnecessary, but magnesium replacement should continue for 3–5 days.[37,38] Additionally, hypomagnesaemia can cause hypokalaemia by increasing kaliuresis.[39] Potassium replacement therapy will not correct the hypokalaemia until magnesium deficits are corrected.[40] Along with these other electrolyte abnormalities, hypophosphataemia resulting from enhanced renal excretion is frequently encountered in patients with alcohol abuse disorders. Hypophosphataemia can be exacerbated during critical illness by concomitant respiratory alkalosis (with stimulation of glycolysis), increased circulating catecholamines that shift phosphate intracellularly, or increased gastrointestinal loss of phosphate from diarrhoea.[41] Phosphate concentrations below 0·32 µmol/L might result in cardiac arrhythmias, respiratory failure, or rhabdomyolysis and therefore should be promptly corrected.[38]

Up to 67% of non-traumatic rhabdomyolysis is recorded in patients with alcoholism, especially after acute intoxication resulting in immobilisation or coma.[42] Direct effects of alcohol on the muscle and co-existing hypophosphataemia and hypokalaemia can be involved in the pathogenesis of rhabdomyolysis. Patients might not have symptomatic muscle pain; however, compartment syndromes can develop in a dependent arm or leg. Although rhabdomyolysis is not defined by creatine phosphokinase concentration, increasing values suggest persistent myocyte damage and impending renal failure. A positive urine dipstick for haemoglobin in combination with no visible red cells on urinalysis is suggestive of rhabdomyolysis.[43] Hyperphosphataemia, hypocalcaemia, and hyperkalaemia can also occur as a direct result of rhabdomyolysis. Dehydration and acidic urine exacerbate the toxic effects of myoglobin on renal tubules. Patients who are thought to be at risk for the development of renal failure should receive intravenous fluids to maintain a urine output of about 200–300 mL/h, with close monitoring of potassium, phosphate, and calcium concentrations.[42] Alkalinisation of the urine should be done with care to avoid hypernatraemia, although there are no randomised trials demonstrating efficacy of urine alkalinisation in prevention of renal failure.[44]

Diagnosis of alcoholic hepatitis should be considered in critically ill patients with jaundice and a history of alcohol abuse. Signs of chronic alcohol abuse (such as spider angiomata) will usually be present in these individuals, and patients may be febrile. Laboratory tests might reveal leucocytosis and high transaminase concentrations, with aspartate transaminase increased out of proportion to alanine transaminase. Extreme elevation of transaminase concentrations (more than ten times normal) is not consistent with alcoholic hepatitis.[45] The patient's hepatic discriminant function can be used to predict a beneficial response to corticosteroid therapy (panel 2).[46] In a meta-analysis, corticosteroids improved 28-day survival in patients with alcoholic hepatitis and a hepatic discriminant function value greater than 32.[47] Steroids should not be used in patients with active gastrointestinal bleeding or in those with sepsis, until appropriate antibiotics have been given for 48 h.[47] Patients with alcoholic hepatitis should also receive appropriate volume replacement to prevent renal dysfunction and nutritional support by nasogastric tube, if required.[45,48]

Patients who abuse alcohol are susceptible to acute hepatic failure, severe liver necrosis, and hepatic coma when taking paracetamol.[49] In those with alcoholism, paracetamol doses as low as 4 g have been reported to cause acute hepatic failure. Therefore, the diagnosis of paracetamol overdose should be considered in all alcoholic patients with abnormal liver function tests. The prompt administration of N-aceyltcysteine is indicated after paracetamol overdose.

About 32% of patients with acute pancreatitis will have a history of alcohol abuse.[50] This diagnosis should be suspected in all patients with abdominal symptoms. A high serum lipase concentration could be helpful to confirm the diagnosis. Up to 30% of patients with acute pancreatitis can develop significant complications that require ICU management.[50] The Ranson's criteria can help predict the development of severe pancreatitis, and a Ranson score of 3 or more on admission can accurately identify patients that will benefit from ICU care (panel 2).[51]

Delirium from alcohol withdrawal

Generalised delirium occurs in more than 80% of critically ill patients who need mechanical ventilation, and is an independent predictor of increased mortality or lengthy hospital stay.[52] Many factors contribute to the onset of delirium in the critically ill, including withdrawal of alcohol. Alcohol withdrawal syndrome is a set of symptoms that develop in alcohol-dependent individuals within 6–24 h after their last drink.[53] The most serious

manifestation of alcohol withdrawal syndrome is alcohol withdrawal delirium, which is also known as delirium tremens. These patients often need ICU care.[54,55] Dependent on the time of their last drink, alcohol withdrawal delirium might be either the main reason for admission to the ICU, or might complicate the clinical course of patients with non-alcohol-related diagnoses.

The symptoms of alcohol withdrawal delirium typically present after 2–4 days of abstinence from alcohol, and can persist for up to 2 weeks.[55–57] The development of this condition is associated with longer stays in hospital and the ICU than for patients with generalised delirium, in addition to increased mortality in postoperative and trauma patients.[58,59] A history of alcohol withdrawal delerium or seizures, previous benzodiazepine use, thermal injuries, and admission for a concurrent acute medical illness are risk factors for the future development of this disorder.[60–63] Both the early signs such as hyperpyrexia, tachycardia, hypertension, and diaphoresis, and the later findings of confusion, agitation, seizures, psychosis, and pronounced autonomic hyperactivity are non-specific in critically ill patients and can be caused by non-alcohol-related problems. Therefore, exclusion of other disorders, including sepsis, cerebral vascular accidents, meningitis, subdural hamatomas, drug toxicity, hepatic encephalopathy, acute haemorrhage, hypoxaemia, hypoglycaemia, and other metabolic abnormalities might be necessary before establishment of a diagnosis of alcohol withdrawal delerium.[64] The pathogenesis of alcohol withdrawal delerium is outlined in figure 2.

In evidence-based guidelines sedative-hypnotic drugs are recommended for alcohol withdrawal delerium.[55] These drugs reduce mortality and decrease the duration of symptoms, with few complications. Benzodiazepines are the most commonly used sedative-hypnotic agents because of their increased safety margin and low abuse potential, compared with barbiturates.[54] However, critically ill patients typically require much higher than normal doses of benzodiazepines to treat alcohol withdrawal symptoms, up to 100-fold in some patients.[67,68] The aetiology of increased tolerance to benzodiazepines in critically ill patients is unclear, but might be related to pronounced neurotransmitter imbalances in the endorphin and noradrenergic systems.[67] Where possible, benzodiazepines should be given with a symptom-triggered dosing regimen rather than with a fixed schedule. Grading of various symptoms of alcohol withdrawal with the revised clinical institute withdrawal assessment for alcohol scale

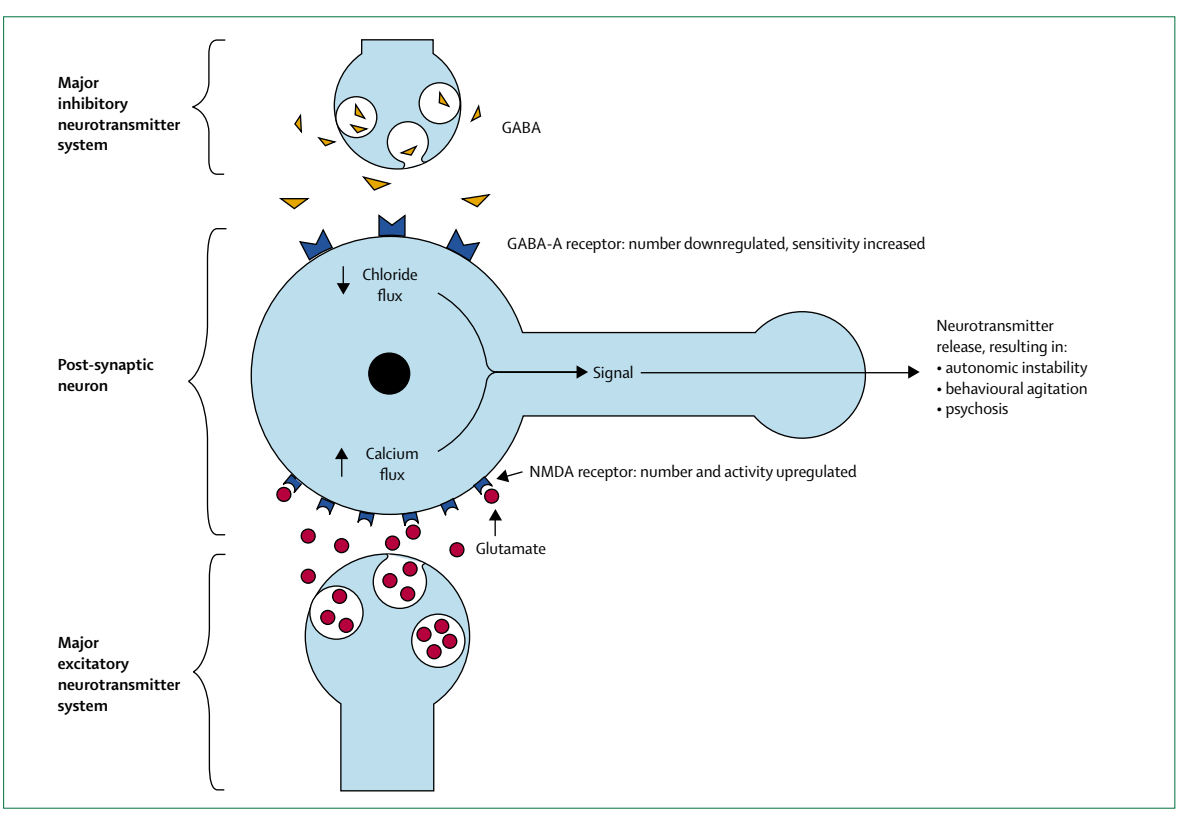

Figure 2: **Pathophysiology of alcohol withdrawal in the central nervous system**
Chronic exposure to alcohol results in increased presynaptic release of glutamate, and downregulation of N-methyl-D-aspartate (NMDA) receptor activity. Additionally, presynaptic γ-aminobutyric acid (GABA) release is also inhibited. As illustrated, the abrupt cessation of alcohol consumption results in up-regulation of NMDA receptor activity, and reduction in GABA-A receptor activity. These changes produce many of the signs and symptoms of alcohol withdrawal delirium, such as autonomic instability, behavioural agitation, and psychosis.[65,66] In patients experiencing this syndrome, the administration of benzodiazepines replaces the effect of alcohol on the GABA-A receptor. Propofol acts in a similar fashion on the GABA-A receptor, but also is an NMDA receptor inhibitor.

See Online for webpanel 2

(CIWA-Ar) (webpanel 2)[55,69] can help titrate the appropriate dosing regimen. Symptom-triggered therapy results in lower incidence of pneumonia, and a shorter duration of ventilatory support and length of ICU stay, compared to a fixed-dose schedule.[69]

In patients whose withdrawal symptoms are not controlled with benzodiazepines, propofol is sometimes recommended, although its benefit has not been validated in randomised trials.[70] Intubation and mechanical ventilation should be initiated before propofol is given, because it has a depressant effect on the respiratory system. Neuroleptic agents should not be used as monotherapy in alcohol withdrawal delerium, although they are commonly and successfully used in combination with sedative-hypnotic therapy in critically ill patients.[54,56,68] Neuroleptics can cause several side-effects, including QT prolongation, reduction in seizure threshold, and development of neuroleptic malignant syndrome.[67] Oral and intravenous ethanol has been used to treat alcohol withdrawal delerium in small, uncontrolled trials.[71,72] The use of ethanol to treat alcohol withdrawal delerium is not recommended because it has an inconsistent pharmacokinetic profile, a narrow therapeutic index, and potential adverse effects.[55] Magnesium has also been reported to reduce the risk of minor withdrawal symptoms, but magnesium therapy specifically for alcohol withdrawal delerium is not recommended.[55,73]

Up to a third of patients who chronically consume alcohol experience seizures during withdrawal. Patients are at enhanced risk for withdrawal seizures if they have had previous withdrawal seizures, which is known as the kindling phenomenon. Such seizures are typically generalised, and occur in the first 8–24 h of abstinence.[56] Up to 60% of patients will have multiple seizures, and the interval between the first and last seizure is usually less than 6 h. Treatment with intravenous benzodiazepines (specifically lorazepam) will greatly reduce the risk of seizure recurrence in these patients.[74] A more thorough neurological evaluation is warranted if focal seizures are present, if the seizures occur later than 48 h after the last alcohol-containing beverage, or if the patient has a history of fever or trauma which relates to the seizure activity.

Pulmonary complications

Individuals with a history of alcohol abuse and dependence are more likely to develop severe or lethal bacterial pneumonia leading to ICU admission and increased total hospital costs.[75–78] Alcohol abuse is sometimes associated with an increased risk of bacteraemia and empyema, extended recovery time, a higher frequency of cavitary disease (18% *vs* 3%), and persistent pulmonary infiltrates on chest radiograph.[75,79,80] Pneumonia in patients with alcoholism is often caused by different pathogens from those that cause pneumonia in non-alcoholic patients, especially anaerobic bacteria and gram-negative organisms such as *Klebsiella pneumoniae*. Possible reasons for the increased occurrence of these organisms could be a higher colonisation rate in the oropharynx, increased frequency of gingivodental disease, or a higher likelihood of aspiration in alcoholics than in non-alcoholics.[81–84] Effects of alcohol on immune function also contribute to the heightened susceptibility to bacterial pneumonia (figure 3).

The acute respiratory distress syndrome is a form of diffuse lung injury, characterised by the sudden onset of severe hypoxaemia in conjunction with bilateral infiltrates that are non-cardiogenic in origin.[99] In two studies in a total of 571 critically ill patients, alcohol abuse was associated with an increased risk of developing acute respiratory distress syndrome.[100,101] In patients with septic shock, alcohol abuse increased the incidence of acute respiratory distress syndrome from 31% to 70%.[101] Similar effects of chronic alcohol abuse on the development of the syndrome have also been recorded after pulmonary resection in patients with non-small-cell lung carcinoma.[102] The mechanisms responsible for this increased susceptibility to develop acute respiratory distress syndrome are outlined in figure 4.

Cardiac and haematological dysfunction

Cardiomyopathy in patients with alcohol abuse is characterised by a dilated left ventricle, and often a subclinical reduction in ejection fraction.[111] Systolic and diastolic dysfunction have been reported in association with alcohol abuse that seems to be dose dependent, but this dysfunction is frequently asymptomatic.[112] Thiamine deficiency can cause a high output cardiac failure (wet beriberi), which has been attributed to vasodilatation and decreased vascular resistance—probably from vasomotor depression and augmented venous return.[113] Common findings that precipitate biventricular failure in the critically ill include increases in sympathetic tone (especially in withdrawal), hypokalaemia, and hypoxia.[114] Cardiac arrhythmias after acute alcohol consumption are also well documented.[115] Acute binge drinking is associated with an increased risk of various arrhythmias, including atrial fibrillation, known as the holiday heart syndrome, in which arrhythmias occur after excessive drinking during weekends or holidays.[116,117] Chronic alcohol abuse is associated with a 34% increased risk of developing atrial fibrillation.[118] These alcohol-related alterations in cardiac function contribute to an increased rate of complications in critically ill patients.[119]

Alcohol can alter haemostasis by increasing bleeding times and inhibiting production of platelets by bone marrow.[120] These changes might cause an increased risk of bleeding, especially in postoperative or traumatically injured critically ill patients.[121] In alcoholic patients, especially those with liver disease, folate deficiency is a common hypovitaminosis, leading to megaloblastic anaemia and impaired enterocyte function. Folate deficiency in these patients is caused by decreased intake, abnormal absorption, metabolism, hepatic storage, and urinary excretion of nutrients. Insufficient folate can also result in problems with postoperative infections and

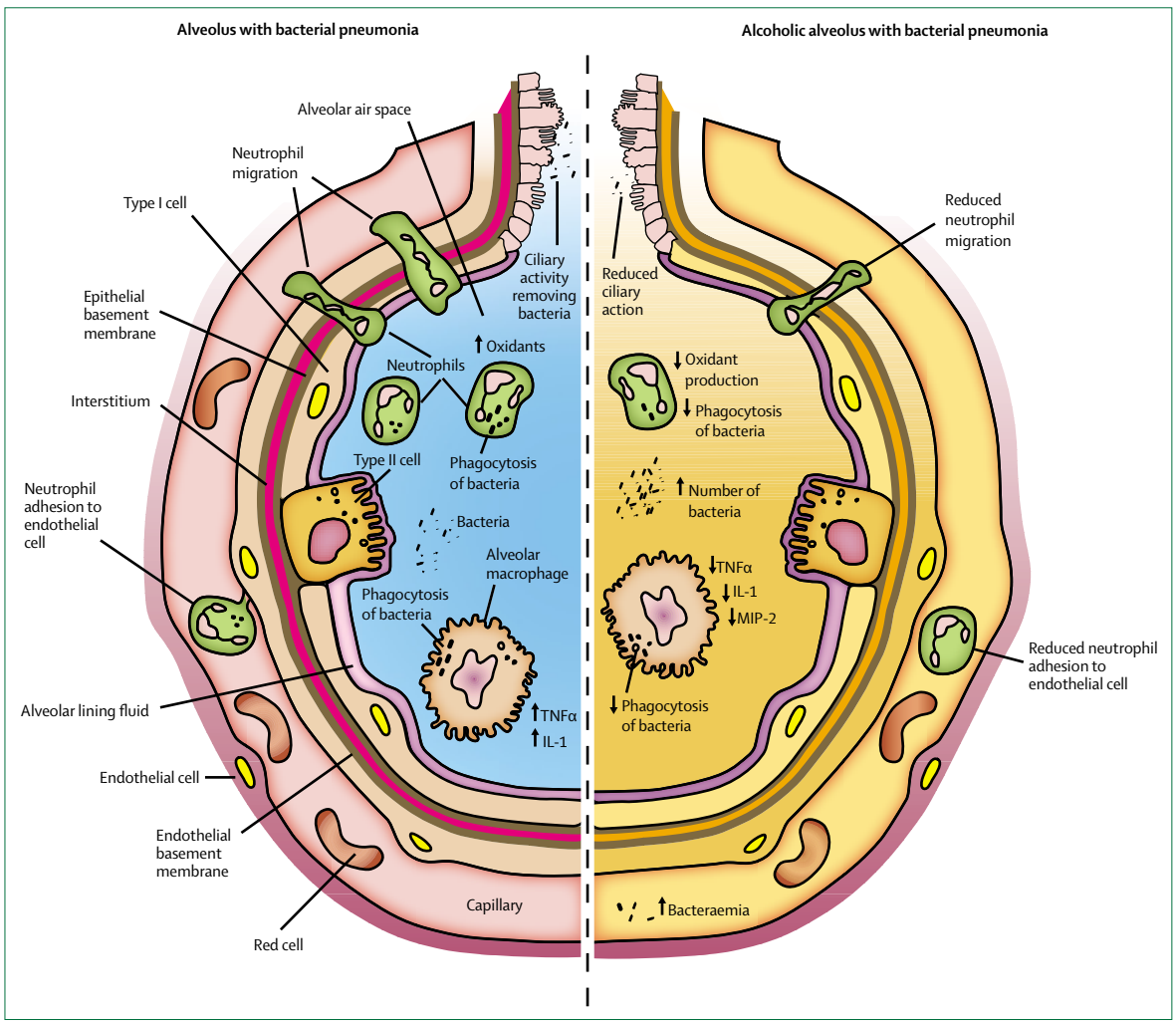

***Figure 3*: Differences in response to bacterial pneumonia in non-alcoholic patients compared with patients with chronic alcohol abuse disorders**
↑=increase, ↓=decrease. Ethanol exposure diminishes chemotaxis of neutrophils to sites of infection by inhibiting upregulation of adhesion molecules, such as CD18, that help bind target receptors, including ICAM-1 on endothelial cells.[85-87] The expression of neutrophil chemotactic cytokines including macrophage inflammatory protein-2 (MIP-2) are also decreased by ethanol.[88] Alcohol exposure suppresses production of pro-inflammatory cytokines, including tumour-necrosis-factor-α (TNFα) and interleukin-1β (IL-1 β) in alveolar macrophages and blood monocytes.[89-92] Alcohol alters cytokine production in macrophages by inhibiting the activation of intracellular messenger nuclear factor-κβ (NFκβ), which is required for the transcription of genes that encode TNFα and other chemokines.[93,94] Lengthened exposure to alcohol results in decreased neutrophil superoxide production, and a potential pro-inflammatory effect with increased plasma concentrations of cytokines IL-6, IL-10, and the endothelial cell adhesion molecule E-selectin.[95,96] Suppression of the serum IL-6:IL-10 ratio is more common in postoperative patients who are alcohol dependent and is associated with an increased rate of infectious complications.[97] Furthermore, T helper cell mediated immunity as measured by suppression of T helper 1:T helper 2 ratio (Th1:Th2) is altered in individuals who are alcohol dependent.[98]

wound healing.[122] Folate replacement therapy should be given as a dietary supplement at a dose of 1 mg per day for several days.[123]

Alcohol and the surgical patient

An increased risk of postoperative complications related to alcohol abuse has been reported after all types of surgery.[119] Nosocomial infections accounted for most of these postoperative complications. Respiratory failure, haemorrhage requiring transfusion and secondary operations, and delayed wound healing have also been reported.[124] Postoperative patients with alcoholism also have high rates of ICU re-admission, need many repeat surgical procedures, and have longer hospital stay than patients without alcoholism.[125] Up to 57% of patients with carcinomas of the upper digestive tract have a history of alcohol abuse or dependence.[59] Postoperatively, the patients with a history of alcohol abuse spent substantially more time on mechanical ventilation, and have an increased risk of haemorrhage necessitating repeat surgery than non-alcoholic patients. Additionally, both anastomotic leakage and post-operative sepsis were only recorded in alcohol-dependent patients. The mortality rate was much higher (9% *vs* 0%) in the patients with a history of alcohol abuse, which is probably a result of this increased rate of post-operative complications.[59]

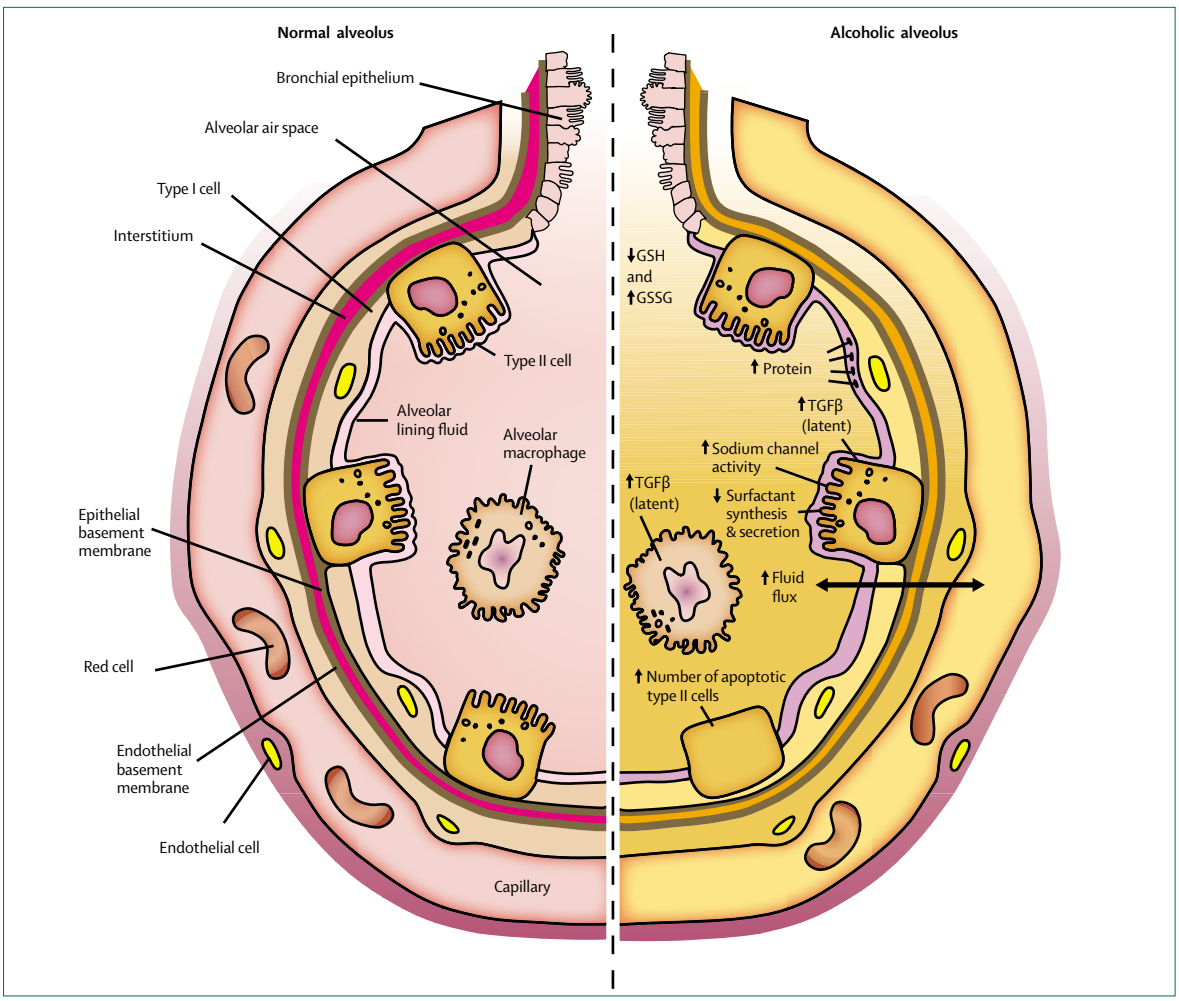

Figure 4: **Basal changes in the alveolus as a result of chronic alcohol abuse**
↑=increase, ↓=decrease. GSH=glutathione. GSSG= oxidised glutathione. Alcohol-induced changes in the lung result in an increased susceptibility to the development of acute respiratory distress syndrome. One of the central changes related to chronic ethanol ingestion is a decreased concentration of the antioxidant glutathione throughout the alveolar lining fluid of the lung and within alveolar type II cells.[103] Deficiencies in pulmonary glutathione result in abnormal surfactant synthesis and secretion, increases in type II cell apoptosis, rises in basal expression of transforming growth factor β (TGFβ), and changes in alveolar-capillary barrier function and permeability.[104-107] In patients with acute respiratory distress syndrome, alcohol abuse magnifies the increase in alveolar capillary permeability and the subsequent accumulation of extravascular lung water and protein in the alveolar lining fluid, and raises concentrations of E-selectin in the lung.[108-110]

Several studies have examined the effects of alcohol abuse and dependence on postoperative complications in patients who had surgery for lung cancer.[102,126,127] Similar to the findings in patients with upper gastrointestinal tumours, lung cancer patients with alcoholism had increased rates of major infectious complications and respiratory failure, defined as mechanical ventilatory support for greater than 48 h.[127] Patients with alcohol dependence also had extended hospital stays (26·1 days *vs* 10·6 days) and more expensive hospitalisations than did non-alcoholics. Similar effects of alcohol use on postoperative complications have been recorded in neurosurgical patients needing subdural haematoma evacuation and urological patients after transurethral prostatectomy.[128,129]

Abstinence from alcohol can result in reversal of subclinical cardiac dysfunction, improvement in haemostasis and wound healing, correction of immunosuppression, and return to normal of the cortisol response to surgical stress.[119] Patients with alcoholism who were scheduled for elective colorectal surgery were randomised to either the regularly scheduled surgery or a month of abstinence and disulfiram treatment, followed by surgery. Patients assigned to abstinence and delayed surgery had strikingly fewer postoperative complications (31% *vs* 74%), less postoperative myocardial ischaemia (23% *vs* 85%), and fewer arrhythmias (33% *vs* 86%) than did those assigned surgery alone.[130] The optimum length of preoperative abstinence remains unknown; however, surgery should be postponed (if possible) until measures of organ

dysfunction have normalised, or at least until the signs and symptoms of withdrawal have subsided.[56,124]

Alcohol and trauma

Trauma patients with alcohol exposure, defined as a measurable blood alcohol, are more likely to be men, less than 40 years of age, screen positive for illicit drugs, lack health insurance, and have sustained their injury during violence.[131] A history of alcohol abuse in trauma patients is associated with an increased rate of haemorrhage requiring transfusion, pancreatitis, and extended mechanical ventilation and ICU stay.[132–135] Alhough there is conflicting evidence in the trauma population, a history of alcohol abuse seems to be associated with an increased rate of infectious complications, especially bacterial pneumonia. Further, a positive blood alcohol level on admission for a trauma-related injury is a risk factor for subsequent trauma-related hospitalisations.[131,136] Although alcohol abuse is not associated with an increased mortality rate in general trauma patients, alcohol-related changes in mortality rate have been seen in patients with thermal injuries. After adjustment for age, total burn surface-area, and inhalational injury, burn victims with a positive blood alcohol concentration on admission had mortality rates six times that of non-alcoholic patients.[137]

Proper identification of alcohol abuse or dependence with subsequent brief interventions can help patients stop drinking and prevent future medical and social problems. Brief interventions usually consist of 10–15 minutes of counselling and feedback about drinking, responsibility, advice, empathy, and goal setting.[6] In the trauma population, brief interventions led to decreased alcohol consumption, decreased readmissions to the emergency department, and a sizable reduction in injuries needing hospital admission.[138] For example, the initiation of brief interventions during an emergency department visit for adolescents with drinking-related injuries reduced the 6 month frequency of future alcohol-related injuries from 50% to 21%.[139] In a randomised trial of trauma patients with a history of alcohol abuse, brief interventions with a follow-up visit after 7–10 days significantly reduced alcohol-related injuries at one year when compared with no intervention.[140]

Long-term complications of critical illness

Hospitalisations that require intensive care can diminish the patient's quality of life for months, or even years, after discharge. In view of the prevalence of alcohol abuse in ICU patients, the existence of specific alcohol-related issues in ICU survivors is possible. Alcohol abuse has deleterious effects on skeletal muscle and can cause myopathy.[111] Muscle wasting and weakness due to critical illness, in addition to chronic myopathy related to alcohol consumption, could synergistically affect quality of life and the ability to undertake activities of daily living.[141] A manifestation of thiamine deficiency with Korsakoff's psychosis or Marchiafava-Bignami disease, acute demyelination, and necrosis of the corpus callosum can cause long-term confusion after ICU discharge.[142] Such problems are a continued challenge to the physician providing critical care and subsequent management for patients with alcohol abuse and dependence. Hopefully, greater appreciation and recognition of the effects of alcohol abuse and dependence in the critically ill will result in improvements in both short and long-term outcomes for these patients.

Conflict of interest statement

We declare that we have no conflict of interest.

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