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Alcoholic liver disease

Assessment and management

Background

Alcohol is a major cause of liver disease in Australia and the incidence of end stage liver disease among young adult Australians is rising.

Objective

This article explores the types of alcoholic liver disease, their pathogenesis and detection, and the investigation and management of these conditions.

Discussion

Alcoholic liver disease is often silent until complications develop; therefore clinicians need a high index of suspicion to detect individuals with heavy alcohol consumption and evolving liver disease. At a population level, strategies to reduce per capita alcohol consumption can be expected to reduce mortality from alcohol related disease. At an individual level, early diagnosis, abstinence and effective treatment of complications are pivotal to reducing mortality. The cornerstone of management of chronic alcoholic liver disease is abstinence from alcohol and good nutrition. Other important aspects of management include care when prescribing medications, immunisations and early referral for complications.

Keywords: liver diseases; alcohol related disorders



The fermentation of grapes, grain and similar carbohydrates to form alcohol was recognised in biblical times; the association of these with liver disease was known in Classical Greece. Today, alcohol is a major cause of liver disease worldwide. In Australia, between 1992 and 2001, an estimated 31 132 people died from alcohol caused disease and injury, with 6825 dying from alcoholic liver cirrhosis.¹ The rising incidence of end stage liver disease among young adult Australians is of particular concern.²

Liver disease due to alcohol is common and presents in a number of guises including fatty liver, alcoholic hepatitis and cirrhosis. It is difficult to estimate the incidence of each, as in many cases the disease may go undiagnosed (particularly fatty liver).

Mortality from alcohol is proportional to per capita alcohol consumption. At a population level, strategies to reduce per capita alcohol consumption can be expected to reduce mortality from alcohol related disease. At the individual level, early diagnosis, abstinence and effective treatment of complications are pivotal to reducing morbidity and mortality.³

Types of alcoholic liver disease

Fatty liver due to alcohol

Fatty liver due to alcohol is usually asymptomatic but may be associated with mild nonspecific symptoms such as nausea. Its major feature is liver enlargement due to the accumulation of fat globules within hepatocytes, which can occur after a single occasion, or 'binge', of alcohol excess and usually regress with abstinence. Other causes of fatty liver include obesity, viral hepatitis and medications. It is therefore a diagnosis of exclusion.

Alcoholic hepatitis

Alcoholic hepatitis is characterised by acute inflammatory changes in the liver and symptoms varying from mild abdominal pain and fever to deep jaundice and coma. It is usually a consequence of binge drinking. Acute changes may reverse if alcohol is avoided. If heavy alcohol consumption continues it leads to cirrhosis. It is more commonly seen in those with concomitant advanced liver disease.



Alcoholic cirrhosis

Alcoholic cirrhosis is characterised by replacement of hepatocytes by fibrosis and the progressive destruction of the normal architecture and loss of liver function. It is generally the consequence of years of consistently heavy drinking and most often occurs in middle aged men.² Cirrhosis is often silent until it presents with complications such as jaundice, bleeding from varices, ascites, infection or neuropsychiatric changes.

Pathogenesis

The manifestations of alcoholic liver disease are best understood by a consideration of the metabolism of alcohol. Alcohol is readily absorbed by the stomach, and in the liver is converted to acetaldehyde by alcohol dehydrogenase (ADH) by the removal of two hydrogens, which enter a cascade. Acetaldehyde is converted ultimately to acetate and metabolised as a potent source of calories. Acetaldehyde is a cell poison and causes inflammatory changes in the liver. In addition, the hydrogen from ADH and acetaldehyde dehydrogenase promotes the production of fatty acids and thus the triglycerides of fatty liver and the elevated serum lipoprotein. Also, the excess lactate in the liver impairs urate excretion and promotes the production of gout.

The rate of alcohol elimination in humans varies significantly between individuals and between races. Alcohol dehydrogenase is encoded in at least four sites with multiple polymorphisms creating differing rates of alcohol metabolism. Acetaldehyde dehydrogenase also has multiple gene loci of varying potency. An example of this is that 50% of Japanese and Chinese people have deficient acetaldehyde metabolism, underlying their impaired alcohol tolerance and flushing after alcohol. There are probably other genetic variations underlying the body's response to alcohol. This may help to explain why only 10–15% of alcoholics have cirrhosis at autopsy.⁴ The average dose producing cirrhosis in males is estimated at 180 g (18 standard drinks) daily for 25 years.⁴ Females are less tolerant of alcohol; whether this is related to lower body mass is unclear.

Detection

With the exception of acute alcoholic hepatitis, alcoholic liver disease is often silent until complications develop. Importantly, stress such as acute infection or surgery, can unmask a previously unrecognised alcoholic. Clinicians need a high index of suspicion to detect individuals with heavy alcohol consumption and evolving liver disease, as presentations with indirect clues may occur during the years before more classic presentations appear. These may include:

- social disruption, including domestic violence, multiple hospital admissions for minor injuries, motor vehicle accidents and impaired work performance
- impotence in males
- a family history of alcohol abuse
- nonspecific symptoms such as morning nausea, brief morning diarrhoea, vague upper abdominal pain.

The CAGE questionnaire can be a useful tool to detect the heavy drinking that may underlie the development of alcoholic liver disease (Table 1).

Table 1. CAGE questionnaire¹²

C	Have you felt the need to C ut down?
A	Have you felt A nnoyed at the suggestion that you might have an alcohol problem?
G	Have you felt G uilty about excessive drinking?
E	Do you need an E ye opener in the morning?
Score 1 for each positive response; scores of 2 or more suggest an alcohol problem	

Detection of heavy drinking is discussed in more detail in the article, 'Problem drinking: Detection and assessment in general practice' by Demirkol, Haber and Conigrave in this issue of *Australian Family Physician*.

Levels of alcohol intake

Recording of alcohol intake is standardised at units of 10 g per day, roughly the content of a standard drink from a glass of beer to a wine glass or a nip of spirits. Based on epidemiological data and modelling of lifetime risks from alcohol consumption the most recent National Health and Medical Research Council guidelines recommend: 'For healthy men and women, drinking no more than two standard drinks on any day reduces your risk of harm from alcohol-related disease or injury over a lifetime'.⁵ Cirrhosis will occur earlier in the presence of cofactors for cirrhosis such as viral hepatitis, obesity or iron overload. Paradoxically, there is evidence that the mortality curve relating to alcohol intake is a J curve. In males, mortality is lowest at an intake of two units per day after which it rises steeply.⁶

Examination

Alcohol excess can present as hypertension,⁷ this may be the only clue on examination (other than the smell of stale alcohol) that the patient is drinking at excessive levels. An enlarged and possibly tender liver may be another early sign of alcoholic liver disease.

Late signs of alcoholic liver disease include:⁸

- peripheral stigmata of chronic liver disease, including bruising, leukonychia (from hypoalbuminaemia), clubbing, palmar erythema, bruising, spider naevi gynaecomastia and testicular atrophy
- signs specific to chronic alcoholism, including Dupuytren contracture, parotidomegaly and proximal myopathy
- liver enlargement (unless cirrhosis is advanced)
- signs of portal hypertension, including splenomegaly collateral veins and ascites
- signs of cardiomyopathy
- the effects of exocrine pancreatic failure from alcohol induced chronic pancreatitis which result in pale, fatty motions which are difficult to flush away.

Investigations to aid detection of disease

No single marker has 100% sensitivity or specificity for alcoholic liver disease. If there is clinical suspicion that the patient is drinking at



levels that may result in chronic liver disease, a raised gamma-GT on liver function testing and macrocytosis in an otherwise unremarkable full blood examination can support this suspicion. Also, the finding of multiple healed fractures of ribs or clavicle on chest X-ray is highly suggestive of alcoholism.

Upper abdominal ultrasound is an important investigation and may obviate the need for liver biopsy. It can demonstrate fat in the liver, the increased echogenicity of liver cirrhosis, splenomegaly and varices when portal hypertension develops, and the less common complication of hepatocellular carcinoma. Calcification of the pancreas can occur in alcohol induced chronic pancreatitis.

Important investigation findings in alcoholic hepatitis include:

- leucocytosis: the magnitude of the white blood cell elevation correlates closely with the severity of the hepatic injury if other causes are excluded
- raised transaminase levels with an aspartate transaminase (AST) higher than the alanine aminotransferase (ALT) in a ratio of 2:1, but with neither above 300 IU/dL
- elevated bilirubin, hypoalbuminaemia and prolonged prothrombin levels (important indicators of severity).

Importantly, iron studies and hepatitis B and C will identify concurrent causes of liver disease such as haemochromatosis and viral hepatitis.

Investigations for monitoring

A serum ethanol level will confirm recent alcohol consumption and may be a useful guide to treatment effectiveness. In a decompensated cirrhotic, a spot urinary sodium is a useful guide to the effectiveness of diuretic therapy (a low level indicating inadequate blockade of sodium reabsorption). Further ongoing monitoring investigations in patients with alcoholic liver disease should be guided by the patient's liver specialist.

Management

The cornerstone of management of chronic alcoholic liver disease is abstinence from alcohol and good nutrition. Other important aspects of management include care when prescribing medications, immunisations, and early referral for complications.

Abstinence

If abstinence from alcohol can be achieved, the outlook, except in the presence of advanced cirrhosis, can be surprisingly good. Even in the presence of advanced disease, patients who become abstinent do better than those who continue to drink, with 5 year survival rates of over 50%.⁹ It is particularly important to counsel hepatitis C positive individuals about avoiding alcohol because of its synergistic effect. Fatty liver due to alcohol and all but severe cases of alcoholic hepatitis will resolve with abstinence. Referral to a local drug and alcohol service for treatment (inpatient or outpatient) and/or medications may be needed to help achieve abstinence. This is covered in more detail in the article, 'Problem drinking: Management in general practice' by Demirkol, Conigrave and Haber in this issue of *Australian Family Physician*.

Nutrition

Malnutrition is frequent among individuals with advanced liver disease due to a combination of poor intake and increased requirements. Management should focus on correcting any vitamin deficiencies and ensuring that patients consume a high energy, high protein diet of 1.0–1.5 g of protein per kg of lean body weight, either by adjusting the content and frequency of meals and/or by the addition of high energy supplements. A snack before bed helps prevent the breakdown of muscle stores overnight. Patients who continue to drink should also receive thiamine supplementation to prevent Wernicke-Korsakoff syndrome. Once ascites has developed, patients need to avoid salt, including foods with a high salt content and its addition to meals.

Prescribing issues

An important prescribing issue is the extent of impaired liver function. In particular, people with cirrhosis are sensitive to sedatives and anticoagulants are contraindicated in those with decompensation. For the unrecognised cirrhotic, surgery and its postoperative course is dangerous. Many other medications can be hepatotoxic. It is important to educate the patient to check with their doctor before starting any new medications.

Immunisations

Immunocompromised and hyposplenic patients have an increased risk of severe sepsis, and in these groups vaccination should be considered against encapsulated organisms including pneumococcal, meningococcal and against influenza. Immunisation against hepatitis A and B is also recommended, particularly for at risk groups (see *Resource*).

Early referral for management of complications

Complications best treated by early referral to specialist care (usually via a hospital emergency department) include variceal haemorrhage, ascites, neuropsychiatric complications and unexplained deterioration. Unexplained deterioration may indicate the development of complications such as spontaneous bacterial peritonitis (SBP) or hepatocellular carcinoma. Patients with alcoholic hepatitis may require hospital admission if they are too unwell to be managed in the community. Ongoing specialist care of alcoholic cirrhotic liver disease involves variceal surveillance as well as monitoring for, and management of, other complications such as decompensation and hepatocellular carcinoma.

Prognosis

Prognosis depends on the extent of liver damage at diagnosis, the ongoing intake of alcohol and the general nutritional state of the patient. A Danish population based study of almost 500 patients with alcoholic cirrhosis found a risk of complications of about 25% after 1 year and 50% after 5 years.¹⁰ Once signs of clinical decompensation



develop, patients with alcoholic cirrhosis who stop drinking have a 5 year survival of about 60% versus 30% for those who do not. The role of liver transplant for advanced disease is achieving prominence. The European Liver Transplant Report found a 10 year survival of 59% in nearly 7000 transplants for alcoholic cirrhosis.¹¹

While patients with alcoholic liver cirrhosis are at increased risk of hepatocellular carcinoma, patients who are actively drinking are more likely to die from noncancer related complications of alcoholic liver disease (eg. liver failure). Indeed, patients with alcoholic cirrhosis who die of hepatocellular carcinoma (HCC) are about 10 years older than patients who die of noncancer causes.

Finally, as noted, alcohol adds to the risk of developing HCC in patients with chronic hepatitis C or B infections.

Conclusion

Excessive alcohol use and alcoholic liver disease can present to general practice in a multitude of ways, from hypertension to abdominal symptoms to psychosocial upheaval. Detection depends on a high level of suspicion and focused investigations. Early diagnosis, abstinence and effective treatment of complications are pivotal to reducing mortality.

Resource

For a list of at risk groups for hepatitis A and B visit: www.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook-home.

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