Review Article

Alcoholic liver diseases and their therapy

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ABSTRACT

Alcohol related toxicity is the third most common cause of morbidity and the fifth most common cause of disease burden worldwide. Alcoholic liver diseases (ALD) are the leading cause of mortality in people aged 15–49 years. Fatty liver develops in about 90% of individuals who drink more than 60 g/day of alcohol. Many heavy drinkers will progress from fatty liver to alcoholic hepatitis and finally to alcoholic cirrhosis over time. The cornerstone of therapy of alcoholic hepatitis is abstinence. However, other therapies like naltrexone and baclofen found to improve abstinence and decrease relapse. An assured therapy of liver transplantation playing a vital role during end stage liver failure. It is the time now to make awareness regarding ALD among the public.

Keywords: ALD, Hepatitis, Naltrexone, Abstinence

Introduction

Liver is a vital organ that performs many essential functions. It filters out harmful substances from your blood, makes bile to digest food, stores energy and nutrients, and manufactures hormones, proteins, and enzymes your body uses to function and ward off disease. Alcoholic liver diseases (ALD) is the leading cause of mortality in people aged 15–49 years, and the total expenditure amounts to billions of dollars.1 Alcoholic liver disease is a term that encompasses the liver manifestation of alcohol overconsumption including fatty liver, alcoholic hepatitis and chronic hepatitis with liver fibrosis or cirrhosis. The National Institute on Alcohol Abuse (NIAA) recommends that both males and females must not drink more than 28 g and 14 g per day, respectively.2

Burden of alcohol-related disease and injury

In 2010, liver cirrhosis, as a result of ALD, was responsible for 493,300 deaths (156,900 female and 336,400 male deaths) worldwide.3 Alcohol consumption is responsible for 3.8% of global mortality and 4.6% of disability-adjusted life-years (DALYs) lost due to premature death.4 Approximately two-thirds of adult Americans drink some alcohol.5 Development of negative social and health consequences of drinking (e.g., unemployment, loss of family, organ damage, accidental injury, or death). More recent data suggest 4.65% meet criteria for alcohol abuse and 3.81% for alcohol dependence in America.6 Young people also account for a disproportionate amount of ALD disease burden, with over 10% and 25% of alcohol-related deaths in female and male youths respectively.
Types of alcohol related liver diseases

ALD is due to excess enough of intake of alcohol. For most of the people moderate consumption of alcohol will not lead to ALD.

Fatty liver

It is otherwise called as steatosis. The disease is characterized by excessive accumulation of fat inside liver cells (Figure 1), which makes it harder for the liver to function. Initially no symptoms followed by enlargement of liver and upper abdominal discomfort. This can be prevented if the patient stops the intake of alcohol.

Figure 1: Fatty liver.

Alcoholic cirrhosis

This type liver disorder is serious form of the liver damage (Figure 2). In this case the normal liver tissue is replaced with nonliving scar tissue. Usually 10-20% of the drunker develop cirrhosis after 10 or more years of drinking. The symptoms include accumulation of fluid in abdomen, high blood pressure in the liver, bleeding from vain of esophagus and enlargement of spleen. Fibrosis is the first stage of liver scarring. When scar tissue builds up and takes over most of the liver, it’s referred to as cirrhosis. Many heavy drinkers will progress from fatty liver to alcoholic hepatitis and finally to alcoholic cirrhosis over time.

Figure 2: Alcoholic cirrhosis.

Alcoholic hepatitis

The disease is characterized by inflammation (Figure 3) and swelling of liver along with destruction of hepatocytes. The heavy drinkers in maximum case are developing alcoholic hepatitis. The symptoms include abdominal pain, fever, jaundice, nausea, vomiting. Alcoholic hepatitis can be last for years and the life threatening complains may occur to the patient. Liver damage can be reversible due to stop intake of alcohol.

Figure 3: Alcoholic hepatitis.

Pathogenesis of alcoholic liver diseases

Ethanol metabolism

Alcohol is metabolized to acetaldehyde by both alcohol dehydrogenase (at low alcohol
concentrations) and CYP2E1 (at higher concentrations, >10 mM), which is further metabolized by aldehyde dehydrogenase to acetate. Acetaldehyde forms protein adducts which causes hepatocyte injury directly or by autoimmune reaction.7

**Oxidative stress**

Decrease in anti-oxidant level (selenium, glutathione,) leads to oxidation of protein, lipid and DNA which produces cell injury by DNA damage, lipid peroxidation and tumour necrosis factor (TNF) production. Apart from excess production of pro-oxidants like NAD phosphate oxidase and inducible nitric oxide synthase from Kupffer cell leading to nitric oxide damage.2

**Factors increase the alcoholic-related liver diseases**

- Obesity
- Malnutrition
- Genetic factors
- Chronic viral hepatitis, particularly hepatitis-C

**Complication of alcohol related liver diseases**

Serious and sometimes life threaten complications from ALD are due to many years of heavy drinking. The complications are-

- Kidney failure
- Liver cancer
- Confusion and coma (due to hepatic encephalopathy)

**Diagnosis of ALD**

- Blood tests to check liver function and rule out other causes of liver disease
- Imaging tests like an ultrasound, CT (compute tomography) or MRI (magnetic resonance Imaging) of the liver
- A liver biopsy may be considered if the diagnosis is uncertain

**Treatment for ALD**

Among the different medications available to treat alcohol dependence, disulfirum is the oldest one, but it has poor tolerability because of sever vomiting sensation. Abstinence is the most important therapeutic intervention for patients with ALD.8 For short-term treatment (inject able extended release form) with opioid antagonists such as naltrexone is useful in lowering the risk of relapse. The GABAB (Gama amino butyric acid-B) receptor agonist, baclofen, is shown to improve abstinence and decrease relapse. It is found to be relatively safety and effective in ALD patient. Recent research is progressed on N-methyl-D-aspartate (NMDA) receptor blockers as a new pharmacological treatment.9

**Liver transplantation**

Liver transplantation or hepatic transplantation is the replacement of disease liver with another healthy liver. It is the treatment option for the patient during end stage liver failure. The most common technique is orthotopic transplantation, in which the native liver is removed and replaced by the donor organ in the same anatomic position as the original liver. The average cost of liver transplantation is around Rs 18 Lakhs. The cost of investigations of the donor and recipient is Rs 2 Lakhs. When patients are too sick and require prolonged stay following liver transplantation, the cost of treatment can escalate; hence it is advisable to patients to have the liver transplantation before they develop complications secondary to the liver disease (cirrhosis).

**Conclusions**

ALD is the most common liver diseases in the western world. Pathological process includes mild fatty infiltration to advance cirrhosis. The better treatment of ALD is the combination of abstinence from alcohol and supportive care include adequate nutrition and awareness. Some cases glucocorticoids can be used to control severe alcoholic hepatitis. In case of end stage...
liver failure the liver transplantation process is the only remedies to over com.

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