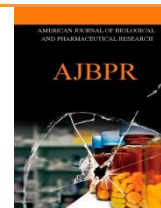




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## ALCOHOL POISONING- AN OVERVIEW

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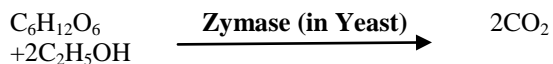
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Article Info	ABSTRACT
<p>Received 29/12/2014 Revised 02/01/2015 Accepted 07/01/2015</p> <p><b>Key words:</b> -Acute, Chronic, Ethanol, Liver and Therapy.</p>	<p>Acute and Chronic alcohol consumption is known to result in hepatic injury, particularly in the general population, and is considered a major risk factor for multi-organ system failure and death. The objective of this paper is to present an overview of the ethanol poisoning, etiology, mechanisms, toxicokinetics, clinical features, diagnosis and current drug therapy. The information has been obtained by searching relevant literature using Chemical abstract, Pubmed, Delnet, Science direct, Dove press, Pharmaintelligence, Medline and other data bases. With the completion of revision of all the data's. We are able to suggest that the controlling of ethanol poisoning in developing countries is still, uncontrolled in the community. So, there is an urgency to develop awareness amongst the individual (ie) to be free from ethanol abuse and also develop a new drug regimen for the proper management of ethanol toxicity.</p>

### INTRODUCTION

Ethyl alcohol is a monohydric alcohols, It is also known as grain alcohols, it is a clear, colorless liquid with a faint fruity odour, sweetish burning taste. [1]. Pharmacology of alcohol is important for its presence in beverages and for alcohol intoxication, rather than as a drug. At low doses, alcohol causes loss of emotional restraint, vivaciousness, feeling of warmth, flushing of skin and mild impairment of judgment. As blood alcohol levels increase, speech becomes slurred and the intoxicated person begins losing motor control. At higher levels, memory is affected and the person becomes stuporous and unable to be aroused. Coma and death can, rarely, ensue

Alcohol is manufactured by fermentation of sugars:



Fermentation proceeds till alcohol content reaches -15%. Then the reaction is inhibited by alcohol itself. Starchy cereals e.g. barley, when soaked produce malt:



This can then be fermented by yeast to produce alcohol. The major source of commercial alcohol is molasses, a byproduct of sugar industry.

Misuse of alcohol is recognized by the national drug strategic framework as one of the most significant causes of drug-related problem in India. This report examines the extent of alcohol -related harm within India and provides information on strategies for reducing that harm. It focuses on the concepts of harm minimization and shared responsibility, which have been hallmarks of Indian government alcohol policy since the national campaign against drug abuse in 1947. Research has shown that there is a high co-morbidity between alcohol misuse and the misuse of other drugs, with a consistent pattern in the uptake of polydrug use being reported: alcohol, followed by marijuana, then other drugs. Frequent abuse of other drugs is often seen in people being treated for alcohol problems,

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**Table 1. Common alcoholic beverages available world-wide [2]**

Types of Liquors	Categories	Alcohol Content (%)	Sources
<b>Malted Liquors</b>	Beers, Stout,	03-06	Cereals
<b>Wines</b>	Light Wines (Claret, Cider)	09-12	Natural Sugars (Cereal, Vegetable or Fruits)
	Fortified Wines (Port, Sherry)	16-22	
	Effervescent Wines (Champagne)	12-16	
<b>Spirits</b>	Rum, Gin, Whiskey, Brandy, Vodka	40-55	Starch
<b>Others</b>	Absolute alcohol	99	Dehydrated alcohol
	Rectified Spirit	90	Molasses
	Proof Spirit	100	

including adolescents, complicating the issue of treatment and resulting in a higher risk of relapse to alcohol or substitution of another drug for alcohol. Adolescents have reported that alcohol removes their inhibitions and alters their judgement, increasing the likelihood of their experimenting with drugs [2].

#### Detection

Bedside test: Place 1mL of unknown solution plus 1mL of acetic acid and 1 drop of H<sub>2</sub>SO<sub>4</sub> in a test tube and heat gently for 1 minute. A characteristic strong fruity odour ( due to ethyl acetate) is positive for ethanol. Saliva has been proposed for the detection of alcohol abuse, e.g., by the determination of salivary aminotransferases and gammaglutamyl- transferase, ethanol , methanol , diethylene and ethylene glycol or sialic acid [4]. In many countries including India, traffic police carry special equipment in the form of breathalyzer to detect alcohol in the breath of a suspect driver in metropolitans cities. It serves as an “on the spot test”. It comes under motor vehicles act 1988 (amended 1994) . In earlier days the individual concerned was asked to blow into a plastic balloon containing a crystalline dichromate-sulphuric acid mixture. If the BAC was above a certain prescribed limit, the crystals would turn green to a predetermined distance. However, today this has been superseded by more

**Table 2. Clinical Manifestations of Ethanol Poisoning [3]**

Stages	Blood alcohol concentration (mg/100mL)	Clinical Features
<b>I</b>	0-50	Normal behavior
<b>II</b>	50-100	Feeling of well-being, sociability, talkativeness, Increased self-confidence, decreased inhibitions, fine movements affected
<b>III</b>	100-150	Emotional instability, impairment of memory and comprehension, increased reaction time, mild ataxia
<b>IV</b>	150-200	Disorientation, confusion, vertigo, diplopia, ataxia, slurred speech, staggering gait.
<b>V</b>	200-300	General inertia, diminished response to stimuli, inability to stand or walk, vomiting
<b>VI</b>	300-500	Unconsciousness, abolished reflexes, subnormal temperature, incontinence of urine and faeces, respiratory compromise
<b>VII</b>	>500	Death due to respiratory failure; Dead drunk.

*I-Sobriety;II-Euphoria;III-Excitement;IV-Confusion;V-Stupor;VI-Coma;VII-Death*

sophisticated versions based on fuel-cell sensing, electrochemical oxidation, infrared photometry and microprocessors which accurately predict the BAC. [5]

#### Toxicokinetics

The absorption of ethanol from the GI tract is within 30 to 60 min after its ingestion. The stomach extracts about 20%, with the remainder of absorption occurring in the small intestine. The absorption of ethanol from the GI tract may be delayed by various factors, including coingested food, drugs, and medical conditions that inhibit gastric emptying. After it enters the portal vein, ethanol first passes through the liver before it distributes to the rest of the body. More than 90% of the ingested ethanol is oxidized to acetaldehyde by liver and gastric mucosal cells; 5 to 10% is excreted unchanged by kidneys, lungs, and sweat. Oxidation of ethanol to acetaldehyde occurs predominantly in the liver by alcohol dehydrogenase (ADH). In addition, hepatic cytochrome P450, principally the isoform 2E1 (CYP2E1) in endoplasmic reticulum, and catalase in peroxisomes, are also able to catalyze the oxidation of ethanol to acetaldehyde. The acetaldehyde formed is further converted to acetate via the action of aldehyde dehydrogenase (ALDH) present in liver mitochondria. Generally, women have a higher peak ethanol concentration than men if exposed to the same



amount of ethanol, due to their lower body water content and the lower level of ADH in gastric mucosal cells. ADH, ALDH, and CYP2E1 exhibit genetic polymorphisms. Polymorphisms of these alcohol-metabolizing enzymes may lead to alterations in the ethanol elimination rate. For example, some Asian people have a facial flushing reaction when they drink alcohol, which is caused by the lower efficiency of their ALDH, leading to accumulated acetaldehyde in blood. In addition, polymorphisms of ethanol-metabolizing enzymes may influence the susceptibility to ethanol-induced diseases such as pancreatitis, liver cirrhosis and esophageal cancer. The average rate of ethanol metabolism in adults is 100 to 125 mg/kg/h in occasional drinkers, and can be up to 175 mg/kg/h in chronic drinkers. For medium sized adults, the blood ethanol level drops at an average rate of 15 to 20 mg/dl/h. [6]

### **Cirrhosis**

It represents the irreversible end-stage of several diffuse diseases causing hepatocellular injury and is characterized by the following 4 features:

1. It involves the entire liver
2. The normal lobular architecture of hepatic parenchyma is disorganized
3. There is formation of nodules separated from one another by irregular bands of fibrosis
4. It occurs following hepatocellular necrosis of varying etiology so that there are alternate areas of necrosis and regenerative nodules

### **Pathogenesis**

Irrespective of the etiology, cirrhosis in general is initiated by hepatocellular necrosis. Continued destruction of hepatocytes cause collapse of normal lobular hepatic parenchyma followed by fibrosis around necrotic liver cells and proliferated ductules and there is formation of compensatory regenerative nodules.

**Fibrogenesis.** Fibrosis in the liver lobules may be portal-central, portal or both. The mechanism of fibrosis is by increased synthesis of all types of collagen and increase in the number of collagen-producing cells. In cirrhosis, there is proliferation of fat-storing to cells underlying the sinusoidal epithelium which become transformed into myofibroblasts and fibrocytes.

**Regenerative nodule.** The cause of compensatory proliferation of hepatocytes to form regenerative nodules is obscure. Possibly, growth factors, and hormonal imbalance play a role in regeneration.

### **Classification**

Cirrhosis can be classified on the basis of morphology and etiology Morphologic classification. There are 3 morphologic types of cirrhosis- Micronodular,

macronodular and mixed. Each of these form may have an active and inactive form.

1. Micronodular cirrhosis. In micronodular cirrhosis, the nodules are usually regular and small, less than 3mm in diameter.
2. Macronodular cirrhosis. In this type, the nodules are of variable size and are generally larger than 3mm in diameter. The pattern of involvement is more irregular than in micronodular cirrhosis
3. Mixed cirrhosis. In mixed type, some parts of the liver show micronodular appearances while other parts show macronodular pattern.

### **ALCOHOLIC LIVER DISEASE AND CIRRHOSIS**

ALD is the term used to describe the spectrum of liver injury associated with acute and chronic alcoholism. There are three sequential stages in alcoholic liver disease, alcoholic steatosis (fatty liver) alcoholic hepatitis and alcoholic cirrhosis.

### **Risk factor for alcoholic liver disease**

The incidence of cirrhosis among alcoholics at autopsy is about 10-15%. Why some individuals are predisposed to alcoholic cirrhosis is not clearly known, but a few risk factors have been implicated.

1. Drinking patterns. Most epidemiologic studies have attributed alcoholic cirrhosis to chronic alcoholism. Available evidence suggests that chronic and excessive consumption of alcohol invariably leads to fatty liver in >90% of chronic alcoholics, progression to alcoholic hepatitis in 10-20% cases, and eventually to alcoholic cirrhosis in more than 10 years.
2. Gender. Women have increased susceptibility to develop advanced alcoholic liver disease with much lesser alcohol intake (20-40g/day)
3. Malnutrition. Absolute or relative malnutrition of proteins and vitamins is regarded as a contributory factor in the evolution of cirrhosis. The combination of chronic alcohol ingestion and impaired nutrition leads to alcoholic liver disease and not malnutrition per se.
4. Infections. Intercurrent bacterial infections are common in cirrhotic patients and may accelerate the course of the disease.
5. Genetic factors. The rate of ethanol metabolism is under genetic control. It is chiefly related to altered rates of elimination of ethanol due to genetic polymorphism for the two main enzyme systems. MEOS (microsomal P-450 oxidases) and alcohol dehydrogenase (ADH)
6. Hepatitis C infection. Concurrent infection with HCV is an important risk factor for progression of alcoholic liver disease. HCV infection in chronic alcoholic leads to development of ALD with much less alcohol consumption, disease progression at a younger age, having greater severity, and increased risk to develop cirrhosis and hepatocellular carcinoma and overall poorer survival.



**Table 3. Mechanisms of diseases caused by ethanol abuse [7]**

Organ System	Lesion	Mechanisms
<b>Liver</b>	Fatty change Acute hepatitis Alcoholic cirrhosis	Toxicity
	Wernicke syndrome Korsakoff syndrome	Thiamine deficiency Toxicity and thiamine deficiency
<b>Nervous system</b>	Cerebellar degeneration Peripheral neuropathy	Nutritional deficiency Thiamine deficiency
<b>Cardiovascular system</b>	Cardiomyopathy Hypertension	Toxicity
<b>Gastrointestinal system</b>	Gastritis	Toxicity
<b>Skeletal muscle</b>	Rhabdomyolysis	Toxicity
<b>Reproductive system</b>	Testicular atrophy Spontaneous abortion	?
<b>Fetal alcohol syndrome</b>	Growth retardation Mental retardation Birth defects	Toxicity

**Pathogenesis**

Exact pathogenesis of alcoholic liver injury is yet unclear. The biomedical and cellular pathogenesis due to chronic alcohol consumption culminating in morphologic lesions of alcoholic steatosis (fatty liver), alcoholic hepatitis and alcoholic cirrhosis can be explained in this review.

1. Direct hepatotoxicity by ethanol
  2. Hepatotoxicity by ethanol metabolites
    - (i) Production of protein-aldehyde adducts
    - (ii) Formation of malondialdehyde-acetaldehyde (MAA) adducts
  3. Oxidative stress
  4. Immunological mechanism
  5. Inflammation
  6. Fibrogenesis
  7. Increased redox ratio
  8. Retention of liver cell water and proteins
  9. Hypoxia
  10. Increased liver fat
1. Alcoholic Steatosis (fatty liver). G/A The liver is enlarged yellow, greasy and firm with a smooth and glistening capsule. The features consist of intial microvesicular droplets of fat in the hepatocyte cytoplasm followed by more common and pronounced feature of

macrovesicular large droplets of fat displacing the nucleus to the periphery. Fat cysts may develop due to coalescence and ruptures of fat-containing hepatocyt. Less often, lipogranulomas consisting of collection of lymphocytes, macrophages and some multinucleate giant cells may be found.

2. Alcoholic Hepatitis. Alcoholic hepatitis develops acutely, usually following about of heavy drinking
  1. Hepatocellular necrosis
  2. Mallory bodies or alcoholic hyaline
  3. Inflammatory response
  4. Fibrosis
3. Alcoholic Cirrhosis. Alcoholic cirrhosis is the most common form of lesion. Constituting 60-70% of all cases of cirrhosis.

Alcoholic cirrhosis classically begins as micronodular cirrhosis (nodules less than 3mm diameter), the liver being large, fatty and weighing usually above 2kg. Eventually over a span of years, the liver shrinks to less than 1kg in weight, becomes non-fatty having macronodular cirrhosis (nodules larger than 3mm in diameter), resembling post-necrotic cirrhosis. On cut section, spheroidal or angular nodules of fibrous septa are seen. Alcoholic cirrhosis is a progressive alcoholic liver disease. Its features include the following

- i) Nodular pattern
- ii) Fibrous septa
- iii) Hepatic parenchyma
- iv) Necrosis, inflammation and bile duct proliferation

**Laboratory Diagnosis**

1. Elevated transaminase: increase in SGOT (AST) is more than that of SGPT (ALT)
  2. Rise in serum  $\gamma$ -glutmyl transpeptidase ( $\gamma$ -GT)
  3. Elevation in serum alkaline phosphatase
  4. Hyperbilirubinaemia
  5. Hypoproteinaemia with reveral of albumin-globulin ration
  6. Prolonged prothrombin time and partial thromboplastin time
  7. Anaemia
- Neutrophilic leucocytosis in alcoholic hepatitis and in secondary infections [8,9]

**Autopsy Features [11]**

- Congested conjunctivae
- Fruity odour in the vicinity mouth, and nose
- Congestion of GI tract
- Pulmonary and cerebral oedema
- Chronic alcoholism includes; Cirrhotic liver; Cardiomyopathy and lesions in other organs.



**Table 4. Management of Ethanol Poisoning [10]**

<b>DO</b>	<b>DON'T</b>
<b>Correction of metabolic abnormalities</b>	Use of activated charcoal
<b>Control of seizures, Intravenous fluids</b>	Use of cathartics
<b>Circulatory support, airway protection</b>	Use of gastric lavage
<b>Malnourished patients administered thiamine 100mg IV and pyridoxine</b>	Patient with acute renal failure and a metabolic derangements that is unresponsive to standard therapy should considered Hemodialysis
<b>Fomepizole should be given loading dose of 15mg/kg followed by 10mg/kg every 12h for 48h, the dose should be increased to 15mg/kg every 12h</b>	Do the Craving for alcohol encourage
<b>Dialysis should continued until ethylene glycol level is less than 20mg/dl, the acidosis has resolved and there are no signs of systematic toxicity</b>	Encourage Peritoneal dialysis and produce more complication
<b>Call 108,104 and stay with the victim ( Indian Patients)</b>	Call 91 and stay with the victim (India)
<b>Usual dose of disulfiram is 250mg/day administer only by the oral route, which may have to be taken for an indefinite period of time</b>	Patient explicitly that while he/she is on disulfiram, alcohol be consumed even in small quantity
<b>Supportive Psychotherapy essential for chronic alcoholic person</b> ➤ <b>There is no membership fee and the organization functions on a self-supporting basis through contributions from the members. Slogan is “ Desire to stop drinking”</b> ➤ <b>Meetings are generally held once a week and are informal affairs conducted in a friendly atmosphere. Generally two or three participants should share their experiences during each session relating to their addiction and recovery</b> <i>Prevention of Hangover effect”</i> <b>Brett Smith, who claims that 15–20 g of spirulina ingested after a night (or full day) of revelry has proved fully effective for hangover prevention, both for himself and his imbibing friends. Intriguingly, this is within the clinical dose range of spirulina estimated to be required to replicate the potent antioxidant/anti-inflammatory benefits of spirulina observed in many rodent studies. [9]</b>	Do individualized psychotherapy is not effective and cost effective therapy

**CONCLUSION**

With the completion of revision of all the data's. We are able to suggest that the controlling of ethanol poisoning in developing countries is still, uncontrolled in

the community. So, there is an urgency to develop awareness amongst the individual (ie) to be free from ethanol abuse and also develop a new drug regimen for the proper management of ethanol toxicity.

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