



Review Paper

Alcohol Abuse and Related Health Issues

Geetanjali², Poonam¹, Veer Babita¹ and Singh Ram^{1*}

¹Department of Applied Chemistry, Delhi Technological University, Delhi - 110 042, India

²Department of Chemistry, Kirori Mal College, University of Delhi, Delhi-110 007, India
singh_dr_ram@dce.ac.in

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Abstract

Alcohol abuse and related health issues are an age old problem. Alcoholism is the reflection of socio-cultural factors of an individual and sometimes society as a whole. For some people, this is a part of daily life. Use and abuse travel on the very tight rope. People who have been drinking excess amounts of alcohol for longer periods of time come under the category of alcohol abuse. These people put themselves in the risk of developing serious and persistent changes in various organs including the brain. The effect of alcohol on the organs may be direct or indirect depending upon the general health status of the person. The studies have suggested that the brain functions are affected due to the interaction of alcohol with multiple neurotransmitter systems. Alcohol abuse also leads to different nutritional deficiencies and diseases. This article will discuss the effect of alcohol abuse and related health issues.

Keywords: Alcohol, Ethanol, Alcoholism, Acetaldehyde, CNS, Nutritional deficiencies.

Introduction

Alcohol, in chemistry, is symbolized as R-OH, where R is an alkyl group. Drinking alcohol is an age-old practice and is thought to be the reflection of socio-cultural factors of the individual and society as a whole¹. All alcohols are not appropriate for drinking purposes. Only the ethyl alcohol (CH₃CH₂OH; ethanol) has been found to be suitable for drinking. Ethanol is being used in the production of alcoholic beverages and is the most widely consumed chemical worldwide. This alcohol is produced by the fermentation of grains and fruits. All the rural and urban societies are involved in the alcohol abuse. People have a total misconception that drinking alcohol releases their stress and tension and makes them happy. But the fact is different. Ethanol is a psychoactive substance and causes more adverse effect on human health which includes various disorders and diseases. Also drinking alcohol is responsible for negative social and economic burden on alcoholics¹.

As per the report of the National Institute on Alcohol Abuse and Alcoholism, in a year, the alcohol related problem takes the life of about 88,000 people. This data makes it the fourth leading cause of death in the United States^{2,3}. Globally, about 3.3 million deaths in 2012 were attributable to alcohol abuse and related health issues⁴. Alcohol directly does not contribute to many diseases but over 200 diseases and injury-related health conditions are alcohol dependent diseases which also includes liver cirrhosis, cancers, and other injuries⁴. The alcohol consumption is directly linked with the economic condition of the country. The higher economic wealth of a country showed more alcohol consumption.

Ethanol is classified as depressant⁵. The damaging effects of this in CNS are possible due to its direct toxic effect. This also damages by an indirect effect through its metabolites or ROS generation (Reactive Oxygen Species). The ethanol drinking slows down the vital functions and results in uneven movement that causes an inability to react quickly, slurred speech and disturbed precipitations. The amount of ethanol consumed determines the type of the effect and health issues. Its overdose causes a more severe depressant effect such as an inability to feel pain, unconsciousness, worse, coma or even death. Ethanol can travel anywhere in our body as they contain both hydrocarbon chain and hydroxyl group and hence the hydrophobic part allows them to move into fat while the hydroxyl group (hydrophilic part) allows moving into water⁴. This article presents an overview of the correlation of alcohol consumption and its impact on our health.

Effect of Alcohol

Effect of alcohol in the brain: The brain gets damaged due to the chronic and excessive consumption of alcohol, i.e. ethanol⁶. The quantity and time period of ethanol consumption plays leading role in the damage and neuro-behavioral changes of any alcoholic person. The effect also depends on age, gender, family history and level of education of the person. The effects of ethanol consumption on brain have been studied by a number of research groups^{7,8}. They have postulated that the effect is basically mediated through the formation of acetaldehyde (CH₃CHO), the first metabolite of ethanol⁸.

Acetaldehyde plays a crucial role in damaging the health of alcoholic people and is responsible for the behavioural,

neurochemical and neurotoxic actions⁸. However, this hypothesis has several doubts and is still under investigation; however, several groups have reported the oxidation of ethanol to acetaldehyde in the brain⁹. The three enzymes that are involved in the metabolic reaction of ethanol to acetaldehyde in the brain are *Catalase*, *Cytochrome P450* and *Alcohol dehydrogenase*¹⁰. The quantity of acetaldehyde in the brain at a particular time period is based on the comparative rate of removal and formation of acetaldehyde. This is because the oxidation of acetaldehyde to acetate is taking place in large quantity. Hence, the exact damage done by the acetaldehyde in the brain is still under investigation.

Effect of alcohol on astrocytes: The entire central nervous system (CNS) is covered by astrocytes which are specialized glial cells¹¹. The population of these cells are 10 to 50 times more than the neurons in the CNS. Ethanol has several targets in astrocytes. This tempts astroglial activation, in combination with up-regulation of several pro-inflammatory cytokines that is responsible for cell apoptosis, neuroinflammation and neurodegeneration¹². Ethanol also affects the synthesis, distribution, intracellular transport, and secretion of N-glycoproteins in astrocytes and neurons resulting in the hindrance of brain development¹³.

Effect of ethanol on neurotransmitters: Neurotransmitters are the chemical compounds that act as messengers which enable neurotransmission by passing signals across a chemical synapse. The chronic alcoholism affects the synaptic structure¹⁴. The N-methyl-D-aspartate receptor (NMDA receptor or NMDAR) is the main target of ethanol in the brain. The interaction of this receptor with ethanol is associated with ethanol tolerance, dependence, withdrawal, craving, and relapse¹⁵. The low level of ethanol concentration inhibits the excitatory activity of the NMDA receptor, which contributes towards the abnormalities like learning disabilities, neuronal losses and cognitive deficits.

The exact mechanism and direct action for changes in the functionality of this receptor by ethanol remains unclear¹⁶. The interference of ethanol with the phosphorylation and compartmentalization of NMDA receptor is a possible mechanism of action¹⁷. The inhibition of the NMDA receptors by ethanol is mainly restricted in the subset of neurons¹⁸. This is because; the different sub-units of the receptors have different sensitivity to ethanol¹⁹.

Ethanol also interacts with another membrane receptor, γ -aminobutyric acid (4-aminobutyric acid, GABA). The three types of GABA receptors are GABA_A, GABA_B and GABA_C. GABA_A and GABA_C receptors are ligand-gated whereas GABA_B receptors are G protein-coupled receptors²⁰. Ethanol does not affect all the subunits of all types of GABA. The interaction of ethanol is only restricted to certain subtypes of some subunits²¹. The chronic alcohol consumption leads to the decreased sensitivity of GABA_A receptor-mediated responses²². The interaction of ethanol to GABA is allosteric which changes

the shape of active site and modulates the receptor activity leading to the stimulation of the flow of chloride ion²³. Some studies have also suggested that the modulation of the GABA_A receptor is also due to phosphorylation / dephosphorylation mechanisms²¹. The ethanol dependence and withdrawal are also responsible for the various polymorphisms in the GABA_A gene²⁴ and there is a possibility of significant functional consequences²⁵.

The enhancement of the GABA_B induced synaptic responses by ethanol results in the inhibition of the cation channels. This results in the hyperpolarization of the membrane and a consequent decrease in neuronal excitability²⁶ and altered mental and motor performance in an acute intoxication phase²⁷.

Ethanol being small molecule interacts with many neurotransmitter systems in the brain like mesocorticolimbic dopamine and serotonin²⁸. Ethanol acutely activates mesocorticolimbic dopamine (DA) system and leads to the functional changes in the brain reward system²⁹. The polymorphic variations in many dopaminergic system genes including the dopamine transporter gene have been observed in alcoholics³⁰ along with severe alcohol withdrawal symptoms³¹. The alcoholism has also been associated with polymorphism of the serotonin transporter³².

Vitamin and Mineral Deficiency due to Alcoholism

The vitamins and minerals that are essential for our life are severely got deficient due to chronic alcoholism. The deficiency is associated with inhibition in breakdown and lowering of absorption. Alcohol slows down the secretion of digestive enzyme from the pancreas and hence inhibits the breakdown of nutrients into usable molecules³³. Also, alcohol damages the cells lining in the stomach and intestines and reduces the nutrient absorption³⁴. Alcohol also affects the transport, storage, and excretion of the digested and absorbed nutrients³⁵.

The chronic alcoholic people have shown deficiencies of minerals like calcium (Ca), magnesium (Mg), iron (Fe), zinc (Zn) etc in their body³⁶. A variety of diseases like skin lesions, zinc-related night blindness and calcium-related bone etc caused due to the mineral deficiencies and are also called mineral deficiency diseases³⁷.

Chronic alcoholics also showed vitamin deficiencies due to decreased food ingestion and impaired absorption, metabolism and utilization. This has been observed that the people who are addicted to ethanol suffer from thiamine (Vitamin B1) deficiencies³⁸. Vitamin B1 is used in combination with other Vitamin B as Vitamin B complexes³⁸. The deficiency of these vitamins has fatal outcome and mainly responsible for the diseases like Korsakoff's syndrome, optic neuropathy and beriberi. Three important pathways are involved in thiamine deficiency due to alcoholism: i. Inadequate nutritional intake, ii.

Decreased absorption of thiamine from the gastrointestinal tract and iii. Reduced uptake and impaired utilization in the cells³⁹. Similarly, the chronic alcohol consumers showed deficiency in vitamin A and hence exposed to the vitamin A deficiency diseases⁴⁰. The diseases like the loss of night vision (nyctalopia), xerophthalmia and blindness are associated with alcoholism⁴¹.

Diseases due to Alcoholism

Alcohol consumption results in the initiation and development of many chronic diseases and conditions. Twenty-five chronic disease and condition codes in the International Classification of Disease (ICD)-10 are entirely attributable to alcohol⁴². Alcohol has been found to be associated with diseases like tumors, cancers, numerous cardiovascular and digestive diseases and neuropsychiatric conditions⁴².

Cancer: Studies have proved that alcoholic beverages are carcinogenic to humans⁴³. Generally alcohol increased the risk of cancers of the upper digestive track, the lower digestive track and the female breast⁴². The stomach cancer has also been linked to alcoholism⁴⁴. Some studies have also shown some positive effect of alcohol, if taken in dose-dependent manner. It has been found that alcohol significantly decreased the risk of renal cell carcinoma⁴⁵, Hodgkin's lymphoma⁴⁶, and non-Hodgkin's lymphoma⁴⁷.

Alcoholic Liver Disease (ALD): ALD is a collection of various liver diseases that are directly or indirectly associated with the alcohol consumption. The three histological stages of ALD includes simple steatosis (fatty liver), alcoholic hepatitis, and chronic hepatitis with hepatic fibrosis or cirrhosis⁴⁸. Cirrhosis is a condition in which the liver is damaged and does not function properly whereas hepatitis is an inflammation of the liver. The widely accepted mechanism for liver damage involves the oxidative and non-oxidative breakdown of ethanol in the liver leading to the formation of free radicals, acetaldehyde, and fatty acid ethyl esters. These chemical species are responsible for the damage⁴⁹.

Pancreatic problems: The inflammation of the pancreas (pancreatitis) is usually observed in alcoholics. The alcoholism increases the risk for acute and chronic pancreatitis⁵⁰. The combination of alcohol drinking with smoking aggravates the pancreatic problem further. The damage pathway for the pancreas is almost similar to the liver⁵¹.

Sexual dysfunction: The sexual dysfunction (SD) is associated with many types of problems that include decreased sexual desire, difficulty in erection and achieving orgasm, sexual aversion disorder and premature ejaculation⁵². Alcoholic people always complain of SD like testicular atrophy, inhibition of testosterone production, and inhibition of spermatogenesis, has been observed in the people with chronic alcohol drinking habit⁵³.

Infertility: The association of alcoholism and male/female infertility cannot be ruled out completely⁵⁴. The exact relationship between alcohol and infertility is not clear. This has been observed that the chronic alcoholic female experienced irregularities in their menstrual cycles and ovulation and also unusual variation in the levels of estrogen and progesterone⁵⁵. Infertility due to ovulatory disorders like anovulation and oligoovulation or endometriosis have been associated with alcohol abuse⁵⁶. Alcoholism was found to be associated with decreased fecundability also⁵⁷.

In case of male, the semen quality is associated with alcoholism⁵⁸. The vitality, survival rate and count of sperm have dose and time effect relationship with alcoholism⁵⁸. The alcoholic nature increases the teratozoospermia and oligozoospermia significantly⁵⁹. The teratozoospermia is a condition where sperm with abnormal morphology are present where as oligozoospermia refers to semen with a low concentration of sperm.

Neurological complications: The chronic and excessive alcohol consumption affects the nervous system. This causes disordered thinking, dementia, numbness and pain in hands and feet, and short-term memory loss⁶⁰. Various studies have proved the association between alcohol and Alzheimer's disease (AD) and vascular dementia⁶¹. The high alcohol consumption is considered a risk for late-onset AD⁶². The initial studies with primary neuron culture had provided information about the ability of ethanol to exacerbate A β toxicity and neuron cell death mechanisms⁶³.

Conclusion

From the beginning of human civilization, ethanol remain one of the most commonly used and abused chemical compound on this earth. The alcoholic people develop various alcohol related health issues. The studies have suggested that the adverse effect of ethanol consumption is mainly due to its first metabolite, acetaldehyde. Acetaldehyde plays a crucial role in the alcoholic people and is responsible for the behavioural, neurochemical and neurotoxic actions. Also, ethanol has several targets in astrocytes and responsible for cell apoptosis neuroinflammation and neurodegeneration.

The interaction of ethanol with multiple neurotransmitter system is associated with ethanol tolerance, dependence, withdrawal symptoms, relapses etc. Alcoholic people suffer from vitamins and minerals deficiencies. Alcohol has been found to be associated with diseases like tumors, cancers, numerous cardiovascular and digestive diseases and neuropsychiatric conditions.

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