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Review Article

Does Alcohol Affect Gastrointestinal Cancer Risk: A Review Updating the Briefings of Related Factors?

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Abstract

Alcohol consumption is a significant risk factor for gastrointestinal cancers that may be controlled. The risk of cancer increases with the amount and duration of drinking. Even occasional drinking can raise cancer risk; 100 g or less per week is presently thought to be the upper limit for low-risk consumption. Alcohol is causally linked to colorectal cancer, hepatocellular carcinoma, gastric cancer, oesophageal squamous cell cancer, and most likely also pancreatic cancer. Alcohol can have a multiplicative effect on the development of gastrointestinal cancer when paired with tobacco usage or being overweight. The recent rises in the incidence of early-onset gastrointestinal cancers in various Western nations may have been influenced by alcohol use. It is important to encourage those who use alcohol in a harmful way to enroll in cancer screening programmes. Eliminating alcohol consumption seems to be effective in lowering the elevated cancer risk that alcohol causes.

Keywords: Cancer; Alcohol; Gastrointestinal cancer; Causes; Risk

Introduction

Alcoholic beverages rank among the most significant products of the global addiction demand. Alcohol drinking frequently poses a serious issue in emerging nations like India because of the diverse socio-cultural traditions that exist there. The World Health Organization (WHO) claims that alcohol drinking causes more than 200 diseases, including suicide and accidents [1]. Alcohol kills 2.6 lakh Indians annually, either directly or indirectly through liver cirrhosis, cancer, or accidents on the roads. The most frequent alcohol-attributable fractions for specific causes of death are 22% for esophageal cancer, 25% for pancreatitis, and 50% for liver cirrhosis [2].

Alcoholism is a serious health problem that affects people all over the world. It can cause addiction and harm to practically all of the body's organs. The WHO Global Burden of Disease Project, which came to the conclusion that alcohol is responsible for about 1.8 million fatalities annually (3.2% of all deaths), provides the most thorough estimates of the death rates caused by alcohol. Cancer is one of the most significant diseases brought on by long-term alcohol usage [3].

An worldwide team of epidemiologists and experts on alcohol gathered in February 2007 at the International Agency for Research on Cancer (IARC) in Lyon, France, to discuss the potential carcinogenic effects of alcohol and its primary metabolite, acetaldehyde, in both experimental animals and humans. Based on the epidemiological information available, this Working Group has determined that drinking alcohol is causally connected to the development of malignant tumours of the mouth, pharynx, larynx, oesophagus, liver, colorectum, and female breast [4]. Alcohol is therefore regarded as a carcinogen for these organ locations.

The gastrointestinal (GI) tract, as the first line of contact with anything ingested into the body, is at particular risk for damage by toxins. Additionally, a growing body of studies indicates that the body's general health is significantly impacted by poor gastrointestinal health. Making the connection, anything that could harm the GI system could have effects that extend far beyond the intestines [5]. In fact, studies have shown that alcohol consumption, especially when done repeatedly and in higher amounts, triggers a process that starts in the gut and encourages inflammation all over the body. The three most significant diseases brought on by alcohol usage are cancer, pancreatitis, and Alcoholic Liver Disease (ALD). This review therefore focuses on how chronic alcohol consumption could lead development of cancers of the upper gastrointestinal tract, the liver, the colorectum and the female breast. It has been demonstrated over the past few decades that risk factors for disease—genetic and non-genetic—as well as alcohol susceptibility rely not only on the amount of alcohol ingested but also on the target organ [6].

Metabolism of Alcohol

General Overview

In addition to the liver, alcohol is also oxidised in the digestive system. The first pass metabolism of alcohol and alcohol-induced tissue toxicity are both affected by this alcohol metabolism, even though it is less than that of the liver. Alcohol Dehydrogenase (ADH) and the microsomal alcoholoxidising system (MEOS), as well as a wide range of microorganisms, can all metabolisealcohol in the gastrointestinal tract [7]. One or the other metabolic pathway for alcohol may be predominate depending on the digestive region. The so-called first pass metabolism of alcohol by stomach ADH affects alcohol blood concentrations not only in the portal vein and consequently in the liver, but also in the systemic circulation [8]. Increased blood alcohol concentrations after oral ingestion of alcohol may happen in these circumstances because stomach ADH activity is lowered in younger women, the elderly, alcoholics, people who are fasting, and those who

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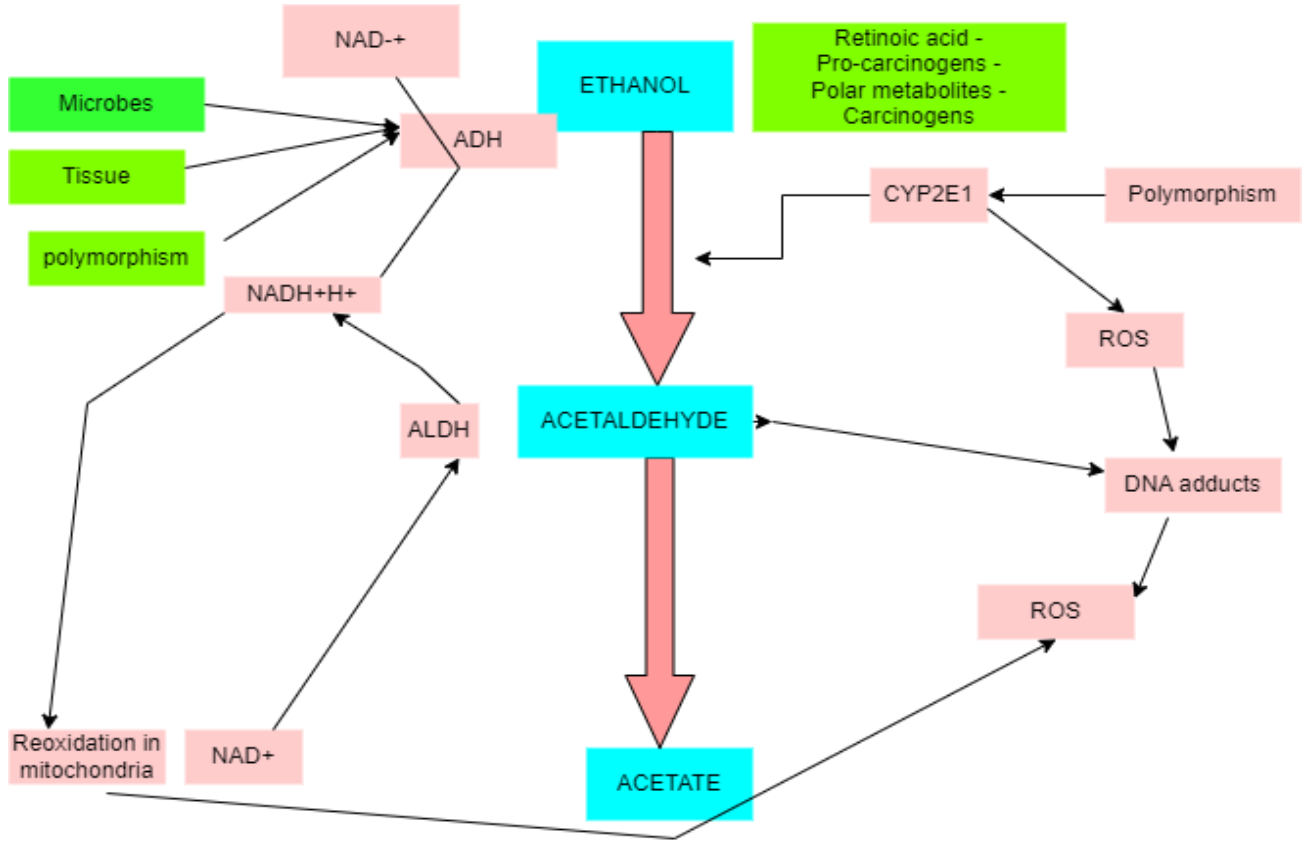

Figure 1: General mechanism of Alcohol metabolism.

have been treated with specific H-2-receptor antagonists. However, the rate of stomach emptying also has an impact on the first pass metabolism of alcohol in addition to ADH activity (e.g. slow gastric emptying leads to increased first pass metabolism) [9]. Finally, first pass metabolism is also influenced by gastric morphology. Gastric ADH activity declines due to chronic atrophic gastritis and Helicobacter pylori-related gastric damage, which may result in a slower first-pass alcohol metabolism. Additionally, the well-known alcohol linked oesophageal cancer growth may be facilitated by the local generation of acetaldehyde from alcohol in the oesophagus, where much more sigma-ADH is present. The colorectum contains several isoenzymes of ADH, and these enzymes can also produce acetaldehyde in high enough concentrations to harm the mucosa. The mixed function oxidase MEOS also metabolises alcohol in addition to ADH[10]. Chronic alcohol use can induce this system, which is involved in the metabolism of several xenobiotics, including procarcinogens and pharmaceuticals. So, this enzyme system's increased activation of dietary procarcinogens could possibly aid in the development of cancer in alcoholics. Additionally, a wide range of bacteria in the digestive tract can convert alcohol to acetaldehyde. In the colorectum, where faecal bacteria, particularly anaerobes in the rectum, can produce high levels of acetaldehyde and this correlates with mucosal hyperregeneration suggesting an acetaldehyde-mediated mucosal injury, this may be of particular significance [10]. (Figure 1) shows general mechanism of alcohol metabolism.

Alcohol-Mediated Carcinogenesis

A group 1 human carcinogen, according to the International Agency for Research on Cancer (IARC), is acetaldehyde generated from alcoholic beverages. This IARC conclusion, which is based on gene-epidemiologic data on alcohol consumers with ALDH2 deficiencies, is particularly concerned about alcohol-related upper digestive tract malignancies. According to the WHO, alcohol usage results in more than 3 million fatalities annually (5.3% of all deaths globally), with cancer accounting for around 13% of those deaths [11]. Alcoholic beverages mostly include alcohol. Alcohol (alcohol) is degraded after consumption by Alcohol Dehydrogenase (ADH) into acetaldehyde, which is then transformed into acetate by Aldehyde Dehydrogenase (ALDH). Acetaldehyde shortens telomere length, inhibits DNA repair processes, and permanently damages DNA strands. Alcohol causes scavenger systems to malfunction and increases the production of ROS, which causes oxidative stress and genomic instability. An key relationship between drinking alcohol and the development of gastrointestinal cancer is the microbiome [12].

Oral and Oesophageal Microbiome and Acetaldehyde Production

A risk factor for oral and oesophageal carcinogenesis is poor oral health. The upper digestive tract mucosa's exposure to acetaldehyde is significantly influenced by the local microbiota. A dysbiotic oral microbiome promotes the growth of opportunistic pathogens (like

Candida yeasts) and can increase local acetaldehyde production by up to 100%. The expression of alcohol- and acetaldehyde-metabolizing enzymes is further altered by organ-specific gene polymorphisms and organ-specific expression patterns. Saliva and oral bacteria, which both play crucial roles in the pathogenesis of alcohol-related upper digestive tract malignancies, connect the oropharynx to the oesophagus and stomach [13].

Millions of drinkers have been randomly exposed to noticeably more local acetaldehyde exposure through saliva and stomach juice due to a point mutation in the ALDH2 gene, increasing their risk of upper digestive tract malignancies significantly. The oropharynx offers a special gene-epidemiologic and gene-biochemical human cancer paradigm for long-term local acetaldehyde exposure due to a single point mutation in the ALDH2 gene. The model firmly establishes the causative relationship between local acetaldehyde and gastric, oesophageal, and throat cancers, in addition to oropharyngeal cancer caused by alcohol. Regarding this gene mutation-based paradigm, it is significant to highlight that individuals with homozygotic ALDH2-deficiency (zero ALDH2 activity) typically are unable to consume alcohol at all due to uncomfortable side effects, including severe "Antabuslike" flushing [14].

Hepatocellular Cancer

Decompensated alcohol-induced cirrhosis carries an annual risk of 1% or less for HCC. Abstinence does not lower the risk, because HCC can develop in a liver that is not cirrhotic. Alcohol usage increases the risk of HCC in chronic hepatitis C by two times over the risk in hepatitis C alone. Additionally, alcohol and hepatitis C may work together to accelerate the development of HCC in some people, causing the disease to manifest earlier in life and with more advanced histological characteristics. According to studies conducted in Italy and the United States, alcohol consumption accounts for 32% to 45% of all HCC cases. Although the exact mechanisms by which alcohol promotes HCC are yet unknown, they may involve chromosomal loss, oxidative stress, a drop in the liver's retinoic acid level, altered DNA methylation, and hereditary vulnerability [15]. Alcohol usage is rising around the globe, which indicates that HCC will continue to be primarily brought on by alcohol.

Obesity and alcohol consumption work together to cause HCC. Due to the high prevalence of excess body weight and alcohol consumption in teenagers, it is possible that these two factors have causally increased the incidence of (early-onset) HCC in high-income nations. Additionally, chronic viral hepatitis (B,C), diabetes, or hemochromatosis can alter the risk of alcohol-induced HCC, increasing the overall risk of the disease. When a patient has non-alcoholic steatohepatitis or liver cirrhosis, HCC is a substantial factor in liver-specific mortality. Patients with liver cirrhosis should be given the option of early detection of asymptomatic HCC by liver ultrasound every six months; this procedure may also be used to find asymptomatic (early-stage) intrahepatic cholangiocellular carcinoma, a condition that some authors also include on their list of cancers linked to alcohol consumption [16].

Pancreatic Cancer

Pancreatic cancer, the deadliest major cancer in the world, still has a 5-year survival rate of only 9%. It is anticipated that by 2030 it will rank as the second most common cancer-related cause of death in the USA, rising to the top spot by 2050. Smoking, previous diabetes, chronic pancreatitis, being overweight, having H. pylori infection, and having a family history of pancreatic cancer are all well-known risk factors. With a 3% population-attributable risk, alcohol consumption is the fourth most significant risk factor for pancreatic cancer [17]. With a 3% population-attributable risk, alcohol consumption is the fourth most significant risk factor for pancreatic cancer. There is (limited) evidence of a non-linear dose-response relationship between alcohol usage and the risk of developing pancreatic cancer at higher alcohol intake levels (above around 40 g of alcohol per day).Tobacco, alcohol, excess body weight, and diabetes interact multiple times to cause pancreatic cancer. Smoking cigarettes and consuming (high-risk) alcohol together appears to raise the overall risk of pancreatic cancer. By altering lifestyle risk factors, the risk of pancreatic cancer may be decreased by 27% or more. Given the prevalence of alcohol use, cigarette use, and obesity among US adolescents, (high-risk) alcohol consumption in combination with either obesity or smoking may have contributed to the recent rises in the incidence of early-onset pancreatic adenocarcinoma [18].

Gastric Cancer

One of the most common cancers in the world is gastric cancer, often known as stomach cancer; over two-thirds of cases and fatalities from gastric cancer take place in less developed nations like India. Despite the fact that the precise influencing elements have not been clarified, it has been hypothesised that the development of stomach cancer is a multi-step process. Many scientists investigating the causes of gastric cancer in the past had divergent theories regarding the contribution of alcohol usage to the development of stomach cancer. The major mechanism is probably connected to the principal metabolites, acetaldehydes, which have a local toxic effect and enhance the risk of gastric cancer, according to recent research that have established that drinking alcohol can increase the risk of gastric cancer [19]. There is a non-linear dose-response relationship between alcohol usage and the chance of developing stomach cancer at higher alcohol intake levels (from 45 g of alcohol per day). Both stomach tumours with and without cardia share the same connection. In contrast, the majority of studies found that occasional light drinking had no discernible impact on stomach cancer. A significant (up to) 50% reduction in the risk of stomach cancer was linked to the EPIC study's healthiest score of the three lifestyle characteristics (no/little alcohol usage, no tobacco use, and adherence to a Mediterranean diet) [20].

Esophageal Cancer

Drinking alcohol can increase your risk of getting some malignancies, such esophageal cancer. According to research, the following factors related to alcohol usage may accelerate the growth of cancer. Alcohol use at any level raises the risk of developing esophageal cancer. However, a person's risk increases as they consume more alcohol. Heavy drinking carries a five-fold greater risk of esophageal cancer compared to abstaining from alcohol. Oesophageal squamous cell carcinoma (ESCC) and adenocarcinoma are the two main histologic forms of the disease, which is the sixth most common cause of cancer-related death worldwide [21]. Alcohol usage and the risk of ESCC are associated nonlinearly in terms of dose. Tobacco use, oral

microbes, folate deficiencies, and gene polymorphisms (ALDH2*1*2, ALDH2*2*2, ADH1B*2, and ADH1C*1) work together to exacerbate the carcinogenic effect of alcohol and cause ESCC. Unfortunately, the majority of drinkers also smoke cigarettes.Alcohol use and concurrent smoking have continuously been linked to favourable, synergistic carcinogenic effects that lead to ESCC, according to epidemiological research [22].

Conclusion

The purpose of this review was to provide an overview of the available data supporting the hypothesis that chronic alcohol use contributes to the burden of cancer globally and the underlying processes. A causal link between persistent alcohol use and upper gastrointestinal tract malignancies has been established by the evidence. The risk of gastrointestinal malignancies is not only dependent on alcohol intake. It's possible to avoid about 40% of gastrointestinal malignancies. In addition to alcohol consumption, other significant modifiable risk factors include tobacco use, excessive body weight, inactivity, bad nutrition, and a few chronic illnesses. Therefore, well-planned cancer prevention programmes can considerably lower the number of fatalities from gastrointestinal cancer. The purpose of this review was to provide an overview of the available data supporting the hypothesis that chronic alcohol use contributes to the burden of cancer globally and the underlying processes. A causal link between persistent alcohol use and upper gastrointestinal tract malignancies has been established by the evidence. The risk of gastrointestinal malignancies is not only dependent on alcohol intake. It's possible to avoid about 40% of gastrointestinal malignancies. In addition to alcohol consumption, other significant modifiable risk factors include tobacco use, excessive body weight, inactivity, bad nutrition, and a few chronic illnesses. Therefore, well-planned cancer prevention programmes can considerably lower the number of fatalities from gastrointestinal cancer.

Conflict of Interest

The authors confirm that this article's content has no conflict of interest.

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