Alcohol and its association with cancer

Background

Although there was already **sufficient evidence on alcohol consumption as a cause for cancer** more than 20 years ago (IARC, 1988), there is still poor public awareness of alcohol as a risk factor for cancer.

Drinking is considered part of the culture in many European Member States, and, although rates and patterns vary across countries, **the EU has the highest rate of alcohol consumption in the world** (WHO 2004).

Alcohol is the common term for ethanol, one of a family of alcohols, produced in the process of fermentation to produce alcoholic drinks. The evidence does not show any 'safe limit' for intake of ethanol, whose effect is irrespective of the type of drink (WCRF and AICR, 2007).

The mechanisms by which alcohol induces carcinogenesis are not fully understood; they may differ by target organ and include polymorphisms in genes. It is hypothesized to include the interaction of cytochrome P-4502E1 (CYP2E1), which metabolizes ethanol to acetaldehyde and is involved in the metabolism of various procarcinogens (Poschl and Seitz, 2004).

For the upper digestive tract, **acetaldehyde**, both from alcohol metabolism in the human body and ingested as a component of fermentation to produce alcoholic drinks, has been recently highlighted as an important likely causal pathway and proposed already in 1987 by the International Agency for Research on Cancer (IARC) as being 'possibly carcinogenic to humans' (IARC, 1987). The average exposure to acetaldehyde from alcoholic beverages has been estimated at 0.112 mg/kg body weight/day. The lifetime cancer risks for acetaldehyde at 7.6 in 10,000 exceed the usual limits for cancer risks from the environment that are commonly set between 1 in 10,000 and 1 in 1,000,000 (Lachenmeier et al., 2009).

In relation to the genetic susceptibility, the major alcohol-metabolising enzymes in humans are the alcohol dehydrogenases (ADH) that oxidise ethanol to acetaldehyde, and the aldehyde dehydrogenases (ALDH) that detoxify acetaldehyde to acetate. Most homozygous carriers of this allele (ALDH2*2/*2) are abstainers or infrequent drinkers, because the enzyme deficiency would cause a strong facial flushing response, physical discomfort, and severe toxic reactions. In heterozygous carriers (ALDH2*1/*2, with about 10% residual ALDH2 activity) these acute adverse effects are less severe, but when they consume alcohol these carriers are at high risk for several alcohol-related aerodigestive cancers (IARC, 2007).

There are other components in alcohol beverages such as **ethyl carbamate**, that are probably carcinogenic to humans. Ethyl carbamate may be formed naturally as a result of fermentation, and it has been detected in a variety of fermented foods and beverages. The concentrations in wine and beer are usually below 100 microgram per litre, whereas higher levels (in the milligram per litre range) have been found in some spirits. There are no epidemiological data available on its potential carcinogenicity in humans although there is sufficient evidence for the carcinogenicity of ethyl carbamate and its metabolites vinyl carbamate and vinyl carbamate epoxide in experimental animals (IARC, 2007).
Alcohol increases the risk of cancers of the oral cavity and pharynx, oesophagus (gullet), larynx (upper airway), and to a lesser extent, cancers of the colon and rectum in a linear relationship.

Alcohol increases the risk of female breast cancer in a dose dependent manner.

Gastrointestinal tract

The risk of these cancers increases linearly from zero consumption (Figure 1). Strong evidence for this finding is provided by the meta-analysis of Corrao et al. (2004), for cancers of the oral cavity and pharynx, oesophagus, larynx, colon and rectum respectively. For all the cancers the direct trends in risks were found starting from the lowest dose of alcohol considered (25g/day; corresponding to about two drinks per day). The relative risk functions obtained by fitting meta-regression models showed the absence of a threshold effect, meaning that from 0 g/day of alcohol consumption, the risk starts to increase for cancers of the oral cavity and pharynx, oesophagus, larynx, colon and rectum (Corrao et al., 2004).

According to an IARC Monographs Working Group (IARC, 2007), a daily consumption of around 50 g of ethanol compared with the risk of non-drinkers:

- Increases the risk of cancers of the upper digestive track two to three times (twofold increase in risk for cancer of the larynx and oesophagus, and threefold increase in risk for cancers of the oral cavity and pharynx). Moreover, the effects of drinking and smoking seem to be multiplicative.
- Increases the relative risk of about 1.4 for colon and rectal cancer.

Breast

The Collaborative Group on Hormonal Factors in Breast Cancer (2002) found strong evidence that alcohol increases the risk of female breast cancer in a dose dependent manner at all ages. The cumulative risk by age 80 years increased from 88 per 1000 non-drinking women to 133 per 1000 women who, at baseline, drank 6 drinks (60g) a day. Daily consumption of about 50g of alcohol is associated with a relative risk of about 1.5 (95% confidence interval 1.3–1.6), compared with that in non-drinkers, and even regular consumption of about 18g of alcohol per day is statistically significantly associated with an increased risk of breast cancer. Each additional 10g ethanol/day is associated with risk higher by 10% (Key et al., 2006). The risk for breast cancer is affected by a variety of hormonal and reproductive factors, and the effect of consumption of alcoholic beverages on the risk for breast cancer does not vary significantly by child-bearing patterns, menopausal status, use of oral contraceptives or hormone replacement therapy or having first-degree relatives with a history of breast cancer (IARC, 2007).
Alcohol and the individual risk of Cancer

Liver

The effect of alcohol consumption on the risk for liver cancer is difficult to quantify because cirrhosis and other liver diseases often occur before the cancer becomes manifest and patients with these disorders generally reduce their alcohol intake. However, chronic infections with hepatitis viruses B and C are the major causes of liver cancer and the increased risk associated with alcoholic beverage intake has been found consistently among individuals infected with hepatitis viruses as well as among uninfected individuals (IARC, 2007). Alcohol is a cause of cirrhosis that predisposes to liver cancer, but the factors that determine why some people are susceptible to cirrhosis are not known (WCRF, 2007).

Other cancers

– **Kidney cancer:** There is consistent evidence, of no increase in risk for renal-cell cancer with increasing alcohol consumption. In several studies, increasing alcohol intake was associated with a significantly lower risk for renal-cell cancer.

– **Non-Hodgkin lymphoma:** Two prospective cohort studies and several large case–control studies showed an inverse association or no association between alcohol consumption and non-Hodgkin lymphoma; most studies showed a lower risk in drinkers than in non-drinkers.

– **Lung cancer:** In most populations, there is a strong correlation between the use of tobacco and the consumption of alcohol. Many studies have reported an increased risk for lung cancer associated with alcohol drinking, but it is not generally possible to exclude residual confounding by smoking, by far the most important cause of lung cancer. The findings from some of the studies that presented separate data on the risk for lung cancer in non-smokers suggest an increased risk with consumption of alcoholic beverages, but others do not. Therefore, lung cancer is not usually included as an alcohol-attributable disease because no biological pathway has yet been identified, and because the higher incidence of lung cancer in drinkers may be due to smoking.

– **Stomach cancer:** Epidemiological studies show inconsistent results for lung cancer, stomach cancer and others.

With alcohol there are no increases in risk for kidney cancer and non-Hodgkin lymphoma, and inconsistent results for lung cancer, stomach cancer and others.

– **Other sites:** For cancers of the pancreas, cervix, endometrium, ovary, vulva, vagina, male breast, urinary bladder, prostate, testis, brain and thyroid, and for skin melanoma, Hodgkin disease, leukaemias and multiple myeloma, the evidence for an association between consumption of alcoholic beverages and risk for the site was generally sparse and/or inconsistent. Although for some sites, e.g. cervix and prostate, some studies of special populations showed positive associations, bias and confounding could not be excluded.
90-95% of cancers have their roots in the environment and lifestyle, as for example, in alcohol consumption (Anand et al., 2008). Therefore, modification of lifestyle by introducing preventive actions, such as reduced consumption of alcohol, can lead to a lower probability of developing cancers.

A few epidemiological studies have examined the effect of stopping drinking on the risk of malignant neoplasms, and the majority of these studies have found a consistent reduction in risk in developing cancers, at least in those of the oral cavity, pharynx, larynx and oesophagus (Rehm et al., 2007).

The reductions in risks are not immediate and it can take decades to decrease to the same levels of never drinkers. Malignant neoplasms can take years to develop, and most people may not stop drinking alcohol in a harmful way until the symptoms have already appeared (Rehm et al., 2007). Therefore, from a public health perspective one of the essentials for cancer prevention should be reduced hazardous and harmful use of alcohol.

The temporal sequence and strength of the decrease of cancer after alcohol cessation vary according to the type of cancer.

Figure 2: Odds ratio following alcohol cessation on oesophageal (left column) and head and neck (right column) cancer (cubic regression). From Rehm et al. (2007).
Cancer in perspective

Alcohol is an important modifiable risk factor for cancer, and, although not consistently prominent in public debates on the health risks from alcohol, nevertheless, there are more than 50,000 deaths due to cancer in the European Union each year arising from alcohol use (Anderson & Baumberg 2006). Unlike most alcohol-related harms, cancers are also a particular risk for women, with 11,000 of the deaths being those of female Europeans dying from alcohol-attributed breast cancer every year. In both cases, alcohol-attributable cancer has a greater negative impact through death than disability, due to a combination of relatively higher age of death (and, therefore, fewer life-years lost) and relatively greater case fatality. Further, given that there is a linear dose-response relationship between alcohol use and the risk of alcohol-related cancers, any reductions in alcohol use bring benefit in terms of reduced risk.

Policy implications

Raising awareness through public education campaigns and consumer labelling

Although public education campaigns and consumer labelling do not by themselves lead to behavioural change, they nevertheless have an important role in imparting information about the health risks of alcohol, particularly for health risks, such as alcohol-related cancers, that are not commonly known. Consideration could be given to mounting public education campaigns that focus on alcohol-related cancers, and, perhaps particularly, breast cancer amongst women. Further, consumer warning labels on alcohol beverage containers and packaging could consider mentioning that alcohol increases the risk of cancer.

Effective alcohol policies will reduce the risk of alcohol-related cancer

Policies and interventions that are known to be effective in reducing alcohol-related harm in general will reduce the risk of alcohol-related cancers. These policies include, for example:

- higher taxes for higher alcohol beverages;
- reducing outlet density; and
- reducing trading hours;

Early identification and brief intervention programmes should mention cancer

Brief interventions are defined as advice provided in primary health care that involves a small number of education sessions and psychosocial counselling. When delivering the brief intervention framework, health care providers could mention the risk of alcohol-related cancers as part of the advice to reduce alcohol consumption.

Screening programmes for alcohol-related cancers should mention alcohol

There are effective screening programmes for two important alcohol-related cancers, breast cancer and colorectal cancers. As part of the screening programmes, cancer risk in relation to alcohol could be mentioned.
References


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