Alcohol

Introduction

Alcohol (ethanol) is generally consumed as beer (2.5-6 vol% alcohol), wine (about 12 %) or spirits (about 40 %). The energy liberated upon oxidation of alcohol in the organism corresponds to 29 kJ per g. At high alcohol consumption the energy efficiency appears to be lower, with relatively higher heat dissipation than with the other energy yielding nutrients (Lieber 1984). Alcohol is efficiently absorbed through passive diffusion in the intestine and is distributed in the total water compartment of the body. Most of it is oxidized in the body but a small amount (5-10 %) is lost with expired air and in the urine.

In the Nordic countries, alcohol accounts for about 3-6 % of energy intake in adults. The intake is very unevenly distributed and about half the population is responsible for most of the consumption.

Nutritional aspects

Replacing part of the food intake with alcoholic beverages may impair the quality of the diet. In particular the consumption of milk products, fruits and vegetables appears to decrease when the intake of alcohol is increased. Some exceptions to this pattern may be noted. A Danish study showed a strong association between fruit and vegetable consumption and wine intake (Tjonneland et al 1999). A high alcohol consumption may result in impaired absorption of nutrients and increased loss in the urine. From a nutritional point of view it is therefore reasonable to recommend moderation in alcohol intake. Among high alcohol consumers,

nutritional status is always affected (Lieber 1988). In particular, deficiencies in ascorbic acid, thiamine, magnesium, phosphorus, vitamin D and protein are frequent (Bøhmer et al 1994, Halvorsen et al 1983).

Alcohol and health

Alcohol is a toxic substance that affects all organs of the body. Both acute and chronic alcohol-induced damage contribute significantly to morbidity and mortality in the population. From a public health perspective it is important to bear in mind that overall consumption is a main determinant of the alcohol-related harm rates in the population (Nordström and Skog 2001). The negative health effects of alcohol are primarily determined by the total amount of alcohol to which the body is exposed. This means that alcohol damage may develop in individuals who have not been visibly drunk. It is likely that a daily consumption of 70 g alcohol per day will result in alcohol damage (Pequignot et al 1978).

Alcohol and cardiovascular disease

Alcohol has been associated with coronary heart disease (CHD), atrial fibrillation (AF), ischemic stroke (IS), hemorrhagic stroke (HS) and congestive heart failure (CHF).

Coronary heart disease

A meta-analysis and review comprising data from 84 prospective cohort studies or in total 3,159,720 study participants assessed association CHD risk among drinkers and non-drinkers (Ronksley et al 2011). The pooled adjusted RR for alcohol drinkers relative to non-drinkers were 0.71 (95% CI: 0.66-0.77) for incident CHD (29 studies) and 0.75 (95% CI: 0.68-0.81) for CHD mortality (31 studies). These results persisted after excluding former drinkers from the category of abstainers. In analyses exploring dose-response, categories of 2.5-14.9 g/day, 15-29.9 g/day and 30-60 g/day were associated with similar and statistically significant reduction in the relative risk of CHD relative to non-drinkers. The highest category (>60 g/day) were associated with a relative risk of 0.76 (95% CI: 0.52-1.09). Hence, there is evidence of a maximal upper range of intake for the cardioprotective effect, but no indication of a higher risk among the most heavily drinking individuals. In contrast, an earlier meta-analysis found that the association between alcohol and CHD risk was J-shaped, implying a minimum relative risk of 0.80 at 20 g/day, a significant protective effect up to 72 g/day and a significant increased risk at intakes above 89 g/day (Corrao et al 2004).

The impact of drinking pattern has been addressed in fewer studies, the majority of which find a non-beneficial or even harmful effect of a drinking pattern that involves drinking large amounts of alcohol per occasion (binging).

The finding that CHD risk is lower in light to moderate drinkers compared with non-drinkers is very consistent across study populations with different distributions of confounders and potential effect modifiers (Ronksley et al 2011). Due to the heterogeneity of the exposure in studies investigating the independent effects of drinking pattern, it is premature to make a firm conclusion of the exact measure of drinking pattern that most exactly captures the non-

beneficial effect. However, most evidence points towards that the significance of drinking pattern in line with the NNR 2004 recommendations (< 10 g/day for women and <20 g/day for men) is not detrimental. In conclusion, the current evidence is in accordance with NNR 2004.

Atrial fibrillation

In a meta-analysis and review comprising data from 5 case control studies and 9 prospective cohort studies (6 of which were hospital based, in total 138,020 participants) high alcohol intake was associated with increased risk of AF (29). In pooled analyses, the relative risk for the highest versus the lowest alcohol category was 1.51 (1.31, 1.74), but the definition of 'high' differed from study to study (Kodama et al 2011). In dose-response analyses, each 10 g/d increment was associated with an increased risk (RR=1.08, 95% CI: 1.05-1.10). Results of the meta-analysis indicate that the risk of AF is probably increased by heavy drinking, while the effect of light to moderate intake is more uncertain due to few high-quality studies. In conclusion, the current evidence is in accordance with the recommendations in NNR 2004.

Stroke

Two meta-analysis and reviews assessed association between alcohol intake and stroke (Ronksley et al 2011, Patra et al 2010), 16 on hemorrhagic stroke and 20 studies on ischemic stroke, in total 737,038 study participants. Results show that high alcohol intake is consistently associated with an increased risk of both hemorrhagic and ischemic stroke. With moderate intakes of up to 3 drinks/day, the results are inconsistent: moderate consumption seems to be protective for ischemic stroke, but neutral or slightly detrimental for hemorrhagic stroke.

In conclusion, the current evidence is in accordance with the recommendations in NNR 2004.

Congestive heart failure

A meta-analysis and review (Padilla et al 2010) included six prospective cohort studies with 164,479 study participants. Compared with never drinkers, the pooled RR of CHF were 1.16 (95% CI: 0.90-1.51) for former drinkers, 0.90 (95% CI: 0.83-0.98), 0.80 (95% CI: 0.73-0.88), 0.78 (95% CI: 0.65-0.95), and 0.77 (95% CI: 0.63-0.95) for current drinkers of 0.1-0.9, 1 to 7, 8 to 14 and >14 drinks/week (Padilla et al 2010). There was no heterogeneity in the findings between the 6 individual studies. Light to moderate drinking is not associated with increased CHF risk, or at best is associated with a lower risk.

In conclusion, the current evidence on this subject is in accordance with the recommendations in NNR 2004.

All-cause mortality

A meta-analysis and review of 34 prospective cohort studies reporting on mortality from Australia, China, Japan, Europe and USA published up to 2005 included 1,015,835 study participants (Di Castelnuovo et al 2006)). A J-shaped relationship between alcohol and total

mortality was found in adjusted analyses, in both men and women. Consumption of alcohol, up to 2-4 drinks per day in men and 1-2 drinks per day in women, was inversely associated with total mortality, maximum protection was 18% in women (99% CI: 13%-22%) and 17% in men (99% CI: 15%-19%). Higher intakes of alcohol were associated with increased mortality. Risk reductions were somewhat lower in analyses adjusting for age, socioeconomic status and dietary markers and were apparent up to 3 drinks for men and up to 2 drinks for women. The calculated reversion point (the dose of alcohol at which the protection against mortality was not statistically significant at the 99% confidence level) was 30 g/d in the adjusted model. Since the relative incidences of alcohol-related diseases and outcomes differ by age, the J-shaped association between alcohol and all-cause mortality also differs by age. The nadir (representing the alcohol intake at the lowest risk of mortality) is achieved at a lower intake in the younger ages. In a British study, the lowest mortality risk among women 16-34 years old and men 16-24 years old was observed among the non-drinkers (White et al 2002). Hence, a beneficial effect of alcohol is not observed among the young, where alcohol is directly associated with mortality.

Results from studies regarding the role of drinking pattern consistently imply an increased mortality risk associated with drinking large amounts of alcohol per session, binge drinking (Rehm et al 2010). Further, there is good evidence that the protective effect of alcohol on cardiovascular disease only occurs if the pattern of drinking is not binging (Rehm et al 2010). Hence, for the J-shaped association between alcohol intake and all-cause mortality depends upon the drinking pattern.

The association between alcohol and all-cause mortality is J-shaped; the nadir of the J reflects a relatively lower risk of coronary heart disease (CHD) among light to moderate drinkers compared with abstainers and the ascending leg of the J is reflecting an increased risk of alcohol-related diseases such as liver cirrhosis, pancreatitis, upper gastrointestinal cancers, cardiomyopathy, polyneuropathy and deaths from accidents and violence among excessive alcohol users. Since the association between alcohol and all-cause mortality thus represent the sum of the numerous disease and outcomes, there are related to alcohol, the shape and nadir of the risk curve depends upon the distribution of other variables such as age, relative incidences of diseases, the prevalence of drunk-driving etc. Hence, the association between alcohol and all-cause mortality does not have the same causal interpretation as associations between alcohol and singular endpoints.

In conclusion, light to moderate drinking is not associated with increased mortality risk, or is at best associated with a lower risk among middle-aged and older adults, who are not having episodes of heavy drinking. For young adults, abstaining totally would be associated with the lowest risk of mortality and binge drinking should be avoided in all age groups.

Alcohol and cardiovascular biomarkers

A comprehensive meta-analysis of intervention studies was made in 2011 (Brien et al 2011). This review is of high quality. By performing meta-analysis of such studies, it was found that alcohol significantly increased levels of high density lipoprotein, and adiponectin and

decreased level of fibrinogen. These favorable changes in the cardiovascular biomarkers provide indirect path physiological support for a protective effect of moderate alcohol use on coronary heart disease.

Alcohol and hypertension

There is convincing evidence that a high alcohol intake is associated with increasing blood pressure (McFadden et al 2005) and risk of hypertension (Taylor et al 2009). During the last few years, there has been some discussion as to whether a light to moderate intake is associated with a lower blood pressure and lower risk of hypertension, especially among women (Taylor et al 2009).

Alcohol, insulin and glucose

Reviews and meta-analyses are sparse on this area, but from single studies it is found that alcohol intake (1-2 drinks per day) is associated with reduced fasting insulin concentration, and improved insulin sensitivity (Davies et al 2002, Flanagan et al 2000, Kiechl et al 1996, Lazarus et al 1997, Paulson et al 2010). Further, fasting glucose levels was similar in non-drinkers and moderate alcohol drinkers in a prospective cohort study (Schooling et al 2009).

Alcohol and cancer

The evidence that intake of alcohol is related to several types of human cancers has increased since the mid-1990s. Alcohol (ethanol) is classified as a human carcinogen by the International Agency for Cancer Research (2010). The 2007 World Cancer Research Fund report includes an extensive systematic review of the available evidence on the association between alcohol intake and the development of cancer (WCRF 2007). Evidence was graded as "sufficient" for an increased risk of cancer of the mouth, pharynx, larynx, esophagus and colorectal cancer among men, and breast cancer among women. There was "probable" evidence for an association between alcohol intake and the risk of liver cancer and colorectal cancer among women. Several subsequent meta-analyses and reviews have been published. For the cancers with sufficient evidence in the WCRF report (WCRF 2007), new studies have supported the evidence of a relation between intake and cancer risk (Hamajima et al 2002, Suzuki et al 2008, Singletary et al 2001, Key et al 2006, Tramacere et al 2010, Purdue et al 2009, Chen et al 2009, Moskal et al 2007, Cho et al 2004, Mizoue et al 2008). This is shown for cancers of the upper aerodigestive tract and colorectal cancer and for breast cancer among women.

The WCRF review concluded that a substantial effect on risk was unlikely with regard to renal cell cancer. A meta analysis by Song et al. (2012) including 20 case-control studies, 3 cohort studies and a pooled analysis of cohort studies reported an inverse association with the greatest reduction at the moderate level of intake, but suggesting the evidence that drinking >15g per day does not confer additional benefit for prevention in renal cell cancer risk.

Other cancers

A meta-analysis by Tramacere from 2010 (Tramacere et al 2010) indicated an increased risk between heavy alcohol intake (≥ 3 drinks/day) and the risk of pancreatic cancer. There was no association between moderate drinking and pancreatic cancer risk. However, since smoking is a strong risk factor for pancreatic cancer, residual confounding is a potential problem in these studies. This could also be the case in the studies between alcohol intake and lung cancer, where a suggestive increased risk have been shown (Chao 2007). No strong association was shown for alcohol intake and the risk of ovarian, endometrial or non-Hodgkin lymphoma (Genkinger et al 2006, Turati et al 2010, Morton et al 2005). A suggested possible protective effect on lymphoma risk might differ by lymphoma type.

There is some evidence suggesting that alcohol increases the risk of liver cancer through alcohol-associated fibrosis and hepatitis (La 2007, WCRF 2007). Liver cirrhosis was found to be present among 80% of patients with liver cancer (McKillop et al 2005).

In a review on alcohol consumption and prostate cancer (Rizos et al 2010) it was concluded that a daily consumption up to about 3 drinks per day does not appear to influence prostate cancer risk, while heavy consumption of 7 or more drinks per day may be associated with an increased risk. However, the data on high exposure were limited to only one prospective study and 4 case-control studies in this review.

In a meta-analysis on alcohol intake and bladder cancer the overall estimate showed no association (Mao et al 2010). Sub-analysis did show a relation between beer and wine intake and a reduced risk of bladder cancer in a dose-response manner, which should be explored further in other studies.

Conclusion: The overall evidence between alcohol intake and cancer does not show any “safe limit” of intake. This is especially true for breast cancer, where even very moderate intake has been shown to increase the risk (Allen et al 2009). The effect is from ethanol, irrespective the type of drink (WCRF 2007). The current evidence on the relation between alcohol and cancer risk is in accordance with the recommendations in NNR 2004.

Weight control

Results from a review including 31 publications with 13 prospective cohort studies and 4 clinical trials, did not show any consistent associations between alcohol intake and weight gain (Sayon-Orea 2011(, although higher levels of consumption (>2-3 drinks/day) were associated with weight gain is some studies. The type of beverage seems to be of importance with a lower weight gain observed for wine compared to beer and spirits. Only four prospective studies reported on the relation between alcohol intake and waist circumference or waist hip ratio. The findings were inconsistent, with both positive, negative and no associations.

Conclusion: The effect of alcohol on weight gain and waist circumference is not clear from the current evidence and no final conclusion could be drawn.

Prenatal alcohol exposure

Alcohol may affect the developing fetus in a dose dependent manner. Alcohol is teratogenenic and may give rise to Fetal Alcohol Syndrome (FAS) characterized by craniocephal abnormalities, physical and mental retardation, cardiac and joint abnormalities (Ornoy et al 2010). These effects are mainly seen with an alcohol intake above 24-48 grams/day.
In a systematic review the effects of low to moderate prenatal alcohol exposure were evaluated (Henderson et al 2007). At low to moderate levels of consumption, no consistently significant effects of alcohol on any of the outcomes considered were found, including miscarriage, stillbirth, intrauterine growth restriction, prematurity, birth weight, small for gestational age at birth and birth defects were shown in this review. However, weaknesses in the evidence preclude the conclusion that drinking at moderate levels during pregnancy is safe.

Alcohol intake during lactation

Although the effect of alcohol consumption for the infant during lactation has not been established, some studies (Little et al 1989) but not all Little and co-workers (2002) have suggested impaired development of infants whose mothers consumed alcohol when lactating. Reduced milk production (Mennella 1998), reduced milk intake (Mennella 2001) and sleep disturbances in the child (Mennella and Garcia-Gomez 2001) have been described. These effects are transient and compensated by the child within 24 hours if the mother does not continue to drink during that time. No medical consequences have been seen in the child if a lactating mother occasionally drinks small amounts of alcohol (Giglia and Binns 2006). Mothers in Sweden are advised that there are no positive effects of alcohol intake while breastfeeding, but also that occasional intake of small amounts (not exceeding 1-2 small glasses of wine 1-2 times per week) is not harmful to the child. In Norway lactating mothers are recommended to abstain completely from alcohol until the child is at least six weeks old. If occasional use occurs later in lactation, it is important to limit the amount. In Denmark lactating mothers are advised to be cautious with alcohol. In Finland it is generally considered that occasional, moderate alcohol use is not a barrier to breastfeeding. In Iceland women who are breastfeeding are advised to avoid alcohol.

Recommendation

Alcohol consumption is associated with both negative and positive health effects and affects diet quality. The evidence shows that regular, moderate alcohol consumption may confer cardioprotective effects among middle-aged and older subjects, whereas alcohol consumption among young adults is detrimental. For most cancers, there is convincing evidence that alcohol consumption increases the risk and it not possible to set any "safe limit" of intake. This is especially true for breast cancer, where even very moderate intake has been shown to increase the risk. Light to moderate regular alcohol consumption is not associated with increased mortality risk among middle-aged and older adults. Among young adults, alcohol consumption is associated with increased mortality.

Based on the overall evidence, it is recommended to limit alcohol intake. Based on estimates of the maximal mortality risk reduction associated with moderate alcohol consumption (16, 17), the intake should not exceed 10 g (approximately 1 unit *) per day for women and 20 g (approximately 2 units *) per day for men. In relation to energy intake, the consumption of alcohol should not exceed 5 energy percent in adults.

Pregnant women, children and adolescents are recommended to abstain from alcohol. Lactating women should also have a limited intake.

* 1 unit is defined as 12 g alcohol (41) corresponding to the alcohol content in one bottle of beer (330 ml), one glass of wine (120 ml) or one glass of spirits (40 ml). The definition of a unit may differ in different countries from approximately 8 g to 12 g (17).

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