Many reports show a 20% decrease in the risk of coronary disease in people taking small amounts of alcohol (5-14 drinks per week), i.e. less than 30 g alcohol per day for men and 15 g alcohol per day for women. On the other hand, diabetes mellitus is associated with the highest rate and earlier development of atherosclerotic changes as compared with the general population, diabetes mellitus being one of the risk factors for coronary disease. Alcohol has an antiatherogenic effect, the possible mechanisms implying alcohol metabolism into acetaldehyde that inhibits the formation of glycosylation endproducts and lipoprotein oxidation, reduces platelet aggregation, and influences vascular relaxation depending on the endothelium mediated by the NO-cyclic guanosine 5-monophosphate system. Thus, moderate alcohol consumption in diabetics does not interfere with normotriglyceridemia if taken at meals. The recommended alcohol intake is 1-2 drinks daily or 5-14 drinks weekly.

Should alcohol intake be recommended in diabetic individuals, and if so, when and in what amounts?

Some Characteristics of Ethanol

Ethyl alcohol (C₂H₅OH) has wide usage, such as a disinfectant, in industry, in alcohol drinks and in household. Various alcohol drinks contain different concentrations of ethanol, e.g., beer 2%-6%, wine 10%-20%, and strong drinks up to 50%. Medical and cosmetic products contain ethanol in concentrations of 0.3% to 68%.
Alcohol is a small molecule of 46 daltons, small volume of distribution (0.6 l/kg), and boiling point at 78 °C. It is soluble in water and lipids.

Lethal dose for adults is 5-6 g/kg body mass, or 300-400 ml of 100% ethanol, which is about 1L of 30% strong drink taken within one hour. The highest concentration in air is 100 ppm.

Alcohol cannot be eliminated from the body but has to undergo oxidation in the liver. Healthy people can metabolize more than 160-180 g ethanol per day.

Drinking 30 mL of whisky, 100 mL of wine or 250 mL of beer results in body intake of 10 g alcohol.

Energy value of 1g ethanol is 7 kcal. Drinks contain about 70-100 kcal from ethanol and other carbohydrates. So, 8-10 alcohol drinks per day provide more than 1000 kcal, however, the components such as vitamins, minerals and proteins are then lacking (2,3).

METABOLISM OF ETHANOL

Twenty percent of the ethanol consumed per os is absorbed in the stomach, and 80% in the small intestine, the absorption being very fast, i.e. 80%-90% in 30-60 minutes. Many factors can influence the absorption, e.g., concentration (best absorption at a concentration of 20%), volume and characteristics of alcohol drinks, motility of the stomach and small intestine (attenuated in the elderly), fasting drink intake, concomitantly of some medicaments, liver function, individual variation, and time lapse of drink consumption. Depending on these conditions, the absorption can be prolonged by up to 2-6 h.

Three enzyme systems are involved in the hepatic oxidation of ethanol to acetaldehyde: alcohol dehydrogenase (ADH), microsomal system of oxidation (MEOS), and catalase. ADH system is most important in the condition of low blood and tissue concentration of ethanol, and is responsible for 80%-85% of oxidation.

ADH turns ethanol into acetaldehyde in the cytosol. Acetaldehyde is a highly reactive and toxic compound that can cause membrane injury in the cytosol and mitochondria, and thus lead to cell necrosis. Therefore, acetaldehyde metabolizing to acetate is of utmost importance. Acetaldehyde oxidation to acetate occurs through acetyl-CoA, primarily by the action of aldehyde dehydrogenase (ALDH) in hepatocyte mitochondria.

The function of ALDH may decline, which can result in the accumulation of acetaldehyde in the liver and circulation, manifested by the symptoms of flushing, tachycardia and circulatory collapse.

Alcohol conversion to acetaldehyde and then to acetyl-CoA is accompanied by the release of hydrogen, its acceptor being NAD (nicotine adenine dinucleotide). Hydrogen changes fatty acids as fuel, which results in the accumulation of fatty acid and potential reduction in fatty acid oxidation. All these steps lead to the accumulation of triglycerides in the liver and an increased synthesis of lipoproteins. The increased concentration of hydrogen acceptors (NADH) has some consequences.

The redox potential of hepatocytes implies changes with inhibition of protein synthesis and increased lipid peroxidation. NADH provides hydrogen needed for pyruvate conversion to lactate, which increases the blood concentration of lactates and urates after alcohol consumption. This mechanism can explain the episodes of gout and hypoglycemia after alcohol ingestion.

The MEOS system is responsible for the metabolism of 10%-15% of alcohol. The critical component of MEOS is the cytochrome P450 (CPY2E1) enzyme that catalyzes not only ethanol oxidation but also many drugs such as paracetamol and halothane. This explains the higher toxicity of customary percentage of these drugs in alcoholics. Chronic consumption of alcohol increases the activity of CPY2E1 enzyme 5- to 10-fold, resulting in accelerated elimination of ethanol in chronic alcoholics. In case of fasting alcohol intake, a high concentration of ethanol will reach liver with the blood and alcohol metabolism will prevail in the first passage through the liver. This in turn will result in an increased concentration of ethanol in the blood. The same amount of alcohol taken postprandially will slowly pass through the liver, thus allowing for the metabolism of ethanol to be completed by the first passage through the liver and resulting in a lower concentration of ethanol in the blood.

Glucose deficit entails higher concentration of NADH, a product of ethanol oxidation. This in turn results in reduced metabolism (pyruvate → lactate and oxalacetate → malate). The increased lactate production leads to lactic acidosis. A decreased concentration of oxalacetate limits gluconeogenesis and favors development of ketoacidosis.
CONSEQUENCES OF ALCOHOL DRINKING

The consequences of alcohol drinking do not only depend on the volume and frequency of alcohol intake but also on the individual features such as sex, age, nutritional status, genetic predisposition, and presence of other diseases. The relations between alcohol drink volume and its consequences are not simple, and there is no clear border between safe and risk alcohol consumption. The relative risk of liver cirrhosis grows exponentially with daily volume of alcohol intake. The relation between the risk of coronary disease and alcohol intake has a configuration of U letter, i.e. there is a proportionate daily intake of alcohol which diminishes the onset of plaques in coronary arteries.

ETHANOL EFFECTS ON BODY SYSTEMS

Central nervous system

Alcohol acts as a depressor of the central nervous system (CNS) and has effects similar to those of anesthetics. Passing through lipid cell membranes of the CNS alcohol compromises normal relationship between lipid cell membranes and functional proteins (receptors, enzymes). Among systems that can be attacked by alcohol, implying neuron function impairment, are the systems of neurotransmitters such as norepinephrine, dopamine, serotonin and enkephalin. CNS can adapt to these effects and develop tolerance. Except for its modifying effects on the psychologic, intellectual and naturopathic features, chronic alcohol abuse also has other effects such as CNS lesions. The pathogenic effect of alcohol also involves other body systems and organs.

Gastrointestinal system

Oral cavity: periodontitis and caries as well as carcinoma of the tongue, ephipharynx and larynx are more common in alcoholics than in nonalcoholics.

Esophagus: inflammation of esophageal mucosa, lower sphincter defects; fivefold prevalence of carcinoma recorded in nonalcoholics, esophageal varices due to stasis in the portal vein system.

Stomach and intestine: gastritis and damage of intestinal mucosa are the most common gastrointestinal complications of alcoholism characterized by vomitus matutinus (morning nausea and vomiting).

Liver cirrhosis: it is a common and severe complication of chronic alcoholism, with an incidence of 10%-15% (4). The prevalence of liver carcinoma is also higher in alcoholics. Besides liver cirrhosis, alcoholic pancreatitis is a typical complication of alcoholism.

Cardiovascular complications

Ethanol in low doses induces peripheral vasodilatation, however, daily intake of a greater volume of alcohol is a cause of hypertension. Alcohol induces congestive cardiomyopathy characterized by hypocontractility of the myocardium, arrhythmias and dilatation of all four cardiac cavities.

Pulmonary manifestations

Hypoxia is common in patients with cirrhosis. In case of normal physical status and radiology finding, it is caused by ventilation-perfusion disbalance and intrapulmonary arteriovenous shunt. Tuberculosis is more common in alcoholics.

Muscular disease

Acute intake of a high volume of alcohol may in chronic alcoholic lead to acute muscular damage with injuries ranging from a mild and transitory increase in muscle enzymes to rhabdomyolysis with myoglobulinuria. Chronic alcoholism leads to progressive muscle atrophy and weakness, especially of proximal leg muscles, in association with peripheral neuropathy.

Endocrine diseases

Alcohol decreases erectile capacity and leads to testicular atrophy. In women it causes amenorrhea, atrophy of ovaries, loss of corpora lutea with infertility and spontaneous abortions. Sustained alcohol abuse in pregnancy may induce fetal alcohol syndrome.
Alcoholics have low gonadal hormones in plasma with hyperestrogenism, which progresses to cutaneous vascular changes and gynecomastia. Direct effects of alcohol on ACTH secretion can induce development of pseudo-Cushing’s syndrome that is clinically identical to Cushing’s syndrome. The diagnosis is based on regression of the disease signs after a period of alcohol abstinence.

Hypoglycemia is a frequent and potentially fatal disorder induced by poor nutrition in chronic alcoholics with deficient vitamins and loss of glycogen reserve.

ALCOHOL AND CORONARY DISEASE

Many reports show a decrease in the risk of coronary disease by 20% in people who drink alcohol in small volume (5-14 drinks per week), i.e. less than 30 g alcohol per day for men and 15 g alcohol per day for women (5). It points to a conclusion that the risk of death is higher in abstinents than in people with moderate alcohol intake. The effect of alcohol is antiatherogenic, and the possible mechanisms are alcohol metabolizing to acetaldehyde, which inhibits the production of glycosylation endproducts and oxidation of lipoproteins, diminishes platelet aggregation, and influences relaxation of blood vessels dependent on endothelium mediated by the NO-cyclic guanosine 5-monophosphate system.

Red wine contains polyphenols that exert an antioxidative effect and are supposed to diminish oxidation of LDL granules and their atherogenic effect (6,7). There are reports on a higher protective effect of white wine (8) and beer (9) when taken in moderate volume, however, all alcohol drinks have some protective effect.

ALCOHOL AND DIABETES MELLITUS

Reports consistently suggest that the acute effects of alcohol induce a state of insulin resistance following oral and/or intravenous glucose load. Contrary to the acute alcohol studies, there is a large body of epidemiologic evidence from cross-sectional studies which suggest that longterm exposure to alcohol is associated with an improvement in insulin sensitivity. There is a nonlinear relation between alcohol intake and the risk of type 2 diabetes. Results from the ARIC study point to a relationship between alcohol intake and risk of type 2 DM in 12,261 middle-aged subjects of both sexes. Men who drank more than 14 alcohol drinks weekly had a 82% higher chance to develop type 2 DM than men who did not drink alcohol habitually (10). Serum insulin and HDL cholesterol explained a low proportion (20%) of the reduction in the risk of type 2 diabetes associated with moderate drinking (11). Light to moderate alcoholic beverage consumption may be associated with a lower risk of type 2 DM among women aged 25 to 42, although this benefit may not persist at higher levels (12). Furthermore, a substantial number of prospective studies point to a protective role of light to moderate chronic alcohol intake against the development of diabetes as well as a protective effect of regular mild to moderate drinking against coronary artery disease in type 2 diabetic subjects (13).

Three prospective cohort studies investigated the association between alcohol consumption and risk of coronary heart disease among diabetics. The results indicated significant risk reductions, ranging from 34% to 79%, associated with light to moderate alcohol intake. The potential mechanisms include increased HDL cholesterol, decreased coagulation, and increased insulin sensitivity. Alcohol intake is also associated with certain risks among diabetics. Consumption of excessive alcohol amounts within a short period of time is associated with hypoglycemia, lactic acidosis and ketoacidosis. Chronic alcohol intake is associated with higher risks of carcinoma, hypertension, liver cirrhosis and symptomatic neuropathy (5,14,15).

However, for moderate alcohol consumption, the benefits would likely outweigh the risks (16). Moderate alcohol consumption is associated with a lower risk of coronary heart disease in men with type 2 diabetes (17-19). These results of the Physician Health Study in 87,938 subjects including 2790 diabetics free from myocardial infarction, cancer or liver disease suggest that light to moderate alcohol consumption is associated with similar risk reductions in coronary heart disease among diabetic and nondiabetic men (19).

Moderate alcohol consumption is associated with a reduced risk of coronary heart disease in women with type 2 diabetes and should not be routinely discouraged. Compared to diabetic women reporting no alcohol intake, the adjusted relative risk of nonfatal or fatal coronary heart disease for diabetic women
reporting a daily intake of 0.1 to 4.9 g alcohol (<0.5 drinks) or ≥5 g (≥0.5 drinks) was 0.72 and 0.45, respectively (18).

**CONCLUSION**

Many studies report on a decrease of mortality in the population with moderate alcohol intake, especially in those at a higher risk of coronary disease (14). The effect of light to moderate alcohol consumption in diabetic patients may be reduction in the risk of coronary heart disease and myocardial infarction (17-20). Whereas diabetes is a risk factor for coronary heart disease, moderate alcohol consumption does not interfere with the state of normotriglyceridemia if taken with a mixed meal. Recommendations for alcohol intake are 1-2 drinks daily or 5-14 drinks weekly, but not 3-5 drinks daily. Diabetics must be cautious not to take a large amount of alcohol within a short period of time, as it may lead to hypoglycemia, lactic acidosis and ketoacidosis. They should be aware of the fact that chronic alcohol intake is associated with higher risks of carcinoma, hypertension, liver cirrhosis and symptomatic neuropathy. They should also pay due attention to the energy part of alcohol in their diet, especially in obese patients and those on sulfonylureas.

If diabetic individuals take one unit of alcohol drink as part of a mixed meal, they have reduced the intake of some other group of food (bread, fats, or meat). Usually one unit of fat is replaced by one unit of alcohol. It is not the same whether the patient is on an 800, 1300 or 1800 kcal diet. We do not recommend moderate alcohol intake for obese patients on reduction diet.

It is not the same whether it is wine or beer. Beer and spirit contain alcohol and sugar, therefore wine without sugar is preferred (21).

Recommendations for diabetic patients should be tailored individually, depending on the patient’s characteristics, readiness for cooperation and compliance, comorbidity, therapy, and specific conditions (e.g., pregnancy, exercise).
REFERENCES


