ALCOHOL AND METHABOLIC SYNDROME – RISK OR BENEFITS, DOES IT MATTER?

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Summary

Health aspects of alcohol have been debated for centuries. Many studies have demonstrated that moderate alcohol consumption promotes health. Metabolic syndrome, a constellation of central obesity, impaired glucose metabolism, dyslipidemia, and hypertension, is associated with subsequent development of type 2 diabetes and cardiovascular diseases. A protective effect of moderate alcohol consumption on the cardiovascular system has consistently been reported, but limited evidence has been produced on the association of alcohol with metabolic factors. The aim of this review was to ask to the question: should alcohol intake be recommended in patient with metabolic syndrome and if so, when and in what amounts.

Rezumat

Alcoholul şi sindromul metabolic – risk sau beneficiu, oare contează?

Influenţa alcoolului asupra sănătăţii este o discuţie ce durează mai multe secole. Multe studii au demonstrat că consumul moderat de alcool promovează sănătatea. Sindromul metabolic reprezintă o constelaţie de simptome, incluzând obezitatea centrală, dereglarea metabolismul glucidic, dislipidemia, hipertensiune arterială şi este asociat cu dezvoltarea ulterioara a diabetului zaharat de tip 2 şi a patologiei cardiovasculare. În mod constant a fost raportat un efect protector al consumului moderat de alcool asupra sistemului cardiovascular, dar există dovezi limitate privind influenţa alcoolului asupra factorilor metabolici. Scopul acestei lucrări a fost răspunderea la întrebare: dacă este necesar de recomandat consumul de alcool la pacienţi cu sindrom metabolic şi, dacă da, atunci când şi în ce cantităţi.

Introduction

Health aspects of alcohol have been debated for centuries. Alcoholic drinks have been used as restoratives, stimulants, appetizers, and even as analgesics for many of the body's aches. In ancient and medieval times, wine and beer were parts of everyday diet, because many places on earth lacked reliable sources of drinking water. Nowadays, they are mostly regarded as regular staples of modern day living and their consumption parallels the increase in welfare. During the last two decades the popularity of alcoholic drinks, especially wine, has received an extra boost because of an assumed beneficial effect on the cardiovascular system.

Metabolic syndrome, a constellation of central obesity, impaired glucose metabolism, dyslipidemia, and hypertension, is associated with subsequent development of type 2 diabetes and cardiovascular diseases (CVD) (1).

Many studies have demonstrated that moderate alcohol consumption promotes health. In recent decades, the association between alcohol intake and cardiovascular disease has received considerable attention. Most of the prospective epidemiological studies have consistently shown that light-to-moderate alcohol consumption (6–48 g/day) is associated with a lower risk of coronary artery diseases, stroke, myocardial infarction and hypertension compared to non-drinkers (2). For example, alcohol consumption of a certain amount and frequency prevents the development of diabetes mellitus (3), reduces the risk of coronary heart disease (4) and elevates high-density lipoprotein cholesterol and adiponectin levels (5). These healthy contributions of alcohol consumption appear equivalent to a reduction in the risk of developing metabolic syndrome. Improved insulin sensitivity by alcohol consumption (6), may be responsible for ameliorating metabolic syndrome, since insulin resistance is a key component of metabolic syndrome (7).

But alcohol consumption has also proven to be associated with liver disease, cardiomyopathy, trauma and injuries, the Wernicke-Korsakov syndrome and some forms of cancer. Heavy alcohol consumption and irregular (binge) drinking are associated with several adverse effects: fetal alcohol syndrome, liver cirrhosis, certain cancers, hypertriglyceridemia, hypertension, hemorrhagic stroke, obesity, alcohol intoxication and dependence (8).

Should alcohol intake be recommended in patient with metabolic syndrome, and if so, when and in what amounts?

Alcohol consumption and cardiovascular protection

Moderate alcohol consumption has been shown to be protective against cardiovascular disease and reduced incidence of morbidity and mortality from coronary heart disease in comparison with abstainers (9). This was first observed in observational studies comparing countries with regard to wine consumption and cardiac mortality (10). Despite a high intake of saturated fats, a significant lower mortality rate of coronary heart disease was observed in France compared with other Northern European countries, a phenomenon which became known as the French paradox (11). This paradox was initially explained by ingredients of the Mediterranean diet, which resulted in much attention to the potential favorable effect of wine. Most physicians and medical organizations, however, stayed critical and reserved towards the promotion of wine drinking, being aware of the other and darker side of the Janus head. Furthermore, later analyses and studies threw doubt on the superiority of red wine over other alcoholic drinks.

Mechanisms of action of alcohol as a protective factor against CVD

Alcohol consumption correlates with modification of several vascular and biochemical factors that have potential cardio protective benefits. Increase in high-density lipoprotein (HDL) cholesterol levels, decrease in platelet aggregation via inhibition of prostaglandin synthesis and changes in fibrinogen, tissue-plasminogen activator are thought to represent major mechanisms to reduce the risk of cardiovascular events.

Mechanisms by which alcohol may increase cardiovascular risk

Heavier alcohol consumption is associated with increased risk of myocardial infarction, arrhythmias and sudden death and binge drinking increases the risk of both hemorrhagic and ischemic stroke, possibly due to variable effects on blood pressure, bleeding tendency and dehydration. The hypertensive effect of regular alcohol drinking has been demonstrated in a number of randomized controlled trials (2). Alcohol is a well-documented cause of cardiomyopathy with a direct toxic effect on myocardial as well as skeletal muscle fibers, even in the absence of hypertension or thiamine deficiency. However, again recent population studies suggest that the incidence of heart failure is less frequent in regular drinkers (4,5).

Nevertheless, both positive and negative reported mechanisms have often been deduced from epidemiologic data, and are not real mechanisms. The actual relevance of inhibition of some enzymes and lipoprotein oxidation is indirect and often questioned. Further basic studies, able to define plausible mechanisms of action are warranted.

The role of the pattern of drinking

The pattern of drinking (defined as regular drinking versus binge) plays a role in the relationship between alcohol intake and cardiovascular risk. Experimental studies (12) suggest that drinking wine at meals provides maximal health effect, by prevention of the development of atheromatous lesions, while a binge pattern of drinking has been associated with higher risk of CVD (13). Phenols from the wine have great antioxidant effect, but need to remember about different toxic substances which used for conservation of wine in modern time. On the other hand, alcohol consumption of 10–30 g/day on 3–4 days/week appeared to be associated with the lowest risk of ischemic stroke when compared with abstention or other amount of alcohol intake. A regular small intake of alcohol, several days per week or even daily, is associated with more favorable outcomes than only occasional or once or twice weekly drinking (14). The subjects who mainly consumed wine had the lowest systolic pressure levels, those who mainly drank beer had the lowest diastolic pressures and those who preferred hard liquor had the highest systolic and diastolic pressures.

Light regular drinking, possibly during meals appears as the ideal behavior, while binge drinking is to be absolutely avoided. The compendium *Regimen Sanitatis Salernitani*, edited by Arnoldo da Villanova at the turn of the thirteenth century, which contains recommendations for a healthy life, says '. . . during meals drink wine happily, little but often . . .' and '. . . avoid harming the body never drinking between meals . . .' (15).

Non-alcoholic fatty liver disease and alcohol

Non-alcoholic fatty liver disease (NAFLD) is also a feature of metabolic syndrome in the liver (16). Recent studies have suggested an inverse association between light alcohol consumption and the likelihood of NAFLD. An analysis of a limited number of morbidly obese subjects suggested that light alcohol consumption reduced the likelihood of non-alcoholic steatohepatitis (17). Other studies performed on a large, general population have also revealed an inverse association between alcohol (18) or wine (19) consumption and unexplained hypertransaminasemia. Furthermore, a cross sectional study on a general population revealed an inverse association of light alcohol consumption with ultrasonographically determined fatty liver (20). These studies indicate that light to moderate alcohol consumption may have a beneficial effect on NAFLD.

Dunn et al. (19) reported a low prevalence of elevated ALT in modest wine drinkers and suggested that both alcohol and non-alcoholic components of wine are possibly associated with the low prevalence of metabolic syndrome features. The liver protective effects of modest wine drinking are supported by other studies (21, 22). Degrace et al. (23) showed that the triglyceride content of liver was significantly decreased by beer or ethanol-free beer treatment in mice. Alcoholic beverages certainly seem to have a beneficial effect on the liver, and the current observations suggest that frequent drinking enhances the effect. Further studies are required to elucidate the underlying mechanism(s) of the association between fatty liver and alcohol consumption, particularly in terms of frequent intake.

On the other hand, excessive alcohol consumption causes alcoholic liver injury, (24) and the molecular mechanisms of alcoholic fatty liver have been indicated (25). Liver cirrhosis and hepatitis may be very sensible for administration even a little amount of alcohol. Therefore, the beneficial effect of alcohol consumption on the liver has not been sufficiently studied and the details remain unclear. Whether the amount (light), frequency or both of alcohol consumption are responsible for the beneficial effect on NAFLD development is unknown, although the association of drinking pattern with the risk of disease progression has been reported in other metabolic syndrome-related diseases, such as type 2 diabetes (3) or coronary heart disease (4).

Alcohol and diabetes mellitus

On the one hand reports consistently suggest acute affects of alcohol to induce a state of insulin resistance following either an oral and/or intravenous glucose load. The paradox to these acute alcohol studies is a large body of epidemiological evidence which in cross sectional studies suggests that long-term exposure to alcohol is associated with an improvement in insulin sensitivity. Further, a substantial number of prospective studies point to a protective role for 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 subject.

Conclusion

Patterns of drinking alcohol were linked to beneficial and detrimental effects on coronary heart disease morbidity and mortality. Likewise, the clinical significance of alcohol's effect on metabolic syndrome requires further investigation. It is, however, clear that there is no compelling evidence at this time for health care professionals to recommend that nondrinkers begin consuming alcohol for medical reasons.

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MANIFESTAREA IDICELUI DE INSULINOREZISTENŢĂ (HOMA$_{IR}$) LA PACIENŢII HIPERTENSIVI ÎN FUNCŢIE DE OBEZITATE

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Summary
Manifestation of the insulinoresistance index (homa$_{ir}$) to the patients with hypertension depending on obesity

In the study were included 80 patients with arterial hypertension of I-II degree. Obesity was determined by calculating the body mass index and measuring the waist circumference. The insulinoresisantce index HOMA$_{IR}$ was established to the patients with arterial hypertension and obesity. Thus, the patients with arterial hypertension and obesity in comparison with those with arterial hypertension and non-obese had more frequently higher values of the insulinoresisance index HOMA$_{IR}$. To the obese patients with arterial hypertension not only the waist circumference, but the body mass index as well as shows a significant direct correlation with insulinoresisantce index HOMA$_{IR}$.

Rezumat

În studiu au fost incluşi 80 de pacienţi cu hipertensiune arterială gradul I-II. Obezitatea a fost apreciată prin calcularea indicelui masei corporale şi prin măsurarea circumferinţei taliei. Pacienţilor hipertensivi obezi li s-a apreciat indicele de insulinorezistenţă HOMA$_{IR}$. Astfel, pacienţii hipertensivi obezi în comparaţie cu cei hipertensivi nonobezi, au prezentat mai frecvent valori sporite ale indicelui de insulinorezistenţă HOMA$_{IR}$. La hipertensivii obezi nu numai circumferinţa taliei, dar şi indicele masei corporale manifestă o corelaţie semnificativă directă cu indicele de insulinorezistenţă HOMA$_{IR}$.

Actualitatea

Asocierea dintre obezitate şi hipertensiunea arterială (HTA) este bine documentată, dar natura exactă a acestei relaţii rămâne neclară. Actualmente, problema asocierii HTA cu obezitatea (în particular – obezitatea abdominală) se află în atenţia medicinei contemporane, cauză fiind invalidizarea precoce, majorarea riscului de dezvoltare a complicaţiilor cardiovasculare, mortalitate precoce [12]. Obezitate este şi un facror de risc (FR) pentru dezvoltarea diabetului zaharat (DZ) tip 2. Creşterea prevalenţei DZ tip 2 este strâns legată de răbufnirea obezităţii [1]. Circa 90% de diabetici prezintă exces ponderal sau obezitate. DZ tip 2 va atinge un nivel pandemic în 2030: de la 171 milioane de diabetici, în 2000, la 366 milioane. Aproximativ 197 de milioane de oameni prezintă toleranţă alterată la glucoză (TAG) [8]. Insulinorezistenţa (IR) este defectul biochimic primar ce face legătură între obezitate, maladiile cardiovasculare şi DZ tip 2 [10]. În favoarea rolului-cheie al IR în dezvoltarea sindromului metabolic (SM) şi al componentelor acestuia se prezintă rezultatele unui studiu populaţional, prezentat de E. Bonora, care indică prevalenţa IR la 58% pacienţi cu HTA, 84% - cu hipertrigliceridemie, 42% - cu hipercolesterolemie, 66% - cu TAG, 95% - cu SM [1]. Sindromul