REVIEW

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Alcohol and health: A drink a day won't keep the doctor away

ABSTRACT

We should not advise patients to start drinking alcohol for its alleged cardiovascular benefits. The negative effects of alcohol are well established, and the evidence of alcohol's benefits comes mainly from epidemiologic studies that were not well controlled for other influences, such as lifestyle factors. Moreover, we have other means of lowering cardiovascular risk that are safe and proven. Those who are healthy and whose drinking history shows little risk of developing alcohol dependency may continue to drink moderate amounts. Heavy drinkers should be advised to quit.

KEY POINTS

Some reports of coronary and mortality benefits of alcohol were based on the use of negligible amounts of alcoholic beverages, indicating that factors other than alcohol might have been involved. The most likely explanation is lifestyle factors associated with moderate drinking.

National guidelines recommend caution when applying the results of epidemiologic evidence of benefit from alcohol consumption to individual patients.

Alcohol consumption was shown to increase levels of high-density lipoprotein (HDL) cholesterol, but the HDL subtype that increased may not be one that is optimal for coronary protection.

Claims that wine is healthier than other alcoholic beverages have not been consistently corroborated.

There is no evidence that moderate drinking is detrimental in people who have shown that they are not prone to develop craving and slip into dependence.

A DRINK A DAY does not keep the doctor away. This is what we should be telling patients who ask if they should start having a drink every day because they heard it lowers the risk of heart attack or stroke.

So far the claims of health benefits from moderate drinking come from epidemiologic studies, some of which involved the use of so little alcohol that other factors (such as high income and healthy lifestyles) must have been responsible for the alleged health benefit. And the results of the studies have not been consistently corroborated.

In short, an evidence-based approach to health care does not support advising patients to start drinking for therapeutic purposes, especially when we already have effective, evidence-based ways to lower cardiovascular risk. Even if moderate drinking turns out to be beneficial in some people, the risk of developing alcohol abuse outweighs any potential cardiovascular benefits.

In this article, I examine the evidence to date for health benefits of moderate alcohol consumption and make recommendations based on this evidence.

EXPLAINING THE APPARENT BENEFITS OF ALCOHOL

Explanations for the apparent health benefits of moderate alcohol consumption have included elevation of high-density lipoprotein (HDL) cholesterol, the presence of congeners that might have antioxidant or antiplatelet properties, interactions with genetic factors, and age.

High-density lipoprotein

Three decades ago, my group reported that rats that were fed alcohol developed hyperlipemia

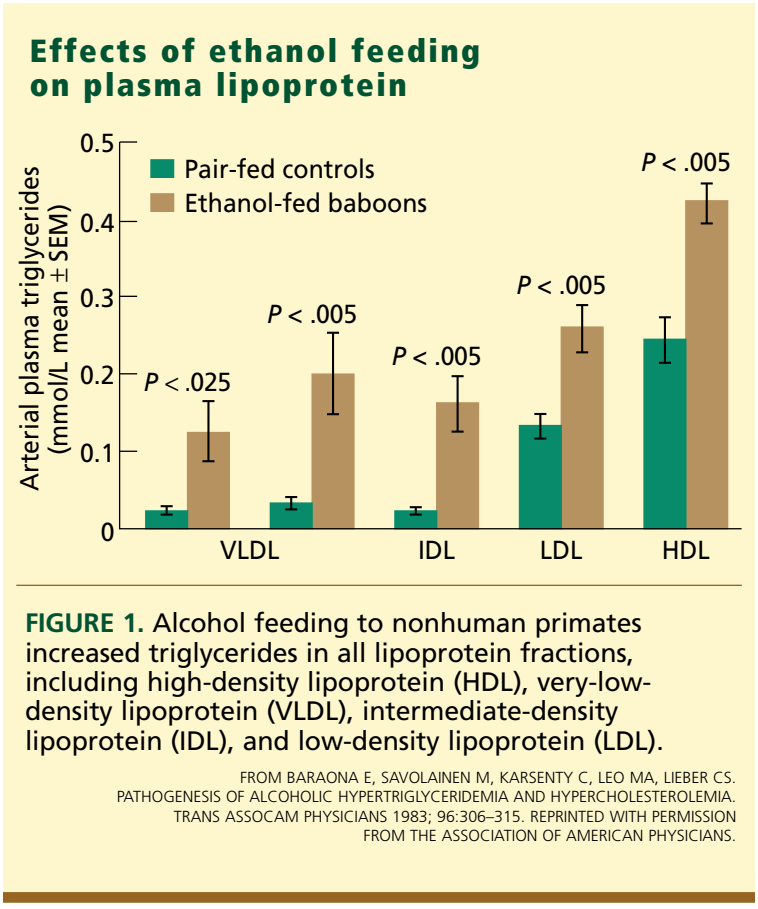

FIGURE 1. Alcohol feeding to nonhuman primates increased triglycerides in all lipoprotein fractions, including high-density lipoprotein (HDL), very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), and low-density lipoprotein (LDL).

FROM BARAONA E, SAVOLAINEN M, KARSENTY C, LEO MA, LIEBER CS. PATHOGENESIS OF ALCOHOLIC HYPERTRIGLYCERIDEMIA AND HYPERCHOLESTEROLEMIA. TRANS ASSOCAM PHYSICIANS 1983; 96:306–315. REPRINTED WITH PERMISSION FROM THE ASSOCIATION OF AMERICAN PHYSICIANS.

involving all lipoprotein classes.[1,2] In subsequent studies, we found that this also occurs in nonhuman primates,[3] with an effect predominant in HDL cholesterol (FIGURE 1). The rise in HDL levels was also confirmed in human studies,[4] and a number of studies indicated that HDL plays an important role in the transport of cholesterol and in preventing its adverse effects.[5]

When Klatsky et al[6] published the first large-scale epidemiologic study showing an inverse association between alcohol and coronary heart disease, the rise in HDL levels was invoked as a possible mechanism for the alcohol effect. Klatsky's study was followed by others that raised the hypothesis of a beneficial effect due to nonalcoholic components of the beverages rather than to alcohol itself. In that regard, the possible additional benefits of wine (especially red wine) received considerable attention. However, close scrutiny revealed weaknesses, and the challenge remains greater than ever to define in any given individual whether moderate drinking is beneficial or not in terms of cardiovascular and other diseases.

Not all HDLs are the same. When the role of HDL in cholesterol transport and its protective effect against atherosclerosis became apparent, it made sense to postulate that the apparent lower incidence of coronary heart disease in moderate drinkers might be due to the ethanol-induced elevation of HDL. However, although clinical laboratories generally report HDL as the combination of all fractions, HDL is in fact a heterogeneous group of lipoproteins with two major subclasses: the less dense HDL_2, epidemiologically associated with a lower incidence of coronary heart disease, and the more dense HDL_3, not clearly related to that disease one way or the other. Indeed, agents or conditions that are thought to affect coronary heart disease through HDL (such as exercise and female sex) have been shown to be associated with HDL_2, not HDL_3.

In one report, the increase in HDL after alcohol consumption apparently involved both HDL_2 and HDL_3, with a major change in HDL_2.[7] By contrast, Gaziano et al[8] reported that the inverse association of moderate alcohol intake with the risk of myocardial infarction is mediated in large part by increases in both HDL_2 and HDL_3.

Conflicting reports. However, these various observations were made in alcoholics with a relatively high intake of alcohol. It is now well recognized that large amounts of alcohol have adverse effects not only on the liver,[9,10] but also on virtually all tissues of the body, including the cardiovascular system,[11] and it is generally agreed that such high intakes are not associated with protection against coronary heart disease.[12] Furthermore, Haskell et al[13] reported that moderate doses of alcohol raised levels of HDL_3 but not HDL_2, and that upon abstention from moderate consumption, levels of HDL_3 decreased, but not levels of HDL_2. In addition, according to a study of Hartung et al,[14] consumption of alcohol in moderation seems to be associated with increased HDL cholesterol levels in inactive men but not in men who run or jog regularly.

Thus, in view of these conflicting studies, we must now reconsider some of the previously derived implications.

Congeners

Various effects of some congeners (components other than alcohol in alcoholic beverages), such as antioxidants or inhibitors of platelet aggregation, have been invoked to explain the apparent decrease in coronary complications with moderate drinking, and with the drinking of wine vs any other alcoholic beverage. These substances include polyphenols. However, according to Corder et al,[15] they are unlikely to account for the beneficial effects. Furthermore, extensive epidemiologic data indicate no substantial difference depending on the type of alcoholic beverages.[16–18]

One group of researchers described an ethanol-induced increase of surface-localized fibrinolytic activity in cultured human endothelial cells,[19] but it is noteworthy that experimental studies showed that neither ethanol nor red wine polyphenols either reduced mature atherosclerosis or changed the collagen content of plaques in apolipoprotein E-deficient mice.[20]

Genetic factors

We still don't know if wine is healthier than other alcohol

It was reported that, compared with homozygosity for the allele related to a fast rate of ethanol oxidation (gamma-1), homozygosity for the allele associated with a slow rate of oxidation (gamma-2) is accompanied by a lower risk of myocardial infarction. Furthermore, moderate drinkers who are homozygous for the slow-oxidizing allele were observed to have higher HDL levels and a substantially decreased risk of myocardial infarction.[21] More recently, however, it was found that the alcohol dehydrogenase genotype does not modify the effects of alcohol on HDL.[22] Further studies are needed to determine how genetic information can be applied to the management of patients who drink.

Age

Recent studies reported that light to moderate alcohol consumption is associated with a lower risk of dementia in people age 55 and older. The effect seemed to be independent of the source of alcohol.[23] Furthermore, Mukamal et al[24] showed consumption of one to six drinks weekly to be associated with a lower risk of dementia among older adults. However, the amount of alcohol involved was so low as to raise doubts that it could explain such benefits.

IS WINE 'HEALTHIER' THAN OTHER ALCOHOLIC BEVERAGES?

Many physicians and patients have heard reports of the "French paradox" or the "Mediterranean diet," in which red wine is supposed to offer significant health benefits. But the data to date do not show that wine is any healthier than any other type of alcoholic beverage.

In some studies, the amount of wine used (as little as one glass a month) was so small that we should doubt whether it could really have been responsible for the beneficial effects observed. The improved outcome could have been due to another factor, such as lifestyle.

For example, the Copenhagen heart study[25] found that wine drinkers had a lower relative risk for coronary artery disease, but also that they consumed twice as much fruit and vegetables.

Furthermore, Mortensen et al[26] showed that wine drinking is a general indicator of optimal social, cognitive, and personality development. Consequently, the association between drinking habits and social and psychological characteristics may explain, in large part, the apparent health benefits of wine. This is also the interpretation of some other investigators, including those of the National Institute of Alcohol Abuse and Alcoholism.[27]

WHAT IS 'MODERATE'?

What constitutes "moderate" drinking is debatable. According to the *Dietary Guidelines for Americans*[28] published every 5 years by the US Department of Agriculture and the US Department of Health and Human Services, moderate means a daily intake of one drink for women and two drinks for men. A drink was defined as one 5-ounce glass of wine, one 12-ounce can of beer, or 1.5 ounces of 80-proof distilled beverage, each of which contains about 14 g of alcohol.

The sex difference is justified by a corre-

sponding difference in susceptibility to the adverse effects of alcohol.[29] For instance, 40 g per day is an amount above which alcohol consumption becomes associated with a detectable increase in the incidence of cirrhosis of the liver in men, whereas in women the corresponding amount is only 20 g (or 1.5 drinks) per day.[30]

In a study of Japanese men,[31] consumption above a similarly low level was found to be associated with an increased risk of rectal cancer in beer drinkers and of lung cancer in whiskey drinkers.

How many drinks to reach the toxicity threshold?

The "threshold" for toxicity may depend on various factors—not only sex, but also congeners, drinking patterns, and genetic predisposition. Consequently, considerable variation exists in individual responses. At present, one's past capacity to keep consumption within socially and medically acceptable bounds is probably the most useful guide in deciding for that patient whether moderate drinking is appropriate or not. In patients for whom such evidence is lacking, we should not recommend even moderate drinking.

DRINKING FOR HEALTH: THE CASE AGAINST

There are a variety of reasons not to advocate moderate drinking for the purpose of reducing cardiovascular risk.

Not all studies are positive

Contrary to some of the positive studies, a 21-year follow-up of 5,766 Scottish men ages 35 to 64[32] found no cardiovascular or other evidence that alcohol consumption reduced mortality for light and moderate drinkers. Furthermore, higher levels of intake (three drinks per day) were associated with increased mortality in men with previous myocardial infarction.[33] Another study of alcohol use in middle-aged people came to similar conclusions.[34]

A meta-analysis of many of the alcohol-cardiovascular studies concluded that "the degree of protection from moderate doses of alcohol should be reconsidered, and further research investigating the effect of drinking patterns on the risk of coronary heart disease should be performed."[35]

Publication bias

In view of the objections raised above, one may wonder why the number of papers reporting positive effects of moderate drinking exceeds the negative ones. It is probable that publication bias led to overestimation of the reported effects.[35]

Confounding factors in abstainers, the 'control group'

In most studies, the effects of moderate alcohol consumption are compared with the events in total abstainers. However, in our society, people who totally abstain from alcohol often either are former heavy drinkers or do so because they have a disease in which drinking is discouraged, such as diabetes mellitus, and this fact might affect the significance of any such comparisons. Some studies have tried to take these factors into account, but the necessary adjustments are not easy to make.

Epidemiologic data not applicable to an individual's risk of alcohol dependency

Although Mukamal et al[36] observed that, in men, the consumption of alcohol at least 3 to 4 days per week was inversely associated with the risk of myocardial infarction, the authors also pointed out that national guidelines recommend caution when applying the results of epidemiologic studies of alcohol consumption to individual patients, since optimal care requires taking into account the many health effects of alcohol and the individual's susceptibility.

'Moderate' means no more than two drinks a day for men, one for women

Underage drinking and traffic accidents

At present, alcohol is the leading drug abused by US teens. Underage drinking accounts for 19.7% of US alcohol consumption. Seventy-eight percent of high school students have tried alcohol. Thirty percent admit to binge drinking at least once a month. The average age of the first drink is 14.[37] Encouraging moderate drinking in adults may unintentionally encourage drinking in those who are under the legal drinking age, which could increase the well-known associated risk of motor vehicle accidents.

Risk of dependence outweighs any alleged health benefit

There are no people in whom moderate drinking is clearly desirable as therapy. Even if moderate alcohol consumption turns out to be beneficial in some people, the risk of developing alcohol dependence would outweigh any potentially benefit in reducing heart disease.

ADVERSE CARDIOVASCULAR EFFECTS OF MODERATE DRINKING

Other reasons not to recommend moderate alcohol consumption relate to possible negative health effects. Although the cardiovascular benefits of moderate drinking are often cited, other studies have found negative effects of moderate drinking.

Stroke

It has been reported that light to moderate alcohol consumption reduces the overall risk of stroke, and specifically the risk of ischemic stroke.[38] However, since the benefit was apparent with as little as one drink per week,[39] it is highly unlikely that the effect was due to alcohol per se.

By contrast, a prospective study of the health effects of alcohol consumption in middle-aged and elderly men[40] found that light and moderate drinkers were actually at increased risk for fatal and nonfatal stroke.

Advocation of moderate drinking may lead to heavy drinking

Blood pressure

Drinking can raise blood pressure. Increased blood pressure has been observed with three drinks a day.[41] In a Kaiser-Permanente study,[42] women who drank two or fewer drinks per day had lower blood pressure than nondrinkers, whereas men and women who took three or more drinks per day had higher systolic pressures. In 1986, the same investigators reconfirmed the relationship of higher blood pressure to alcohol use in both men and women.[18] The vasopressor effect of ethanol may explain the association between long-term consumption of alcohol and hypertension. Furthermore, alcoholics have elevated levels of plasma homocysteine,[43] which has been linked to premature vascular disease.

Other cardiovascular effects

Orlando et al[44] reported that drinking either 2 or 5 ounces of ethanol aggravates exercise-induced angina pectoris and increases associated ischemic ST-segment depression.

TO DRINK (MODERATELY) OR NOT TO DRINK: MY RECOMMENDATIONS

In view of the lack of definitive evidence for beneficial effects of moderate drinking, Goldberg[45] proposed to settle this issue by assigning patients with cardiovascular disease to an alcohol treatment study. However, such a study would be ill advised, because of the risk that a former abstainer might develop alcohol dependence. The consequences for the individual and for society could be catastrophic.

Nearly 20 years ago, in a *New England Journal of Medicine* editorial,[46] I stated that whether a patient should start drinking must take special circumstances into account, and that still holds true today.

When intact judgment and motor coordination are essential, as in driving, temporary cessation of alcohol intake is of course indicated. Abstinence is also advisable under other special circumstances, such as pregnancy, since even moderate amounts of alcohol may adversely affect the fetus.

Advising abstainers to take up moderate drinking to protect their coronary arteries puts them at risk for alcohol dependency and its associated social and medical problems. However, there is no compelling reason to advise abstinence to our patients who are already drinking at a moderate level and have demonstrated the capacity to keep their drinking at an acceptable level.

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