



Review Article

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Regular Moderate Alcohol Consumption Reduces the Incidence of Cardiovascular Diseases: Review of Evidences and Plausible Mechanisms

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Abstract

Background: Inappropriate consumption of alcohol contributes to the occurrence of chronic diseases, social and economic burdens though moderate consumption is proven to be beneficial. Moderate alcohol consumption is generally considered to be in the range of 1-3 drinks/day.

Objective: The present narrative review was aimed to disclose the putative mechanisms of cardioprotective role of moderate alcohol consumption.

Design: Narrative review of published studies.

Evidence acquisition: This review was conducted by collecting clinical, epidemiological and translational research evidences from PubMed, Google scholar and Cochrane databases.

Results: Several clinical and epidemiological studies outlined that drinking regularly of moderate amount of alcohol might decrease the incidence of debilitating cardiovascular diseases. Moderate Alcohol consumption increases high-density lipoproteins and reduces the oxidation of low density lipoprotein. It has also a capacity to induce the expression of endothelial nitric oxide synthase and synthesis of nitric oxide. In addition, moderate alcohol consumption induces the expression of putative cardio-protective proteins in the heart during ischemic conditions. Furthermore, it reduces unnecessary platelet aggregation and blood coagulation, facilitates smooth muscle cell proliferation during vascular insult, enhances insulin sensitivity and probably plays its cardioprotective role by reducing acute and chronic psychosocial stress which exerts allostatic load not only on cardiovascular system but also on the body.

Conclusion: Cardiovascular diseases, Ethanol, Moderate ethanol consumption.

Keywords

Coronary heart disease; Myocardial reperfusion injury; Remote ischemic preconditioning; Cardiac biomarkers; Percutaneous coronary intervention; Troponin-I; Angioplasty.

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Introduction

Chemistry and source of alcoholic beverages

Alcohol is a broad term used to describe a class of organic compounds having common properties with a distinct chemical group (R-OH). It is volatile and water soluble. There are five basic kinds of alcoholic beverages: beers, table wines, dessert or cocktail wines, liqueurs or cordials, and distilled spirits. The form of alcohol found in alcoholic beverage is called ethanol, which has a chemical formula of C_2H_5OH . Although alcohol is not considered as a nutrient, it is a source of energy approximately 7.1 Kcal/g [1].

Alcohol consumption

Alcohol is a psychoactive substance with a potential of precipitating to dependence. Its lipid solubility allows easy crossing of the blood brain barrier. The dependency and addiction property of alcohol consumption is associated with inhibitory and stimulatory effect of it on neurotransmitters. Alcohol inhibits the action of glutamate (excitatory neurotransmitter) and stimulates the action of Gamma-Aminobutyric Acid (GABA) (inhibitory neurotransmitter). By acting directly on GABA receptors, alcohol potentiates the effects of GABA [2]. Inappropriate consumption of alcohol contributes to the occurrence of chronic diseases, social and economic burdens though moderate consumption is proven to be beneficial [3]. The type, frequency and amount of alcohol consumed increases enormously, and there are several healthrelated problems related to alcohol consumption. The public health study found that public consumption of alcohol has risen in recent decades, with the bulk of this rise occurring in developing countries [4]. Worldwide, adults (age 15 years and older) drink an average of 5 liters of pure beer, wine and spirits annually. In 2010, world consumption was equivalent to 6.2 liters of pure alcohol consumed per person 15 years age or older [4].

Concept of light to moderate consumption of alcohol

Alcohol intake is usually expressed in 'drinks' or 'units'. It may be divided in to light, moderate and heavy categories depending upon the amount of alcohol consumed in terms of pure ethanol per day [5].

Light to moderate alcohol intake is usually known to be within the range of 1-3 drinks a day, resulting in blood alcohol levels of around 0.046 to 0.092 gram in 100 ml of blood [6]. A drink is described as about 355 ml bottle of beer (4%-5% ethanol), or 118 ml glass of wine (10%-12% ethanol), or 4ml shot of liquor or spirits (40% ethanol).

Binge drinking is a typical pattern of excessive alcohol use and a 'binge' pattern, according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA), is a drinking pattern that corresponds to 5 or more drinks for males, or 4 or more drinks for females, in around 2 hours [7]. Binge drinkers have higher risks for major coronary events like myocardial ischemia or infarction than abstainers, even when the overall volume of drinking is low. Evidence showed that there was an association between binge alcohol consumption and a two-fold greater mortality after acute myocardial infarction [8]. It is thus apparent that in addition to the volume of consumption, the pattern of drinking should be considered in the assessment of the effect of alcohol.

The association between alcohol use and health consequences is complex [3]. It is related by intermediate pathways with long-term health and social consequences including dependency, acute intoxication and physiological effects. The present review tried to explore the plausible mechanisms of moderate ethanol consumption and its role in minimizing the risk of cardiovascular disease in its direct and indirect biological effects on systemic organs and cells.

Objective

The aim of this review was to summarize the available evidences in support of the potential role of regular moderate alcohol consumption in the prevention of the occurrence cardiovascular diseases and the possible mechanism by it reduces diseases incidents.

Methods

This review was conducted by collecting clinical, epidemiological and translational research evidences from PubMed, Google scholar and World Health Organization reports.

Results and Discussion

Moderate alcohol consumption increases High-Density Lipoproteins (HDL)

An increase in HDL level inversely correlates with the incidence of coronary artery disease [9]. HDL inhibits low density lipoprotein oxidation, vascular wall inflammation, and thrombosis critical for abnormality of the cardiovascular system and enhances the number of endothelial progenitor cells. Moderate alcohol intake raise HDL concentrations though the metabolic pathway by which alcohol increases HDL concentrations is not well understood. However, moderate alcohol consumption results in dose dependent increases in plasma concentrations of the major HDL components (HDL-C, apoA-I and -II) through an increase in the HDL apolipoprotein Transfer Rate (TR). The main protein in HDL, apolipoprotein A-I, is capable of removing LDL lipid hydroperoxides in vitro, after injection into mice in vivo, and after infusion into humans in vivo and hence preventing the occurrence of atherosclerosis secondary to oxidation [10].

Alcohol drinking increases the plasma concentration of apolipoprotein AI and apolipoprotein AII, the main components of HDL particles. Based up on epidemiological data, it has been estimated that an average individual consuming 30g of alcohol per day would show an 8 mg/dl increase in the plasma concentration of apolipoprotein AI, primarily due to increased synthesis in liver [11].

Ethanol ingestion also enhances the capacity of Reverse Cholesterol Transport (RCT), in which HDL accepts cholesterol from peripheral cells and transports it to the liver for removal from the body [12]. According to Rimm and his colleagues, a 16.8% reduction in coronary heart disease is directly attributable to increased HDL from consuming 30g alcohol per day [11].

Consumption of red wine induces oxidation of Low Density Lipoprotein (LDL)

The chance of developing coronary artery disease is very high in individuals with elevated LDL cholesterol [13]. Oxidized LDL affects the arterial wall more than native LDL. It is easily trapping in the arterial wall when it modified by free radicals. LDL cholesterol can be oxidized or modified by free radicals or Reactive Oxygen Species (ROS) generated by a variety of cells in the arterial wall [13]. Expressive

ROS production at sites of vascular injury or inflammation may overcome the normal antioxidant defenses system and may lead to diseases, including cardiovascular disease. Oxidized LDL can impair the production of nitric oxide which ultimately decreases the dilation characteristics of blood vessels [14]. Certain alcoholic beverages contain polyphenolic components which are good antioxidants. For example, the consumption of red wine reduces the susceptibility of LDL to oxidation [15].

Moderate alcohol consumption induces the expression of Endothelial Nitric Oxide Synthase (eNOS)

The endothelium is an important regulator of vascular tone and play a key role in atherogenesis. The development of cardiovascular diseases is often linked with endothelial dysfunction as it facilitates the formation of atheromatous plaque [16]. The endothelium, under normal conditions, produces functionally important substances that modulate the vascular tone, prevent the tendency of unnecessary blood clotting and affect the growth of smooth muscle cells. One such vasoactive agent is Endothelium Relaxing Factor (EDRF), which is known as Nitric Oxide (NO) [17].

NO plays a key role in controlling blood flow by inhibiting the contraction and the proliferation of smooth muscle cells and the aggregation and adherence of platelets [18]. Moderate ethanol intake is believed to be beneficial as ethanol induces the activity of endothelial nitric oxide synthase. Study has speculated that ethanol facilitates the dilation of coronary vasculature which in turn enhances myocardial blood flow [19]. It has an activation role on Transient Receptor Potential Vanilloid 1 (TRPV1) channels responsible for the release of the potent vasodilator calcitonin gene-related peptide. In addition, polyphenols found in red wine also enhance the activity of nitric oxide synthase and consumption of red wine increases blood flow in human brachial arteries [20].

The effect of ethanol on prostacyclin has been also studied. Prostacyclin is a potent vasodilator and inhibitor of platelet aggregation which derived from derived from endothelium. Ethanol increases prostacyclin production in cultured human umbilical vein endothelial cells and high level of prostacyclin in plasma was found in volunteers [21]. Therefore, ethanol's modulatory effect on prostacyclin production could also contribute to its cardio-protection effects in vivo.

Moderate alcohol consumption induces the expression of cardio-protective proteins

As demonstrated by improved post-ischemic ventricular function and decreased myocardial infarction and cardiomyocyte apoptosis, alcohol may protect the heart from the adverse effects of ischemia reperfusion injury [22]. Alcohol has also resulted in increased expression of many cardiovascular proteins, including Heat Shock Protein70 (HSP70), Hemeoxygenase-1(HO-1) and Manganese Superoxide Dismutase (MnSOD), indicating that these proteins could be integral in the cardioprotective capabilities of alcohol [22].

Moderate alcohol consumption reduces coagulability of blood and platelet aggregation

Alcohol consumption may affect several hemostatic factors, including fibrinogen concentration, platelet aggregability and the fibrinolytic factors: tissue-type plasminogen activator and plasminogen activator inhibitor-1 [23]. The link between an inhibition of platelet function by ethanol and the cardio-protective

effects of moderate drinking likely relates to the role of platelets in the complication of atherosclerosis. Platelets are involved in the generation of atherosclerotic lesions by formation of mural thrombi at sites of endothelial injury and by stimulation of smooth muscle cell proliferation by the release of platelet-derived growth factors [13]. Platelets also accumulate over ruptured atherosclerotic plaques leading to the generation of platelet fibrin thrombi and thromboembolic phenomena. It has been shown that there are also additional factors which may modulate the effect of ethanol on the platelet functions. Inappropriate concentration of coagulation factors have been linked with the risk of atherosclerotic diseases. Ethanol has multiple effects on hemostasis, affecting platelets, coagulation factors, and the fibrinolytic system. Light-to-moderate alcohol use was associated with lower levels of fibrinogen, plasma viscosity, factor VII, and Von Willebrand factor [24].

Moderate alcohol consumption increases insulin sensitivity and decrease insulin resistance

Insulin resistance and hyperinsulinaemia are prominent predictors of risk for the development of diabetes mellitus and may promote atherosclerotic diseases because of the association with multiple vascular risk factors and direct atherogenic effects [25]. Insulin resistance measured by the glucose clamp technique has been shown to be associated with high triglycerides and low high density lipoprotein cholesterol levels in subjects without diabetes mellitus, in subjects with impaired glucose tolerance and in patients with non-insulin dependent diabetes mellitus [25]. Furthermore, insulin resistance has been found to be associated with hypertension [26]. Based on these evidences it is reasonable to expect that resistance to insulin-stimulated glucose uptake would play a crucial role in the pathogenesis of atherosclerotic vascular diseases. Moderate alcohol intake is associated with a reduction in insulin resistance, which may explain in part the cardioprotective effect of alcohol [27]. In a study by Furuya and colleagues in male wistar rat showed that moderate ethanol consumption is associated with enhanced insulin sensitivity. In this study, chronic treatment of male wistar rat with 3% (v/v) ethanol in the drinking water over a period of four weeks resulted in enhanced sensitivity, while lower or higher concentrations of ethanol in the drinking water has no such effect [28]. The mechanism responsible for the insulin sensitizing activity of alcohol remains uncertain. However, McCarty indicated that the metabolism of acetate in peripheral tissues generates adequate amounts of Adenosine Monophosphate (AMP) responsible for activation of protein kinases, which in effect induces the synthesis of certain proteins that function to increase insulin sensitivity and fat oxidation [29]. In a multicenter, randomized, clinical intervention trial study done at the Ben-Gurion University of the Negev, Israel, outlined patients with type 2 diabetes who had previously abstained from alcohol, initiation of moderate daily alcohol consumption reduced fasting plasma glucose. Patients with higher hemoglobin A1C may benefit more from the favorable glycemic effect of alcohol [30].

Moderate alcohol consumption reduces stress

Stress implies a challenge that requires behavioral, psychological, and physiological changes associated with a state of hyper arousal that initiates necessary counteracting reactions. Stress responses orchestrated by several physiological mechanisms that are dependent on the hypothalamus, the pituitary gland and the adrenal gland [31]. These neuroendocrine systems are coordinated to maintain internal

homeostatic conditions to preserve the integrity of the body even under extremely demanding conditions otherwise known as allostatic load. A chronic allostatic load has a deleterious impact on biological functions include the cardiovascular system. Mental or psychosocial stress is associated with endothelial dysfunction and atherosclerosis. Stress induces the development and progression of atherosclerosis. It has been demonstrated to increase oxidative stress and induce endothelial injury- processes mediated via sympatho-adrenal activation (β 1-adrenoceptor activation) that lead to atherosclerosis and the risk of coronary artery disease [32]. Furthermore, animal models have illustrated the critical role of sympathetic arousal, associated with stress, in the development of hypertension. Immediate increment in arterial blood pressure can be precipitated by stressful situations. This is probably due to vasoconstriction, triggered by enhanced sympathetic activity [29]. It is a common activity in day to day bases people drink to feel relaxed. Moderate drinkers in the midst of stress have less depression than people in other patterns of drinking. Low and moderate doses of alcohol improve affective overall speech, joy and euphoria, and feelings of satisfaction and carefreeness. Therefore, light to moderate alcohol consumption might offer protective effect against cardiovascular disease by reducing behavioral and psychosocial stress which might otherwise increase the risk of developing cardiovascular disease.

Conclusion

Cardiovascular disease is the world's leading cause of death and morbidity. Heavy alcohol consumption is one of the risk factors for the cardiovascular disease incident along with cigarette smoking, diabetes mellitus, hypertension, obesity and others. Although large epidemiological and clinical studies showed that heavy consumption of alcohol is the risk factor for the development of cardiovascular disease, light to moderate consumption of alcohol (i.e. 1-2 drinks/day) have to be protective against atherosclerosis, sudden cardiac death and arrhythmia, coronary artery disease and hypertension. Light to moderate consumption of alcohol is believed to play its cardio-protective effect through at least on its effect on high density lipoproteins and prevention of low density lipoprotein oxidation, reduction of platelet function (i.e. prevention of aggregability) and enhancing the process of fibrinolysis and preventing thrombus formation which are major risk factor for incidence of cardiovascular disease. Light - moderate ethanol intake also exert its protective effect by mildly lowering the blood pressure, by decreasing the insulin resistant and enhancing sensitivity and reducing mental and psychosocial stress which might trigger the incidence of the disease or further exacerbation to mention a few. This review was organized from publications most of which are epidemiological and clinical evidences which may not show the cellular and molecular mechanisms of light – moderate ethanol consumption. Therefore, it is very important to search the detailed mechanism of action so that recommendations are set about the cardioprotective role of moderate alcohol consumptions. Additionally, the definition of amount and pattern of consumption and alcoholic content of each beverage may vary from country to country; therefore, it's mandatory to take considerations of these parameters in a study in order to avoid inappropriate results and conclusions. Furthermore, it is not well recognized whether the effect of alcohol on the body is associated with the ethanol itself or its metabolites or additional compounds found in alcoholic beverage. Therefore, further study is needed to address these discrepancies.

Authors contribution

A.G. and G.S. contributed to the idea and the design of the review, A.G. worked out the writing up of the review, A.G. and G.S. contributed to the preparation and revision of the manuscript.

Competing interests

There is no conflict of interest.

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