

## The Relation between Alcohol and Hypertension

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**Keywords:** Alcohol-Induced Hypertension, Hypertension, Alcohol Absorption, Alcohol Metabolism, Mechanisms, Alcohol Consumption, Alcohol Effects.

**Abstract:** Alcohol is a depressant found in any liquor that can numb the nerves. It slows brain function, consequently causing difficulty in speech, thinking, and biological movements. When referring to alcohol, the chemical formula  $\text{CH}_3\text{CH}_2\text{OH}$ , or ethanol, can be used. Alcohol abuse is becoming common, especially among teenagers. When people choose to consume alcohol for entertainment, they also introduce several health risks to their bodies, including hypertension. Hypertension is the elevation in blood pressure. It is a serious disease that harms body health and can lead to further fatal diseases. To understand hypertension, the underlying mechanisms of alcohol-induced hypertension are summarized. As discussed in this review, alcohol abuse is one of the causes of hypertension, while there might be slight differences between females and males. Finally, hypertension can lead to fatal diseases, including but not limited to heart failure and kidney malfunction. People should be more aware of the consequences that alcohol usage can bring.

### 1. Introduction

Fermented beverages and alcoholic drinks have existed for thousands of years. In many early civilizations, around 7000 BC, alcohol already existed. In the sixteenth century, alcohol, what people called "spirits" at that time, was used largely for medicinal purposes. In the nineteenth century, people's attitude toward alcohol changed and began promoting moderate alcohol use. Although alcohol is a numbing depressant, research indicates that low-to-moderate drinking can reduce the risk of cardiovascular diseases, lower blood pressure, and increase longevity [1, 2]. For men younger than 65, two drinks a day are defined as "moderate drinking"; for women of any age and men aged 65 and older, one drink a day is moderate drinking [3, 4]. Noticeably, the definition of "a drink" is determined by the types of alcohol. Different types of alcohol are considered to have a different amount of alcohol for "a drink". However, studies revealed that excessive alcohol consumption is life-threatening. Based on a large amount of cross-sectional and prospective epidemiological studies, researchers demonstrated that heavy drinkers and alcoholics have a higher risk of cardiovascular diseases (such as hypertension) and mortality. In addition, chronic high level of alcohol intake most commonly causes hepatic, gastric, and nervous injuries, which lead to physiological dysfunctions. According to the National Institute on Alcohol Abuse and Alcoholism, in the United States, approximately 95,000 people die from alcohol-related diseases annually [5]. Drinking alcohol is a common phenomenon at present, and alcohol abuse is one of the major public health problems in most human societies in the world. Previous studies confirmed that the relationship between alcohol consumption and blood pressure is causal. The review focuses on alcohol absorption and metabolism, possible mechanisms of alcohol-induced hypertension, effects of alcohol consumption on blood pressure, and prevention and treatment of hypertension.

### 2. Alcohol Absorption and Metabolism

Alcohol absorption is closely related to human digestion. When alcohol enters the mouth cavity, a small portion is absorbed directly by the tongue and mucosal lining of the mouth [6]. The remaining portion will be passively digested in the stomach and small intestine, respectively.

## 2.2 Absorption

The presence of food in the stomach triggers the pyloric sphincter, which is the muscle located between the stomach and small intestine that controls the peristalsis, to contract and hence block the pathway into the small intestine. Since the epithelial lining in the stomach is less than that in the small intestine due to surface area difference, the alcohol absorption in the stomach will be inhibited and slower to some extent [7]. The absence of food in the stomach leads to alcohol directly moving down to the small intestine, where contains more epithelial cells for comparatively faster absorption due to its large surface area. After alcohol contacts with the epithelial cells, it slowly passes through interstitial space and eventually diffuses into the capillaries, further transporting the alcohol content into every organ.

## 2.3 Metabolism

Alcohol metabolism occurs mainly in the liver. The enzyme alcohol dehydrogenases are secreted into three systems, alcohol dehydrogenase (ADH) system, microsomal ethanol-oxidizing (MEOS) system, and acetaldehyde dehydrogenase (ALDH) system, responsible for degrading alcohol down to acetaldehyde, acetate, and carbon dioxide sequentially [8] in the citric acid cycle.

The chemical formula of alcohol breakdown [9] can be described as:



Alcohol dehydrogenases (ADH) in the liver catalyze the oxidation reaction of ethanol to acetaldehyde ( $CH_3CH_2OH$ ), which is a toxic compound that needs to be rapidly oxidized. Two aldehyde dehydrogenases (ALDH) are responsible for the further process of breaking down alcohol. ALDH1 oxidizes a small portion of acetaldehyde in the cytosol, while ALDH2 oxidizes the rest into the mitochondria using a different pathway. The product will be in the form of acetic acid ( $CH_3COOH$ ). A reversible reaction may also occur where the acetic acid interacts with water ( $H_2O$ ) and forms acetate ( $CH_3COO^-$ ) [10].

In both of the oxidation processes,  $NAD^+$  (nicotinamide adenine dinucleotide) functions as the oxidizing agent that gains the electron, or hydrogen ion, from ethanol and acetaldehyde.

## 3. Potential mechanism of alcohol-induced hypertension

How alcohol causes a high level of blood pressure specifically is not confirmed yet. Scientists have suggested several possible mechanisms that may underlie alcohol's effects on blood pressure.

### 3.1 Damage to the Endothelium

The endothelium is undoubtedly a key modulator of vascular function. Endothelial dysfunction is an early indicator of vascular injury and atherosclerosis and an important prognostic factor of future cardiovascular diseases [11]. Several research showed that in *vitro* animal studies, low doses of alcohol increase the release of nitric oxide (NO) and augment endothelium-mediated vasodilatation, while high levels of alcohol intake constrict most blood vessels and inhibit endothelium-dependent vasodilation [12].

Soardo et al. reported that Endothelin and nitric oxide had been shown to be involved in alcohol-induced vasoconstriction. Alcohol increased the levels of endothelin-1, NO, plasminogen activator inhibitor-1 and oxidative stress in vivo and in vitro. As a result, alcohol affected endothelial function and activated oxidative stress play a role in this process of alcohol-induced endothelial dysfunction. However, the data suggested that the endothelial responses depend on the different doses of alcohol. Low to moderate doses of alcohol may translate into vascular protection, but high doses of alcohol may translate into vascular damage [13].

At ethanol concentrations up to 20mM, alcohol stimulates and increases endogenous nitric oxide synthase (eNOS) expression in cultured human vascular endothelial cells via the PI3K/Akt pathway [14]. In an animal experiment in 2008, to further confirm the effects of ethanol on blood pressure and eNOS expression and NO production in vascular endothelial cells, rats were fed a liquid diet that

contained low to moderate doses of ethanol for 6 weeks. The results show that chronic ethanol intake reduced mean arterial pressure, increased eNOS expression and NO production in the aortic vascular wall, and enhanced endothelium-dependent relaxation responses to acetylcholine [15]. Nitric oxide benefits the regulation of vascular tone. Due to NO production, eNOS functions as a protective tool in the cardiovascular system. Conversely, in another animal study, higher daily ethanol (blood alcohol levels >29 mM) for 6 weeks in an animal model was associated with decreased eNOS expression, increased release of endothelial-derived vasoconstrictor prostanoids, and greater responsiveness of mesenteric arterioles to phenylephrine [16]. To sum up, high levels of alcohol intake would reverse the positive effects of lower alcohol intake on nitric oxide. This may lead to higher risks of hypertension or other cardiovascular events [17].

### **3.2 Effects on the Nervous System**

The World Hypertension League points out that alcohol has a relatively greater effect on systolic blood pressure than diastolic blood pressure, indicating an imbalance between the central nervous system factor that affects cardiac output and the effect of alcohol on peripheral blood vessels [18]. More evidence suggests that alcohol triggers and activates both central and peripheral responses, which synergistically increase blood pressure. In addition, alcohol causes an increase in sympathetic outflow. This may be associated with the release of corticotropin hormone. The increase of sympathetic outflow may lead to adrenoceptor-mediated responses, such as vasoconstriction and increased heart rate, and stimulates oxidation responses [19].

### **3.3 Cortisol**

Research indicates that the subjects showed a significant increase in plasma cortisol levels after drinking, and plasma cortisol levels decreased after stopping drinking. The cortisol levels in regular drinkers elevate probably because alcohol stimulates corticotropin hormone and strengthen the vasopressin corticotropin [20]. The effects on blood pressure may be due to an allergic reaction to cortisol or catecholamine mineralocorticoid [21].

## **4. Alcohol and Hypertension**

Currently, the causal reason for alcohol-induced hypertension remains unclear. Although no significant association between alcohol and hypertension is discovered, there is still increasing evidence suggesting possible factors that may directly or indirectly lead to hypertension.

### **4.1 Genetic Polymorphism Effects on Alcohol-Induced hypertension**

Aldehyde dehydrogenases (ALDH), as the enzymes that oxidizing and detoxifying the intermediate product acetaldehyde ( $\text{CH}_3\text{CHO}$ ) of ethanol metabolization, has the potential on the increasing risk of hypertension once they are mutated or inactivated [22]. If the acetaldehyde accumulates, ALDH2 (mitochondrial aldehyde dehydrogenases) tend to be altered in their properties and subsequently forms ALDH2 variants that significantly raise the systolic blood pressure [23].

### **4.2 Alcohol Effects on Cardiovascular System**

Research suggests alcohol directly upregulate voltage-gated  $\text{Ca}^{2+}$  channels, inhibit  $\text{Ca}^{2+}$ -ATPase from removing  $\text{Ca}^{2+}$  and relaxing muscles, and affecting  $\text{Mg}^{2+}$  depletion, which builds up intracellular sodium ion by inhibiting the sodium-potassium ion pump [24]. These serial reactions eventually increase intracellular calcium ions. The flow of calcium ions from extracellular into intracellular space prompts the stress hormone norepinephrine, increasing blood bumping and raising blood pressure to function. When acutely consuming alcohol, the flow of calcium ions is enhanced. Hence, the  $\text{Ca}^{2+}$  independent vasoconstriction occurs more rapidly due to increased  $\text{Ca}^{2+}$  sensitivity by binding to arterial and arteriolar smooth muscle cells [24]. Abnormal vasoconstriction triggers the heart to beat faster, consequently may causing higher blood pressure.

### **4.3 Alcohol Dependency**

Not only the narrowing of blood vessels contributes to the diagnosis of hypertension, but also alcohol dependence can affect one's blood pressure status. According to research conducted in China, among 36,157 individuals, 22.20% (3854/17501) of the males and 1.74% (324/18656) of the females were classified as alcohol dependent [25]. A significant association ( $P < 0.01$ ) between alcohol dependence level and blood pressure was found [25]. Furthermore, systolic blood pressure positively correlated with alcohol dependence, while diastolic blood pressure existed as an independent risk factor for hypertension [25].

### **4.4 Gender-Related Differences on Alcohol-Induced Hypertension**

As discussed in 2.2, alcohol can affect blood pressure very differently by gender. It is also crucial to review gender-related difference to understand the effects of alcohol have on hypertension. Epidemiological data indicate a higher risk of alcohol-induced hypertension in men than women. A positive relation between alcohol consumption level and the risk of developing hypertension is observed in women, that low average alcohol consumption (5-20g/day) decreases the hypertension risk. In contrast, higher-level alcohol consumption increases the risk. Contrastingly, the relationship is linear in men, and even the risk of hypertension increases under low levels of alcohol consumption [26].

In another research among 43810 men and women, who were separated into five different groups based on daily alcohol intake (non/very light ( $< 10$ g per day), light ( $\geq 10$  g and  $< 20$  g per day), moderate ( $\geq 20$  g and  $< 30$  g per day), and heavy ( $\geq 30$  g per day)), a conclusion of "the blood pressure is more prone to be elevated by alcohol drinking in men than in women" [27] was drawn. The male moderate/heavy drinkers had a considerable higher systolic blood pressure than non-drinkers, while only female heavy drinkers had significantly higher systolic blood pressure. Furthermore, all light/moderate/heavy drinkers from both men and women had significantly higher diastolic blood pressure [27]. The overall systolic and diastolic blood pressure differences between drinkers and nondrinkers in men were greater than in women [27].

## **5. Prevention and Treatment**

### **5.1 Prevention**

Reducing alcohol intake is effective in reducing high blood pressure and normal blood pressure. This may also help prevent the development of high blood pressure related to alcohol. According to research, alcoholics who reduce moderate drinking can reduce systolic blood pressure by 2 to 4 millimeters of mercury (mm Hg) and diastolic blood pressure by 1 to 2 millimeters of mercury (mm Hg). Heavy drinkers who intend to lower their blood pressure should reduce their alcohol intake over a week or two rather than stop drinking immediately. This is because this action can cause alcohol withdrawal syndrome, resulting in a rapid rise in blood pressure [1].

To prevent high blood pressure and reduce the risks of other cardiovascular diseases, it is significant to maintain the blood pressure within a good and healthy range, which is normally below 120/80 mm Hg. This can be achieved by having a healthy lifestyle [28]. Having overweight is one of the risk factors of hypertension. A heavier body needs more blood to supply oxygen and nutrients to the tissues. With the increase of blood flow through the blood vessels, the artery walls would suffer more pressure. Moreover, being physically active prevents high heart rates. Once the heart rates get higher, the heart must work harder with each contraction, leading to cardiovascular diseases [29]. Therefore, healthy living habits, such as getting regular physical activity and keeping at a healthy weight, can effectively prevent hypertension.

### **5.2 Treatment**

The specific medication type for hypertension should be determined based on each patient's blood pressure measurement, age, and overall health. Five medications are used widely to treat hypertension:

CCBs, ACEI, ARBs, diuretics, and beta blockers. The combination of two or more drugs often can be more effective than merely one [28]. However, there is no accurate clinical data on the specific drugs for alcohol-induced hypertension treatment. Dexamethasone (2 mg/per day) can inhibit acute alcohol hypertension. ACE inhibitors can increase the cardiac output of patients with cardiovascular disorders and are therefore useful in treating alcohol-induced high blood pressure [30]. Moreover, another study showed that Angiotensinogen type 1 receptor blockers could protect against alcoholic cardiomyopathy in the dog. Since calcium channel blockers may be associated with the possible mechanisms of the development of alcoholic hypertension, it may also be the drug of choice for alcohol-induced hypertension treatment [31].

## **6. Potential Threats Led by Hypertension**

Not only does hypertension itself negatively affect human body health to a great extent, but also it can introduce the body to a few consequent diseases that are led by elevated blood pressure and can be fatal.

### **6.1 Heart Failure**

Hypertension can lead to serious damage to health in many ways. According to NCBI (National Center for Biotechnology Information), hypertension can be an underlying risk of heart failure [32]. Heart failure can be fatal as it is chronically causing abnormal pumping patterns in which only a little blood and oxygen are transported to organs [33]. As the blood pressure is elevated, the blood vessels are narrowed. The blood is hence traveling the circulation system slower and more difficult, causing a larger workload to the heart [33]. The heart muscles, specifically the left ventricle, are thickened to pump more blood to the rest of the body organs to accommodate the workload. However, a larger heart can mean a lower work efficiency. Consequently, the heart can fail to supply blood and oxygen to the body. According to increasing data, gender can also play a role in affecting hypertension-led heart failure differently. In research on hypertensive heart disease, the outcome indicates that women have a slightly greater chance of heart failure that result from hypertension [34]. Women are also more prone to unstable blood pressure and are less affected by antihypertensive medications [34].

### **6.2 Kidney Malfunction**

As the kidney functions to remove any wastes that the body produces [35], it is essential in the purification of the body. The kidney also regulates the release of angiotensin and aldosterone [36], which are two hormones that affect blood pressure. As the blood pressure is elevated to a level that harms the body, kidney scarring or glomerulosclerosis and kidney failure can occur. Kidney scarring is the damage within the kidney that causes the organ cannot filter waste effectively and eventually lead to kidney failure [37]. Severe kidney failure may require a kidney replacement. Blood pressure is closely related to kidney performance, that the control of blood pressure may effectively control kidney damages caused by hypertension. According to S Mennuni and his colleagues from their research, "an adequate control of high blood pressure, obtained through an appropriate therapeutic intervention, still represents the key strategy to achieve a satisfactory control of renal damage in hypertension" [38].

## **7. Conclusion**

Alcohol has the potential to lead to hypertension. The more alcohol consumed, the higher risk of developing elevated blood pressure, and consequently causing hypertension. Multiple proposed mechanisms can be references when examining how alcohol-induced hypertension is developed. The relation between alcohol and hypertension can be approached from different angles, including genetic and gender effects. In addition, hypertension can be contributing to several subsequent diseases, such as heart failure and kidney malfunction. To prevent and provide treatment for hypertension and possible future diseases, the consumption of alcohol needs to be stopped.

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