

Association between Ethanol Consumption and Hypertension Risk

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Abstract

Ethanol consumption has been linked to many physiological changes including hypertension. This review examines the mechanisms of how ethanol affects blood pressure through the nervous system, endocrine hormones, and local factors in blood vessels. Moreover, recent epidemiological literatures on the roles of gender, age, ethnic backgrounds, and abstinence in the association between ethanol consumption and the risk of hypertension are summarized and compared.

Introduction

Humans have been involved in the production and consumption of ethyl alcohol, C₂H₅OH, for thousands of years for medicinal, antiseptic, analgesic, nutritional, and religious purposes^[1,2]. Ethanol is also used as a recreational substance for social settings because individuals tend to feel more socially comfortable after moderate consumption^[2]. Studies have shown that ethanol consumption affects various neurotransmitters in the brain that are associated with behaviors^[1,3,4]. Other than psychosocial effects, ethanol consumption has also been linked to physiological changes. Some studies have suggested that consuming small amounts of alcoholic beverages daily lowers blood pressure and benefits the cardiovascular system^[5], while other studies found ethanol consumption offered little to no protection in mortality^[6]. Understanding of the association between ethanol consumption and the risk of hypertension can be vital in the treatment of patients with hypertension or developing hypertension. Focusing on recent literatures on regulatory mechanisms and epidemiological surveys primarily published in the last ten years, this review article seeks to summarize and compare current evidences supporting the association between ethanol consumption and the risk of hypertension, with the considerations of gender, age, ethnic backgrounds, and abstinence.

Mechanisms of how ethanol affects blood pressure

Blood pressure can be regulated by the nervous system, endocrine hormones, and local factors in blood vessels. Studies have shown that ethanol induces changes in all these three aspects. In the nervous system, selective impairment of baroreceptors, which are responsible for the regulations of heart rate and blood pressure, was triggered by ethanol microinjection and led to ethanol-induced hypertension^[7,8]. Rostral ventrolat-

eral medulla (RVLM) in the brain is also a target of ethanol to elicit modest increases in blood pressure in rats^[9]. At the onset of ethanol-induced hypertension, an increase of sympathetic nerve activity was observed^[10], which may directly contribute to the elevation of blood pressure^[11,12]. Epinephrine and norepinephrine, the neurotransmitters used in the sympathetic nervous system, showed increasing plasma concentrations after ethanol consumption. The rise of epinephrine occurred sooner than norepinephrine^[13,14].

In addition to the changes in the nervous system, the endocrine system responds to ethanol in multiple ways including the activations of the renin-angiotensin-aldosterone system (RAAS) and one of the targets of RAAS, vasopressin^[15-26], both of which contribute to decreased plasma and urinary volumes^[26], and therefore the increase of blood pressure^[27,28]. Interestingly, ethanol reduced vasopressin V1b receptors in the basolateral amygdala in non-ethanol-dependent rats, but the receptors were restored when ethanol-dependence was established^[29].

At the local level in blood vessels, ethanol may increase blood pressure via inflammatory/oxidative injury to the endothelium^[30,31], decreasing the production of vasodilators such as nitric oxide (NO)^[32-35], increasing the production of vasoconstrictors endothelin-1 and endothelin-2^[36,37], or the elevation of intracellular Ca²⁺ levels in smooth muscle cells^[38]. In endothelia, both acute and chronic ethanol ingestions suppressed the production of vasodilator nitric oxide (NO) by inhibiting inducible NO synthase (iNOS) activity^[32-35] or endothelial NO synthase (eNOS) expression^[36]. iNOS and eNOS may have opposite changes after ethanol intake^[37]. On the other hand, the productions of two potent secretory peptide vasoconstrictors endothelin-1 and endothelin-2 were increased in vascular endothelial cells when stimulated by ethanol^[38,39]. In addition, exposure of cultured cells to ethanol increased the intracellular Ca²⁺ level concentration 2-3

fold^[40-44], which contributes to the hyper excitability of the vascular smooth muscle cells and the vasoconstriction^[45,46].

Table 1: The possible means in which ethanol raises blood pressure are summarized below.

N e r v o u s System	● Decreased baroreceptor activity ^[7-8]
	● Ventrolateral medulla (RVLM) ^[9]
Endocrine system	● Increase in activity of sympathetic nervous system and release of adrenaline, epinephrine, and norepinephrine ^[10-14]
	● Release of sympathetic amines, adrenaline, and corticotropin-releasing hormone ^[10-14]
	● Increase in activity of renin ^[15-19]
	● Elevated angiotensin II level ^[20,21]
	● Increase in angiotensin converting enzyme ^[20-23]
Endothelium	● Aldosterone ^[24,25]
	● Vasopressin and its receptor ^[26,29]
	● Inflammatory/oxidative injury to the endothelium ^[30,31]
	● Decrease in vasodilator nitric oxide (NO) ^[32-37]
	● Increase in endothelin-1 and endothelin-2 secretion ^[38,39]
	● Elevation of intracellular Ca ²⁺ levels ^[40-46]

Gender, age, and ethnic differences in the association between hypertension and ethanol consumption

Early studies identified regular drinking (three or more drinks of alcohol per day) as a risk factor for hypertension^[47,48] with a slightly stronger association observed in males, whites, and persons 55 years of age or older^[49]. In more recent reports that examined groups with different drinking levels, ethanol seems to have differential effects on blood pressure between males and females. A study published in 2008 followed 28,848 women and 13,455 men in the U.S. for over 20 years and found the risk of hypertension was decreased by 10% in women with light-to-moderate ethanol consumption (less than 4 drinks per day)^[50]. In men, however, the risk of hypertension increased in all drinkers regardless of the total amount of ethanol they consumed^[50]. In heavy drinkers, the risk was 26% higher than that in the men that rarely or never drank^[50]. Similar results were seen in a recent study published in 2015 with 6,997 men and 13,505 women ages 18 to 74 years living in rural China^[51]. Ethanol intake slightly lowered blood pressure in women regardless of the type of alcoholic drinks, but increased blood pressure in male drinkers of beer and liquor, but not rice wine^[51]. In a similar study published in 2014 consisting of 37,310 men and 78,426 women in Japan, blood pressure was found to be higher in male heavy drinkers (>60 g of ethanol per day), but lower in female heavy drinkers, given the small sample size of female heavy drinkers^[52]. Another study published in 2013 and done on elderly subjects from a rural Greek population observed that ethanol consumption increased the risk of hypertension only in heavy drinkers (>300 g of ethanol per week, in both men and women)^[53]. The authors proposed that the “Mediterranean diet” may contribute to the reduced risk of hypertension in light or moderate drinkers.

In men, two studies with Japanese subjects showed higher risk of hypertension was associated with drinking^[54,55]. One observed 3,900 Japanese men ages 10 to 59 years and found an ethanol intake of more than 200 grams of ethanol per week was associated with a significantly greater blood pressure^[54]. The other studied 5,275 Japanese male office workers who were 23 to 59 years old and concluded that ethanol consumption of any amount caused an increase in blood pressure^[55]. It is interesting that the two studies done in the same country had partly different results, suggesting other factors such as age or working habit seen in these two studies may play additional roles. It is also important to note that different ethnic groups may have different responses to ethanol due to their varying life styles in different regions of the world and their genetic background^[56]. A good example is the prevalence of aldehyde dehydrogenase (ALDH) deficiency in East Asian populations^[57].

In women, one study published in 2009 showed that moderate ethanol consumption was associated with a decreased risk of total mortality among Caucasian and hypertensive women, but not African American women^[58]. The authors pointed out that this was possibly due to the fact that African-American non-hypertensive women who abstained from drinking had a low mortality rate^[58].

The relationship between hypertension and ethanol withdrawal in chronic alcoholics is of particular interest in clinical practices. Early research found that alcoholics during withdrawal showed transitory (<72 hr) elevations in blood pressure and cardiovascular dysregulations continued during a time span of up to 4 weeks of abstinence^[59-61]. A more recent study^[62] examined 147 male and female chronic alcoholics. 55% of the chronic alcoholics had hypertension at the beginning after withdrawal. However, a sharp and sustained decrease in blood pressure was observed after continuous abstinence. Only 21% of the subjects continued to have hypertension even after 18 days. Correlations between blood pressure, years of at-risk drinking, and the severity of alcohol withdrawal syndrome were also found. Another research found stress tasks induced multiple cardiovascular effects including an increase in diastolic blood pressure, a higher peripheral resistance index, and a reduced cardiac efficiency index in some but not all female alcoholics after 3 to 4 weeks of abstinence^[63]. These effects appeared more severe and with a lower threshold level of chronic drinking in women than in men.

Overall, the majority of studies concluded that ethanol consumption is associated with increased risk of hypertension especially in male or heavy drinkers. Many other factors, such as gender, age, ethnic backgrounds, and the type of alcoholic drink, may apply their effects and alter the risk of hypertension in other groups. Although light to moderate ethanol consumption appeared to be linked to lower hypertension risk in some groups, such as women^[50-52,58] and a rural Greek population^[53], the benefit of limiting of ethanol consumption most likely outweighs the potentially beneficial effect of ethanol on hypertensive patients. This is consistent with current guidelines in many regions of the world^[64-68]. In addition, it is common to observe a transitory hypertension at the beginning of abstinence but a sustained decrease in blood pressure after continuous abstinence should be expected in most patients.

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