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ALCOHOLIC BEVERAGES-INDUCED HYPERTENSION AND ITS MANAGEMENT

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ABSTRACT

Alcoholic (ethanol containing) beverages have been part of human culture for thousands of years around the world. They are divided into three general classes namely bears, wines and spirits and typically contain 5%, 12% and 40% alcohol by volume. Preclinical and clinical studies have revealed the association between consumption of alcoholic beverages and elevation of blood pressure or hypertension. The exact mechanism of alcoholic beverages-induced hypertension remains elusive. However several possible mechanisms have been reported: an imbalance of the nervous system, stimulation of the renin-angiotensin-aldosterone system, increased cortisol levels, increased intracellular calcium levels, induction of vascular endothelial oxidative stress. For the management of alcoholic beverages-induced hypertension non-pharmacological strategies are: reduction of alcoholic beverage intake, weight reduction, reduction of salt and caffeine intake, smoking (nicotine) cessation and promotion of physical activity. Pharmacologic treatment includes dexamethasone for acute alcoholic beverage-induced hypertension, angiotensin-converting enzyme inhibitors, angiotensin II type 1 receptor blockers and calcium channel blockers are recommended for chronic alcoholic beverages-induced hypertension.

KEYWORDS: Alcoholic beverages; Hypertension; Mechanisms; Management; Non-pharmacological; Pharmacological.

INTRODUCTION

Alcoholic beverages or drinks (containing ethyl alcohol or ethanol, C_2H_5OH) have been consumed for thousands of years. Alcoholic beverages have common feature of being produced through anaerobic fermentation of carbohydrates by yeast. Beverages vary with respect to their raw materials, method of production and alcohol content. Alcoholic beverages are usually classified as fermented alcoholic beverages (beers and wines), or distilled alcoholic beverages (spirits or liquors). They typically contain 5%, 12% and 40% alcohol by volume (ABV), respectively. The proof is twice the percentage of alcohol by volume at 60 degrees Fahrenheit (e.g. 80 proof = 40% ABV). The earliest alcoholic beverages made from berries or honey was at least 10,000 years ago.[1] The fermented alcoholic beverages used in China dating 7000 BC, in Persia dating back to 5000 BC, in Egypt around 4000 BC, in India 3000 B.C, in Babylon 2700 BC, in Palestine around 1200 BC, in Mexico dating 1000 BC and in Greeks dating 450 BC.[2] The discovery of distillation during 500–1500 CE resulted in the production of distilled spirits. During the first century and a half the North American Colonies (United States) widely used alcoholic beverages. Although distilled spirits were used largely for medicinal purposes during sixteenth century.[1] However during eighteenth and nineteenth century, distilled alcoholic beverages were heavily used in most of the countries around the globe.

Research studies in the past suggest that mild to moderate consumption of fermented alcoholic beverages is beneficial to cardiovascular system and lowering blood pressure while excessive use is harmful to cardiovascular system and causes elevation in blood pressure.[3,4] It has been used as an analgesic to relieve the pain.[5] The first report of excess wine drinking and hepatic inflammation was reported by a physician practicing in Constantinople during eleventh century.[1] Current research demonstrates that mild to moderate drinking of fermented or distilled alcoholic beverages is beneficial to the cardiovascular system, lowers the blood pressure and increases the longevity.[6-9] Preclinical studies are also in support of the above beneficial effects of the alcoholic beverages.[10,11] Mild to moderate drinking is generally considered to be: Two alcoholic drinks a day for younger men, one drink a day for older men and one drink a day for women. A standard drink is 355 milliliters of beer, 148 milliliters of wine or 44 milliliters of distilled spirits or liquors. Heavy drinking, defined as having more than three alcoholic drinks per day, may contribute to high blood pressure or hypertension. The molecular mechanisms and possible mediators through which the consumption of alcoholic beverages causes hypertension or high blood pressure remain

elusive. This review focuses the commonly used alcoholic beverage by the modern human society and the link between consumption of alcoholic beverages and hypertension, mechanisms implicated with alcoholic beverages-induced hypertension and strategies to manage, prevent or to treat alcoholic beverages-induced hypertension.

Alcoholic beverages consumption by human societies around the world

Today, alcoholic beverages are consumed regularly by most of the human societies in the world and most widely used as recreational drug**s**. Regular consumption of alcoholic beverages is a habit of at least 50% of the world population.[12] Whereas, heavy drinking of alcoholic beverages in about 39% of the population.[13, 14] According to the data from WHO, worldwide total per capita (15+ years) consumption of alcoholic beverages was estimated to be 13.5 g per day.[15] Spirits/liquors accounted for 50% of total consumption of recorded alcoholic beverages, followed by beers (35%) and wines (8%).[15, 16] The consumption of alcoholic beverages is responsible for 3.3 million deaths worldwide per year and is a causal factor in developing over 200 diseases and injury related conditions including liver cirrhosis, cancers and cardiovascular diseases.[17] In the United Kingdom, consumption of alcoholic beverages is one of three leading risk factors contributing to disease and death[18], with alcohol related harm estimated to cost the UK over £20 billion annually.[19] In United States alcoholic beverages affects more than 20 million individuals leading to loss of 100,000 lives annually.[11, 20]

The table 1 summarizes all types of alcoholic beverages and raw material used in modern world. Beers are the best-known member of the malt family of alcoholic beverages. It is made from malt, corn, rye, barley, wheat, rice, honey, milk, coconut, ginger and hops. Beers have in alcoholic content 2-8%. Commonly used beers are Ales, Budweiser, Lagers, Stout and Weizen. Wines are alcoholic beverages that have been fermented from fleshy fruits such as apples, grapes, peaches, pears, apricots, pine apple, bananas, cherries, berries and plums. Wines generally contain 8-14 % alcohol. Commonly used wines are Bordeaux, Burgundy, Chianti, Champagne, Muscatel, Port, Red wine, Sauterne, Sherry and White wine. The spirits or liquors are first fermented using grains, fruits, or other ingredients then distilled. Commonly used spirits or liquors are Whiskeys (Scotch), Bourbon, Brandy, Gin, Rum and Vodka. Spirits/Liquors have in alcohol content 40-75 %. Binge drinking is especially bad for blood pressure in men, the researchers found. Drinking more than five drinks in one day, especially if this is done more than once a week, is considered frequent binge drinking and

increases both systolic and diastolic blood pressure. The risk is directly related to the amount of alcohol consumed.[21] A moderate intake of alcohol (2–4 drinks/day) has showed to have health benefits[22], A standard drink is equal to 14 grams (0.6 ounces) of pure alcohol, more than enough to raise the blood pressure by 1 mm of Hg and this amount of pure alcohol is found in: 12-ounces of beer, 5-ounces of wine and 1.5-ounces of spirit. The researchers concluded that any amount of alcohol above 10 grams raises systolic blood pressure. This information contradicts the previously held belief that small amounts of alcohol (less than 2 drinks a day for men and less than 1 drink a day for women) actually lowers the blood pressure. Research indicates that cardiovascular disease (CVD) incidence is lower in wine-drinking countries than other countries, suggesting that moderate wine consumption may be more beneficial than the consumption of other alcoholic beverages, such as beer and spirits.[23] This hypothesis is further strengthened by studies reporting differential[24-29] associations between alcoholic beverages and CVD risk, mostly in favor of wine consumption.[30-33] Okamura T et al[34] reported that the effect of alcohol consumption on blood pressure does not depend on the type of alcoholic beverage consumed.

Link between alcoholic beverages consumption and hypertension

Alcoholic beverages and blood pressure association has been known since the 1960's and hypertension remains the leading cause of cardiovascular disease, the biggest killer worldwide. Recent epidemiological and clinical studies have demonstrated that chronic ethanol consumption (more than three drinks per day, 30 g ethanol) is associated with an increased incidence of hypertension and an increased risk of cardiovascular diseases.[24-29] The magnitude of the increase in blood pressure in heavy drinkers averages about 5 to 10 mm of Hg, with systolic increases nearly always greater than diastolic increases.[35] Similar changes in blood pressure were also reported in preclinical studies.[10,36-41] However, preclinical studies have also shown a linear relationship between blood pressure and ingestion of alcohol.[10]

The relation between regular alcoholic beverages consumption and blood pressure has been described in several epidemiological surveys.[31, 42-45] Consumption of a single alcoholic drink may cause an acute rise in blood pressure that resolves within 2 hours.[46-48] Clinical studies with small sample sizes of subjects have suggested that alcohol consumption over several days may cause a more sustained rise in blood pressure.[49-53] In alcoholics, hypertension is common but settles after withdrawal from alcohol[54, 55-57] estimated 7-day retrospective

alcohol intake and 24-hour intake on separate occasions and showed the same magnitudes of correlation between both these estimates of alcohol consumption and blood pressure.

Intake of alcoholic beverages can have a serious long-term effect on blood pressure and research has shown that heavy drinking can lead to increased risk of hypertension for both men and women.[28, 58] A significant linear association between alcoholic beverages consumption and the risk of incident hypertension was consistently observed in middle-aged and older men and women.[59] Mac Mahon[60, 61] reviewed 30 cross sectional studies and reported that the J-shaped association, with a higher blood pressure among nondrinkers than among drinkers of 1 to 2 drinks per day, was observed in 40% of the studies. However, meta-analyses of high-quality cohort studies of alcoholic beverages consumption and incident hypertension[10, 62, 63] showed a significant linear association. Barboriak et al[64] reported that higher alcohol consumption was significantly related to higher systolic and diastolic blood pressure only among patients aged ≥50 years. Klatsky et al[44] reported that the relationship between alcohol consumption and higher blood pressure was slightly stronger among individuals aged ≥60 years. Wakabayashi et al[65,66] reported that only among men aged ≥40 years; the mean blood pressure was higher in light drinkers than in nondrinkers. However, Nakanishi et al [67, 68] conducted a 4-year longitudinal study and found consistent liner associations between alcohol consumption and the incidence of hypertension among all of the age groups. There are over forty population studies demonstrating an association between regular alcoholic beverages consumption, blood pressure levels and prevalence of hypertension. The largest of these, the Kaiser-Permanente Health Screening Survey[44], showed an average rise of 1 mm Hg of systolic blood pressure for each standard glass of alcoholic drunks per day. However, the increased risks of alcoholic cardiomyopathy (ACM), hypertension, stroke and myocardial infarction (MI) related to heavy drinking, either in the form of chronic alcoholism or occasional binge drinking, counteract these protection.[6-8,29,45,69-71] A study attributed alcoholic beverages as the cause of hypertension in 34.5% of men and 2.6% of women in a Japanese population.[72] This gender discrepancy was also seen in a prospective study in the women. This large study showed that light-to-moderate drinking was associated with reduced hypertension risk in women and increased hypertension risk in men.[28] Racial considerations further complicate the light-drinking-hypertension picture. Relative to abstinence, black men consuming low-to-moderate amounts of alcohol appear to have a higher risk of hypertension compared to black women or Caucasians of either gender.[73] Moreover, for men at any level of alcohol consumption, the risk of developing

hypertension may be higher in Asian populations than non-Asian populations.[74] A recent meta-analysis combined 16 prospective studies on alcohol consumption and hypertension risks. For male, though lacking statistically significant association, there was a trend toward increased hypertension risks with low to moderate drinking, and heavy drinking significantly elevated hypertension risks. For female, a J-shaped association existed between drinking and hypertension. Less than 10 g/day of alcohol intake rendered protective effects, while drinking more than 20 g/day significantly increased hypertension incidence.[75] Similarly, a J-shaped relationship was found between drinking and all-cause mortality among hypertension patients.[76, 77] Only a few studies have addressed the relationship between alcohol and hypertension in the elderly, and most of them have shown a strong association between hypertension prevalence and alcohol intake. [39, 40]

Mechanisms of alcoholic beverages-induced hypertension

Despite long history, the interaction between alcohol and cardiovascular health especially hypertension is still poorly understood. Several mechanisms have been proposed for the relationship between consumption of alcoholic beverages and elevated blood pressure as illustrated in Figure 1.

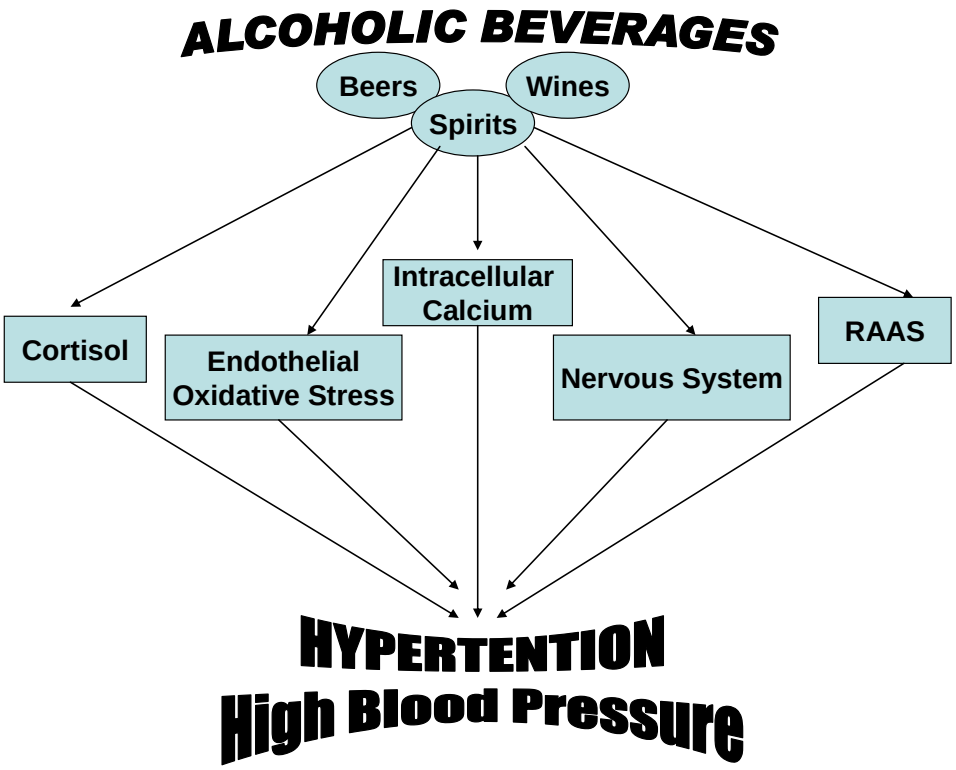

Figure 1: Mechanisms of alcoholic beverages-induced hypertension. RAAS: Renin-angiotensin and aldosterone system.

The putative pathology of alcohol-induced hypertension is through the effects of alcohol on cardiac function, acetaldehyde, blood vessels, neural conduction, sympathetic activity, noradrenaline metabolism, renin–angiotensin system, plasma vasopressin, plasma cortisol and ACTH (adrenocorticotropic hormone), and calcium metabolism.[49, 50, 78] Choudhury et al.[79] reported that there was little difference in sodium and potassium intake between Japanese male drinkers and nondrinkers.

An immediate effect of alcohol ingestion is vasodilation in some vascular beds. Sustained intake accompanied by high blood alcohol levels, however, results in short-term elevation of BP.[30] In addition, BP levels usually correlate best with alcohol intake within the prior 24 hours, and fall within hours to days after cessation or reduction in intake.[13, 14] Therefore, it is likely that the effect of alcohol on BP is not mediated by long-term structural alterations, but by neural, hormonal, or other reversible physiologic changes. The possible mechanisms of alcoholic beverage induced hypertension include an imbalance of nervous system, stimulation of the endothelium to release endothelin, inhibition of endothelium-dependent nitric-oxide production and stimulation of rennin-angiotensin-aldosterone system (RAAS) or cortisol; calcium or magnesium depletion and increased intracellular calcium or other electrolytes in vascular smooth muscle, possibly mediated by changes in membrane electrolyte transport.

1) Nervous system in alcoholic beverages-induced hypertension

It is speculated that the greater effect of alcoholic beverages on systolic blood pressure compared with diastolic blood pressure indicates an imbalance between CNS factors influencing cardiac output and the peripheral vascular effects.[49, 50] There is increasing evidence that alcohol initiates central as well as peripheral reactions which in a synergistic manner have a hypertensive action. In addition, alcohol induces an increased sympathetic outflow, most probably linked to secretion of corticotropin-releasing hormone.[80] Some investigators have suggested that the association between alcohol and hypertension is related to the temporal sequence of alcohol use and blood pressure measurement.[26, 61] The results of plasma catecholamine measurements after the short-term ingestion of alcohol in humans are conflicting but direct recordings of sympathetic-nerve activity suggest that short-term alcohol ingestion in humans and both short and long-term administration of ethanol in rats stimulate sympathetic-nerve discharge.[81-84] Several studies reported increased sympathetic nervous system activation and discharge of sympathetic amines after alcohol consumption.[42, 81, 82, 85]

Alcohol may cause hypertension by affecting the autonomic nervous system.[49, 50, 80] The increased sympathetic outflow is expected not only to induce adreno-receptor-mediated reactions (vasoconstriction, heart rate increase) but to stimulate oxidation reactions.[49,50,80] Direct recordings of sympathetic-nerve activity suggest that short-term alcohol ingestion in humans and both short and long-term administration of ethanol in rats stimulates sympathetic-nerve discharge.[80, 81, 83, 84] Moreover, in rats the alcohol-induced increases in blood pressure and sympathetic activity is centrally mediated.[84] It is possible that alcohol may stimulate adrenals to release adrenaline, resulting in increased heart rate cardiac output and systolic blood pressure.[46] Randin et al[85] have also reported that alcohol induces hypertension in rats by sympathetic activation that appears to be centrally mediated. Alcohol also perturbs the baro reflex by interacting with receptors in the brain stem.[80] Other investigators reported that baroreceptor reflex curves, which indicate the gain in baroreceptor reflex sensitivity, were shifted up and reduced slope in ethanol fed rats when challenged with vasoconstrictors (phenylephrine and angiotensin II) compared with controls.[80, 86] This findings and others[50, 80, 83, 86-88] suggest the impairment of baroreceptor control and sympathetic system. A greater decrease in heart rate in ethanol treated rats compared with control rats during β-adrenoreceptor blockade with propranolol indicates that the ethanol treated rats had an increased sympathetic activity. An increase in sympathetic activity is consistent with impairment of the baroreceptors that, when activated, inhibit the sympathetic nervous system.[84, 86] However this mechanism is more likely implicated in acute alcoholic beverages-induced hypertension.

2)Renin-angiotensin-aldosterone system (RAAS) in alcoholic beverages-induced hypertension.

The renin-angiotensin-aldosterone system (RAAS) plays an important role in the regulation of blood pressure. Angiotensin-II (Ang II) is a vasoconstrictor released by proteolytic cleavage of the precursor molecule, angiotensinogen (AGT) by renin and angiotensin-I converting enzyme (ACE). Overexpression of human AGT in transgenic animals results in blood pressure elevation while AGT gene-knock out reduces blood pressure in mice.[89] **C**hronic alcoholic beverages exposure followed by binge alcohol exposure causes increased mRNA level of AGT in mice.[90] Formation of increased Ang II can be anticipated from increased synthesis and secretion of AGT. Recent studies have demonstrated a significant increase in blood and aortic angiotensin II levels after alcohol exposure to rats.[40, 91] Prolonged elevation of serum ACE activity in alcoholics suggests elevated angiotensin II

levels due to activation of ACE activity.[92] The serum levels of vasoactive substances such as renin-aldosterone have been reported to be affected by alcohol ingestion in vivo or ethanol in vitro.[93, 94] Antihypertensive drugs are shown to offer protection against alcohol induced responses in cultured human endothelial cells suggesting the possible involvement of renin-angiotensin system (RAS).[94] It has been reported that a significant increase in plasma renin activity in patients consuming heavy alcohol compared to mild or moderate alcohol consumption.[93-96] Other studies reported an expansion of the extracellular fluid after alcohol consumption which has been shown to elevate the systolic blood pressure in rats.[97, 98] Chan and Sutter [97] have proposed that expansion of the extracellular fluid is the result of elevated plasma vasopressin levels and plasma renin activity, indicating increased sympathetic stimulation. Alcohol ingestion in dogs caused sustained RAS activation with progressive increases in plasma levels of Angiotensin II, renin activity, left ventricular ACE enzyme activity, and left ventricular myocyte Ang II AT1 receptor expression.[94,99] This mechanism is more likely implicated in alcohol-induced hypertension.

3) Cortisol in alcoholic beverages-induced hypertension

The role for adrenal corticotropic hormone in alcoholic beverages-induced hypertension was suggested by Linkola associates.[100] The role of cortisol was also responsible, since plasma-cortisol levels increase following acute alcoholic beverages ingestion, and a Cushing's-like syndrome (hypertension) has also been reported in chronic alcoholic beverages drinkers. There are few studies reported the role of cortisol in alcoholic beverages-induced hypertension.[53, 101, 102] Potter et al[48] have reported a significant elevation in plasma cortisol levels following intake of alcoholic beverages and when consumption of alcoholic drinks was discontinued the plasma cortisol levels dropped. The elevation of cortisol levels in chronic alcoholic beverages drinkers may likely be due to direct stimulation of adrenocorticotropin hormone (ACTH) or potentiation of corticotrophin releasing hormones (CRH) by arginine vasopressin.[102] This hypertensive response may likely be due to the mineralocorticocoid activity of cortisol or hypersensitivity to catecholamines.[101] In animal studies alcoholic drinks stimulate the release of CRH [101, 103, 104] leading to stimulation of cortisol secretion [105], stimulation of sympathetic activity leading to elevation in blood pressure. In humans dexamethasone, possibly by its inhibitory effect on CRH release, inhibits insulin-induced sympathetic activation.[106] Further study indicated that alcoholic drinks increase postganglionic sympathetic-nerve discharge[85] which was consistent with oral administration

of alcoholic drinks in human.[81, 82, 85] However this mechanism is more likely implicated in acute alcoholic beverages-induced hypertension.

4) Intracellular calcium in alcoholic beverages-induced hypertension

In experimental studies alcoholic beverages demonstrated constriction of blood vessels [107] due to greater shifts in the binding of the calcium ion (Ca^{++}) in arterial and arteriolar smooth muscle cells causes increased sensitivity to endogenous vasoconstrictors. This finding is consistent with other reports showing the shifts of the extracellular Ca^{++} to intracellular space increase the vascular sensitivity to vasoconstrictor norepinephrine.[81, 82, 98] It is proposed that alcohol increases intracellular Ca^{++} by a) direct upregulation of voltage-gated Ca^{++} channels; b) inhibition of Ca^{++}-adenosine triphosphatase (Ca^{++}-ATPase) that extrudes Ca^{++} from the cells and c) magnesium ion (Mg^{++}) depletion that inhibits the sodium ion (Na^{+})-potassium ion (K^{+}) pump (Na^{+}/K^{+}-ATPase), causing a build up of intracellular Na^{+} . This reaction in turn inhibits the Na^{+}/Ca^{++} exchanger, thereby increasing the intracellular calcium ion.[81,82,98,105,107,108] Chronic alcohol ingestion has been reported to induce a deficiency of blood and intracellular magnesium, which influences cellular Ca^{++} homeostasis through attenuation of plasmalemmal ATPase activity.[109] Vasdev et al[110] have shown that increases in cytosolic free calcium and calcium uptake are associated with ethanol-induced hypertension in rats. Intra-arterial infusion of ethanol has been shown to reduce hand and forearm blood flow in humans.[111] This effect could be the result of a direct vasoconstriction or of a loss of endothelium dependent vasorelaxation.[112] However earlier studies in rats demonstrated no significant response of alpha-adrenergic receptor-mediated constriction of aorta after chronic ethanol ingestion in rats.[37,86,113,114] On the other hand, the endothelium-dependent relaxation elicited by acetylcholine was diminished in chronic alcohol-induced hypertension.[112] Our earlier study also demonstrated the role of endothelium-independent responses in the aorta of chronic alcohol treated hypertensive rats.[37,40,41,112,113,115] Because of inconsistencies among several reports this mechanism of alcoholic beverages-induced hypertension is less likely to be implicated.

5) Endothelial oxidative stress in alcoholic beverages-induced hypertension

The oxidative stress is referred to imbalance of cellular oxidants and antioxidant system is implicated in cardiovascular diseases including hypertension.[116,117] Alcoholic beverages-induced oxidative stress in the cardiovascular system is well known.[117-119] The perturbation in the vascular angiotensin II, endothelin-1 and nor-epinephrine, vascular endothelial growth

factor (VEGF) and nitric oxide (NO) may play a major role in alcoholic beverages-induced hypertension. In vitro study has demonstrated that alcoholic beverages dose –dependently stimulate the release of vasoconstrictor endothelin 1 and 2 from vascular endothelium.[120] Alcoholic beverages have also been shown to increase the vasoconstrictor angiotensin II levels in the circulatory system.[40,121] Endothelin 1 and 2 as well as angiotensin II are known to regulate the tone of the vascular system.[40,53,92,121] Angiotensin II stimulates superoxide production via AT_1 receptor, by activating NADPH oxidase in the vascular wall.[122,123] Superoxide productions through NADPH oxidase activation ($p22^{phox}$ expression) has been demonstrated in rats made hypertensive with angiotensin II infusion.[124] Chronic ethanol ingestion induces hypertension which is correlated with elevated tissue angiotensin II levels and activation of NADPH oxidase activity causing endothelial injury in rats.[40,41,78] It is possible that alcohol ingestion raises the blood pressure by decreasing the vasodilators such as nitric oxide (NO) in the vascular endothelium either due to inhibition of endothelial nitric oxide synthase (eNOS) or inflammatory/oxidative injury to the endothelium. Earlier studies have also shown that chronic ethanol consumption either interferes with NO production or release of NO from endothelial cells.[40,53,96,125-127] The diminished NO bioavailability may either be related to reaction with superoxide anion to form peroxynitrite radicals [128] or oxidative inactivation/uncoupling of endothelial nitric oxide synthase (eNOS) by ethanol-induced free radicals.[40,41,129,130] The production of NO in the endothelium is critically dependent on the function of endothelial NO synthase (eNOS) which is regulated by vascular endothelial growth factor (VEGF).[40,131,132] Alcohol inhibits the enzyme that converts arginine into NO[133] as well as eNOS protein expression.[40,115,133] In the endothelium, depletion of NO production or NO reaction with superoxide anion to form toxic peroxynitrite radical which causes endothelial injury, impairment and hypertension in alcohol treated rats.[37,38,40,41,66,117,134] Recent studies have shown that chronic ethanol ingestion induces hypertension which was related to increased aortic inflammation, elevated angiotensin II levels, induction of NADPH oxidase causing endothelial injury, depletion of antioxidants, down-regulation of endothelial NO generating system and impaired vascular relaxation in rats.[10,37,39,40,113,115,117,135] These data clearly indicate that this mechanism is most likely implicated in chronic alcoholic beverages-induced hypertension.

MANAGEMENT OF ALCOHOLIC BEVERAGES-INDUCED HYPERTENSION

There are strategies for the management, control, prevention and treatment of alcoholic beverages-induced hypertension as shown in Figure 2. Keeping the blood pressure normal (120/80 mm/Hg) helps reduce the risk of cardiovascular disease including stroke through non-pharmacological treatments such as life style intervention.

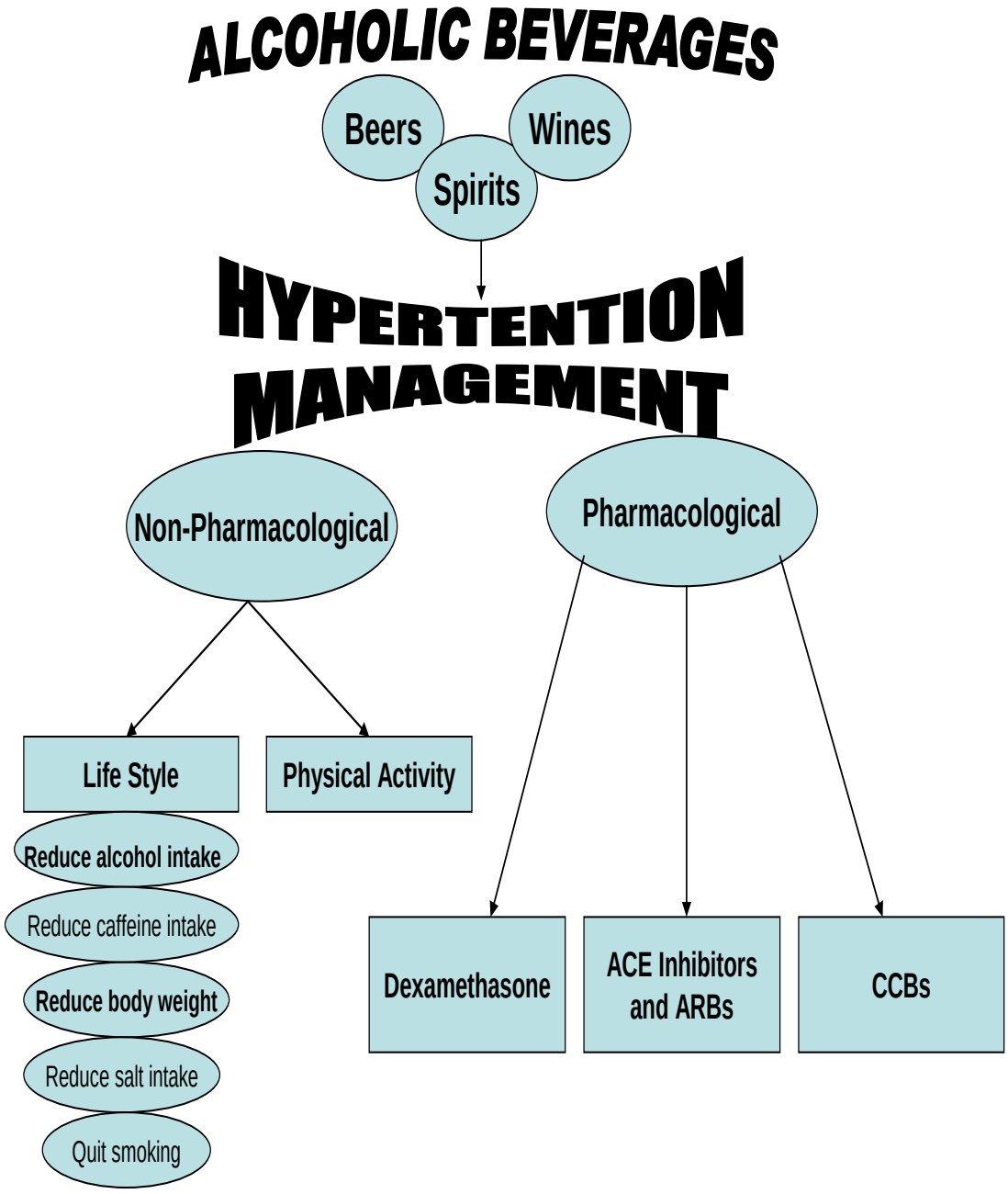

Figure 2: Management of alcoholic beverages-induced hypertension. ACE: Angiotensin-converting enzyme; ARBs: Angiotensin II type 1 receptor (AT_1) blockers; CCBs: Calcium channel blockers.

Table 1: Commonly used fermented and distilled alcoholic beverages in the world and their raw materials used for production.

Alcoholic Beverages	Raw Material Used	Names of the beverages
Beers/Wines (Fermented)	Apple	Cider
	Banana	Chuoi, Cauim
	Barley	Ale, Lager
	Coconut	Toddy
	Corn	Chicha, Tesguino
	Ginger	Ale
	Grape	Champagne, Port
	Honey	Mead, Tej
	Milk	Kumis, Kefir
	Pear	Perry, Poire
	Pine apple	Tepache
	Rice	Huangjiu, Sake, Sonti
	Sugar cane	Basi
	Rye	Kvass
	Wheat	Weizen
Spirits/Liquors (Distilled)	Apple	Applejack
	Apricot	Palinka, Kaisieva rakia
	Banana	Majmunovaca
	Barley	Scotch whisky, Soju
	Berry	Gin, Borovicka
	Coconut	Arrack
	Corn	Moonshine, Vodka
	Grape	Brandy, Vermouth
	Honey	Mead
	Milk	Arkhi
	Pear	Brandy, Poire Williams
	Plum	Slivovitz, Umeshu
	Rice	Awamori, Baijiu, Soju
	Rye	Whisky, Vodka, Korn
	Sugar cane	Rum, Pinga
	Sweet potato	Sochu, Soju
	Wheat	Whisky, Vodka, Soju

Life Style Intervention

Cutting back on alcoholic beverages drinking is one of the proven methods for reducing blood pressure. American Heart Association (AHA) recommended limiting the alcoholic beverages consumption to no more than 2 drinks per day for men and no more than one drink per day for women. Reduction of heavy drinking of alcoholic beverages to moderate drinking can lower systolic blood pressure by 2-4 mm of Hg and diastolic blood pressure by 1-2 mm of Hg. Importantly the effects of alcoholic beverages on elevating blood pressure are considered reversible.[136,137] Even in alcoholic beverages drinkers, 50% of whom have blood

pressures >160/90 mm of Hg, high blood pressure values have been reported to normalize when they reduced and abstained from drinking.[14,31,55,56] Heavy alcoholic beverages drinkers who want to lower blood pressure should slowly reduce the drinking over one to two weeks. If heavy drinkers suddenly stop drinking then they are at risk of developing severe hypertension for several days. Therefore a reduction in alcoholic beverages consumption should be included in the initial management plan rather than abstaining from drinking. The observed reductions in blood pressure following decreased alcoholic beverages intake in randomized, controlled trials are comparable to or quantitatively greater than the differences found for most other lifestyle interventions.[45,136-139] However, a meta-analysis of 15 randomized controlled trials in which alcohol reduction was the only intervention between active and control groups found that alcoholic beverage reduction lowered systolic as well as diastolic blood pressure.[73] Furthermore a randomized controlled crossover trial found that after an alcoholic beverages-reduction-induced drop in blood pressure, the resumption of baseline alcohol intake increased blood pressure back to pre-study levels.[55-57,73] These data clearly show that a reduction in alcoholic beverages intake is effective in lowering the blood pressure both in hypertensive and normotensive individuals and may help to prevent the development of hypertension.

The consumption of alcoholic beverages contributes to weight gain because it provides extra calories and weight gain is one of the risk factors for hypertension. Weight reduction was most effective in reducing blood pressure by 2.3-2.9 mm of Hg.[140,141] These data were comparable to the data of alcohol intervention.[142,143] It is also important to avoid smoking as nicotine is also one of the risk factors for hypertension. Healthy diet helps to lower blood pressure.[79] It is important to avoid consuming too much salt as this can increase blood pressure. Low sodium intake significantly reduced blood pressure by 0.9-1.7 mm of Hg.[143] These data were comparable to the data of alcohol intervention.[142] Blood pressure may be increased by drinking more than four cups of coffee per day. The drinking of coffee (caffeine) should be cut down to a minimum as it can raise heart rate and blood pressure.[79,142] These data clearly support the non-pharmacological intervention of alcoholic beverage-induced hypertension.

Physical Activity intervention

Keeping active physically and avoiding leisure activity is important for managing blood pressure. Physical activity is defined as any bodily movement produced by skeletal muscle

contraction resulting in increased energy expenditure above the resting energy expenditure. Physical activity in the broad sense includes all movements performed in daily life and cannot be reduced only to sport, whether recreational or competitive. It is recommends doing at least 150 minutes (2 hours and 30 minutes) of moderate-intensity aerobic activity a week. Additionally some muscle-strengthening activities should be performed at least twice a week. Physical conditioning or exercise training is another non-pharmacological intervention of alcoholic beverages-induced hypertension. Exercise has known to reduce the blood pressure.[141] There is a physiological basis for effect of physical conditioning on chronic alcohol-induced hypertension in a rat model. Exercise increases the utilization of oxygen in the body and up-regulate the antioxidant defense system in the cardiovascular system.[38,41,144-151] Exercise training also generates NO in the cardiovascular system by induction of nitric oxide synthase.[38,41,113,147,148,152] Recent studies have shown the beneficial role of physical training in the control of blood pressure in humans [141,144,145,149,153,154] and experimental animals.[38,41,147,155,156] Physical inactivity and overweight trigger hypertension[157-159] whereas; regular physical activity has been shown to decrease the BP and body weight.[141,154] Studies have shown that physical conditioning is beneficial in lowering the BP through suppression of weight gain in chronic ethanol treated hypertensive rats.[38,41,141,147,154] Physical conditioning attenuates the chronic ethanol-induced hypertension by augmenting the NO bioavailability and reducing the oxidative stress response in rats.[38,41,141,147,154,160] Stress is also one of the factors raises blood pressure. Therefore relaxing techniques such as yoga, meditation and stress management may also reduce the hypertensive response of the alcoholic beverages.

Pharmacological intervention of alcoholic beverages-induced hypertension

Alcoholic beverages can interfere with the effectiveness and increase the side effects of certain blood pressure medications through drug-alcohol interaction. There are limited clinical reports available on the efficacy of specific drugs for the intervention of alcoholic beverages-induced hypertension. Increase in the heart rate during the consumption of alcoholic beverages is thought to be mediated sympathetically because they are abolished by propranolol.[81,83,88] The increase in the heart rate after dexamethasone was similar to those after placebo, not greater, even though suppression of the pressor response would be expected to result in the removal of baroreflex restraint on heart-rate responses.[85] Therefore, it appears that dexamethasone also attenuated alcohol-induced stimulation of sympathetic outflow to the heart. It is also recommended the angiotensin converting enzyme (ACE)

inhibitors/angiotensin II receptor type 1 (AT_1) blockers, because of their ability to increase the cardiac output in patients with alcohol-induced cardiomyopathy will be useful in the treatment of alcohol-induced hypertension. In an experimental study by Cheng et al [99] have demonstrated that angiotensin II type 1 receptor blockade prevents alcoholic cardiomyopathy in dogs. An in vitro study has demonstrated that calcium channel blocker attenuated the alcohol-induced endothelial oxidative stress.[94] Therefore the calcium channel blockers may also likely be the drug of choice for the treatment of alcoholic beverages-induced hypertension.

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