Divergent Effect of Acute and Chronic Alcohol on Arterial Stiffness

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To study the effects of alcohol on large artery function we measured arterial wave reflection in the aorta as augmentation index (AI%) by applanation tonometry in 324 subjects (18 to 86 years, 223 male). In eight subjects, when ingested acutely, red wine containing alcohol (0.8 g/kg), but not dealcoholized wine, reduced (P < .01) blood pressure (BP), pulse wave velocity, and AI%. Men with an excessive alcohol consumption (>21 units/week) had a higher AI% (12 ± 2 vs 5 ± 2, P < .05) and BP, particularly aortic systolic, than did those with a lesser intake. This study suggests that alcohol when ingested acutely may reduce arterial stiffness, although alcohol when ingested chronically, in excess, increases it. Am J Hypertens 2002;15:240–243 © 2002 American Journal of Hypertension, Ltd.

Key Words: Alcohol, blood pressure, arterial stiffness.

Numerous mechanisms have been proposed to explain the cardioprotective effect of wine. These include an effect on platelet aggregation, an increase in HDL cholesterol, and an antioxidant effect—particularly of flavonoids, which are found in significant quantity in grape products. On the other hand, increasing consumption of alcohol, in particular, more than four drinks daily, is associated with high blood pressure (BP). Curiously, however, BP may decrease acutely after alcohol consumption. Red wine may improve endothelial dysfunction and is cardioprotective. The common experience of flushing when consuming alcohol suggests it may have a direct vasodilatory effect on blood vessels, but the effect may vary throughout the vasculature. On the other hand, chronic ingestion of large amounts of alcohol increases large artery stiffness assessed by pulse wave velocity (PWV) in middle-aged Japanese men. Therefore, to explore further the vascular effects of alcohol, we examined its effect on large artery properties both acutely and in the long term.

Methods

Study Population

We examined 324 subjects (223 male, 101 female), aged 18 to 86 years. The subjects included healthy university and hospital staff, as well as 128 patients who were undergoing evaluation for hypertension (BP >140/90 mm Hg) but who were not on any medication. We studied the acute effect of alcohol in a subset of eight healthy normotensive subjects who were nonsmokers (three men and five women, aged 21 to 40 years, with a body weight of 70 ± 3.9 kg and a height of 1.7 ± 0.2 meters, mean ± SEM), with an average alcohol intake of 10 ± 3.8 units/week. Subjects were not taking any medication or vitamin supplements. The protocol was approved by the Institutional Ethics Committee, and informed consent was obtained from all subjects.

Study Protocol

For both studies, all the subjects were studied supine after a 15-min rest before measurement of arterial wave reflection, BP, and aortic stiffness (PWV) in a quiet room at 20° ± 1°C. Subjects were asked to abstain from all caffeine-containing beverages in the 12 h before each visit as well as alcohol in the 24 h before the visit. The acute study consisted of two visits at least 1 week apart. Each subject, studied while fasting, consumed 500 mL of red wine (0.8 g/kg ethanol) or 500 mL of red wine without alcohol within 10 min in a double-blind, randomized, crossover fashion. After a stable baseline, subsequent hemodynamic measurements were made 30, 60, and 90 min after ingestion of either drink.

Blood Pressure Measurements

Brachial BP and heart rate were measured (mean of three) in the left arm with an automated digital oscillometric BP monitor (Omron model HEM 705-CP, Vernon Hills, IL).
Table 1. Hemodynamic variables categorized by sex and alcohol intake

<table>
<thead>
<tr>
<th></th>
<th>Men (n = 223)</th>
<th></th>
<th>Women (n = 101)</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Alcohol Excess</td>
<td>Normal</td>
<td>Alcohol Excess</td>
</tr>
<tr>
<td>Number</td>
<td>156</td>
<td>67</td>
<td>73</td>
<td>28</td>
</tr>
<tr>
<td>Brachial systolic BP</td>
<td>133 ± 2</td>
<td>143 ± 3*</td>
<td>133 ± 3</td>
<td>135 ± 4</td>
</tr>
<tr>
<td>Brachial diastolic BP</td>
<td>80 ± 2</td>
<td>87 ± 2†</td>
<td>79 ± 2</td>
<td>82 ± 3</td>
</tr>
<tr>
<td>Augmentation index (%)</td>
<td>5 ± 1</td>
<td>12 ± 2†</td>
<td>16 ± 2</td>
<td>16 ± 3</td>
</tr>
<tr>
<td>Aortic systolic BP</td>
<td>118 ± 2</td>
<td>128 ± 3†</td>
<td>119 ± 3</td>
<td>121 ± 2</td>
</tr>
<tr>
<td>Aortic diastolic BP</td>
<td>82 ± 2</td>
<td>88 ± 2†</td>
<td>79 ± 2</td>
<td>82 ± 2</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>70 ± 1</td>
<td>70 ± 1</td>
<td>72 ± 2</td>
<td>71 ± 2</td>
</tr>
</tbody>
</table>

BP = blood pressure.
Data are given as mean ± SEM.
* P < 0.05; † P < .01.

Derivation of the Aortic Pressure Waveform

Immediately after recording BP, the same arm was used for applanation tonometry. A high-fidelity micromanometer (BPAS-1, PWV Medical, Sydney, NSW, Australia) was used to flatten the radial artery and the peripheral radial pulse continuously recorded. The central aortic waveform was derived with radial tonometry, and augmentation index (AI%), a measure of arterial wave reflection calculated, by using a previously validated transfer factor relating peripheral to aortic waveform within the software package (Sphygmocor, PWV Medical), as previously described.5

Pulse Wave Velocity Measurements

Carotid-femoral (PWV) was determined with the foot-to-foot method using a validated technique (Complior, Colson, Dupont Medical, Pantin, France). The simultaneous recording by two pressure-sensitive transducers of the carotid and femoral waveform and measurement of the time delay of successive records from the foot of each wave divided by the distance, measured over the body surface, between the transducers allows calculation of PWV (meters/sec).

Statistical Analysis

Data were analyzed with JMP software version 3 for Windows (SAS Institute, Cary, NC), using analysis of variance. Time-related hemodynamic changes were studied by two-way analysis of variance for repeated measures applied to a crossover design and testing treatment and period effect. As there was no significant difference between the two groups, it was assumed that there was no carryover effect, and further data analysis was based on ignoring the order in which subjects received their treatment. In addition, as arterial hemodynamics parameters may be influenced by BP, we carried out a complementary analysis on PWV and AI% adjusted for the changes in BP at the time they were measured. Values are expressed as mean ± SEM, with P < .05 considered to be statistically significant.

Results

Chronic Effects of Alcohol

Subjects were divided into those with an excessive alcohol intake during the previous year of >21 units (210 g) weekly for men (n = 67) or >14 units (140 g) weekly for women (n = 27) or less. Their hemodynamic measurements are shown in Table 1. Both systolic and diastolic BP in the aorta and brachial artery were higher in men with excessive alcohol intake. The increase in systolic pressure in the aorta was more marked than the increase in the brachial systolic pressure (P < .05, Table 1). The AI% was significantly higher in the men who consumed excessive alcohol than in men with lower alcohol intake, but the difference in AI% was not significant when corrected for BP.

Acute Effects of Alcohol: Brachial Blood Pressure

There was no significant difference in the baseline hemodynamic parameters on the 2 study days. There was a significant decrease (P < .05) in brachial systolic and diastolic BP only after ingestion of red wine containing alcohol; from baseline 110 ± 3/68 ± 2 to 108 ± 3/67 ± 2 at 30 min, 107 ± 3/64 ± 1 at 60 min to 104 ± 4/62 ± 2 mm Hg at 90 min. Heart rate increased significantly after red wine with alcohol but not with dealcoholized wine (P < .05) from 58 ± 3 beats/min at baseline to 62 ± 3 at 90 min.

Changes in Aortic Pressures and Arterial Wave Reflection

Both aortic systolic and diastolic BP decreased significantly after consumption of red wine containing alcohol; aortic systolic pressure decreased from 93 ± 4 at baseline to 89 ± 3 at 90 min (P < .05) and aortic diastolic pressure from 66 ± 2 to 62 ± 2 mm Hg (P < .05) at 90 min. No
such changes were seen with the dealcoholized red wine (Fig. 1).

The AI% decreased significantly from 5% ± 2% at baseline to 1% ± 3% (*P < .05) at 90 min after red wine with alcohol only (Fig. 1). The decrease in AI% was still significant when corrected for the fall in BP (*P < .05).

Changes in Pulse Wave Velocity

At baseline, PWV was significantly (*P < .05) correlated with brachial systolic (*r = 0.59*) and diastolic BP (*r = 0.46*). The PWV decreased significantly after ingestion of red wine containing alcohol, from 7.6 ± 0.2 meters/sec at baseline to 6.9 ± 3 meters/sec at 90 min (*P < .001*) but no change was seen with dealcoholized wine (Fig. 1). The change in PWV was significant even when adjusted for BP changes (*P < .05*).

Discussion

In this study, acute ingestion of red wine containing alcohol reduced PWV and decreased arterial wave reflection in the ascending aorta, as well as decreasing aortic and brachial BPs. The changes in arterial stiffness were still significant when corrected for the fall in BP. In contrast, chronic ingestion of alcohol at levels greater than those recommended shows evidence of increased stiffness and BP.

Only red wine containing alcohol produced an acute reduction in BP, an effect seen in some (but not all) previous studies.1-2 This may be attributed in part to the amount of alcohol, the population under study, and the duration of observation.3 In hypertensive subjects, acute alcohol intake initially lowered BP through systemic vasodilation.7 In normal men who were given 15, 30, and 60 g of alcohol, for the higher dose, mean BP, using 24-h ambulatory BP monitoring, was 4/2 mm Hg lower in the period immediately after alcohol but 7/4 mm Hg higher at night.8 The pressor effect is usually greater on the day after alcohol withdrawal.2 Alcohol-induced changes in magnesium and calcium have been advanced to explain these seemingly paradoxical effects on vasculature.9 At low alcohol concentrations arterial relaxation is potentiated by a reduction in intracellular calcium, but at high concentrations magnesium depletion occurs with intracellular calcium overload and vascular contraction. Such ethanol-induced contraction may be abolished by caffeine pretreatment.9 We excluded caffeine from our study, as it has been shown that caffeine may itself have a pressor effect and acutely increases arterial stiffness.10 Of interest combining alcohol and caffeine generally offset the pressor effects observed with either of these substances administered alone.11

Although there is evidence that some of the vascular effects of wine, such as flow-mediated dilation of the brachial artery3 and increasing coronary flow vascular reserve,12 may be attributable to constituents of the grape (in particular, flavonoids), the acute effect on BP, as seen in this and other studies,8 is due to a direct vascular effect of alcohol. Our data also suggest that the acute effect on stiffness may be partly independent of BP. In contrast, the
effects of chronic, excessive consumption of alcohol included stiff arteries in the male subjects, which may be secondary to the higher BP in these men. Women who had no increase in AI% also had no increase in BP after chronic, excessive consumption of alcohol. Although the slightly higher BP in women with excessive alcohol consumption was not significant, because a pressor effect has been seen in larger epidemiologic studies, we believe that our results may be attributed to the relatively small number of women studied, and that alcohol intake is generally less in women than in men with excessive intake.

The increase in systolic pressure in men was almost twice as high in the aorta as in the brachial artery. Such a preferential effect of alcohol in aortic systolic pressure over brachial pressure may be the underlying mechanism of increased aortic stiffness after excessive alcohol intake in the long term. We believe that the effect on stiffness is important. Although related to BP, increased aortic stiffness may be an independent risk factor in hypertensive individuals and in persons with end-stage renal disease. Indeed, a fall in PWV rather than BP was the important prognostic determinant in a 12-year follow up of patients with renal disease.

It is therefore clear that, depending on the vascular territory, the amount of alcohol and its vehicles (wine, beer, etc) and period of ingestion may have disparate, and sometimes opposite, effects. Acutely, alcohol may reduce arterial wave reflection and pulse pressure amplification of adding angiotensin II receptor blockade in resistant hypertension. J Hum Hypertens 2000;14:541–546.

References