Alcohol Potentiates Orthostatic Hypotension
Implications for Alcohol-Related Syncope

Krzysztof Narkiewicz, MD, PhD; Ryan L. Cooley, MD; Virend K. Somers, MD, PhD

Background—Alcohol consumption may be linked to syncopal events. The mechanisms by which alcohol may induce syncope are unknown. Impairment of the response to orthostatic stress may be involved. Using a double-blind, randomized, placebo-controlled study, we tested the hypothesis that short-term alcohol intake causes orthostatic hypotension because of an impairment in the vasoconstrictor response to orthostatic stress.

Methods and Results—We examined the effects of alcohol on blood pressure, heart rate, and forearm vascular resistance (FVR) during orthostatic stress achieved by stepwise increases in lower-body negative pressure (LBNP) in 14 healthy young volunteers. During the placebo session, blood pressure did not change significantly during LBNP at −5, −10, and −20 mm Hg. A significant decrease in blood pressure was evident only at −40 mm Hg. In contrast, blood pressure fell significantly at all levels of LBNP during the alcohol session. Compared with placebo, alcohol potentiated the hypotensive responses to LBNP, particularly at −40 mm Hg, when the decrease in systolic blood pressure after alcohol intake (−14 mm Hg) was double that after placebo intake (−7 mm Hg). FVR increased with LBNP after placebo. However, after alcohol intake, FVR did not increase during LBNP despite the potentiated decrease in blood pressure. FVR responses during LBNP were reduced during alcohol compared with placebo consumption (P<0.04).

Conclusions—Short-term alcohol consumption elicits hypotension during orthostatic stress because of impairment of vasoconstriction. These findings have implications for the understanding of the hemodynamic effects of alcohol and, in particular, for understanding syncopal events that occur in association with alcohol intake. (Circulation. 2000;101:398-402.)

Key Words: alcohol ■ blood pressure ■ hypotension
session and an alcohol session. Each session was conducted at the same time of day on 2 separate days. Vasovagal responses or discomfort during LBNP in 5 subjects resulted in completion of studies examining the effects of both alcohol and placebo in only 14 subjects (13 men, 1 woman; mean age, 26±2 years).

Heart rate was measured continuously by an ECG. Systolic, diastolic, and mean blood pressures were measured each minute by an automatic sphygmomanometer (Life Stat 200, Physio-Control Corp). Forearm blood flow was measured by venous occlusion plethysmography as previously described.1 FVR was calculated by dividing mean arterial pressure by flow and is expressed in arbitrary units. In 6 subjects, measurements of central venous pressure (CVP) were obtained during both placebo and alcohol sessions with a catheter inserted percutaneously into an antecubital vein and advanced into an intrathoracic vein.

Protocol and Interventions
Subjects were studied in the supine position. After undergoing baseline measurements for 10 minutes, alcohol (1.0 g/kg body weight, diluted in 400 mL of water) or placebo (400 mL water) was administered orally over a 30-minute period. A flavoring (Crystal Light) was added to these solutions to prevent the subjects from being able to detect alcohol during the placebo session. A value of 0.001 versus placebo). During the alcohol sessions, plasma alcohol increased from 0 to 105±5 mg/dL at 60 minutes after alcohol intake (P<0.001). Alcohol produced only mild levels of intoxication. All subjects were able to walk after completion of the study and were not inebriated. Plasma alcohol was undetectable during the placebo session.

Effects of Alcohol on Resting Measurements
Resting blood pressure, CVP, and FVR did not change significantly after alcohol compared with placebo intake (Table 1). Alcohol increased baseline heart rate from 57±2 to 63±2 bpm (P<0.001 versus placebo).

Effects of Alcohol on Responses to LBNP
CVP decreased progressively during graded LBNP (Table 2 and the Figure). Changes in CVP were similar after both alcohol and placebo intake (Table 2). During the placebo session, blood pressure did not change significantly during LBNP at −5, −10, and −20 mm Hg. A significant decrease in blood pressure was evident only at −40 mm Hg (Table 2). In contrast, blood pressure fell significantly at all levels of LBNP during the alcohol session (Table 2). Compared with placebo, alcohol potentiated the hypotensive response to LBNP (Table 2 and the Figure), particularly at −40 mm Hg, when the decrease in systolic blood pressure after alcohol consumption (−14 mm Hg) was double that after placebo intake (−7 mm Hg).

FVR increased with LBNP after placebo intake (Table 2 and the Figure). After alcohol intake, however, FVR did not change significantly during LBNP (Table 2), despite the accompanying decrease in blood pressure. FVR responses during LBNP were reduced during alcohol compared with placebo intake (P=0.04; the Figure). Heart rate increased during LBNP at −40 mm Hg during both sessions (Table 2 and the Figure). Despite a significantly greater decrease in blood pressure with orthostatic stress during the alcohol session, the heart rate response was not statistically different between the 2 sessions (Table 2). In a cross-sectional analysis, no relationship between alcohol concentration and hemodynamic responses was evident across subjects.

Discussion
One important and novel finding of this study is that mild orthostatic stress (LBNP of −5 to −20 mm Hg) lowers blood pressure significantly in healthy subjects after alcohol but not placebo intake. Another is that alcohol results in a 2-fold increase in the hypotensive response to more marked orthostatic stress (LBNP of −40 mm Hg). A third is that alcohol disrupts the vasconstrictor response to orthostatic stress. During LBNP (which should stimulate cardiopulmonary reflex vasoconstriction) and despite the accompanying lower

### TABLE 1. Effects of Placebo and Alcohol Intake on Blood Pressure, CVP, and Heart Rate*

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Placebo</th>
<th>Alcohol</th>
<th>Session-by-Time Interaction, P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP, mm Hg</td>
<td>115±2</td>
<td>111±3</td>
<td>0.72</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>62±2</td>
<td>61±2</td>
<td>0.23</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>81±2</td>
<td>79±2</td>
<td>0.49</td>
</tr>
<tr>
<td>CVP, mm Hg</td>
<td>8.6±1.3</td>
<td>8.9±1.4</td>
<td>0.92</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>59±2</td>
<td>57±2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; and HR, heart rate.

*Values are mean±SEM; n=14 except for CVP (n=6). P values are for the session-by-time interaction term (ANOVA).

Results

### Plasma Alcohol Levels
During the alcohol sessions, plasma alcohol increased from 0 to 105±5 mg/dL at 60 minutes after alcohol intake (P<0.001). Alcohol produced only mild levels of intoxication. All subjects were able to walk after completion of the study and were not inebriated. Plasma alcohol was undetectable during the placebo session.
blood pressure (which should trigger arterial baroreflex mediated vasoconstriction), there was no vasoconstrictor response evident after alcohol. This blunted response is in striking contrast to the effects of LBNP after placebo, when forearm vasoconstriction was clearly present, even though blood pressure was much higher during placebo and LBNP.

Previous studies examining the effects of alcohol ingestion on erect blood pressure in normal subjects report conflicting results, showing either a decrease\(^\text{12}\) or no change\(^\text{13}\) in blood pressure. A low dose of alcohol (0.5 g/kg body weight) tended to lower systolic blood pressure after 10 minutes of 45° head-up tilt, but this decrease was not statistically significant.\(^\text{14}\) In the present study, we used higher doses of alcohol (1.0 g/kg body weight). Thus, the potentiated decrease in orthostatic blood pressure after alcohol may be dose dependent. Levels of alcohol consumption and blood alcohol levels achieved during this study were relatively modest and are frequently exceeded in real-life situations. Thus, excessive alcohol consumption may elicit more profound disruption of orthostatic tolerance and consequent symptomatic hypotension\(^\text{15}\) than described in this article. Within our subject group, however, a cross-sectional analysis revealed no relationship between hemodynamic responses to LBNP and plasma alcohol levels.

It is important that alcohol induces orthostatic hypotension even in young, healthy subjects. These responses may vary in subjects who are habitual drinkers or in whom other disease states are present. In the setting of preexisting impairment of orthostatic tolerance, alcohol may elicit more profound orthostatic hypotension, leading to symptomatic hypotension.

**TABLE 2. Effects of Graded LBNP on Blood Pressure, FVR, CVP, and Heart Rate During Placebo and Alcohol Sessions**

<table>
<thead>
<tr>
<th>LBNP, mm Hg</th>
<th>0</th>
<th>-5</th>
<th>-10</th>
<th>-20</th>
<th>-40</th>
<th>Session-by-Time Interaction, P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>117±3</td>
<td>115±2</td>
<td>114±2</td>
<td>113±3</td>
<td>110±3‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol</td>
<td>113±3</td>
<td>110±3‡</td>
<td>108±3§</td>
<td>106±3§</td>
<td>99±3§</td>
<td></td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>65±2</td>
<td>64±2</td>
<td>62±2</td>
<td>62±2</td>
<td>60±2‡</td>
<td>0.25</td>
</tr>
<tr>
<td>Alcohol</td>
<td>61±2</td>
<td>59±2‡</td>
<td>59±2‡</td>
<td>57±2‡</td>
<td>53±2‡</td>
<td></td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>84±2</td>
<td>83±2</td>
<td>81±2</td>
<td>81±2</td>
<td>80±3‡</td>
<td>0.01</td>
</tr>
<tr>
<td>Alcohol</td>
<td>80±2</td>
<td>78±2‡</td>
<td>77±2‡</td>
<td>75±2§</td>
<td>72±2§</td>
<td></td>
</tr>
<tr>
<td>FVR, U</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>42±4</td>
<td>50±5</td>
<td>51±5</td>
<td>61±7‡</td>
<td>60±6‡</td>
<td>0.04</td>
</tr>
<tr>
<td>Alcohol</td>
<td>50±7</td>
<td>45±5</td>
<td>50±6</td>
<td>53±6</td>
<td>55±5</td>
<td></td>
</tr>
<tr>
<td>CVP, mm Hg</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>9.0±1.3</td>
<td>7.5±1.1‡</td>
<td>6.1±1.0§</td>
<td>4.1±1.2§</td>
<td>1.5±0.5§</td>
<td>0.98</td>
</tr>
<tr>
<td>Alcohol</td>
<td>9.4±1.3</td>
<td>7.7±1.6‡</td>
<td>6.2±1.5§</td>
<td>3.9±1.3§</td>
<td>1.7±0.6§</td>
<td></td>
</tr>
<tr>
<td>HR, bpm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>58±2</td>
<td>57±2</td>
<td>58±2</td>
<td>60±2</td>
<td>77±2§</td>
<td>0.07</td>
</tr>
<tr>
<td>Alcohol</td>
<td>63±2</td>
<td>62±2</td>
<td>63±2</td>
<td>67±2</td>
<td>88±3§</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1. *Values are mean±SEM; n=14 except for CVP (n=6). P values are for the session-by-time interaction term (ANOVA).

\(\dagger P<0.05, \ddagger P<0.01, \§ P<0.001\) for comparison with 0 mm Hg LBNP.

Changes in mean arterial pressure (MAP), FVR, and heart rate (HR) in response to LBNP during placebo (○) and alcohol (●) sessions. Decreases in MAP were greater and increases in FVR were smaller during alcohol than during placebo session. Data are mean±SEM. *P<0.05 for session-by-time interaction for all levels of LBNP.
orthostatic responses, such as in elderly subjects and diabetics, we speculate that orthostatic hypotension after alcohol intake may be especially pronounced. Furthermore, effects of orthostatic hypotension on cerebral perfusion may be exacerbated in patients with underlying cerebral vascular disease and consequent impaired cerebral autoregulation. Indeed, in patients with primary autonomic failure, alcohol enhanced the decrease in blood pressure during head-up tilt. In patients with congestive heart failure, short-term alcohol intake decreased blood pressure even in patients in the supine position. Systematic studies in patients with neurally mediated syncpe show an attenuation of the sympathetic vasoconstrictor response to orthostatic stress. Thus, in these and other populations, orthostatic stress after alcohol intake may result in significant hypotension and frank syncpe.

Important strengths of this study include the double-blind study design and the graded levels of orthostatic stress. Simultaneous measurements of FVR allowed us to identify the impaired vasoconstriction as a key component in orthostatic hypotension after alcohol. CVP changes with LBNP were very similar during both placebo and alcohol intake. Therefore, the blunted vasoconstriction after alcohol was not explained by higher cardiac filling pressures after alcohol compared with placebo consumption. However, our data do not clarify whether the impaired vasoconstriction is secondary to an attenuated sympathetic vasoconstrictor response to orthostatic stress or whether the sympathetic response is preserved but the vasoconstriction attenuated by direct vasodilator effects of alcohol. Previous studies indicated that short-term alcohol administration impairs baroreflex sensitivity. In the present study, sympathetic traffic was not measured, and baroreflex function was not formally tested. However, the heart rate response to the decreased blood pressure during LBNP suggests possible blunting of the baroreflex by alcohol administration. A reduced baroreflex gain after alcohol ingestion would also contribute to the impaired vasoconstriction observed in our study.

The augmented hypotension evident during orthostatic stress may thus result from an interaction between several potential mechanisms. Direct vascular effects of alcohol would elicit vasodilation. The consequent reduction in blood pressure could potentially be augmented by impairment of reflex cardiopulmonary and/or arterial baroreceptor responses, which may themselves be attenuated by effects of alcohol on their sensory afferents or on central brainstem mechanisms modulating these reflexes. An additional consideration is the possibility that alcohol may conceivably act peripherally to attenuate the vasoconstrictor and/or chronotropic responses to sympathetic activation.

Our findings have several important implications. The first involves our understanding of the hemodynamic effects of alcohol in the ambulatory setting. During ambulatory blood pressure measurements, repeated hypotension in response to standing may explain why alcohol raises supine blood pressure but lowers ambulatory blood pressures. The second involves our understanding of the possible mechanisms underlying micturition syncpe. Bladder distention (due in part to the diuretic effect of alcohol) induces increases in blood pressure, which would oppose any alcohol-induced postural hypotension. We speculate that micturition, and consequent bladder emptying, would thus remove the pressor effect of bladder distention, allowing unopposed alcohol-induced postural hypotension with consequent syncpe. Third, our results may help in the understanding of some cases of unexplained syncpe. In an overview of syncopal events of obscure nature, Fisher has noted in a number of cases the involvement of a combination of alcohol intake and subsequent assumption of the erect posture.

In summary, these data demonstrate that in healthy young subjects, short-term alcohol consumption elicits hypotension during orthostatic stress because of impairment of vasoconstriction. These findings have implications for understanding of the hemodynamic effects of alcohol, particularly for understanding the syncopal events that occur in association with alcohol intake.

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References


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