Acute Effects of Ethanol on Left Ventricular Performance

By Lawrence D. Horwitz, M.D., and James M. Atkins, M.D.

SUMMARY

The cardiac effects of ethanol were studied in six conscious dogs chronically instrumented for analysis of left ventricular pressure, internal transverse diameter, and outflow. Successive intravenous infusions of ethanol produced blood levels of 120 ± 16 (SEM) mg% (infusion #1) and 311 ± 19 mg% (infusion #2). Stroke volume decreased from 20.1 ± 1.6 ml preinfusion to 17.2 ± 1.9 ml after infusion #1 (P < 0.01) and 13.6 ± 1.9 ml after infusion #2 (P < 0.01). Left ventricular end diastolic pressure increased 2.5 mm Hg with infusion #1 (P < 0.05) and 6.0 mm Hg with infusion #2 (P < 0.05). Left ventricular dp/dt max fell 17% with infusion #1 (P < 0.001) and 30% with infusion #2 (P < 0.01). Left ventricular diameter increased at end diastole and end systole with ethanol. Heart rate was unchanged with infusion #1 and increased with infusion #2; left ventricular systolic pressure was unaltered. Studies after pharmacological autonomic denervation with propranolol and atropine demonstrated changes in left ventricular dp/dt max, left ventricular end diastolic pressure, and stroke volume similar to unblocked results. Thus ethanol at blood levels commonly encountered in social usage is a potent myocardial depressant.

Additional Indexing Words:
Myocardial contractility Autonomic denervation Stroke volume

Although ethyl alcohol has been imbied, abused, admired, and deplored since the beginning of recorded history, the acute hemodynamic effects of alcoholic beverages have been incompletely studied. Most available information is based on data from anesthetized animal preparations or fragmentary observations in man and has suggested that ethanol may be a myocardial depressant. This study was undertaken to assess the acute effects of ethyl alcohol in conscious dogs which had been chronically instrumented for analysis of left ventricular function. The results establish that dosages of ethyl alcohol encountered commonly in social usage produce myocardial depression and potentially deleterious hemodynamic alterations.

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Methods

Six mongrel dogs weighing 11.3–19.5 kg underwent a sterile thoracotomy under sodium pentobarbital anesthesia. Through a stab incision on the anterior wall just above the apex, a Konigsberg P18 high-fidelity, solid-state pressure transducer was implanted within the left ventricle. A Zepeda electromagnetic flow probe was placed around the ascending aorta. Eighteen-gauge polyvinyl catheters were inserted into the right and left atria. The dogs were allowed seven to ten days for recovery before experiments began.

In two of the dogs discoid sonocardiometer transducers were implanted within the left ventricle through a stab incision on the anterior wall during a brief occlusion of the superior and inferior venae cavae. The transducers were positioned across the greatest internal transverse diameter of the left ventricle, one on the anterior and the other on the posterior endocardial wall.

The solid-state pressure transducers have a natural frequency in excess of 3000 Hz and do not change in sensitivity during implantation. At the beginning of each study day-to-day zero drift was corrected for by assuming that left ventricular end diastolic pressure was equal to the simultaneous mean left atrial pressure measured via the implanted catheter with a Statham P23Db manometer. The left ventricular pressure was differentiated by an active RC network; there is a decrease of 3 db at 100 Hz.

Aortic phasic flow was recorded with a Zepeda EDP2 square wave flowmeter. Flow probes were calibrated in vitro prior to implantation. It was assumed that flow was zero at end diastole. Stroke volume was obtained.
by integrating the systolic portion of the phasic flow signals with an active RC network. All signals were recorded on a Beckman RM oscillograph and an Ampex PR 500 tape recorder. In two dogs left ventricular internal transverse diameter was obtained with a sonocardiometer which measured the transit time of 5-MHz ultrasound between the two piezoelectric crystal transducers at a sampling rate of 5000 times/sec. The resolution of the instrument is to the nearest 0.07 mm.

During experiments the animals lay quietly in a sling. After initial control measurements were obtained, ethanol 0.5 g/kg was infused into the right atrium over a 10-minute period. The infusate was a 50% ethanol solution made by mixing equal amounts of pure ethanol and one-half normal saline. Immediately after this infusion, designated infusion #1, all hemodynamic measurements were repeated and a left atrial blood sample was drawn for measurement of the blood ethanol levels. Subsequently, an additional 1.0 g/kg of ethanol was administered over the next 10 minutes, as infusion #2. Immediately after this infusion all measurements were repeated. Three days later, the ethanol infusions were repeated after pharmacological autonomic denervation. Proparanolol hydrochloride 1 mg/kg and then atropine sulfate 0.1 mg/kg were administered through the right atrial catheter. Fifteen minutes later control measurements were obtained and the ethanol infusions were given as on the first experimental day. Blood ethanol levels were measured according to the method of Kingsley and Current. Statistical analyses were performed by paired t tests using each animal as its own control.

**Results**

In three dogs control experiments were performed by infusing a solution of 1/2 normal saline and 5% dextrose in water mixed in equal volumes at identical infusion rates and under the same conditions as the ethanol infusions. There were no consistent changes in any hemodynamic parameters. In two animals identical controls were performed with autonomic blockade and again no consistent changes were noted.

The mean blood ethanol level immediately after infusion #1 was 120 ± 16 (SEM) mg%. After infusion #2 the level rose to 311 ± 19 mg%. Ethanol-induced hemodynamic changes are shown in table 1 for studies with intact autonomic innervation and in table 2 for studies with pharmacological denervation. A representative recording is shown in figure 1.

**Heart Rate and Stroke Volume**

With intact autonomic innervation heart rate did not change during infusion #1 but increased significantly with infusion #2. With autonomic blockade the preinfusion heart rate was set at a high level which fell slightly after infusion #1 and returned toward the preinfusion level after infusion #2.

With intact autonomic innervation, stroke volume fell in all six dogs with infusion #1 and subsequently fell further with infusion #2. With autonomic blockade, the preinfusion stroke volume was low and did not change with infusion #1. However, there was a significant reduction in stroke volume after infusion #2.

**Left Ventricular Pressure and dp/dt Max**

Mean left ventricular end diastolic pressure rose significantly after infusion #1 and rose further after infusion #2 during both intact and autonomic blockade studies. Left ventricular peak systolic pressure did not change significantly after ethanol infusions.

**Table 1**

<table>
<thead>
<tr>
<th>Hemodynamic Effects of Ethanol With Autonomic Innervation Intact</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
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<tr>
<td></td>
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<tr>
<td>Stroke volume (ml)</td>
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<tr>
<td></td>
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<tr>
<td>Left ventricular end diastolic pressure (mm Hg)</td>
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<tr>
<td></td>
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<tr>
<td>Left ventricular peak systolic pressure (mm Hg)</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Left ventricular dp/dt max (mm Hg/sec)</td>
</tr>
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</tbody>
</table>

Mean measurements of hemodynamic variables during control period and after ethanol infusion #1 (0.5 g/kg) and after ethanol infusion #2 (additional 1.0 g/kg). Values are ± standard error of the mean. NS = P > 0.05.
Table 2

**Hemodynamic Effects of Ethanol With Pharmacological Autonomic Blockade**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Infusion #1</th>
<th>Infusion #2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>160 ± 9</td>
<td>145 ± 7</td>
<td>133 ± 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>P</em> &lt; 0.05</td>
<td>NS</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>14.6 ± 1.7</td>
<td>14.9 ± 1.6</td>
<td>12.3 ± 1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NS</td>
<td><em>P</em> &lt; 0.01</td>
</tr>
<tr>
<td>Left ventricular end diastolic pressure (mm Hg)</td>
<td>0.5 ± 1.0</td>
<td>2.5 ± 1.0</td>
<td>7.5 ± 2.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>P</em> &lt; 0.05</td>
<td><em>P</em> &lt; 0.01</td>
</tr>
<tr>
<td>Left ventricular peak systolic pressure (mm Hg)</td>
<td>101 ± 5</td>
<td>105 ± 6</td>
<td>108 ± 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Left ventricular dp/dt max (mm Hg/sec)</td>
<td>1926 ± 211</td>
<td>1673 ± 156</td>
<td>1343 ± 117</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>P</em> &lt; 0.05</td>
<td><em>P</em> &lt; 0.01</td>
</tr>
</tbody>
</table>

The maximum first derivative of the left ventricular pressure (dp/dt max) fell significantly after ethanol. This change occurred in all six dogs. With autonomic innervation intact, the reduction from the preinfusion level was 17% after infusion #1 and 30% after infusion #2. Autonomic blockade decreased the preinfusion dp/dt max in most animals; the reductions from the preinfusion level were 13% after infusion #1, and 30% after infusion #2.

**Left Ventricular Diameter**

As shown in table 3, left ventricular internal transverse diameter was measured in two dogs with intact autonomic innervation. Both end diastolic diameter and end systolic diameter increased in response to ethanol. The increase at end systole exceeded that at end diastole.

**Discussion**

Although acutely administered ethanol appeared to be a myocardial depressant in most previous studies, there has been some disagreement. Various investigators have concluded that ethanol improves,5 has little or no effect,6,7 or impairs9-11 cardiac function. In anesthetized animals, Regan10 found myocardial depression at blood levels of 110 mg/100 ml but Webb et al.6 found no depression in heart-lung preparations at levels up to 900 mg%.

![Figure 1](http://circ.ahajournals.org/)

**Figure 1**

Hemodynamic effects of ethanol 0.5 mg/kg body weight intravenously (infusion #1) and 1.5 g/kg intravenously (infusion #2) in a conscious dog with intact autonomic innervation. Ethanol resulted in reductions in the maximum first derivative of the left ventricular pressure (LV dp/dt) and stroke volume, and elevation in the left ventricular end diastolic pressure.
Table 3

Effect of Ethanol on Left Ventricular Diameter

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Infusion #1</th>
<th>Infusion #2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EDD</td>
<td>ESD</td>
<td>EDD</td>
</tr>
<tr>
<td>Dog #3</td>
<td>25.0</td>
<td>16.8</td>
<td>26.1</td>
</tr>
<tr>
<td>Dog #4</td>
<td>33.3</td>
<td>26.6</td>
<td>33.5</td>
</tr>
</tbody>
</table>

Measurements in mm of left ventricular internal transverse diameter at end diastole (EDD) and end systole (ESD) in two conscious dogs.

Riff, Jain, and Doyle\(^7\) found no changes in myocardial function in normal human volunteers, with blood levels ranging from 85 mg/100 ml to 136 mg/100 ml, either at rest or with exercise. Blomqvist, Saltin, and Mitchell\(^8\) reported no change in maximal oxygen uptake by human volunteers performing graded exercise, although there was evidence that mechanical efficiency was decreased during submaximal exercise. However, after oral ingestion of only 2 oz of Canadian whiskey, Gould, Zahir, DeMartino, and Compreg\(^1\) reported myocardial depression in patients with cardiac disease, although they detected little or no effect in normal patients. Conway\(^12\) found evidence of myocardial depression in patients with coronary artery disease who drank 0.5 g/kg of ethanol. Paradoxically, the findings of Juchems and Klobe\(^9\) can be interpreted as demonstrating improved myocardial function at blood ethanol levels of 39 and 120 ml/100 ml.

Since anesthetics are themselves myocardial depressants, the variation in anesthetized animal experiments may reflect difficulty in distinguishing superimposed changes in a subnormal preparation. The studies of human subjects were hampered by the low sensitivity of routine cardiac catheterization procedures. Measurements of cardiac output by Fick or dye dilution methods and pressure measurements with conventional fluid-filled catheter systems may not have been adequate for detection of subtle changes. An additional problem with some human studies was the use of extremely small dosages of oral ethanol, which would have produced very low blood levels at the time of study. The present investigation in chronically instrumented conscious dogs circumvents these difficulties. There is no anesthetic, and a high-fidelity pressure system and a sensitive electromagnetic flowmeter provide optimum measurements for assessment of left ventricular function. The validity of left ventricular end diastolic pressure changes as an indication of preload changes was confirmed in two dogs by measurement of left ventricular internal diameter, which varies directly with left ventricular volume.\(^13\) The dosages of ethanol are high but equivalent to levels commonly encountered in the adult population.

The finding of consistent decreases in the maximum first derivative of the left ventricular pressure and elevations in left ventricular end diastolic pressure, without significant alteration in left ventricular systolic pressure and either no change or increases in heart rate, unequivocally demonstrates a diminished myocardial contractility in these conscious dogs. These changes represent a diminished rate of force development by the myocardial muscle fibers and an increase in preload through the Frank-Starling mechanism. In addition, the decreases in stroke volume are evidence, in this setting, that the extent of muscle fiber shortening is decreased. The presence of a Frank-Starling response and diminished shortening was confirmed in two animals by left ventricular diameter measurements which showed small increases at end diastole and larger increases at end systole.

Aortic pressure was not measured, since to do so would have required additional surgery with sacrifice of a carotid artery. It can be assumed that aortic systolic pressure did not change in response to ethanol, because left ventricular systolic pressure did not change. Systemic vascular resistance, estimated from the cardiac output and left ventricular pressure during ejection, did not change consistently. Inasmuch as the maximum rate of pressure rise occurs prior to the time at which the aortic valve opens, it is independent of the level of aortic diastolic pressure. Accordingly, it is highly unlikely that significant changes in aortic pressure either occurred or influenced the changes in left ventricular dynamics.

The demonstration of myocardial depression in response to ethanol during pharmacological autonomic denervation establishes that the effects of the alcohol infusions on the myocardium are direct and not mediated through autonomic mechanisms. Tachycardia occurred after the higher ethanol dosage when autonomic innervation was intact, but not during autonomic blockade. This may represent a compensatory mechanism to maintain cardiac output in the presence of a diminished stroke volume, and could be related to distention of stretch receptors by the elevated filling pressures and either diminished vagal tone or enhanced sympathetic tone.\(^14\)

The blood alcohol levels after the first infusion were the equivalent of those in averaged-sized

* Circulation, Volume XLIX, January 1974
human subjects drinking 4-5 oz of 90 proof whiskey, and are compatible with mild intoxication. It is a level slightly below the 150 mg% legal limit for safe operation of an automobile. The second infusion would require the equivalent of a 10-11 oz ingestion in a human subject and would be associated with moderate intoxication in most individuals. The finding of detectable evidence of myocardial depression with dosages commonly encountered among the population may have considerable clinical significance. Popular conceptions of alcohol as a stimulant to improved physical performance appear to be questionable. Although the degree of myocardial depression observed may not greatly threaten a normal individual who is not engaged in stressful activity, those with heart disease may be placed at risk of development of or acute exacerbation of heart failure during a drinking bout.

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References
15. HIMWICH HE: The physiology of alcohol. JAMA 163: 545, 1957

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