ELECTROPHYSIOLOGIC CHANGES PRODUCED BY INTRAVENOUS ALCOHOL

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SYNOPSIS

The effect of alcohol (.1 mg/kg) on the sinus node and atrioventricular node was studied in 9 mongrel dogs. The sinus node function was evaluated by the sinus node recovery time and the atrioventricular node by the highest atrial pacing rate at which Wenckebach periodicity was developed. The effect was studied for 45 minutes. Three groups were identified: Group I, Low Concentration of Alcohol (.063 ± .012 mg%); Group II, Medium Concentration of Alcohol (.118 ± .026 mg%); and Group III, High Concentration of Alcohol (.240 ± .52 mg%).

In Group I alcohol lengthened the sinus node recovery time of 16% (p less than .05), and reduced the heart rate by 5.7% and had no effect on Wenckebach periodicity. In Group II alcohol lengthened the sinus node recovery time of 22% (p is less than .01) and reduced the heart rate by 9.8% (p is less than .01) and the Wenckebach rate by 31% (p is less than .005). The correlations were excellent between alcohol concentration and sinus node recovery time (r=0.90), heart rate (r=0.90), and rate of Wenckebach (r=0.90). The corrected sinus node recovery time was lengthened by 38% from baseline values to peak values obtained at the highest alcohol concentration (393 ± 80 msec to 640 ± 120 msec, p is less than .005).

Autonomic blockade with atropine and propranolol prevented these changes. Thus, alcohol produced a sick sinus-like syndrome. The prevention of this by autonomic blockade suggests that these abnormalities are mediated via the autonomic nervous system.

INTRODUCTION

Due to the prevalent problems of alcoholism, several researchers have investigated the chronic and acute effect of this drug on the heart. Without doubt, myocardial damage is produced by alcohol which may finally end in a cardiomyopathy (Bidgen & Robinson, 1964; Evans, 1969). Several investigators have described some of the cardiac conduction abnormalities and arrhythmias produced by

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alcohol (Ettinger et al., 1976; Muehlinger, 1969), but the reasons for these electrophysiologic abnormalities have not been described. The purpose of this study was to describe the acute effect of alcohol on sinus and atrioventricular node function. By observing the effect of alcohol after autonomic blockade, we determined whether alcohol has an effect directly on the sinus node or via the autonomic system. These changes may explain the arrhythmias seen in alcoholics.

**MATERIALS AND METHODS**

Nine mongrel dogs (canis domesticus) were studied after being anesthetized with intravenous phenobarbital. Two catheters were localized in the atrium. Right atrial pacing was performed via the catheter located at the junction of the superior vena cava and right atrium. The other catheter was used to record the intracavitary atrial electrogram. The Leads I, II, and III electrocardiograms and atrial electrograms were continuously recorded. The sinus node recovery time was measured as the interval from the last paced atrial depolarization potential to the first spontaneous atrial depolarization potential. The corrected sinus node recovery time was calculated by subtracting the basic sinus cycle from the sinus node recovery time.

A baseline value for each dog was recorded. Atrioventricular node function was measured as the highest pacing rate at which Wenckebach periodicity developed.

An infusion of ethyl alcohol was made using a dose of 1mg/kg of body weight. Sinus node recovery time, atrioventricular function, and heart rate were measured at 5 minutes, 15 minutes, and 30 minutes. At each recording time a sample of blood for alcohol analysis was obtained. This sample was analyzed by the method of Levison and Mcfate. After the data were analyzed we realized that as the alcohol was being infused the alcohol concentration increased. The levels were divided as low concentration (Group I) during the early infusion phase, medium concentration (Group II) during the middle of the infusion phase, and high concentration (Group III) which occurred during the final phase of the infusion. These alcohol concentrations are comparable to the human intoxicating doses. The mean alcohol concentration was found for each group. The mean change in sinus node recovery time, corrected sinus node recovery time (CSRT), heart rate, and change in Wenckebach rate were found for each dog. Comparisons of the data were made using the Student t Test for paired values. The correlations of the increasing alcohol concentration in each dog with the electrophysiologic parameters at the recorded level were analyzed by standard techniques.
The above measurements were made in 5 additional dogs after autonomic blockade using .2 mg/kg of propranolol and .04 mg/kg of atropine. Autonomic blockade was performed to separate extrinsic (autonomic dysfunction) from intrinsic sinus node dysfunction as described by Jordan and associates (1978).

RESULTS

The alcohol concentration of each group were as follows: Group I (Low Concentration), .063 ± .012 mg%; Group II (Medium Concentration), .118 ± .026 mg%; and Group III (High Concentration) .240 ± .052 mg%. Group I showed a 16% lengthening in sinus node recovery time ($p$ is less than .05); Group II, a 22% lengthening ($p$ is less than .01); and Group III, a 45% lengthening ($p$ is less than .005). (See Figure 1). Table 1 shows the baseline corrected sinus node recovery time and at the end of the infusion at the (highest alcohol concentration.) The change in sinus node recovery time was 393 ± 80 msec to 640 ± 120 msec ($p$ is less than .005). The average percent reduction in Wenckebach rate was: no change in Group I; 32% in Group II ($p$ is less than .05); and 31% in Group III ($p$ is less than .005). The reduction in the heart rate was of 5.7% in Group I (N.S.), 9.8% in Group II ($p$ is less than .01), and 14.4% in Group III ($p$ is less than .05).

Changes Observed in the Corrected Sinus Node Recovery Time (CSRT) After Intravenous Alcohol

<table>
<thead>
<tr>
<th>DOG</th>
<th>BASELINE (MSEC)</th>
<th>END OF EXPERIMENT (MSEC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>360</td>
<td>447</td>
</tr>
<tr>
<td>2.</td>
<td>340</td>
<td>800</td>
</tr>
<tr>
<td>3.</td>
<td>500</td>
<td>766</td>
</tr>
<tr>
<td>4.</td>
<td>439</td>
<td>800</td>
</tr>
<tr>
<td>5.</td>
<td>450</td>
<td>620</td>
</tr>
<tr>
<td>6.</td>
<td>217</td>
<td>667</td>
</tr>
<tr>
<td>7.</td>
<td>433</td>
<td>587</td>
</tr>
<tr>
<td>8.</td>
<td>450</td>
<td>507</td>
</tr>
<tr>
<td>9.</td>
<td>348</td>
<td>507</td>
</tr>
<tr>
<td>MEAN PLUS STANDARD DEVIATION</td>
<td>393 ± 80 ($p$ less than .005)</td>
<td>640 ± 120</td>
</tr>
</tbody>
</table>
The correlations in the 8 dogs between sinus node recovery time and alcohol concentration at different stages of infusion ranged between 0.87 and 0.99.

The correlation between alcohol concentration and rate of Wenckebach ranged between 0.76 and 0.99 (Figure 3), and correlation between alcohol concentration and heart rate ranged between 0.83 and 0.98 (Figure 4). As the alcohol concentration increased the heart rate for Wenckebach periodicity and the heart rate decreased. Four dogs developed spontaneous atrial fibrillation and 1 dog showed a bradytachycardia syndrome during high alcohol. These events lasted for about an hour. No attempt was made to convert them back to normal sinus rhythm.

After the autonomic blockade, the rate producing Wenckebach periodicity was reduced by 3.25%; the sinus node recovery time lengthened 7.8%; and heart rate reduced by 30%. The same infusion of alcohol (as in previous 9 dogs) induced no change in the sinus node recovery time nor in the rate to develop Wenckebach at increasing plasma levels of alcohol (Figures 5 and 6).

Two dogs had the same pacing protocol but with an infusion of saline; none showed the effects in the sinus node recovery time and the rate for Wenckebach as the dogs having an alcohol infusion.

**DISCUSSION**

The central nervous system controls the heart by way of the sympathetic and parasympathetic nerve fibers terminating in the sino atrial node (Crawford, 1933; Hutter & Trautwein, 1956; Robinson et al., 1966). Robinson and co-workers suggested that in the supine resting state, parasympathetic restraint is the dominant influence in the heart rate and the accelerating effects of sympathetic stimulation are minor, and that the speeding of the heart in response to mild exercise appears to result largely from withdrawal of parasympathetic inhibition. They also showed that the increase of the heart rate by tilting was abolished by double blockade.

Cardiac conduction abnormalities and rhythm disturbances are common clinical findings in alcoholics. Bundle branch block (Ettinger et al., 1978; Good Kind et al., 1975), atrial fibrillation, ventricular ectopic beats, and other arrhythmias have been reported (Ettinger et al., 1976 a; Green Spoon et al., 1979).
Ettinger and collaborators (1976 a, b) studied dogs with chronic alcohol intake and found (1) slower heart rates, (2) progressive increase in the (H-O) interval, and (3) prolongation of the QRS complex during chronic ingestion, but not during an acute infusion. They observed that alcohol toxicity was cumulative and was not produced by acute alcoholism or short termed alcoholism. Luck and Engel (1983) showed an increase in atrial vulnerability during alcohol ingestion, and Greenspon and Schaal (1983) suggested also some myocardial influence in the production of the arrhythmias. They found normal sinus node function in their patients. Goodking and co-workers (1975) showed that alcohol depressed both atrioventricular node and intraventricular node conduction. They concluded that alcohol has a direct depressant effect on intracardiac conduction.

Acute alcohol intake produces intermittent atrial fibrillation and other arrhythmias. Although, several investigators have suggested a direct effect of alcohol on the myocardium, the direct effect of alcohol on the sinus node has not been reported, except lately by Greenspon and Schaal (1983). Our data show that as the alcohol concentration increases in blood there is a prolongation of the sinus node recovery time as well as the corrected value. The atrioventricular conduction is lengthened with slowing of the heart rate. A criticism in the experiment can be: why were the A-H and the H-V intervals not measured? Ettinger and associates (1976 a, b) have shown no effect in the H-V interval during acute infusions. Due to this observation we concluded that the changes in the development of Wenckebach periodicity were changes in the atrioventricular node area. As discussed earlier, the parasympathetic system has a great influence on the sinus and atrioventricular nodes. Thus, an acute infusion of alcohol may exert more of its influence through the parasympathetic system of the central nervous system. Why Greenspon and co-workers did not find a prolongation in the sinus node recovery time may be explained on basis of the effect of the alcohol metabolites. The first metabolite of alcohol is acetaldehyde. Mizoi et al., (1979) and Altura and Altura (1982) have shown that although normal human subjects with moderate facial flush have similar peak levels of ethanol, they have higher levels of acetaldehyde and a greater increase in pulse rate. In view of the known sympathomimetic effects of acetaldehyde, they suggested that most of the hemodynamic effects of acetaldehyde resulted from release of catecholamines from the sympathetic nerve endings and the adrenal medulla. Probably, the different electrophysiologic effects observed by us can be explained on this basis as well. However, the possibility must be recognized that oral alcohol intake will produce higher acetaldehyde levels than the intravenous route and that the true effect of pure alcohol in the sinus and atrioventricular nodes are the ones observed by us.
Jordan and co-workers (1978) described that by producing autonomic blockade, the primary sinus node dysfunction can be separated from autonomic dysfunction. The observation of no effect of alcohol on the sinus and atrioventricular node function after autonomic blockade indicates that the effect of alcohol on the conduction system in this experiment was mediated through the autonomic nervous system, especially the parasympathetic system. We decided not to block the individual systems alone, because we wanted to do the experiment as fast as possible and in this way reduce the possible effect of the metabolites in the conduction system. Our observations may have therapeutic significance in the management of the arrhythmias observed by alcoholics because the observed rise of systemic blood pressure, heart rate, cardiac output, and left ventricular dp/dt produced by acetaldehyde is also deferred by alpha and beta adrenergic blockade.

Pohorecky (1982) and Katz (1982) have explained the abnormalities in both the Na+, K+ -ATPase and calcium pump produced by acute and chronic alcohol intake. They offered evidence that chronic alcohol intake reduces the sensitivity of these activities to a new challenge of alcohol. This may be another explanation for the differences found by Greenspon and associates and by us. In our case, this was the first exposure of the dogs to alcohol.

In our opinion, intravenous alcohol produces a relative sinus and atrioventricular node dysfunction of different degrees depending on the alcohol concentration. The effect is not observed after autonomic blockade with propranolol and atropine. Probably, the production of arrhythmias in alcoholics is a combination of an elevation of the atrial vulnerability, and sinus and atrioventricular node depression by alcohol or by the metabolites of alcohol.

**BIBLIOGRAPHY**


Figure 1. The average percent change in sinus recovery time, heart rate, and rate to develop Wenckenbach, as the alcohol level increased. (S.A.R.T. = sinus recovery time.)

Figure 2. The relations in 8 dogs between sinus node recovery time and alcohol concentration. Each line represents the lengthening of the sinus recovery time of a given dog as the alcohol concentration was increased. (r = correlation coefficient.)
Figure 3. The relations in 4 dogs between alcohol concentration and rate to develop Wenckebach periodicity. Each line represents the lowering of pace heart rate to develop Wenckebach, as the alcohol concentration was increased in a given dog. (The other 5 dogs showed similar effects.)

Figure 4. The relations between alcohol concentration and heart rate. Each line represents a given dog; each shows the lowering of the heart rate as the alcohol concentration was increased.
Figure 5. The relations between the sinus recovery time and alcohol concentration in 2 dogs after autonomic blockade. No lengthening was observed. (The other 3 dogs showed similar effects.)

Figure 6. The relations between the pacing rate to develop Wenckebach periodicity and alcohol concentration in 2 dogs. No lowering of the pace heart rate to develop Wenckenbach was observed. (The other 3 dogs showed similar effects.)