Netherlands
The Journal of Medicine

PR and QTc interval prolongation on the electrocardiogram after binge drinking in healthy individuals

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ABSTRACT

Background: Acute, excessive alcohol intake has been associated with an increased cardiovascular mortality in otherwise healthy individuals. It predisposes to accelerated atherosclerosis resulting in acute coronary events but also arrhythmias have been described, such as atrial fibrillation and life-threatening re-entrant ventricular arrhythmias. QTc prolongation is associated with an increased risk of ventricular tachyarrhythmias and an independent risk factor for sudden cardiac death. The aim of the study is to investigate the effect of binge drinking on the conduction intervals in healthy individuals.

Methods: Ten of the volunteers drank red wine while the other ten volunteers drank a sweet designer drink. A follow-up of blood pressure, heart rate, ECG and laboratory findings was performed at an ethanol level of 0, 0.4 and 0.8%, respectively.

Results: Fifteen volunteers showed a prolongation of the PR interval, 13 of the QRS complex, 9 of the QT interval and 13 of the QTc interval. PR interval increased from 149 ± 16 ms to 163 ± 11 ms ($p<0.05$). The heart rate-adjusted QT interval increased from 400 ± 24 ms to 426 ± 52 ms ($p<0.05$). Heart rate and systolic blood pressure did not significantly change due to the ingestion.

Conclusion: Acute ingestion of alcohol in a healthy population can induce prolongation of PR and QTc interval.

INTRODUCTION

Alcohol is widely used and in contrast to moderate intake, which can reduce the risk of coronary heart disease, chronic and excessive use is associated with increased cardiac morbidity and mortality.[1,2] In chronic alcoholism, patients first develop diastolic dysfunction and later a systolic dysfunction with hypertrophy and dilatation of the ventricular chambers. This results in a decrease in ventricular ejection fraction and possible symptoms of heart failure.[3,4] Electrocardiographic changes may develop after long-term alcohol consumption, such as prolonged heart rate-adjusted QT interval, conduction disturbances, nonspecific T-wave changes and shortening of the action potential. These changes can predispose to the development of atrial fibrillation.[5-7] Binge drinking is also associated with an increased cardiovascular mortality in otherwise healthy individuals. The exact definition of binge drinking is not provided in the literature but it is considered as an acute and excessive alcohol intake. This drinking pattern causes an acute inhibition of fibrinolysis and may predispose to accelerated atherosclerosis resulting in acute coronary events.[8] Atrial fibrillation but also life-threatening re-entrant ventricular arrhythmias have been described after a binge.[9-12] Because QTc prolongation is associated with ventricular tachyarrhythmias and sudden cardiac death we invested the effect of binge drinking on the conduction intervals in individuals without any signs of cardiac heart disease. We chose for alcohol ingestion instead of infusion in order to imitate oral intake and compared red wine with a sweet designer drink to differentiate between a possible alcohol effect as compared with the effect of polyphenols in wine.

METHODS

Study design

A prospective study was performed among 20 healthy individuals, 24 to 56 years of age, without a history of atherosclerosis, hyperlipidaemia, diabetes mellitus, hyperhomocystenaemia or cerebrovascular disease. Exclusion criterion was the use of prescribed medication, with an exception of oral contraceptives. The average alcohol consumption before entering the study was 1.5 drinks daily. Before entering the study a medical check was performed involving history taking, ECG and general laboratory assessment (*table 1*). The study was designed to achieve an ethanol level of 0.4 and 0.8% after ingestion of 40 and 60 g of alcohol, respectively. Ten individuals ingested a sweet designer drink (Bacardi breezer, 275 ml with 5.0 vol% alcohol, adding up to 11.0 g of alcohol). The other ten volunteers drank red wine (Rioja, 110 ml 13.0 vol% of alcohol, adding up to 11.4 g of alcohol per glass). As one glass of wine contains 11.4 g ethanol and a sweet designer drink contains 13.75 g ethanol, volunteers had to drink four to six glasses of wine and three to four designer drinks, respectively, to reach an ethanol level of 0.8%. Three glasses of wine and two designer drinks were consumed in 45 minutes and after the last drink, 45 minutes were allowed for alcohol uptake in the circulation. After these 90 minutes, ECGs were obtained and alcohol level was measured by blood sampling using an enzymatic method (t = 0.5). If the alcohol level did not reach the 0.45%, the amounts of alcohol were adjusted. Hereafter, the cycle was repeated and 180 minutes after starting ECGs and blood samples were again collected (t = 1). Pasters were used for the precordial location determination in serial electrocardiography. A Siemens ambulant electrocardiography machine was used to obtain all the electrocardiograms. All subjects had not eaten or smoked for four hours before entering the study and participants gave informed consent. The medical ethical committee of the Meander Medical Centre approved the study protocol.

Table 1
Baseline subject characteristics (mean and range)

	N=20	(RANGE)
Sex (male/female)	14/6	
Age (years)	35.5	(21-56)
Systolic blood pressure (mmHg)	116	(105-140)
Diastolic blood pressure (mmHg)	62	(55-80)
Ethanol intake (g/week)	175	(0-532)
Daily ethanol intake (consumption)	1.5	(0-4)
CDT%	2.2	(1.6-5.8)
Smokers	7	
Cholesterol (mmol/l)	4.65	(3.3-6.2)
LDL cholesterol (mmol/l)	2.85	(1.7-4.0)
Triglyceride (mmol/l)	1.2	(0.5-2.8)
HDL cholesterol (mmol/l)	1.3	(0.7-2.0)
Cholesterol/HDL	4	(2-6)

CDT% = carboxyl deficient transferring; LDL = low-density lipoprotein; HDL = high-density lipoprotein.

ECG analysis

The ECGs were analysed for heart rhythm, heart rate, PR interval, QRS interval, QT interval and the heart rate-adjusted QT interval. The intervals were hand-measured. The QTc interval was calculated by using Bazett's correction formula $QTc = QT/\sqrt{RR}$. Furthermore, bundle branch block, ST segment elevation (≥0.1 mV) and/or depression (≥0.05 mV), T-wave morphology and ECG criteria for LVH and U-wave presence were analysed. Left ventricular hypertrophy is considered to be present when the S wave in lead V1 and V2 plus the R wave in lead V4 to 6 is more than 3.5 mV (5.3 mV in patients younger than 25 years), R + S >4.0 mV in the precordial leads, R in lead I >1.5 mV, R in lead aVL >1.3 mV (and no signs of left anterior hemiblock), R in lead aVF >2.0 mV (and no signs of left posterior hemiblock) and R in lead I and S in lead III >2.5 mV (and no signs of left anterior hemiblock).

Statistical analysis

Data were analysed using the Student's paired t-test. The comparisons of the intervals between the two study groups were made by the χ^2 test. These results are expressed as relative risks. A p value <0.05 was regarded as statistically significant.

RESULTS

In 18 volunteers, an ethanol level of ≥0.45% (t = 0.5) was measured after ingestion of 20 to 30 g of ethanol. In 19 persons a level of ≥0.8% (t = 1.0) was reached after ingestion of 40 to 60 g of ethanol. At a level of 0.4% 12 individuals had a prolongation of the PR interval, 8 of the QRS complex, 6 of the QT interval and 12 of the QTc interval. At a level of 0.8%, 15 persons showed a prolongation of the PR interval, 13 of the QRS complex, 9 of the QT interval and 13 of the QTc interval (*table 2*). PR interval increased from 149 ± 16 ms to 163 ± 11 ms (p<0.05). The QRS complex increased from 90 ± 4 ms at baseline to 95 ± 1 ms at t = 1 (NS). QT interval was 383 ± 25 ms at t = 0 and rose to 393 ± 29 ms (p<0.05) at t = 0.5. However, at t = 1, the QT interval was 385 ± 33 ms (NS). The heart rate-adjusted QT interval increased from 400 ± 24 ms to 426 ± 52 ms (p<0.05). The systolic blood pressure was 116 ± 3 mmHg before ingestion and 110 ± 2 mmHg after consumption of alcohol (NS). The diastolic blood pressure did not change during intake. The heart rate at baseline was 67 ± 1 beats/

min and after ingestion 67 ± 8 beats/min (NS) (*table 3*). There was no significant difference in conduction intervals between the red wine and sweet designer drink group after ingestion of alcohol. Sixteen volunteers showed nonspecific T wave changes. ECG changes like ST-segment depression and first-degree atrioventricular block occurred in one volunteer. A U wave developed in three persons during the ingestion of ethanol. Arrhythmias did not occur in any of the subjects.

DISCUSSION

The current study shows that binge drinking can cause a prolongation of the PR and QTc interval in a healthy study population. These intervals show a statistically significant prolongation at an ethanol level of 0.8%. However, prolongation of the PR interval (>200 ms) and QTc interval (>450) ms occurred in one and in three individuals, respectively. Prolongation of the heart rate-adjusted QT interval has been described before but after intravenous infusion and in patients with stable coronary heart disease. Rossinen *et al.* studied whether acute alcohol after intravenous infusion prolonged the ventricular repolarisation in patients with stable heart disease. At an ethanol level of 1.2 ± 0.2% the QTc interval increased on average by 12 to 23 ms (p<0.005) over a 12-lead ECG in the study group as well as in a healthy control group. These authors concluded that alcohol indeed prolongs the QTc interval which reflects abnormal repolarisation and may increase the risk of life-threatening arrhythmias.[7]

The question remains whether the prolongation is due to depolarisation or repolarisation. The PR interval reflects the time needed to activate the atria, to conduct the impulse to the AV node and His bundle and start the ventricular depolarisation. The QTc interval reflects ventricular depolarisation and repolarisation. Even if the delays are mainly due to repolarisation, considering the fact that the QRS intervals did not significantly increase during alcohol intake, Cardy *et al.* demonstrate P wave and QRS complex length-

Table 2
ECG characteristics after 40-60 g ethanol ingestion

	SWEET DRINK (N)	RED WINE (N)	RR (CI)	P
PR interval prolongation	8	7	1.14 (0.69-1.9)	NS
QRS complex prolongation	6	7	0.86 (45-1.64)	NS
QT interval prolongation	4	5	0.8 (0.3-2.13)	NS
QTc interval prolongation	5	7	0.63 (0.31-1.25)	NS
ST-segment elevation	0	1	-	-
ST-segment depression	1	0	-	-
Aspecific T wave change	9	5	1.8 (0.94-3.46)	NS
U wave presence	3	0	-	-
Bundle branch block	0	0	-	-
Nonspecific conduction disturbance	0	2	-	-

RR = relative risk; CI = confidence interval; NS = nonsignificant.

Table 3
Conduction intervals, blood pressure and heart rate after ingestion of 20-40 and 40-60 g of alcohol

	BASELINE T = 0	20-40 G T = 0.5	P	40-60 G T = 1	P
PR	149 ± 16	170 ± 11	0.001	163 ± 11	0.01
QRS	90 ± 4	95 ± 7	NS	95 ± 1	NS
QT	383 ± 25	393 ± 29	0.002	385 ± 33	NS
QTc	400 ± 24	411 ± 28	0.016	426 ± 52	0.036
SBP	116 ± 3	114 ± 2	NS	110 ± 2	NS
DBP	62 ± 6	68 ± 2	NS	62 ± 0	NS
MBP	80 ± 3	83 ± 4	NS	90 ± 8	NS
Heart rate	67 ± 0.7	67 ± 5	NS	67 ± 8	NS

Conduction intervals in milliseconds, blood pressure in mmHg, heart rate in beats per minute, NS = not significant; SBP = systolic blood pressure; DBP = diastolic blood pressure; MBP = mean blood pressure.

ening after ingestion of ethanol and might explain in some part the purported changes.[13] They investigated whether atrial and ventricular signal-averaged electrocardiograms change after acute ingestion of ethanol in ten healthy volunteers. They reported P wave and QRS complex prolongation in nine of ten and ten of ten subjects, respectively, after acute alcohol intake with peak alcohol levels of 0.75 ± 0.05%. In their control group, who only drank fruit punch, prolongation of the P wave and QRS complex was also shown. The difference between the experimental and control group was significant. These studies elicit the question of what would have happened in the present study if the volunteers had drunk a nonalcoholic drink on another occasion.

The exact mechanism causing alcohol-induced arrhythmias remains unclear. Alcohol and its metabolite acetaldehyde can indirectly stimulate the release of catecholamines, which are capable of increasing P wave duration.[10] An exaggerated sympathetic reaction on alcohol can predispose to atrial fibrillation.[12] Furthermore alcohol is capable of inhibiting Na-K-ATPase. Decreases in the activity of this pump could eventually alter the resting membrane potential across the sarcolemma, as well as the intracellular and extracellular ionic homeostasis. Also the calcium binding and transport by the cardiac sarcoplasmatic reticulum may be delayed by alcohol. Alcohol consumption may affect the number of calcium ions entering the cardiac cell through voltage-dependent calcium channels during the plateau of the action potential and the amount of activity of these channels located on the sarcolemma.[6] Therefore, the ventricular repolarisation, which depends on the reduction in L-type Ca current and an increased outward K current, may be prolonged by the effect of alcohol.[6,7] Recently O'Leary reported the results of inhibition of the cloned DNA HERG potassium channel by alcohol, cocaine and cocaethylene (a metabolite of cocaine and alcohol).[14] The HERG channel is responsible for the rapidly activating component (I_{Kr}) of the delayed rectifier potassium current which plays a major role in myocardial repolarisation and is the important determinant of action potential duration. The cloned HERG channel resembles the I_{Kr} of the delayed rectifier current. Inhibition of the cDNA HERG channel by ethanol prolongs the repolarisation time and increases the QT interval.[14] This may be an explanation for the significant prolongation of the QTc interval in our study population.

There was no significant difference in conduction interval between the red wine and sweet designer drink group. Therefore the prolongation of the intervals should be attributed to alcohol rather than other compounds in wine. Wine contains more than 500 compounds. These include water, alcohols, organic acids, sugars and glycerol and polyphenols, also known as flavonoids. Polyphenol-rich beverages are tea, cocoa, fruit juices and wine. Wine contains 500 mg/l of flavonoids in contrast to beer which contains no more than 60 mg/l. Polyphenols exhibit a wide range of biological effects as antioxidants, inhibitors of platelet aggregation, and modulators of prostaglandin and nitric oxide metabolism and might have a potential role in atherosclerotic disorders.[15] The positive effect of flavonoids on the cardiovascular morbidity and mortality seems to be related to long-term low intake of alcohol. It is not to be expected that acute ingestion of red wine will result in a positive effect of the flavonoids.

In the present study systolic blood pressure decreased, although not significantly, after ingestion of alcohol. Heart rate did not show any change. This phenomenon has been described earlier.[7] Alcohol primarily causes vasodilatation resulting in a decline in blood pressure. Heart rate will increase as a reflex mediated by baroreceptors. On the contrary, by increasing the total circulating volume by the alcohol intake, this effect of vasodilatation is overruled and heart rate will not rise. The total amount of fluid ingested in the two groups was different. In the sweet designer drink group a total amount of 1650 ml was ingested as compared with 660 ml in the red wine group. Despite this difference, there was no significant difference in blood pressure, heart rate or conduction intervals between the two groups.

CONCLUSION

In conclusion, this study shows that acute, excessive ingestion of alcohol in a healthy study population can result in a significant increase in the PR and QTc intervals. However, there was no comparison with a control group. A larger, randomised and controlled study is mandatory to investigate the effect in individuals subjected to the same volume challenge, without alcohol.

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