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ORIGINAL ARTICLE

ECG changes in patients with acute ethanol intoxication

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Abstract

Objectives. To assess how ethanol in potential lethal serum concentrations affects features of the ECG that may be associated with cardiac arrhythmias. *Design.* We included 84 patients, who were hospitalised with assumed acute ethanol intoxication. In the emergency room resting ECG was recorded and blood was collected for serum osmolality measurement used as a proxy for ethanol level. Thirty-two also had ECG recorded at discharge. Twenty-seven hospitalised patients without known alcohol ingestion served as controls. ECG segment durations were compared with controls and related to intoxication level. *Results.* In subjects with moderately elevated to high serum osmolality, the P wave and QTc intervals were prolonged compared with sober subjects. P wave, PR, QRS and QTc intervals were longer when the subjects had high blood ethanol levels (at admission) than at discharge (p-values: 0.0001, 0.0002, 0.010 and <0.0001 for P wave, PR, QRS and QTc intervals. $n=32$). *Conclusions.* Ethanol at high to very high blood concentration causes several changes in the ECG that might be associated with increased risk of arrhythmias.

Key words: *Alcohol intoxication, ECG, P wave, PR interval, QRS duration, QTc interval*

Ethanol intoxication is common worldwide, and is potentially lethal. In a recent study, the mean serum ethanol concentration in deaths caused by ethanol intoxication was 0.32% (range 0.23–0.50%) (1). The exact mechanism by which ethanol intoxication contributes to death is unknown, although ventricular tachyarrhythmias degenerating into fibrillation is a possible cause (2). In alcoholics, cardiac arrhythmias may occur during a binge or shortly after (3–5); however arrhythmias have also been reported when non-alcoholics drink alcohol (6).

In general, no single variable in ECG can predict cardiac arrhythmias, though some changes have been associated with later development of arrhythmia. Thus, an association has been established between prolonged corrected QT interval (QTc) and sudden death (7–10). Previous studies on the effects of ethanol on ECG in humans have used subjects with lower serum ethanol concentrations than potentially lethal levels. Small to moderate serum ethanol concentrations are known to prolong the QTc and the PR intervals (9,11). However little information is available on the relationship between ethanol intake and other ECG variables.

In this study of patients hospitalised with assumed acute ethanol intoxications we wanted to explore how high to very high ethanol concentrations influence some features of the ECG that might be associated with cardiac arrhythmias. This study is the first to include patients with ethanol concentrations at potentially lethal levels, and the patients were assessed both when they were intoxicated and in the immediate abstinence/hangover phase.

Subjects and methods

Subjects and study design

Between November 1, 1999 and October 31, 2000, 118 patients were admitted to Akershus University Hospital with acute ethanol intoxication. In the present study we included 84 subjects in whom ECG and serum osmolality was recorded at admission, among whom 32 subjects also had ECG recorded at discharge (Figure 1). The diagnoses

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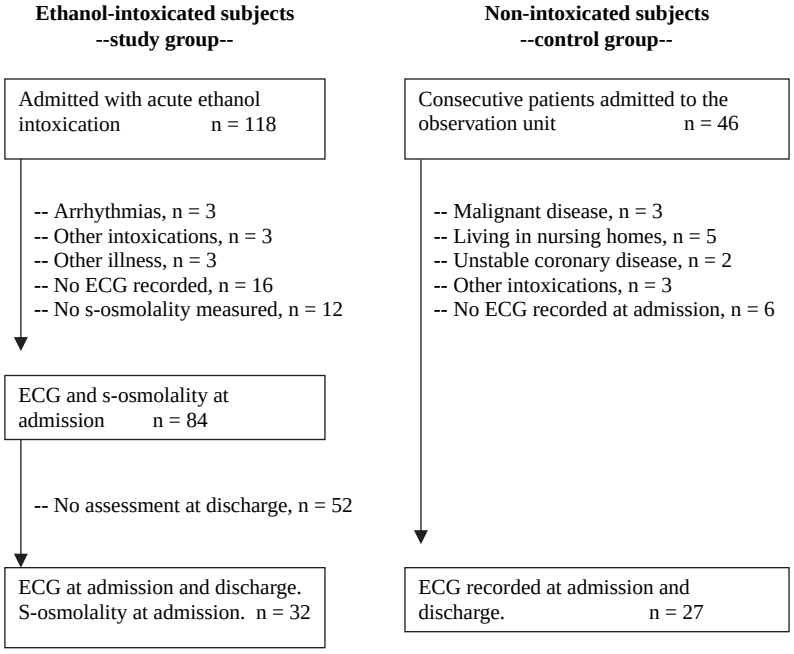

Figure 1. Flow chart of patient selection in the study.

were based on patient interviews at admission and at discharge, examination of the patients and laboratory findings. To establish a control group of patients without ethanol intoxication, we later recruited all patients who during a 2-week period were admitted to the hospital's medical observation unit and had their ECG recorded both at admission and discharge (n = 27) (Figure 1).

We excluded patients with incomplete data, those having consumed other toxic alcohols, patients living in nursing homes or other institutions and those presenting with cardiac arrhythmias, AV-blocks or bundle branch blocks, unstable coronary heart disease, heart failure, other severe symptoms than those of intoxication or daily use of greater than five medications at hospital admission (Figure 1).

At admission, the attending physician recorded regular medication and other drug use combined with the ethanol intoxication (Table I). During hospitalisation ten patients (31%) in the ethanol-intoxicated group (n = 32) received specific medical treatment (4 N-acetylcystein, 5 carbamazepine, 1 naloxone and flumazenil and 6 miscellaneous neuroleptics), and five patients (19%) in the control group (n = 27) (1 antibiotics, 1 acetylsalicylic acid, 2 low molecular heparin, 1 esomeprazol, and 1 ketomidon).

Laboratory examinations and ECGs

At admission for ethanol intoxication, serum osmolality (mOsm/Kg H_2O) was measured, using freezing point depression technique, to estimate the approximate serum ethanol concentration. To obtain an estimate of serum ethanol concentration in ‰, adapted to our laboratory, we derived a regression equation for conversion from a sample of consecutive patients who later were admitted to the hospital and had both serum ethanol and osmolality measured (n = 62, adjusted $R^2 = 0.92$): $C_{Ethanol} = (C_{osmolality} - 295)/28$.

The ECGs were recorded on paper with speed 50 mm/s, using a Marquette Mac 6 (Marquette Electronics Inc, Milwaukee, USA) or a Siemens Sicard 460 (Siemens Elena, Germany) apparatus. PR, QRS, QT intervals and heart rate were obtained from the automatic ECG analysing programs, however always controlled manually. If the manual control indicated that the analysing program had misinterpreted the ECG parameter, that parameter was excluded from further analysis. Thus four QT values and two PR values were excluded. P wave duration was measured manually. Five P-wave values were excluded because they were impossible to measure accurately. The QT intervals were corrected for heart rate into QTc intervals by the automatic analysing program with manual control using Bazett's formula (12). In the ethanol-intoxicated group (n = 32) the mean time between ECG at admission and discharge was 20 hours (range 6–44), compared with 17 hours (range 4–31) in the control group (n = 27).

Statistical analysis

Results are presented with means and SD or SE. For group comparison we used the t-test or χ^2 test. For

Table I. Sample descriptive statistics at admission for patients admitted for acute ethanol intoxication and hospitalized controls, mean (SD) unless stated otherwise.

	Ethanol intoxication			Controls	
Time for ECG recording	Admission only (n = 52)	Admission and discharge (n = 32)	p	Admission and discharge (n = 27)	p[a]
Age (years)	38 (16)	39 (16)	0.90	53 (20)	0.004
Male sex, number (%)	34 (65)	18 (56)	0.40	16 (59)	0.82
S-osmolality (mOsm/kg H_2O)	362 (24)	367 (27)	0.40		
Comorbidity, number (%)	16 (36)[1]	11 (37)[2]	0.92	17 (63)	0.03
Heart disease	10 (22)	5 (16)	0.68	6 (22)	0.52
Mixed intoxications, number (%)	14 (27)	15 (47)	0.06		
Benzodiazepines	6 (12)	8 (25)			
Codein and acetaminophen	6 (12)	4 (13)			
Acetaminophen	2 (4)	1 (3)			
Neuroleptics	6 (12)	5 (16)			
Regular medication, number (%)			0.83		
0	27 (63)[3]	21 (70)[2]		17 (63)	
1	6 (14)	3 (12)		3 (11)	
≥2	10 (23)	8 (27)		7 (26)	
Heart rate, min^{-1}	83.2 (14.9)	88.4 (15.9)	0.13	77.6 (17.6)	0.02
S-Sodium	144.2 (3.2)	143.3 (3.2)	0.25	139.4 (3.3)	<0.001
S-Potassium	4.2 (0.4)	4.0 (0.4)	0.03	3.9 (0.4)	0.60

[1]n = 45, [2]n = 30, [3]n = 43. [a]Control group vs. ethanol intoxication with ECG recorded at admission and discharge (n = 32) (column 2).

comparison of groups according to levels of ethanol concentration, we dichotomized the ethanol-intoxicated patients with ECG at admission into a moderately elevated and a high serum osmolality group using the median serum osmolality as cut-off. In addition we used the control group as a comparison group without influence of ethanol. We checked if groups differed in serum sodium, serum potassium, age, sex or comorbidity. When these differences were statistically significant, we adjusted for this and for heart rate in comparisons of the ECG parameters.

Analysis of covariance (ANCOVA) was used for comparing mean ECG parameters between the groups with high, moderately elevated or undetectable ethanol concentration, adjusted for age, heart rate, comorbidity and serum sodium. The adjusted values represent the predicted score for a subject with the average age, heart rate, comorbidity and serum sodium. Here we used Bonferroni correction of p-values because of multiple comparisons. To demonstrate a possible dose-related response, we also assessed Pearson's correlation coefficients between the calculated ethanol concentrations and P-wave and QTc duration in the ethanol-intoxicated subjects at admission.

We compared ECG parameters between the ethanol-intoxicated and controls at discharge, using ANCOVA, adjusting for age, heart rate and comorbidity. The comparison of the QTc intervals was adjusted only for age and comorbidity.

For each subject in the study and control groups we calculated changes in heart rate, P wave, PR, QRS and QTc intervals from admission to discharge (Δ-values = discharge value − admission value). Intra-subject changes in each group were tested using the one sample t-test.

We chose a 5% significance level using two-sided tests. The SPSS version 12.0 (SPSS Inc., Chicago, Ill.) or Statview version 5.0.1 (SAS Institute, Inc., Cary, NC) were used for statistical analysis.

Results

The study group with ECG recorded both at admission and discharge (n = 32) had slightly lower serum potassium at admission, but otherwise differed little from those with ECG recorded at admission only (n = 52) (Table I). The mean P wave and QTc interval were longer at admission in the 32 who had ECG recorded both at admission and discharge compared with the 52 with ECG recorded at admission only (P wave 109.2 ms vs. 100.9 ms, p = 0.002 and QTc interval: 446.2 ms vs. 434.8 ms, p = 0.02). Patients in the study group (n = 32) were younger than the controls (n = 27), had faster heart rate and higher serum sodium (Table I). One of the 32 patients in the study group developed transitory atrial fibrillation approximately 12 hours after admission. No other arrhythmias were detected; however, telemetry ECG was not utilized.

P wave and QTc interval were longer in the ethanol-intoxicated group compared with the control group, after adjusting for age, heart rate, comorbidity and serum sodium (Table II). There

Table II. ECG variables at admission according to serum osmolality as a proxy for ethanol level in combined sample of ethanol intoxicated and control group, adjusted marginal mean values (SE), adjusted for age, comorbidity, serum sodium and heart rate.

	High (>358[a])	Moderate (<358[a])	Control (no ethanol)	P[b]		
S-osmolality[a], mean (SD)	384.5[c] (18.5) n=43	343.6[c] (9.7) n=41	Normal n=27	High vs. moderate	Moderate vs. control	High vs. control
P wave, ms	105.7 (2.2)[1]	101.1 (2.1)[2]	95.0 (2.8)	0.41	0.27	0.02
PR interval, ms	166.4 (4.4)[3]	160.4 (4.3)[4]	168.1 (5.9)[5]	0.99	0.92	1.00
QRS duration, ms	94.5 (1.9)[3]	93.3 (1.8)[4]	96.5 (2.4)	1.00	0.89	1.00
QTc interval, ms[d]	442.9 (3.8)	437.9 (3.8)[6]	398.7 (4.9)	1.00	<0.001	<0.001
QT, ms [e]	378.9 (4.8)	373.8 (5.1)	376.9 (6.1)	0.46	0.69	0.79
Heart rate, min^{-1} [e]	84.8 (2.3)	85.5 (2.5)	77.6 (3.4)	0.83	0.06	0.07

[1]n=36 [2]n=35 [3]n=38 [4]n=37 [5]n=25 [6]n=40. [a]S-osmolality in mOsm/kg H_2O. [b]After Bonferroni adjustments for multiple comparisons. [c]Estimated serum ethanol concentrations: S-osmolality 384.5 0.32%. S-osmolality 343.6 0.17%. [a]Adjusted only for age, comorbidity and s-sodium in the analysis. [e]Not adjusted in the analysis.

was no difference in any ECG parameters between the groups with moderately elevated and high serum osmolality (Table II). Among the ethanol-intoxicated patients (n=84) the Pearson's correlation of the estimated ethanol levels with the P wave duration was 0.20 (p=0.09) and with the QTc interval 0.14 (p=0.22). There was no difference between the ethanol-intoxicated and controls in any of the ECG variables at discharge, after adjusting for age, heart rate and comorbidity (data not shown).

The P wave, PR, QRS and QTc intervals were all longer at admission than at discharge (i.e. negative Δ-value) (Table III). Thus Δ P was negative in 56% (18/32), Δ PR in 74% (23/31), Δ QRS in 63% (20/32), and Δ QTc in 90% (28/31) of the subjects. Heart rate did not differ from admission to discharge (Table III).

Discussion

The P wave, PR, QRS and QTc intervals were all longer in patients hospitalised with acute ethanol intoxication compared to the day after intoxication. Compared to the non-intoxicated control group only the P wave and the QTc interval were longer during ethanol intoxication. Thus, ethanol has complex influences on the investigated parameters in the EGG, causing prolongation in some parameters in the intoxication phase and normalization, or may be shortening in some parameters the abstinence/hangover phase. We could not find any linear dose-response relationship among the intoxicated patients.

To our knowledge this is the first study to describe the influence of ethanol at potentially lethal levels on parameters of human ECGs. No previous investigators have compared ECG parameters in patients during acute ethanol intoxication with the same patients in the abstinence/hangover phase.

Atrial fibrillation may be caused by alcohol abuse (3,6,13). Whether prolongation of the P wave, measured in a standard 12 lead ECG, is associated with atrial fibrillation or not is still a matter of debate. In one recent study P wave duration >135 ms in lead II was a risk factor for recurrence of atrial fibrillation after cardioversion (14). Longer P wave duration on a signal averaged ECG after intake of ethanol have been described, but the prolongation was not visible in standard limb lead II (15), in contrast Uyarel et al. found that the maximum P wave duration, but not the minimum P wave duration, was longer when the subjects had drunk a moderate amount of alcohol compared to juice (16). The present study is the first to describe P wave prolongation in standard ECG in ethanol-intoxicated humans.

Table III. Change in ECG between admission and discharge, mean (SD).

	Ethanol intoxication (n=32)		Controls (n=27)	
	Δ[a]	p	Δ[a]	p
P wave, ms	−9.8 (14.5)	0.001	−0.4 (5.7)	0.74
PR interval, ms	−13.6 (23.3)	0.002	−0.84 (9.4)[1]	0.66
QRS duration, ms	−3.5 (7.4)	0.010	1.0 (7.4)	0.47
QTc interval, ms	−33.5 (25.9)[2]	<0.001	10.7 (27.8)[3]	0.07
QT interval, ms[b]	−9.3 (36.0)[2]	0.16	−0.8 (23.6)	1.00
Heart rate, min^{-1}	−3.9 (18.3)	0.23	−2.6 (13.9)	0.33

[1]n=25 [2]n=31, [3]n=24. [a]Δ=value at discharge−value at admission.

In a recent study the PR interval was longer (170 ms) in healthy subjects with serum ethanol concentration of 0.04% than before drinking (149 ms) or when serum ethanol concentration reached 0.08% (163 ms) (11). We found no difference between the moderately elevated and highly intoxicated groups. Thus the PR interval increases at low serum ethanol concentrations, but does not further increase in a dose-responsive manner. On the other hand, the PR interval was longer when the subjects were intoxicated with ethanol than at discharge, (mean difference 13.6 ms) indicating that the PR interval is shortened during the metabolisation of ethanol.

The QRS duration was longer in intoxicated subjects than in the same subjects in the abstinence/hangover phase, but not compared to the controls. QRS prolongation is previously found to be associated with arrhythmias in patients with tricyclic antidepressive intoxications (17). Another study identified QRS duration as an independent predictor of mortality (18). The observed differences in QRS duration in this paper were small and the clinical implication of this finding is therefore uncertain.

Previous studies have described prolongation of the QTc interval caused by ethanol in different patient categories (7–10). Mean QTc interval in our study was 439 ms in the ethanol-intoxicated group and 402 ms in the control group at admission. A previous study reported that the QTc interval increased gradually from 400 ms in the sober subjects to 411 ms at 0.04% ethanol and 426 ms at serum ethanol concentration of 0.08% (11). In the present study we found no increase in QTc interval from mean serum ethanol concentration of 0.17 to 0.32%, and no apparent dose-response relationship. Hence, there might be a levelling off of the effect at a certain serum ethanol concentration.

Prolongation of the QTc interval is associated with arrhythmias (7–10). Although deaths caused by ethanol intoxication have been reported at low serum ethanol concentrations, the majority of these deaths happen in persons with high concentrations (1). Acute ethanol intoxication or abstinence/hangover influence many physiological mechanisms in the heart, for example the autonomic nervous system (19,20), ion channels involved in the action potentials (21,22), and modulation of receptor proteins (22).

The present study has several limitations, such as the difficulty in obtaining accurate information from intoxicated patients, both at admission and the following day. Some patients received medication that may have affected the results. For instance carbamazepin and the neuroleptics thioridazil and haloperidol that were used as treatment and given between ECGs (n = 32), may have prolonged several of the ECG intervals at discharge, thereby confounding our results. The ECGs obtained before hospital discharge do not represent a normal situation for the patients. Some of them were discharged before elimination of all the ethanol, or in a situation with symptoms of hangover or abstinence that affected the ECGs.

We used serum osmolality as an indicator of the level of ethanol influence. The use of an indirect measure is a weakness of the study because serum osmolality is influenced by many osmotically active substances. On the other hand previous studies have found a close association between serum values of osmolality and ethanol (23). In some patients with alcoholic acidosis the osmolal gap may not accurately reflect the serum ethanol concentration (24). Ethanol at potential lethal serum concentrations may change the regular ethanol metabolism and result in the formation of different substances with osmolal activity. We therefore prepared an algorithm in our hospital to estimate the approximate serum ethanol concentration from measured serum osmolality.

In an experimental situation it would be unethical to intoxicate humans to the high levels of serum ethanol concentrations attained in the present study.

In conclusion, despite some methodological difficulties our data suggest an association of both high serum ethanol concentration and hangover/abstinence, with changes in some parameters of the ECG that are associated with cardiac arrhythmias.

References

1. Aasebø W, Erikssen J, Jonsbu J. Dødsfall i norske politiarrester. Tidsskr Nor Laegeforen. 2003;123:1066–7.
2. Kupari M, Koskinen P. Alcohol, cardiac arrhythmias and sudden death. Novartis Found Symp. 1998;216:68–85.
3. Ettinger PO, Wu CF, De La Cruz C, Weisse AB, Ahmed SS, Regan TJ. Arrhythmias and the "Holiday Heart": Alcohol-associated cardiac rhythm disorders. Am Heart J. 1978;95: 555–62.
4. Greenspon AJ, Stang JM, Lewis RP, Schaal SF. Provocation of ventricular tachycardia after consumption of alcohol. N Engl J Med. 1979;301:1049–50.
5. Fuenmayor AJ, Fuenmayor AM. Cardiac arrest following holiday heart syndrome. Int J Cardiol. 1997;59:101–3.
6. Thornton JR. Atrial fibrillation in healthy non-alcoholic people after an alcoholic binge. Lancet. 1984;2:1013–4.
7. Day CP, James OF, Butler TJ, Campbell RW. QT prolongation and sudden cardiac death in patients with alcoholics liver disease. Lancet. 1993;341:1423–7.
8. Brooksby P, Batin PD, Nolan J, Lindsay SJ, Andrews R, Mullen M, et al. The relationship between QT intervals and mortality in ambulant patients with chronic heart failure. Eur Heart J. 1999;20:1335–41.

9. Rossinen J, Sinisalo, Partanen J, Nieminen MS, Viitasalo M. Effects of acute alcohol infusion on duration and dispersion of QT interval in male patients with coronary artery disease and in healthy controls. Clin Cardiol. 1999;22:591–4.
10. Straus SM, Sturkenboom MC, Bleumink GS, Dieleman JP, Van Der Lei J, de Graeff PA, et al. Non-cardiac QTc-prolonging drugs and the risk of sudden cardiac death. Eur Heart J. 2005;26:2007–12.
11. Lorsheyd A, de Lange DW, Hijmering ML, Cramer MJM, van de Wiel A. PR and QTc interval prolongation on the electrocardiogram after binge drinking in healthy individuals. Netherl J Med. 2005;63:59–63.
12. Malik M. If dr. Bazett had had a computer. Pacing Clin Electrophysiol. 1996;19:1635–9.
13. Koskinen P, Kupari M, Leinonen H. Role of alcohol in recurrences of atrial fibrillation in persons <65 years of age. Am J Cardiol. 1990;66:954–8.
14. Raitt MH, Volgman AS, Zoble RG, Charbonneau L, Padder FA, O'Hara GE, et al. Prediction of the recurrence of atrial fibrillation after cardioversion in the atrial fibrillation follow-up investigation of rhythm management (AFFIRM) study. Am Heart J. 2005;151:390–6.
15. Steinbigler P, Haberl R, König B, Steinbeck G. P-wave signal averaging identifies patients prone to alcohol-induced paroxysmal atrial fibrillation. Am J Cardiol. 2003;91:491–4.
16. Uyarel H, Ozdol C, Karabulut A, Okmen E, Cam N. Acute alcohol intake and P-wave dispersion in healthy men. Anadolu Kardiyoloji Dergisi. 2005;5:289–93.
17. Thorstrand C. Clinical features in poisonings by tricyclic antidepressants with special reference to the ECG. Acta Med Scand. 1976;199:337–44.
18. Kalahasti V, Nambi V, Martin DO, Lam CT. QRS duration and prediction of mortality in patients undergoing risk stratification for ventricular arrhythmias. Am J Cardiol. 2003;92:798–803.
19. Mäki T, Toivonen L, Koskinen P, Navari H, Harkonen M, Leionen H. Effect of ethanol drinking, hangover, and exercise on adrenergic activity and heart rate variability in patients with a history of alcohol induced atrial fibrillation. Am J Cardiol. 1998;82:317–22.
20. Reed SF, Porges SW, Newlin DB. Effect of alcohol on vagal regulation of cardiovascular function: Contributions of the polyvagal theory to the psychophysiology of alcohol. Exp Clin Psychopharmacol. 1999;7:484–92.
21. Deitrich RA, Dunviddie TV, Harris A, Erwin G. Mechanism of action of ethanol: Initial central nervous system actions. Pharmacol Rev. 1989;41:489–537.
22. Narahashi T, Kuriyama K, Illes P, Wirkner K, Fischer W, Mühlberg K, et al. Neuroreceptors and ion channels as targets of alcohol. Alcohol Clin Exp Res. 2001;23:182–8.
23. Pappas AA, Gadsden RH, Taylor EH. Serum osmolality in acute intoxication: A prospective clinical study. Am J Clin Pat. 1985;84:74–9.
24. Braden GL, Strayhorn CH, Germain MJ, Mulhern JG, Skutches CL. Increased osmolal gap in alcoholic acidosis. Arch Int Med. 1993;153:2377–80.