

# Acute alcohol intake and P-wave dispersion in healthy men

## Sağlıklı erkeklerde akut alkol alımı ve P-dalga dispersiyonu

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### ABSTRACT

**Objective:** P-wave dispersion (Pd), defined as the difference between the maximum and the minimum P-wave duration (Pmin), and maximum P-wave duration (Pmax) are electrocardiographic (ECG) markers that have been used to evaluate the discontinuous propagation of sinus impulses and the prolongation of atrial conduction time, respectively. The incidence of cardiac arrhythmias, particularly atrial fibrillation (AF), following acute alcohol intake has been previously reported. Prolonged P-wave duration and Pd have been reported to represent an increased risk for AF. However, the association between Pd and acute alcohol intake has not been studied previously in normal subjects.

**Methods:** In a randomized crossover study, 10 healthy male volunteers, aged  $30.0 \pm 2.1$  years (range 25-33) received either ethanol and/or placebo (juice). Alcohol group drank moderate dose ethanol;  $0.97 \pm 0.12$  g/kg body weight (range 0.80-1.25 g/kg), and the other group consumed same amount of juice in one-hour period. After 48-hours washout period, alcohol group took juice and juice group drank alcohol. Pmax, Pmin and Pd were measured as milliseconds (ms) on baseline ECG, after alcohol period (AP) and after juice period (JP).

**Results:** In comparison with baseline, Pmax values were significantly prolonged after AP but not after JP (baseline:  $95.3 \pm 5.3$  ms, after AP:  $103.7 \pm 9.5$  ms, after JP:  $94 \pm 7$  ms,  $p=0.027$ ,  $p=0.102$ , respectively). Pmin values did not change significantly. And also, in comparison with baseline, Pd values were significantly prolonged after AP but not after JP (baseline:  $27.0 \pm 7.6$  ms, after AP:  $42.7 \pm 12.8$  ms, after JP:  $27.0 \pm 6.7$  ms,  $p=0.021$ ,  $p=0.891$ , respectively).

**Conclusion:** Acute moderate dose of alcohol intake in short time is associated with an increase in Pmax and Pd. (*Anadolu Kardiyol Derg 2005; 5: 289-93*)

**Key words:** P-wave duration, P-wave dispersion, acute alcohol intake

### ÖZET

**Amaç:** Maksimum P-dalga süresi (Pmak) ve minimum P-dalga süresi (Pmin) arasındaki fark olarak tanımlanan P-dalga dispersiyonu (Pd), Pmak ile birlikte sırasıyla sinüs impulslarının uygunsuz dağılımını ve atriyal ileti zamanındaki uzamayı değerlendirmede kullanılan elektrokardiyogramın (EKG) ölçütleridir. Kardiyak aritmilerin ve özellikle de atriyal fibrilasyonun (AF), akut alkol alımı sonrası sıklığı daha önce rapor edilmiştir. Uzamış P-dalga süresinin ve Pd'nin artmış AF riskini yansıttığı da bildirilmiştir. Bununla birlikte, normal bireylerde Pd ve akut alkol alımı arasındaki ilişki daha önce çalışılmamıştır.

**Yöntemler:** Randomize çapraz çalışmada, yaş ortalamaları  $30.0 \pm 2.1$  yıl olan (25-33 yıl arası) 10 sağlıklı erkek gönüllü, etanol ve placebo (meyve suyu) içtiler. Bir saatlik sürede alkol grubu orta düzeyde etanol içerken;  $0.97 \pm 0.12$  g/kg (0.80-1.25 g/kg arası), diğer grup hacim olarak aynı miktarda meyve suyu içti. Aradan 48 saat geçtikten sonra, alkol grubu meyve suyu, meyve suyu grubu da alkol içti. Pmak, Pmin ve Pd süreleri, bazal, alkol ve meyve suyu alımı sonrası alınan EKG kayıtlarında milisaniye (ms) olarak ölçüldü.

**Bulgular:** Bazale göre, alkol alımı sonrasında Pmak sürelerinde anlamlı uzama varken, meyve suyu alımı sonrasında fark yoktu. (bazal:  $95.3 \pm 5.3$  ms, alkol alımı sonrası:  $103.7 \pm 9.5$  ms, meyve suyu alımı sonrası:  $94 \pm 7$  ms,  $p=0.027$ ,  $p=0.102$ , sırasıyla). Pmin süreleri arasında fark yoktu. Ve yine bazale göre Pd değerleri alkol alımı sonrası anlamlı derecede uzamışken, meyve suyu sonrası anlamlı değişim yoktu. (bazal:  $27.0 \pm 7.6$  ms, alkol alımı sonrası:  $42.7 \pm 12.8$  ms, meyve suyu alımı sonrası:  $27.0 \pm 6.7$  ms,  $p=0.021$ ,  $p=0.891$ , sırasıyla).

**Sonuç:** Kısa sürede akut orta doz alkol alımı artmış Pmak ve Pd süreleri ile ilişkilidir. (*Anadolu Kardiyol Derg 2005; 5: 289-93*)

**Anahtar kelimeler:** P-dalga süresi, P-dalga dispersiyonu, akut alkol alımı

### Introduction

Alcohol has long been suspected as a cause of atrial fibrillation (AF) in those with and without heart disease (1-3). It has been observed that most hospital admissions or emergency department visits for atrial arrhythmias occurred during weekends

or holidays when alcohol intake was more marked. This was termed the holiday heart syndrome (HHS) (4). Its clinical course is benign and specific antiarrhythmic therapy usually is not indicated. Several mechanisms are theorized to be responsible for the arrhythmogenicity of alcohol. Alcohol can cause AF by several mechanisms including its acute effects on atrial refractoriness

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and conduction. These include an increased secretion of epinephrine and norepinephrine, a rise in the level of plasma free fatty acids and an indirect effect through acetaldehyde, the primary metabolite of alcohol. By these effects, alcohol may alter sympathetic and parasympathetic inputs into the heart, important factors in arrhythmogenesis (5,6).

P-wave abnormalities, detected from the electrocardiogram (ECG), have been thought to reflect left atrial enlargement (7), left atrial hypertension (8) and altered conduction (9). Two simple ECG markers, P-wave maximal duration (Pmax) and P-wave dispersion (Pd), have been used to evaluate the intraatrial and interatrial conduction times and the inhomogeneous propagation of sinus impulses which are well known electrophysiologic characteristics of the atrium prone to fibrillation (10,11). P-wave dispersion was defined as the difference between Pmax and Pmin (10). Prolonged P-wave duration and Pd have been reported to represent an increased risk for AF in patients with no underlying heart disease (10,11) and those undergoing coronary artery bypass surgery (12). P-wave dispersion in normal subjects has been reported to be influenced by the autonomic tone, which induces changes in atrial size and the velocity of impulse propagation (13).

The aim of the investigation was to study whether there is an association between Pd and acute alcohol intake in normal subjects.

## Methods

### Study population

For this study, 12 physically and mentally healthy male volunteers were recruited. Two of them were excluded because of electrocardiographic P-wave measurement criteria were not obtained. Therefore this study included 10 healthy male volunteers, aged  $30.0 \pm 2.1$  years (range 25-33 years). All subjects had normal findings on physical examination, 12-lead ECG and chest radiography. Thyroid function tests and other laboratory parameters were normal. None of subjects had hypertension, severe arrhythmia, valve disease, hypertrophic cardiomyopathy, congenital heart disease, bundle branch block, diabetes, coronary artery disease, known psychiatric comorbidities and drug history. Demographic data were inquired. Body mass index (BMI), age, smoking and alcohol consuming pattern were recorded. Of ten patients seven (70%) were smokers. All of the subjects were very light drinkers (0.1-4.9 g daily). Subjects were informed about the study protocol, and consent was obtained from each subject and local ethical committee approval was undertaken.

### Study design

In a randomized crossover study, 10 healthy male volunteers received either ethanol or/and placebo (juice). After three days of alcohol abstinence period, on the study day, subjects consumed the same standard 1600 kcal meal with low fat content at 5:00 PM. Two hours later after meal, baseline ECG recordings, heart rate and blood pressure measurements of the subjects were recorded. Subjects were divided into two groups randomly. Each group consisted of 5 subjects. In one-hour period, one group consumed six 12-oz cans of beer (76.8 g of ethanol) and the other group consumed same amount of juice. The average level of consumed ethanol was  $0.97 \pm 0.12$  g/kg body weight (range 0.80-1.25 g/kg body weight). One hour later after drink-

ing period, ECG recordings, heart rate and blood pressure measurements of all subjects were recorded again. After 48-hours washout period, alcohol group took juice, juice group drank alcohol. And the same procedures were repeated. All subjects were asked to refrain from smoking between 24-hours before alcohol intake day and end of washout period.

### P – Wave Dispersion Measurements on 12 Lead ECGs

All standard 12-lead ECGs were obtained simultaneously using a recorder (Hewlett Packard, Pagewriter 300 pi) set at a 50 mm/s paper speed and 2mV/cm standardization. All recordings were performed in the same quiet room during spontaneous breathing, following 10 minute of adjustment in the supine position. The ECGs were numbered and presented to the analyzing investigators without name and date information. All measurements of P-wave duration were made blindly by 2 medically qualified observers (C.O, A.K.). The P-wave duration was measured manually in all simultaneously recorded 12 leads of the surface ECG. The mean P-wave duration for at least 3 complexes were calculated in each lead. The onset of the P wave was defined as the point of first visible upward slope from baseline for positive waveforms and as the point of first downward slope from baseline for negative waveforms. The return to the baseline was considered as the end of the P-wave. The Pmax measured in any of the 12 leads of the surface ECG was used as the longest atrial conduction time. The difference between the Pmax and the Pmin was calculated and defined as Pd (10).

### Statistical Analysis

All statistical studies were carried out with SPSS program (version 10.0, SPSS, Chicago, Illinois, USA). All data are presented as mean  $\pm$  SD. Statistical comparison of quantitative data and change percentages (%) in Pmax, Pmin and Pd values were performed by Wilcoxon test. Pearson's correlation analysis was performed for reproducibility of P-wave duration and Pd. A p level of  $<0.05$  was considered statistically significant.

## Results

Average body mass index of the subjects was  $25.2 \pm 1.6$ . There were no significant differences in systolic, diastolic blood pressures and heart rates between baseline, after AP and after JP intake (Table 1). P wave measurements are represented

**Table 1. Comparison of systolic, diastolic blood pressures and heart rate after alcohol and after juice periods according to baseline**

	Baseline	Alcohol	Juice
Systolic BP, mmHg	120.0 $\pm$ 14.8	120.8 $\pm$ 15.1	119.4 $\pm$ 13.7
Diastolic BP, mmHg	74.2 $\pm$ 11.6	74.6 $\pm$ 7.8	75.3 $\pm$ 7.3
Heart rate, beat/minute	74.8 $\pm$ 12.3	75.8 $\pm$ 9.3	74.7 $\pm$ 7.3

BP: Blood pressure

**Table 2. Comparison of Pmax, Pmin and Pd after alcohol period, after juice period according to baseline**

	Baseline	Alcohol	Juice
Pmax, ms	95.3 $\pm$ 5.3	103.7 $\pm$ 9.5*	94 $\pm$ 7
Pmin, ms	68.3 $\pm$ 11.1	61.0 $\pm$ 8.6	67.0 $\pm$ 10.6
Pd, ms	27.0 $\pm$ 7.6	42.7 $\pm$ 12.8†	27.0 $\pm$ 6.7

Pmax: Maximum P-wave duration, Pmin: Minimum P-wave duration, Pd: P-wave dispersion, ms: milliseconds \*p=0.027, †p=0.021

ted in the Table 2. In comparison with baseline, Pmax values were significantly prolonged after AP but not after JP. Although Pmin values decreased after JP and especially after AP, the difference was not statistically significant. However, in comparison with baseline, Pd values significantly increased after AP but not after JP (Table 2, Fig. 1, Fig. 2). Change percentages in Pmax, Pmin and Pd values were calculated after AP and after JP according to baseline: Pmax increased by 9.1% after AP and decreased by 1.2% after JP ( $p=0.027$ ); Pmin decreased by 10.3% after AP and by 1.5% after JP ( $p=0.18$ ); Pd values increased by 59.2% after AP but there was no change after JP ( $p=0.021$ ). There were no complications and arrhythmia in subjects during study period. Blinded intra- and interobserver reproducibility of the P-wave duration and Pd measurement were evaluated, and comparison revealed a Pearson correlation coefficient of 0.85 and 0.87 for the P-wave duration, 0.93 and 0.91 for Pd, respectively ( $p<0.001$ ).

### Discussion

Our results showed that acute moderate dose of alcohol intake is associated with an increase in Pmax and Pd, which have been reported to represent an increased risk for AF in patients with no underlying heart disease (10,11).

The electrophysiological properties of atrial myocardium prone to fibrillate due to atrial conduction abnormalities could possibly result in prolonged and highly variable P waves that can be reflected in differently oriented ECG leads. P-wave dispersion is derived from a standard, simultaneously recorded 12-lead ECG and is used as a marker of the interlead variation in P-wave duration (10,11). In accordance with this hypothesis, Pmax and Pd have been shown to distinguish patients with paroxysmal or postoperative AF (10-12). Aytemir et al. (14) found Pmax to be significantly higher in patients with paroxysmal AF compared to healthy controls. In the same study, Pd was also significantly higher in the patient group than in controls. Dilaveris et al. (15) found Pmax to be a significant independent predictor of the recurrent paroxysms of AF. Ozer et al. (16) studied Pd in hypertensive patients with and without a history of paroxysmal AF and concluded that  $Pd > 44$  ms, significantly discriminated patients with a history of paroxysmal AF than those without.

The connection between alcohol intake and AF in healthy subjects has been observed in clinical studies (3), but its role in inducing other supraventricular arrhythmias remains controversial (17). The mechanism of alcohol's arrhythmogenic effect is

not known, but increased adrenergic activity, changed conduction and refractory times, vagal reflexes, and myocardial damage have been suggested. Detrimental effects of alcohol on the heart comprise a decrease in myocardial contractility, hypertension, atrial and ventricular arrhythmias, and secondary non-ischemic dilated cardiomyopathy. After consuming large quantities of alcohol over years, alcoholic cardiomyopathy may develop, which presents with dilation and impaired contractility of the left or both ventricles. Endomyocardial biopsies of patients with alcoholic cardiomyopathy reveal in up to 30% of all cases myocarditis with lymphocytic infiltrates (18). Kim et al. (19), using an animal model of alcoholism, investigated whether 4 months of ethanol consumption was associated with a preclinical stage of alcoholic cardiomyopathy. In this study, the only cardiac structural feature characteristic of a preclinical alcoholic cardiomyopathy was a decrease in relative wall thickness. Denison et al. (20) studied 19 healthy alcoholic men attending a detoxification ward after 24 to 72 hours of last alcohol intake. Alcoholics had a higher mean heart rate, but a lower rate of supraventricular premature depolarizations than nonalcoholic healthy men. The urine catecholamine excretion was higher and some electrolyte disturbances were detected. The main finding was sinus tachycardia, possibly due to increased catecholamine excretion. But in our study, there was no difference in systolic, diastolic blood pressure and heart rate after AP and after JP according to baseline. In a study by Koskinen et al. (21), acute intake of alcohol induced a decrease in the heart rate variability due to diminished vagal modulation in healthy men. In other study (22), alcohol caused a decrease in vagal modulation with a later shift to sympathetic predominance in patients with coronary artery disease. However, most patients were taking beta-blockers as well as nitrates.

Frost et al. (23) prospectively examined the association between alcohol consumption and risk of AF or atrial flutter among 47949 participants (mean age, 56 years) in the Danish Diet, Cancer, and Health Study. They found that consumption of alcohol was associated with an increased risk of AF or atrial flutter in men. In women, moderate consumption of alcohol did not seem to be associated with risk of AF or atrial flutter. Djousse et al. (24) showed that there is little association between long-term moderate alcohol consumption and the risk of

AF, but a significantly increased risk of AF among subjects consuming  $>36$  g/day (approximately  $>3$  drinks/day).

Although HHS was defined previously as an acute cardiac rhythm and/or conduction disturbance, most commonly supra-

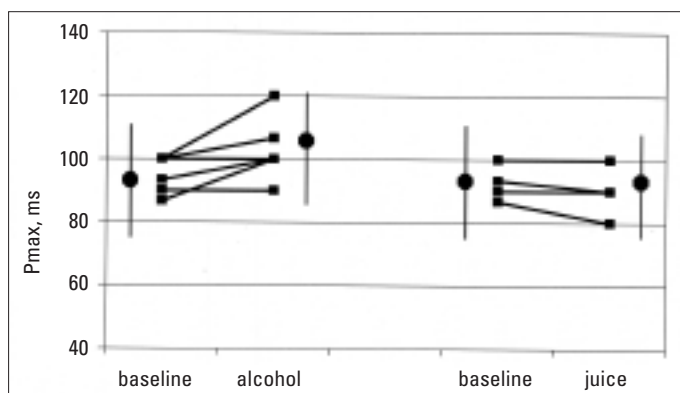


Figure 1. Pmax values in ms after alcohol and juice periods according to baseline ECG. ECG – electrocardiogram, Pmax – P-wave maximal duration

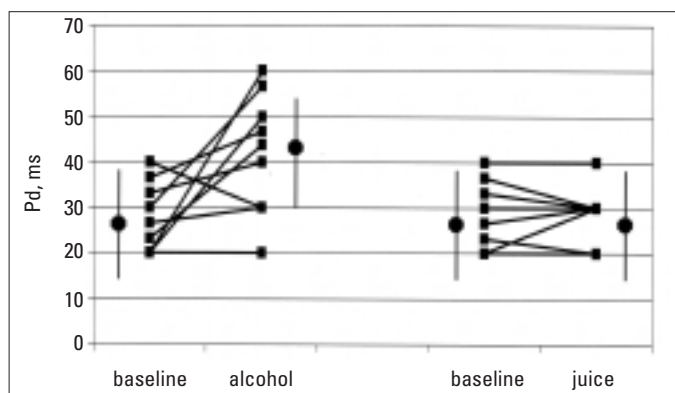


Figure 2. Pd values in ms after alcohol and juice periods according to baseline ECG. ECG – electrocardiogram, Pd – P-wave dispersion

ventricular tachyarrhythmia, associated with heavy ethanol consumption in a person without other clinical evidence of heart disease (1-3), subjects in our study consumed moderate dose of ethanol (range 0.80-1.25 g/kg body weight). But all of them were very light drinkers (0.1-4.9 g daily). . Recently it has been shown, that HHS most commonly refers to the association between alcohol use and new-onset AF, in apparently healthy people. Interestingly, even modest alcohol intake can be identified as a trigger in some patients with paroxysmal AF (25-27).

In general, after the consumption of one standard drink, the amount of alcohol in the blood (blood alcohol concentration, or BAC) peaks within 30 to 45 minutes. A standard drink is defined as 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of 80-proof distilled spirits, all of which contain the same amount of alcohol (28). In the light of this knowledge, ECG recordings, heart rate and blood pressure measurements of all subjects were taken one hour later after drinking period. A number of factors influence the absorption process, including the presence of food and the type of food in the gastrointestinal tract when alcohol is consumed (29,30). The higher the dietary fat content, the more time this emptying will require and the longer the process of absorption will take. One study found that subjects who drank alcohol after a meal that included fat, protein, and carbohydrates absorbed the alcohol about three times more slowly than when they consumed alcohol on an empty stomach (31). Women absorb and metabolize alcohol differently from men. They have higher BAC's after consuming the same amount of alcohol and are more susceptible to alcoholic liver disease, heart muscle damage (32), and brain damage (33). Alcohol consumption affects the metabolism of a wide variety of other medications, increasing the activity of some and diminishing the activity, thereby decreasing the effectiveness, of others (34). Therefore in our study, all of the subjects were male and they ate standard same 1600 kcal meal with low fat content at same time. And also none of them had drug intake history.

#### Study Limitations

All measurements were obtained in a blinded manual conventional manner. But manual measurement of P-wave duration in standard 12-lead ECGs is feasible and more stable and reliable when performed on the high-resolution screen of a digital ECG system than with more conventional methods involving paper-printed ECGs (35). Therefore, manual measurement of P-wave duration performed on standard paper-printed ECGs is of limited accuracy.

Information on how the body metabolizes alcohol permits us to calculate, for example, what our BAC is likely to be after drinking, including the impact of food and gender differences in the rate of alcohol metabolism on BAC. But we had no chance to look for blood alcohol level.

In this study, we evaluated the acute effects of alcohol on P-wave parameters only in healthy subjects and did not include patients with AF. We did not observe AF in our study group. So we do not know whether increased Pmax and Pd levels predict AF or not. For this purpose, further large-scale prospective studies are needed to determine if increased Pmax and Pd levels could predict AF development after acute alcohol intake. It should be also noted also that we evaluated short-term effects of alcohol ingestion on ECG changes and did not follow up these changes further.

## Conclusion

Our study shows that acute moderate dose of alcohol intake in short time is associated with an increase in Pmax and Pd, which may express greater susceptibility to AF.

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