Original Article

J Babol Univ Med Sci
Vol 20, Issu 3; Mar 2018. P:7-14

Compare the Effects of Caffeine on QTc Interval and Blood Pressure During Isometric and Isotonic Contractions in Male Athletes and Non-Athletes

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J Babol Univ Med Sci; 20(3); Mar 2018; PP: 7-14
Received: Jun 2nd 2017, Revised: Oct 14th 2017, Accepted: Dec 10th 2017.

ABSTRACT

BACKGROUND AND OBJECTIVE: QTc fluctuations, in rest and exercise lead to arrhythmias and sudden cardiac death. Caffeine is an energy source and it may moderate this bad fluctuation. The purpose of this study was to compare the effect of caffeine on QTc and blood pressure during isometric and isotonic contractions in athletic and non-athletic men.

METHODS: in this semi-experimental study, 20 healthy men were randomly selected and placed in two groups of athletes and non-athletes. Pre-test: at first, each subject pressed the dynamometer handle at maximum power for 30s (isometric). After 25 min rest, the isotonic activity was performed in 15 repetitions of 5 seconds. At the end, each subject takes 400 mg of caffeine, and after 60min, the post-test similarly, was repeated as a pre-test. QTc changes and blood pressure were checked before and after the test.

FINDINGS: The average weight of individuals was 76±13.93 kg. Caffeine in the athlete group resulted in a decrease in QTc during isometric and isotonic contractions of 11.5 ms and 15ms respectively. But in nonathlete groups, QTc during isometric and isotonic contractions were respectively 0.7ms increase and 4.1 ms decrease. There was no significant correlation between QTc in both groups, but diastolic blood pressure increased significantly (p=0.02).

CONCLUSION: The results of the study showed that caffeine consumption had no significant effect on QTc interval but it affected diastolic blood pressure.

KEY WORDS: *QTc interval, Caffeine, Blood pressure, Isotonic, Isometric, Athletes and nonathletes*.

Please cite this article as follows:

Kashef M, Nejatmand N, Kashef A, Ghyratmand R. Compare the effects of caffeine on QTc interval and blood pressure during isometric and isotonic Contractions in Male athletes and non-athletes. J Babol Univ Med Sci. 2018;20(3):7-14.

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[DOR: 20.1001.1.15614107.1396.20.3.1.9]
[DOI: 10.22088/jbums.20.3.7]

Introduction

The beneficial effects of exercise on the cardiovascular system have been proven (1). Measurement of cardiovascular response during and after exercise is very important for identifying people at risk (2, 3). Classical sports tests have studied more ST segment variations. But QT Interval QT provides more information (4). The QT interval (from the beginning of the QRS complex to the end of the T wave) in the electrocardiogram represents the left ventricular repolarization during the diastole phase (5). The most common heterogeneity index in ventricular repolarization is the rate of dispersion of QT intervals (the difference between the longest and shortest QT intervals) in standard twelve electrocardiograms leads (6). Short or prolonged QT increases the risk of developing arrhythmia and has a high correlation with Cardiac Sudden Death (CSD) (7).

QT interval based on heart rate was corrected using the Bazzet formula and expressed as QTc (6). In a healthy person, the QTc distance is 400 milliseconds, which is slightly longer in women than men (8). According to the international guidelines, men with ms400 QTc> and women with ms460QTc> have considered abnormal beatings (9). In addition to genetic disorders and drug agents that lead to fluctuations in the QTc interval, other factors such as age, gender (women> men), blood pressure, heart rate, autonomic nervous system, body mass index and low calorie diet, leads to intense QTc interval changes (10, 11). QTc during resting and exercise has many clinical consequences.

Although exercise causes a change in the activity of the autonomic nervous system, its effect on QTc is not very clear and varies greatly (12, 13). Performing isometric and isotonic exercises during a short period or a regular period have different effects on the heart. Changes in cardiovascular parameters along with these exercises have been well studied, but electrocardiogram changes, especially the QTc interval, are less compared. In a study, Bhandari et al. examined the effect of low intensity isometric and isotonic exercises on QTc interval in healthy young men. The results showed the opposite effect of these two exercises on QTc. After isotonic exercises, heart rate, systolic and diastolic blood pressure and QTc interval increased significantly compared with baseline. On the contrary, after isometric exercise, only the heart rate was significantly increased and no significant changes were recorded in QTc and other cardiovascular parameters. Therefore, it can be concluded that isometric exercises may not be useful in assessing cardiovascular status or predicting cardiovascular events (14).

On the other hand, there is a difference between athletes and non-athletes regarding the QTc parameter and blood pressure. In a study by Toufan et al., QTc interval in non-athlete group was higher than QTc in both groups of isometric and isotonic athletes. However, QTc interval was lower in isotonic athletes compared to isometric athletes. This study also showed significant changes in systolic pressure between athletes and non-athletes. Meanwhile, this pressure in isotonic athletes was less than isometric athletes (15). Since a low calorie diet also leads to an intense change in the QTc interval, enough use of caffeine as energetic supplement, during exercises can prevent its fluctuations (10-13).

Caffeine affects organs and tissues, such as the nervous system and the cardiovascular system (16). Caffeine is a strong catecholamine's releasing stimulant, which increases the activity of the sympathetic nervous system and blood pressure (17, 18). Increasing caffeine concentration can lead to calcium release and inhibition of phosphodiesterase enzyme, which leads to an increase in cAMP concentration, followed by an increase in energy intake (19). In addition, caffeine is a competitive antagonist with adenosine, increasing its concentration, leading to the occupancy of the receptors of the type A1 and A2A adenosine, and prevents adenosine binding and vasodilation, which results in increased blood pressure and heart rate abnormalities (19, 20).

On the other hand, increased vascular resistance and blood pressure are one of the undeniable consequences of exercise. Even the type of exercise can affect cardiovascular changes, so that resistance exercises that increase the blood pressure proportionate to the nature of the exercise, in contrast to aerobic and endurance exercises, increases blood pressure. (21). Endothelial coronary function plays an important role in ventricular diastole. Endothelial function is evaluated based on FMD = Flow mediated dilatation (flux-dependent dilatation index). Caffeine leads to changes in the FMD (6).

The consumption of caffeine decreases the brachial artery FMD and increases the FMD with decaffeination. There is a lot of controversy about cardiovascular effects of caffeine (6). In a study by Buscemi et al., the blood pressure changes and QT

[DOR: 20.1001.1.15614107.1396.20.3.1.9]
[DOI: 10.22088/jbums.20.3.7]

intervals at an hour after taking Contains Caffeine or Decaffeinated coffee were measured. Both diastolic blood pressure and systolic blood pressure increased at an hour after CC. There was also a significant increase in QT intervals after an hour of DC. However, there was no significant change in QTc interval based on heart rate, following CC and DC (5).

QTc during resting and exercise has many clinical consequences, and its fluctuations lead to arrhythmias and cardiac sudden death (12, 13). Considering that isometric and isotonic exercises are among the most important and common exercises and it is usually inevitable in everyday life and in various sports fields, and because a low calorie diet also results in a significant change in QTc interval, enough consumption of caffeine as an energetic supplementation during exercises can prevent its fluctuations (10-13). Therefore, this study was conducted to determine the effect of caffeine on QTc and blood pressure in isometric and isotonic contractions in athletic and non-athletic men.

Methods

This quasi-experimental study was carried out in the form of pre-test and post-test design, after approval at the Ethics Committee of the Sport Sciences College of Tehran's Shahid Rajaee secretary with code 102.1396 IR.SRTTU.SSF and registration in clinical practice, with system No. 1N201712160379O6IRCT: on 20 healthy male students from the school of Sport Sciences University of Shahid Rajaee Teacher Training of Tehran who were randomly selected and divided into two groups: athlete (n=10) and non-athlete group (n=10).

Athletes are referred to people who carry out activities aimed at developing, maintaining or creating a particular type of physical fitness. Such people are directly involved in sports activities and exercise at least 10 hours a week regularly. Basically, professional athletes fit into this group (22). Non-athletes were people with low activity who did not exercise regularly during the week (23). All subjects completed the health questionnaire and all of them were healthy and had not history of cardiovascular disease. Exit criteria were high blood pressure, diabetes, cardiovascular disease, cardiovascular drug use and smoking. Subjects were asked to avoid taking caffeine containing foods such as chocolate, coffee, etc. on the day before and after the test. To observe ethical considerations, all stages of the work, such as caffeine supplementation and exercise tests, were first described for all subjects, and all of them were fully satisfied with the study. At first, anthropometric indices (weight, body mass index, and fat percentage) of all subjects were calculated using the OMRON Chinese Company's BMI (BF511 model). The athlete group had better BMI and less fat percentage than the non-athlete group, and the pretest was used to prevent the effect of this factor on the results. The height of the subjects was calculated using the Beurer Scales device GS49-BMI (Germany).

Then, at rest status, systolic and diastolic blood pressure (before caffeine ingestion) of each subject was measured and recorded using a Germany mercury blood pressure monitor, Richter brand (0124, Riester model). The sports research contract was, respectively, the maximum isometric and isotonic contraction using the American Digital Hand Grip Dynamometer (JAMAR model, SH5003). The arrangement of the sports contract was as follows: first, the subjects became familiar with how they handled the manual dynamometer, and then they were asked to press the dynamometer (with isometric contraction) with the superior hand and with full force in 30 seconds. Maximum (first seconds) and minimum power (thirtieth second) of each subject were recorded. The hand was completely open in this contraction (14). Systolic and diastolic blood pressure was immediately measured and recorded. Isotonic contraction was performed 25 minutes after isometric contraction to relieve fatigue and re-energization. In this contraction, the subjects performed 15-set 5-second (with 5 seconds rest between sets) with their superior hand in full force and using a dynamometer.

The hand in this contraction was located on the elbow area (90 ° angle) and adjacent to the body (24). Immediately after this contraction, systolic and diastolic blood pressure was measured and recorded. QT interval was evaluated in all three resting conditions, isometric and isotonic contraction using the CORTO PORTAL ECG. QT was corrected based on heart rate using the Bazzet formula and expressed as QTc (25).

$$QTc = \frac{QT}{(RR)^{1/2}}$$

The average blood pressure in resting conditions and exercise was calculated by the following formula (27).

Rest: MAP=1.3 (SBP-DBP)+DBP

Sports activity: MAP=1.2 (SBP+DBP)

[DOR: 20.1001.1.15614107.1396.20.3.1.9]
[DOI: 10.22088/jbums.20.3.7]

After completing these steps, each subject consumed two 200 mg tablets of caffeine supplementation with the DUBIS brand made in Canada (Food and Drug Administration Registry No. 2518359435571020) purchased from the pharmacy in Lavizan. Generally, for most adults, taking 400 mg of caffeine per day is safe, and most of the dose results in dizziness, muscle tremor, insomnia, irritability, and increased heart rate (26). After 60 minutes, all pre-test steps were repeated again in the post-test. It takes about an hour for caffeine tablets to be completely absorbed into the bloodstream and have full effect (26). Since the implementation of this test is involuntary in the pre-test phase and due to controlling the disturbing variables, there was no need for covariance analysis. After ensuring the normal distribution of data and homogeneity of variances (using Kolmogorov-Smirnov and Levine tests), the data were analyzed by repeated measure ANOVA and analyzed in significance level ($p \leq 0.05$).

Results

The average age of the athlete group was 20.5±1.71 years, weight 70.53±10.63 kg, height 176±7 cm, fat percentage 12.94±7.34%, and body mass index 77±3.71 (22 kg/m2). The non-athlete group also had an average age of 22.1±2.47 years, weight 47.18±15.5 kg, height 174±6 cm, fat percentage 24.24±6.5% and body mass index was 74.43±3.84 kg/m2.

QTc interval: With caffeine supplementation consumption QTc in athlete's group was increased by 5.8 (2.13%) in resting conditions, but during isometric and isotonic contractions, decreased about11.5 ms and 15 ms (2.71 and 3.9 Percent). In contrast to the athlete group, in non-athlete group with consumption of caffeine, QTc, under rest and isometric contraction were increased 2.8 and ms 0.7 ms (0.24 and 0.16% respectively) and during isotonic contraction decreased about 1.4 ms (0.96%) (Table 1). Comparison of both groups showed that QTc increased in both groups at rest. Conversely, QTc decreased in both groups during isotonic contraction, which was more tangible for athletes. However, under isometric contraction, QTc for both athletes and non-athletes was slightly decreased (Table 1).

Statistically, QTc of athletic and non-athlete groups did not show significant fluctuations with consumption of caffeine supplementation (Table 2). The average resting blood pressure of the athlete group decreased to 1.34 mg after caffeine consumption and increased to 1 and 2.5 mmHg after isometric and isotonic activity respectively. In non-athletes and after caffeine consumption, the mean resting blood pressure increased by 4.9 mg. In this group, the mean blood pressure after isometric and isotonic activity was decreased by 1.15 mg and increased by 1 mg (Table 1). The results showed that consumption of caffeine supplementation had a significant effect on diastolic blood pressure (p=0.02) (Table 2).

Table1. Average QTc and mean arterial pressure before and after caffeine consumption in both groups

Group / Status		Athlete		Non-athlete	
		Without caffeine	With caffeine	Without caffeine	With caffeine
		Mean±SD	Mean±SD	Mean±SD	Mean±SD
Rest	Systole(mg)	117±7.14	116±5.67	120.9±8.6	123±6.32
	Diastole(mg)	81±5.16	79.5±4.37	76.2±6.03	82.5±6.77
	MAP(mg)	93±5.82	91.66±4.8	91.1±6.88	96±6.62
	QTc (ms)	398.8±22.6	407.3±25.5	400.9±25.4	409.±22.6
After isometric contraction	Systole(mg)	117±6.74	118.5±9.14	124.8±12.88	119.5±8.64
	Diastole(mg)	77±5.86	77.5±7.16	76±9.06	79±6.14
	MAP (mg)	97±6.3	98±8.15	100.4±10.97	99.25±7.39
During isometric contraction	QTc (mg)	424±52.5	4125±51.7	424.3±48.6	425±50.3
After isotonic contraction	Systole (mg)	114.5±5.5	117±4.83	121±9.06	120±8.81
	Diastole(mg)	74.5±5.5	77±5.86	75±6.66	78±7.52
	MAP (mg)	94.5±5.5	97±5.34	98±7.86	99±8.16
During isotonic contraction	QTc (mg)	420.3±36	405.3±32.9	425±33.6	420.9±37.2

[DOR: 20.1001.1.15614107.1396.20.3.1.9]
[DOI: 10.22088/jbums.20.3.7]

Table 2. Analysis of variance of repeated measures of the effect of caffeine supplementation on QTc and blood pressure during isometric and isotonic contraction in both groups

Effect			df	F	P	Eta
Stage agent	QTc		5	1.71	0.14	0.08
	Blood pressure	Systole	5	0.59	0.70	0.03
		Diastole	5	2.67	0.02	0.12
Group agent	QTc		1	0.33	0.57	0.01
	Blood pressure	Systole	1	3.52	0.07	0.16
		Diastole	1	0.00	0.98	0.00
Group and Stake Interaction	QTc		5	0.19	0.96	0.01
	Blood pressure	Systole	5	0.93	0.46	0.04
		Diastole	5	1.1	0.36	0.05

* At the level of $p \leq 0.05$ is significant.

Discussion

The results of this study showed that, after caffeine supplementation, QTc in both groups decreased during isotonic activity. Athletes QTc decreased during isometric activity but increased in non-athletes. Diastolic blood pressure increased significantly. Cardiovascular responses to both types of exercises are the same and dependent on high loading, increased sympathetic activity and parasympathetic inhibition (14). The QTc interval is affected by sympathetic and parasympathetic nerves activity (14).

Autonomic tone changes can directly affect QTc interval (28). In this study, caffeine supplementation led to non-significant QTc decrease in both groups during isotonic contractions. Bhandari et al., Evaluated the effect of isotonic and isometric low-intensity activities on QTc interval in healthy young men, concluded that QTc did not change significantly after isometric activity. But after the isotonic activity, there was a significant increase. Therefore, isometric activity may not be useful in assessing cardiovascular conditions or other predictable events (14). Ogedengebe et al. showed that men QTc increased significantly after the isotonic activity of the bicycle ergometer (29).

Makarov et al. also showed that QTc increased during exercise, especially at the early stages of exercise (30). Caffeine is one of the strongest sympathetic nerve stimulators that eases heart work and modulates the QTc interval. (28). Since low calorie diets are one of the factors that lead to severe changes in QTc intervals (10, 11), caffeine (at standard dosage level), stimulates the central nervous system, increases the activity of adenosine phosphatase sodium-potassium pump and intracellular calcium mobilization, and increasing the concentration of catecholamine, especially norepinephrine, facilitates cardiac function and increases muscle strain (31). This may inhibit over-prolongation of QTc during isotonic activities. White and colleagues showed that caffeine resulted in a significant increase in QTc following Bruce's test (28).

Given that the dose of caffeine in the Hite study was also 400 milligrams, one of the possible reasons for the difference between the findings is the type of protocol. The heart rate response during exercise is strongly dependent on the duration of contraction (32). Given that QTc interval for a healthy person is 400 milliseconds (8). In the present study, it has been observed that QTc of some of the participants after taking caffeine in resting status are close to 500, which can be very dangerous. Long QT syndrome (LQTS) is one of the causes of developing adrenergic ventricular tachycardia (VT), which results in sudden cardiac death (SCD) in young athletes. One of the reasons for long QT syndrome is a long QTc interval (500QTc) and a family history. QTc> 500 is a very strong suggestion that expresses LQTS.

Detection of corrected long-term QT interval based on heart rate (QTc) increases the detection ability of ventricular tachycardia in athletes and disqualifies them from engaging in competitive sports, including intense and moderate activity (9). Another remarkable result of the present study is a non-significant increase in QTc interval in resting mode (after caffeine consumption) in both groups. Inappropriate performance of myocardial channels can lead to increased sodium penetration or decreased potassium excretion, followed by prolonged repolarization and long QTc intervals (8). Clinically, the prolonged QTc

[DOR: 20.1001.1.15614107.1396.20.3.1.9]
[DOI: 10.22088/jbums.20.3.7]

interval, the patient's prone susceptibility to syncope, seizure, irregular heartbeat, and ventricular Therefore, a significant increase in diastolic blood pressure was observed in this study. Probably the mechanism of caffeine's effect is more related to the effect of sympathetic vessels contraction. Caffeine, by inhibiting adenosine receptors, also prevents adenosine vasodilation on the arteries (33).

Tachycardia (TDPs=Torsades de pointes, a kind of polymorphic ventricular tachycardia that is shown in the electrocardiogram as a prolongation of its QTc interval) and can lead to sudden death (8). Brian et al. examined the effects of hemodynamic and electrocardiography of food supplements containing ephedrine and caffeine and showed that these supplements increased QTc interval and systolic blood pressure, and advised patients to not to use these supplements until getting more information (25). According to the results of this study, QT has increased non significantly after taking caffeine in resting conditions, and this is a sign of danger. Excessive consumption of caffeine is likely to lead to autonomic rejection, parasympathetic suppression and sympathetic suppressive inhibition during post-exercise recovery that increases the risk of sudden cardiovascular death (28). Therefore, it is recommended that avoid excessive consumption of this supplement until information is completed in this field. Limitations: This study was conducted on healthy young people, so the results cannot be related to patients with cardiovascular disease. There is also no direct measurement of caffeine concentration in the blood..

Conflict of Interest: No conflicts of interest.

Acknowledgment

Hereby, we would like to thank the Supervisors of Sports Physiology Laboratory of Shahid Rajaee Teacher Training University of Tehran, especially Dr. Salehpour, and Dr. Jafari as well as all students to cooperate in the investigation.

[DOR: 20.1001.1.15614107.1396.20.3.1.9]
[DOI: 10.22088/jbums.20.3.7]

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