INCREASES OF QT DISPERSION, CORRECTED QT DISPERSION, AND QT INTERVAL IN YOUNG HEALTHY INDIVIDUALS DURING RAMADAN FASTING

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Abstract- Ramadan fasting is one of the most important religious duties of Muslims, that its effect on the heart has not been determined yet. Our objective was to evaluate the effect of Ramadan fasting on ventricular repolarization as assessed by QT interval, corrected QT interval, QT dispersion or corrected QT dispersion. Sixthy healthy subjects aged 20 to 35 years were dispersion included in this study. QT interval, corrected QT interval (QTc) QT dispersion QTc dispersion, RR interval and QRS axis were measured in 12-lead surface electrocardiogram, once during fasting (10 to 11. 5 hours of absolute fasting from food and liquid) and another time, 15 to 60 minutes after eating food at sunset. All of the subjects had been fasting 11 to 12 hours each day at least for 25 days during Ramadan. The study was performed at Amir Alam hospital in the year 2000. Maximal QT interval, mean QT interval and RR-interval, were longer during fasting ($P<0.05$), and both QT dispersion and QTc dispersion were increased ($p<0.05$). (QT dispersion: mean ± SD= 57.2± 20.1 ms during fasting Vs 41.6 ± 15.1 ms after meal, QTc dispersion =75.4±24.6 ms during fasting Vs 64.1 ± 22.8 ms after meal). But mean QTc interval, maximal QTc interval and QRS axis showed no significant difference. Prolongation of QT interval and RR interval during fasting, instead of no significant changes in corrected QT interval may primarily suggest that prolongation of RR-interval causes QTc interval not to have significant difference. But increases of QT dispersion and corrected QT dispersion (QTc dispersion) during fasting-that are more reliable indicators of ventricular repolarization-support the idea that ventricular repolarization may be changed during Ramadan fasting.

QT dispersion in cardiac patients is showed to increase from normal values of 30-40 to 67-138 ms, but in our study their increases did not reach critical value.

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Key Words: QT dispersion, Ramadan fasting, QT interval, corrected QT interval

INTRODUCTION

Ramadan fasting is one of the most important religious duties of Muslims. During Ramadan Muslims absolutely refuse to eat and drink from sunrise to sunset.

Effect of Ramadan fasting on the heart has not been determined yet. In a study performed in Turkey, in all patients with a diagnosis of acute coronary mycardial syndrome in one main hospital of Ankara from 1991 to 1997 studied retrospectively, it was observed that the number of hospitalized acute coronary mycardial syndrome patients in CCU ward was less in Ramadan than the other months (P= 0.03) (1). Saidi stated that Ramadan fasting not only does not increase the severity of coronary artery disease and does not cause acute coronary events, but also improves the general condition of about one-third of patients (2). Some studies have reported substantial weight loss, signs of dehydration, raised serum concentrations of uric acid and cholesterol, etc. during Ramadan. However, these changes are unlikely to have much effect on healthy individuals, because generations of Muslims have undertaken fasting year after year. In conclusion, the observance of the Ramadan fast may produce some ill effects in patients with some disease, e.g. hypertension, hypercholes-terolaemia, hypoglycemia, and heart, liver and kidney diseases (3).

There are some reports suggesting cardiac repolarization changes with fasting and feeding. Nagy et al. reported that a-500 kcal formula meal increased corrected QT interval 15-60 minutes after meal consumption, but in 8 of their subjects who drank isovolumic water instead of solid diet no increases

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were observed (4). Also hypoglycemia may influence cardiac repolarization and the risk of arrhythmia may increase with low serum glucose levels (5). So we attempted to find out whether Ramadan fasting makes any difference in cardiac repolarization, heart rate and axis comparing within some minutes after meal ingestion after sunset, that is called "Eftar".

QT dispersion which is the difference between the maximal and minimal QT intervals in 12-lead electrocardiogram, seems to be more specific and sensitive than QT interval and corrected QT interval (QTc) in assessment of cardiac repolarization (6). Age and gender demonstrate a complex interaction on indices of myocardial repolarization with different measures behaving differently (7). Kassotis et al. found that men had a longer QT dispersion, which may explain the increased risk of SCD. However, women have a longer QT interval with a smaller QT dispersion (8). A longer minimal QT interval as opposed to a longer maximal QT interval, is responsible for the shorter QT dispersion in women. This long minimal QT interval in women may predispose to an increased risk of drug induced torsade de pointes (8). Readon et al. showed that QTc interval is longer in women (9).

We aimed to evaluate cardiac repolarization during Ramadan fasting and compare it with the time of food consumption, so we considered measuring QT dispersion and QTc dispersion as well as QT interval and QTc interval as indicators of cardiac repolarization.

MATERIALS AND METHODS

Subjects: A total of 60 healthy subjects were enrolled in our study. These subjects were randomly selected from hospital staff, students of medicine or healthy volunteers. Informed consent was obtained. Sixty seven percent of them were men and 33% were women. The age of our study group ranged 20 to 35 years with an average of 28.55±3.75 (mean ± SD). The study was a quasi-experimental study and performed in Amir Alam Hospital, in December 2000 when days lasted 11 to 12 hours.

All of the subjects had been fasting 11 to 12 hours each day from sunrise to sunset, at least for 25 days during Ramadan. If the subjects were cigarette smokers, had a previous history of cardiac disease, history of sudden death in family, diabetes mellitus, liver or kidney disease or were consuming anti-arrhythmic drugs, we did not include them in the study. Patients were excluded from the study if they had arrhythmia, abnormal electrocardiograms, such as ST-segment and T-wave changes and evidence of left ventricle hypertrophy or data from> 3 leads in 12-lead surface electrocardiogram (ECG) were not available. The entire study group was fed with the same food at the time of sunset (Eftar). They were free to drink as much liquid (tea or water) that they wished, but they were asked about the volume consumed cups of liquid (Each cup equaled 100 ml).

Electrocardiographic recordings: Surface 12-lead electrocardiograms were recorded at 25 mm/s using cardio-test EK 51 recorder. Records were obtained two times for each individual, once during fasting, (2 hours before sunset after 10-11.5 hours of fasting) and another time 15 to 60 minutes after taking "Eftar" . Electrocardiograms were recorded at the end of Ramadan and all the subjects had been fasting at least for 25 days. We had initially planned to record control electrocardiograms one month after Ramadan, 1-3 hours after a meal but unfortunately, only 20 of our subjects completed the study and others avoided completing the study because of their individual problems. These control electrocardiograms were almost all obtained from men and data was not complete. We decided to perform our analysis on those records obtained during Ramadan. A single experienced observer (second author) evaluated all of the electrocardiographic records.

Electrocardiographic variables: 1, 2. QT-interval: QT intervals were measured manually in blinded fashion from the first deflection of the QRS complex to the point of T-wave offset. The point of T-wave offset was defined as the return of T-wave to baseline. If a U-wave was present, the nadir between the T and U-wave was defined as T wave offset (10). If the end of T-wave could not be reliably determined, data from those lead were not included in the data analysis. Each measurement was given as the mean value of 2 consecutive beats. We considered 2 variables for assessment: "maximal QT interval" that is the maximal QT interval among 12-lead ECG and " mean QT interval that is an average of QT intervals in 12-lead ECG.

3, 4. Heart rate corrected QT interval (QTc interval) was calculated by using Bazett's formula (QTc = QT interval divided by the square root of RR interval). We considered "maximal corrected QT interval (QTc)", among 12 leads as a variable. "Mean QTc interval" was referred to an average of QTc intervals in 12-lead ECG.

5. QT dispersion was defined as the difference between maximal and minimal QT interval

measurements occurring in any of the 12 leads on a standard electrocardiogram.

6. QTc dispersion was defined as the difference between maximal and minimal corrected QT interval measurements (QTc) occurring in any of the 12 lead on standard electrocardiogram.

7. RR-interval and heart rate: an average of RR-interval in 12 lead was defined as RR- interval. Heart rate was calculated using RR-interval.

8. QRS axis was calculated using this formula: Arc Cos [$aSin\theta / a^2 + b^2 + 2ab\ Cos\ \theta$] in which "a" is the resultant of QRS measurement in first ECG lead and "b" is the resultant of QRS measurement in any other different lead, and "θ" is the angle between them.

Statistical analysis: Data are presented as mean ± SD. Statistical analysis was performed with paired student t-test, using software of SPSS. Linear regression tests were done as appropriate. P values of< 0.05 were considered significant.

RESULTS

Of the 60 subjects enrolled in this study, 2 were excluded from evaluation because one of them showed arrhythmia in his electrocardiogram and in the other > 3 leads were not available for QT analysis. Results of our electrocardiographic measurement and analysis are summarized in table 1. As we have showed in this table, maximal QT interval and mean QT interval are significantly longer during fasting (P<0.05). (In our study in that measurements by the same experienced observer were used for statistical comparison of QT dispersion, the intra-observer variation was 8.5 ms.) Also we came to the same conclusion when we analyzed maximal QT interval and mean QT interval in male and female separately (P<0.05). Our study did not show any significant difference in maximal QTc interval and mean QTc interval during and after fasting, but QT dispersion and QTc dispersion were increased during fasting (P< 0.05).

RR-interval as an indicator of heart rate was longer during fasting (P< 0.05). These results were confirmed when we analyzed the data for male and female separately. In our study heart rate was increased from mean value of 67.24 during fasting to 78.63 after taking Eftar (P<0.05). No significant axis changes were seen during fasting in our study.

Table 1. Electrocardiographic variables during fasting and after meal (Eftar)

Variable	Fasting	After meal (Eftar)	P-value
Maximal QT interval	402.9±24.8	373.5±24.4	P< 0.0001*
Mean QT interval	385±28	362.3±27.4	P< 0.0001*
Maximal QTc interval	449.4±20.3	450.8±24.3	P> 0.05
Mean QTc interval	414±19.7	420±20.1	P> 0.05
QT dispersion	57.27±20.1	41.66±15.1	P< 0.0001*
QTc dispersion	75.44±24.6	64.09±22.8	P< 0.05*
RR interval	892.3±164.7	763±120.7	P< 0.0001*
Axis	55.33±46.78	66.03±57.9	P> 0.05

*P< 0.05

The first number is mean standard deviation. All the measurement units are milliseconds, except for axis that is measured through degrees. Statistical analysis has been performed by means of paired t-tests. Mean values are given for comparison.

Table 2. Differences of some electrocardiographic variables between male and female

Variable	Male	Female	P-value
Mean QT interval	368.8±26.6*	348±24.1	P< 0.01
Fasting mean QT interval	391±28.2*	372.7±23.8	P< 0.05
Mean QTc interval	406±12.5	428.1±19.4*	P< 0.05
Fasting mean QTc interval	399.9±13.6	422.2±18.1*	P< 0.05
Maximal QTc interval	438.2±17.7	458±25*	P< 0.05
Fasting maximal QTc interval	442.6±20.8	454±19.4*	P< 0.05
QT dispersion	50.54±18.8*	37.89±11.5	P< 0.05
Fasting QT dispersion	65.45±17.64*	53.55±20.68	P< 0.05
RR-interval	810±105*	667±89.4	P< 0.001
Fasting RR-interval	944±159*	786±120	P< 0.05

* Greater values are marked with this sign. The first number is mean standard deviation. All the measurement units are milliseconds. Fasting, electrocardiograms were obtained, 2 hours before sunset after 10-11.5 hours of fasting. The other electrocardiograms were obtained 15 to 60 minuets after eating"Eftar". Statistical analysis has been performed by means of unpaired t-test. Only those results with P< 0.05 are presented.

Other data from our study showed that mean QT interval, QT dispersion and RR-interval were longer in men compared to women both during fasting and after Eftar (P< 0.05)(Table 2), but mean QTc interval was conversely longer in women (p<0.05). The volume of liquid consumption was not a predictor of increases in any of studied electrocardiographic variables.

DISCUSSION

Prolongation of QT interval and RR interval during Ramadan fasting, instead of no significant changes in corrected QT interval may primarily suggest that prolongation of RR-interval causes QTc interval not to have significant difference. But increases of QT dispersion and corrected QT dispersion (QTc dispersion) during fasting that are more reliable indicators of ventricular repolarization (6) support the idea that ventricular repolarization may be changed during Ramadan fasting.

In the previous studies, increased QT dispersion has been shown to be related to an increased risk of serious ventricular arrhythmia (6). QT dispersion has been identified as an indicator of arrhythmic cardiac death in patients with myocardial infarction (11), and it has been increased in coronary heart disease (11), prolonged QT syndrome (12), hypertrophic cardiomyopathy (13), chronic heart failure (14) and drug related arrhythmia (15). But notice should be taken that although great prolongation of QT interval has been shown to be associated with increased risk of malignant ventricular arrythmias or even sudden cardiac death, it may exist without the development of torsade de pointes if the QT dispersion is not significantly altered (15). Normal value of QT dispersion has been reported to be 30-40 ms (16). In our study mean QT dispersion after Eftar was 41.6±15.1 with a Confidence Interval of 37.71 to 45.49 that is in normal limits. In cardiac patients QT dispersion is increased to 67-138 ms (11). In our study QT dispersion increased during fasting to an average of 58.1 with a confidence interval of 52.95 to 63.25 ms.

However this increase of QT dispersion in Ramadan fasting is a novel finding, and whether this increase of QT dispersion is harmful or even causes malignant ventricular arrhythmias in cardiac patients, should be studied later in another study planned for cardiac patients.

Nagy et al. reported that a-500 kcal formula meal increased corrected QT interval 15-60 minutes after taking meal, in 11 subjects, but in 8 of their subjects who drank isovolumic water instead of solid diet no increases were observed (4). In our study RR interval decreased after Eftar (p<0.05) but increases of QTc interval was not statistically proved. Also the volume of liquid consumed was not a predictor of the changes of any of our parameters. Notice should be paid that the study group of Nagy et al. was not going on fasting; they included only 11 subjects, and finally their study group either drank liquid or ate a-500 kcal formula, but we could not ethically prevent our subjects from drinking, because they had not drunk any liquid during fasting.

In previous studies it has been shown that hypoglycemia causes QT dispersion and QT interval to increase (5). In another study according to Morris et al decreases in bicarbonate ion has been an indicator for prolongation of QT dispersion after hemodialysis (17). Similarly we can attribute the increases of QT dispersion and QTc dispersion during fasting in our study to acidosis and decrease of bicarbonate or hypoglycemia (5), that may all cause a decrease in outward current during replarization period. However confirmation of this hypothesis needs further survey.

Acceleration of heart rate and shortening of RR-interval after food consumption may be due to stimulation of autonomic nervous system or noradernergic release after meal but this remains to be confirmed later. RR-intervals were longer during fasting in contrast to control electrocardiograms but this was not statistically proved. This finding shows that relative bradycardia may occur during Ramadan fasting. Maybe the greater peace of mind, that is created by fasting and obedience of God, may cause daily stresses and sympathetic activity to decrease or may cause endorphins to increase. However confirmation of this hypothesis needs further survey because our data set were not complete in control electrocardiograms.

In our study mean QT interval and RR-intervals were longer both during fasting and after meal in men comparing with women and QT dispersion was greater in men (P<0.05), but conversely mean QTc interval was longer in women during and after fasting (P<0.05). Husain stated that males experienced a greater reduction than females in resting heart rate during Ramadan fasting (18). Readon et al. came to the conclusion that QTc interval is longer in women (9). So it seems that the effect of RR-interval increase in men is stronger than the effect of increased QT interval so that corrected QT interval is longer in women. Readon et al. stated that longer QTc interval in women may be due to fibrosis or myocardial amyloidosis (9). Gender related differences in corrected QT interval observed in the adult population,

are not present at birth and appear only after puberty, suggesting a possible impact of sex hormone levels on the corrected QT interval duration (19). Because of these differences in QT interval, QTc interval and RR-interval in different genders, we analyzed mean and maximal QT interval, mean and maximal QTc interval, RR-interval, QT dispersion and QTc dispersion separately in men and women during fasting and after meal and came to the same conclusion. So it seems that gender does not influence the effects of fasting on cardiac repolarization and heart rate.

Study limitations:

In some studies it has been shown that QTc interval and aging are related to each other (9). So we performed our study on a special age group, aged 20-35 years to eliminate the effect of age on QTc interval.

We had initially decided to record another series of control electrocardiograms one month after Ramadan, 1-3 hours after a meal. But we could only find 20 of our study group and others were missed. When we completely analyzed this part of the study, by means of paired t tests we concluded that our electrocardiographic variables including mean and maximal QT interval, mean and maximal QTc interval, QT and QTc dispersion, RR-interval and axis had no statistically significant difference in Ramadan after Eftar and one month later 1-3 hours after a meal ingestion (as control). So we decided to perform our analysis in all 60 individuals just in Ramadan during fasting and after Eftar.

The effects of Ramadan fasting on cardiovascular disorders especially arrhythmia or palpitation may need another study aimed to consider patients instead of healthy individuals.

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