Impact of Gender on QT and QTc Interval in Relation to Exercise

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Abstract: The QT interval on the electrocardiogram (ECG) has gained clinical importance. Prolongation of QT interval can predispose a person to fatal ventricular arrhythmia. Clinical and experimental studies suggest that QTc is longer in women than in men. Exercise is believed to affect the QT interval in both gender. But not many studies have been done with regard to QT & QTc interval in relation to exercise and gender. The aim of this study is to compare the QT & QTc interval between male & female. Before start of exercise, i.e basal ECG 2. Immediately after exercise and 3. Fifteen minutes after exercise. Fourty nine healthy subjects of both genders in the age group 17-22 years were selected for the study. ECG was recorded before exercise, immediately after exercise and 15 minutes after exercise with bicycle ergometer. The data was analysed in SPSS version 20 and their statistical significance was noted using student ‘t’ test with P <0.05 taken as significant. Under basal condition- QT interval did not show any gender difference but basal QTc was significantly longer (p<0.05) in females than in males. Immediately after exercise - these parameters did not show any significant differences in both the groups. However 15 mins after exercise i.e during the recovery phase - QTc showed significant increase in females (p <0.05) compared to males. These gender differences in cardiac activity are supposed to be due to action of sex hormones.

Keywords: Bazett formula, Gender, QT interval ,QTc interval , ventricular arrhythmia.

INTRODUCTION

This is the era of women empowerment. Women population constitutes around 50% of the world population. Women are equally competent to men in many socio-economic activities. We see women in all field of activity be it academic or sports like basket ball, cricket, volley ball etc army – navy, air force, military ,mountaineering etc. so it must be made mandatory to evaluate the cardiovascular status before recruiting female subjects in jobs requiring physical exertion. Recently, more research is being undertaken on women's health issues. A simple evaluation for cardiovascular status is the QT & QTc interval in ECG recordings. QT & QTc is one of the important marker for cardiac status. It is important for diagnosis of cardiac dysfunction. Prolongation of QT interval is a predictor to fatal ventricular arrhythmia. Bazett [1] noted that QT interval in female is longer than men. Women have a higher prevalence of sick sinus syndrome, inappropriate sinus tachycardia, atrioventricular nodal reentry tachycardia, idiopathic right ventricular tachycardia, and arrhythmic events in the long-QT syndrome [2]. Also literature studies have proved, some of the drugs prolong the QT interval in women because of which greater caution should be used when prescribing QT-prolonging drugs in women. Similarly in the women the incidence of arrhythmias is increased during pregnancy[3]. The mechanisms of these gender differences are unclear but may be related to hormonal effects. Data available shows that there is a male & female differences in the expression of ion channels. This gender difference in QTc is due to the influence of sex hormone on the ion channels[4,5,6,7] oestrogen prolongs QT (repolarisation) by opening ‘slow Na+ channel’ & Prolonged opening of Ca2+ channels. Testosterone shortens QTc (repolarization) by inhibiting L-type Ca2+channel, slowly activating delayed rectifier K+.
channels. Due to these actions estrogen is pro-arrhythmic in nature making women more prone to arrhythmia testosterone is cardio-protective in nature by reducing risk of arrhythmia. QT interval is part of QRS complex that extends from the beginning of QRS complex to the end of T wave. Functionally, it represents the electrical activity of the ventricular myocardium that includes depolarization and repolarisation. The normal value for QT interval is 0.4 sec (seconds) and it ranges between 0.4 to 0.43 sec [8]. Clinically, QTc is preferred to QT. QTc is the corrected QT interval. As QT interval depends on the HR (heart rate) and HR variation occurs even under physiological conditions, correction factor has to be applied to get real time of the QT interval. This was done by using Bizet formula named after the Physiologist Henry Cuthbert Bazett. The formula is QTc = QT/ √RR where QTc is the QT interval corrected for heart rate, RR is the interval between the peak of two R waves in the QRS complex. The QTc interval in men is 450 ms, in women QTc interval is 470 ms.

Population studies has established that prolonged QT interval has increased risk of ventricular arrhythmias and sudden death in the general population [9, 10, 11]. Although exercise has overall beneficial effects, it has been shown that the risk of sudden death is increased dramatically during and immediately after unaccustomed exercise [12,13] compared with sedentary periods. But whether the increase in QT, QTc with exercise is similar or not between genders is to be explored. Gender differences in resting QTc have been well documented. But the effect of exercise has been less explored. This study explore the QT & QTc interval between male & female in relation to exercise.

**Aim:**
To assess the QT and QTc interval in male and female subjects 1. Before the start of exercise 2. Immediately after the exercise. 3. 15 minutes after exercise. To compare the QT & QTc interval between males & females in relation to exercise 49 healthy male and female volunteer in the age 17 to 22 years were selected randomly for the study. Sample size was determined by using the formula \( n = \left[ \frac{Z_{a/2} \sigma}{E} \right]^2 \) They were divided into two groups [17] female (group-1) and 32 male (group – 2)

**Statistics:**
The data were analysed in SPSS version 20.0 using students t test. P value of < 0.05 was considered to be statistically significant. Comparison of HR QT and QTc between genders in relation to exercise was done.

**Selection of the subjects**

**Inclusion criteria:** subjects not suffering from any clinical conditions were selected for the study.

**Exclusion criteria:** Subjects with hypertension, congenital heart disease, valvular heart disease, respiratory disease, neurological disorders, asthmatics, diabetics, smokers, and alcoholics were excluded from the study. Those who were on medication and athletes were also excluded from the study. The study was approved by the Institutional Ethical Committee and the written informed consent was obtained from the participants after explaining the procedure to them.

**Procedure** The subjects were given instruction to avoid caffeinated beverages for at least 12 hours prior to the test. They reported at 11 AM to the Research laboratory of the Department of Physiology in the institution and were allowed to rest for 10 min. After recording the anthropometric variables (age, sex, height and weight), the basal ECG was recorded for one minute in supine position using electrocardiograph (Model – Cardiart 108T (MK V1). The QT interval was calculated from lead II in the ECG of standard bipolar limb leads. Three QT intervals were chosen randomly from the recorded strip and the average of these QT intervals was taken as the reliable value. From this value QTc was calculated using Bazett formula. Heart rate was also calculated. Bicycle ergometer - Model : Vmax 7380 Magnetic Recumbent Bike was used for exercise. Subjects were asked to pedal at 60 rpm for 6 min Loading wattage of 125 selected for male and 100 for female. ECG was recorded immediately after exercise and 15 minutes after exercise and similarly heart rate, QT interval and QTc interval was calculated from the ECG.

**RESULTS**
The table 1 shows the heart rate of both the genders in the three time periods of the exercise. The difference of mean heart rate before exercise between male and female is statistically significant. However during exercise and 15 minutes after exercise, the difference in mean heart rate is not statistically significant.

The table 2 shows the QT interval of both the genders in the three time periods of the exercise. The QT interval between male and female before exercise, immediately after exercise and 15 minutes after exercise is not statistically significant.

The table 3 shows the QTc interval of both the genders in the three time periods of the exercise. The QTc before exercise between male and female is statistically significant with p value of < 0.05, immediately after exercise the p value of > 0.05 which is statistically insignificant and 15 minutes after exercise the p value is < 0.05 is statistically significant. Under basal condition, QTc interval did not show any difference between males and females. However, basal QTc was significantly longer (p<0.05)
in females than in males. Immediately after exercise, these parameters did not show any significant differences in both the groups. However 15 minutes after exercise i.e during the recovery phase QTc showed significant increase in females (p <0.05) compared to males .Highly significant increase in QTc ( p < 0.005 )was seen in female before exercise and during recovery ( p < 0.005 )compared to male There is no such change in QTc during exercise.

Table 1: Comparison of HR between genders in relation to exercise

<table>
<thead>
<tr>
<th>Gender</th>
<th>Before exercise</th>
<th>During exercise</th>
<th>After 15 minutes of exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>74.15</td>
<td>128.61</td>
<td>75.67</td>
</tr>
<tr>
<td>Female</td>
<td>79.76</td>
<td>122.59</td>
<td>79.76</td>
</tr>
<tr>
<td>P value</td>
<td>p&lt;0.05</td>
<td>p&gt;0.05</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

Table 2: Comparison of mean QT interval between genders in relation to exercise

<table>
<thead>
<tr>
<th>Gender</th>
<th>Before exercise QT0</th>
<th>During exercise QT1</th>
<th>After 15 minutes of exercise QT2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>0.3500±0.035</td>
<td>0.3281±0.03</td>
<td>0.3413±0.027</td>
</tr>
<tr>
<td>Female</td>
<td>0.3553±0.019</td>
<td>0.3147±0.032</td>
<td>0.3365±0.025</td>
</tr>
<tr>
<td>P value</td>
<td>p&gt;0.05</td>
<td>p&gt;0.05</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

Table 3: Comparison of mean QTc interval between genders in relation to exercise

<table>
<thead>
<tr>
<th>Gender</th>
<th>Before exercise QTc0</th>
<th>During exercise QTc1</th>
<th>After 15 minutes of exercise QTc2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>0.3838±0.035</td>
<td>0.4100±0.073</td>
<td>0.3813±0.028</td>
</tr>
<tr>
<td>Female</td>
<td>0.4106±0.027</td>
<td>0.4118±0.033</td>
<td>0.4012±0.023</td>
</tr>
<tr>
<td>P value</td>
<td>p&lt;0.05</td>
<td>p&gt;0.05</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

DISCUSSION
Kenneth A et al [14] showed gender has an effect on the QT interval, with women having longer QT interval lengths than men when the heart was less than 100/min, but when the heart rate was more than 110 there was no gender difference Similar result was noted in our study. Simonetta Genovesi et al [15] have shown that with exercise training, QT & QTc showed no difference with gender. Chauhan VS et al [16] had demonstrated that although healthy women showed longer QTc interval they showed greater adaptation with exercise. Burke et al [17] confirmed that women have longer resting, Bazett-corrected QTc intervals than men, and suggested that differences in autonomic tone and menstrual cycle variability was not responsible for the gender difference. Lehmann et al [18] in their study of familial long QT syndrome, also found that women have longer QTc (rate corrected) intervals than men. Stramba-Badiale et al [19] in their study found that women have longer QT duration than men at long RR duration, but the difference disappears at short cycle lengths. Klipgfield et al [20] noted a similar finding in their study of the QT interval. Prince J. Kannankeril et al [21] has demonstrated that QT interval shortens with exercise as demonstrated in our study but the shortening is only in the initial portion of repolarisation and not in the terminal portion of repolarisation leading to increased risk of sudden death during exercise and during recovery but comparison between male and female was not studied. Our study shows QTc is longer in female than in male. This is more true regarding QTc interval Although QTc is longer in female than male it is not abnormally prolonged. During exercise and during the recovery phase sympathetic parasympathetic balance come into play and prevents the re-enterant arrhythmia. Thus healthy women exhibit greater QTc- rate adaptation with exercise & recovery than men Greater the QTc prolongation with decreasing heart rate, more the risk of arrhythmia in women [22]

CONCLUSION
The path physiology of sudden cardiac death is not completely understood. According to literature study cause of sudden death could be alteration of ventricular repolarization, autonomic tone, and exercise. Although exercise has overall beneficial effects, risk of sudden death is increased during and immediately after exercise [22] compared with sedentary periods.

Under normal physiological condition gender is not a risk factor because of other regulatory mechanism like autonomic influence which come into play. But it becomes risky with condition like diabetes, obesity, unknown genetic mutation, pregnancy. QT & QTc is subjected for gender variation due to hormones .Exercise accelerates this risk. It has to be made mandatory for clinicians to subject the female for physical & clinical examination to rule out the susceptibility for exercise induced cardiovascular risk. So in female subjects, while issuing medical certificate
cardiovascular status evaluation should be included. ECG with QT & QTc interval evaluation is a simple and not time consuming for assessment cardiac status

**Future prospective:** Studies on effect of oral contraceptive pill on QT interval is meager. Effect of oestrogen and progesterone on the cardiovascular system in reproductive age group taking OCP pills has to be evaluated. Further research is needed on the safety of OCP

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