

Sex Hormones and Repolarization Dynamics During the Menstrual Cycle in Women Treated with QT-Prolonging Drugs

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BACKGROUND

Females with long QT syndrome (LQTS) have a higher risk of life-threatening cardiac events after the onset of adolescence, possibly due to a modulating effect of female sex hormones on cardiac repolarization. Clinical research data suggests that women account for most cases of drug-induced QT prolongation and torsade de pointes, indicating that there are sex-related differences playing a role in repolarization duration. However, the predisposition to ventricular arrhythmias in women treated with drug-induced QT prolongation is not well understood. We hypothesized that the effect of sex hormones on cardiac ion channel function may modify propensity for ventricular tachyarrhythmia during the menstrual cycle in women who are treated with QT-prolonging drugs.

OBJECTIVE

To assess the association between sex hormones and QT interval changes in ECG during the menstrual cycle in women treated with sotalol or dofetilide for atrial fibrillation.

METHODS

Study Population:

- 20 women of reproductive age treated with dofetilide or sotalol as per standard of care for atrial fibrillation.
- 20 healthy women subjects of reproductive age.

Study Procedures:

- All subjects underwent three 7-day ECG monitoring acquired using M5 Recorder ECG monitoring (Figure 2).
- The three recording cycles were planned within pre-specified periods of the menstrual cycle (Figure 1), collected on days 3-9, days 13-19, and days 22-28.
 - Simultaneous saliva samples for sex hormone level testing were obtained on the first day of each recording cycle (days 3, 13, and 22).

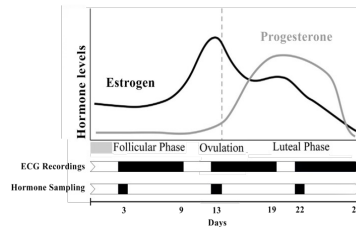


Figure 1. Study procedure with repeated 7-day ECG monitoring and collection of saliva samples for measurement of hormone levels during the menstrual cycle.



Figure 2. Wearable M5 Recorder used for ECG for Monitoring.

Hormonal changes may affect predisposition for ventricular tachyarrhythmia in women who are treated with QT-prolonging drugs.



END POINTS

Primary:

- QT-Apex (a marker of early repolarization)
- QT (a marker of total repolarization time)

RESULTS

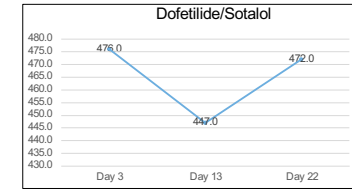


Figure 3. QTc dynamics during the menstrual cycle in women treated with QT-prolonging drugs: sotalol or dofetilide

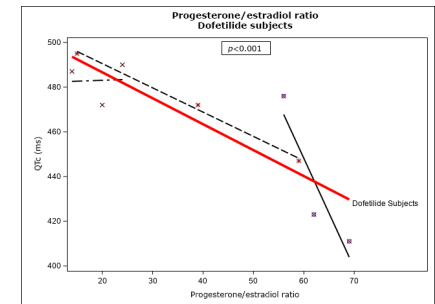


Figure 4. Correlation between QTc and progesterone/estradiol Ratio in Women Treated with QT-Prolonging Drugs

DISCUSSION

This is the first study to prospectively assess correlations between repolarization dynamics and sex hormone levels during the menstrual cycle in women treated with QT-prolonging drugs. Our findings show unique correlations of sex hormones with total cardiac repolarization during the menstrual cycle that may affect propensity for ventricular tachyarrhythmia in women who are treated with QT-prolonging drugs.

DISCLOSURE INFORMATION

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