PEDIATRIC ENDOCRINE SOCIETY

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Drug and Therapeutics Committee

Risk of Prolonged QT Interval with Gonadotropin Releasing Hormone Agonists

The risk of Gonadotropin Releasing Hormone Agonist (GnRHa) therapy causing prolonged QT interval was originally reported during treatment of men with prostate cancer and was proposed to relate to changes in circulating testosterone concentrations (Garnick MB, et al, J Clin Oncol 2004;(suppl):22. abstract 4578). There have not been reports of prolonged QT interval in women associated with GnRHa use. Prolonged QT interval increases the risk of developing torsades de pointes (TdP), a ventricular arrhythmia that can lead to sudden cardiac death. In individuals with congenital long QT syndrome, the risk of TdP increases exponentially as the heart rate–corrected QT interval (QTc) increases. Risk factors for developing TdP in hospitalized adults include concurrent use of more than one drug known to cause prolonged QT, cardiac disease, female sex, electrolyte abnormalities and diuretic therapy (Drew, BJ, et al. Circulation. 121:1047, 2010). This is a dose-dependent relationship for most medications known to cause prolonged QT. The list of medications known to cause prolonged QT interval is updated regularly at www.crediblemeds.org and a smartphone app linking to that information is available. Currently, the only GnRHas reported to increase the risk of prolonged QT interval are leuprolide and degarelix. However, it remains unclear whether this is a class effect and whether other members of the GnRHa class may also confer increased risk.

Other classes of medications that cause prolonged QT interval include anti-psychotics (typical and atypical), anxiolytics and anti-depressants. Therefore, concern has been raised about using GnRHa therapy in individuals receiving these medications. In particular, because mental health conditions requiring pharmacotherapy are a frequent co-morbidity in gender-dysphoric youth, the issue of a possible interaction between GnRHa therapy and psychopharmacotherapy has been raised.

Among conditions treated with GnRHa in pediatrics, gender dysphoria in adolescent males is the clinical circumstance most closely resembling that in which the risk of prolonged QT interval with GnRHa has been described, i.e., males with previously normal adult levels of testosterone lowered by GnRHa.

In discussion with our cardiology and pharmacy colleagues, the Drug & Therapeutics Committee has generated the following recommendation for individuals receiving GnRHa therapy.

1. Before starting GnRHa therapy, providers should inquire about other medications the individual is taking and any symptoms concerning for an arrhythmia.
2. A screening ECG is recommended if the individual:
    a. Is receiving other medications known to cause prolonged QT interval,

OR

b. Has a history of congenital heart disease, arrhythmia or Long QT Syndrome,
OR

c. Has a family history of Long QT Syndrome or sudden cardiac death,
OR

d. Has symptoms concerning for Long QT Syndrome including syncope.

3. If a screening ECG is performed, repeat ECG should be performed when the GnRHa dose has reached steady state.
4. Referral to cardiology should be made if the individual has Long QT Syndrome, which includes a prolonged QTc, or other ECG abnormalities, symptoms or family history of Long QT Syndrome or sudden death.
5. Providers should counsel their patients about symptoms of arrhythmia, including palpitations and syncope.
6. Providers should continue to inquire about new medications during ongoing GnRHa therapy.

Further studies are necessary to investigate the risk of GnRHa therapy causing prolonged QT in children and young adults.

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Version 10/18/2017