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Original article

Borderline and Long QT Syndrome in Adolescent Athletes Taking Medications



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ABSTRACT

Purpose: Adolescent athletes undergo preparticipation screening for long QT syndrome. Medications that are associated with QT interval prolongation are increasingly being prescribed to pre-college students. The side effect profile of these medications during exercise is unknown. The aims of this study were to (1) measure the prevalence of medications known to be associated with QT interval prolongation taken by adolescents participating in athletics and (2) to determine the association between the use of these medications and QT interval prolongation in adolescents participating in athletics.

Methods: Sports preparticipation exams were performed on 484 students at an urban high school. This consisted of a physical examination, 12-Lead electrocardiogram, and health history including current prescription and over-the-counter medications. Electrocardiograms were interpreted by a pediatric cardiologist using Bazett's correction formula. Descriptive statistics were used to characterize the cohort. The participants' parents consented to the preparticipation examination before history and physicals.

Results: No athletes exhibited a corrected QT interval >500 ms. Borderline long QT was identified in 6.65% of the subjects. In this study, 7.64% of the subjects reported that they were taking medications associated with QT prolongation. After controlling for age and gender, medication usage was not significantly related to the presence a borderline long QT interval.

Conclusions: Although adolescent athletes are taking medications associated with QT interval prolongation, their side effect profile during exercise is unknown. Although there was no significant association between medications and borderline long QT, these data were taken from adolescent athletes at rest. The prevalence of adolescents participating in athletics and taking medications associated with QT interval prolongation was significant. There appears to be a very low risk of QT prolongation >500 ms at rest in this cohort.

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IMPLICATIONS AND CONTRIBUTION

It is known that the preparticipation screening examination for adolescent athletes misses a small percentage of those with long QT syndrome. A medication history is not a standard part of this screening examination. This study measures the potential impact of medications taken by adolescents participating in athletics. Medications should be documented as a part of the preparticipation screening examination, and those participating in athletics taking medications that prolong the QT interval should have an EKG during exercise to ensure safety.

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High school and college athletes commonly undergo a preparticipation screening which includes a standard, directed 12-element history and physical examination. Although not standard, many of these athletes also receive an electrocardiogram (ECG). Athletes with abnormal ECGs are routinely referred to a cardiologist for further examination. Because of the significant fear of sudden cardiac death in those with ECG

abnormalities such as QT interval prolongation, some health care providers recommend athletes with ECG abnormalities discontinue participation in exercise and athletics [1].

Long QT syndrome (LQTS) has a prevalence of approximately one in 2,500. Among the 12 known genotypes, LQT1 is the most common (25%–35%) [2]. A defect in LQT1 is typically associated with cardiac dysrhythmias from exercise-related triggers and adrenergic stimulation, and it has been demonstrated that postexercise epinephrine infusions significantly prolong QT intervals [2]. Swimming has been classically associated with cardiac event provocation in those with LQT1 [3].

Additional complexity is added by those adolescents with prolonged QT intervals. Conventionally, individuals identified with QT intervals >500 ms are typically diagnosed with long QT syndrome. There is an overlap, however, between normal patients and patients with QT intervals in the range of 450–490 ms [4]. Previous work has demonstrated that 33% of patients who appear to have a borderline long QT interval on ECG test gene positive for LQTS1 [5]. On the other hand, 25%–50% of gene positive LQTS patients have a nondiagnostic corrected QT (QTc) [6].

Medications that are associated with QT interval prolongation, such as certain asthma medications, antidepressants, and antipsychotics, are increasingly being prescribed to precollege students. The side effect profile of these medications during exercise is unknown. A risk of ventricular dysrhythmias and sudden cardiac death secondary to overdose of these medications has been reported [7]. However, this risk has not been assessed at therapeutic doses during exercise.

Interestingly, medication history is not part of all recommended standard preparticipation screenings. Previous research indicates that standard history and physical examinations do not identify all young athletes at risk of sudden cardiac death [8]. Should a medication history be a part of the standard preparticipation screening? Furthermore, should an athlete's use of certain medications necessitate an ECG? The aim of this study was to measure the prevalence of medications known to be associated with QT interval prolongation taken by precollege students who participate in athletics. In doing this, we also endeavor to better understand the risk for borderline long or long QT syndrome in adolescent athletes taking medications known to prolong the QT interval.

Methods

Patients

This study was approved by the university institutional review board. Sports preparticipation examinations were performed on 484 children and adolescents at an urban high school in May 2012. This process consisted of a physical examination, 12-Lead ECG, and health history requiring subjects to report past medical history, past surgical history, and current prescription and over-the-counter medications. Each of these examinations was performed in the presence of a parent or guardian. All subjects were precollege students who intended to participate on a school sports team in the upcoming Fall semester.

Electrocardiographic analysis

All ECGs were interpreted by a single pediatric cardiologist who was blinded to patient demographic information, medical history, and physical examination results. Bazett's correction

formula was applied to all ECGs, and manual measurement was used to confirm the computer derived QT and QTc. QTc values were performed on all ECGs with heart rate less than 60 or greater than 100 beats per minute. QT intervals in Lead II were measured when possible. Borderline long QT was defined as QTc of 450–500 ms in males and 460–500 ms in females to account for the gender difference in which females have longer QTc intervals than males. Long QT was defined as QTc greater than 500 ms.

Medications

The University of Arizona Center for Education and Research on Therapeutics list of medications associated with QT interval prolongation was used to determine medications of interest for this study (www.azcert.org). The Arizona Center for Education and Research on Therapeutics board constantly reviews the scientific literature, FDA announcements and analyzes case reports to maintain an accurate and up-to-date list. The list is updated at least every 90 days.

Statistical analysis

Descriptive statistics were used to summarize demographics and clinical characteristics of the cohort. Continuous variables were reported as means \pm standard deviations, and categorical variables were reported as frequency (n) and percentage (%). Chi-square test and student's *t* test, when appropriate, were used to compare the distribution of demographic and clinical characteristics among subjects that did versus did not meet the definition of a borderline long QTc interval according to previously published criteria. Variables significantly different between two QTc interval groups were considered as potential confounding variables in subsequent statistical models. A multivariable logistic regression analysis was used to test the relationship between medication usage and the presence of a borderline QT interval. Because of the fact that QT interval was modeled as a categorical variable in the logistic regression analysis, a secondary, multiple-linear regression analysis was used to test the relationship between medication usage and QTc interval length, in milliseconds (ms).

Results

None of the athletes exhibited a QTc interval >500 ms. The presence of a borderline long QT was identified in 6.65% (95% confidence interval [CI]: 4.43%–8.88% of the subjects evaluated. There was a significant difference in age ($p = .0074$) and gender ($p = .0189$) between subjects that presented with a normal QT interval compared with subjects that presented with a borderline long QT interval. There was no difference in race ($p = .5578$), ethnicity ($p = .3339$), or body mass index percentile ($p = .7226$) between the two QTc interval groups (Table 1).

At the time of the preparticipation examination, 7.64% (95% CI: 5.28%–10.01%) of the subjects reported that they were taking medications associated with QT prolongation. In the multiple logistic regression analysis, male gender (odds ratio: 2.92, 95% CI: 1.10–7.77, $p = .0319$) and decreasing age (odds ratio per year: 1.22, 95% CI: 1.04–1.44; $p = .0147$) were significantly related to the presence of a borderline long QT interval. After controlling for age and gender, medication usage was not significantly related to the presence a borderline long QT interval ($p = .7980$). Additional

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