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Secondary long QT syndrome: Prevention and management

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Abstract

Long QT syndrome is characterized by prolongation of the corrected QT (QTc) interval on the surface electrocardiogram and is associated with precipitation of torsade de pointes, a polymorphic ventricular tachycardia that may cause sudden death. The prevalence of Long QT syndrome is close to 1/3000-1/5000. The QT interval duration is physiologically variable: the QTc is calculated using the Bazett's formula. Acquired long QT syndrome is an important issue for clinicians and a significant public health problem concerning the large number of drugs with this adverse effect with a potentially fatal outcome, the large number of patients exposed to these drugs, and our inability to predict the risk for a given individual. In this paper, we focus on mechanisms underlying QT prolongation, risk factors for torsades de pointes and describe the short- and long-term treatment of acquired long QT syndrome.

Keywords: long QT syndrome, treatment

Introduction

Long QT syndrome (LQTS) is a cardiac conduction disorder characterized by prolongation and increased dispersion of ventricular repolarization, manifested by lengthening of the QT interval on the electrocardiogram (ECG). This abnormal repolarization can lead to the formation of reentry circuits and may present with syncope, seizures, or torsades de pointes (TdP), ventricular fibrillation and, therefore sudden cardiac death [1].

Traditionally, LQTS is divided into congenital (c-LQTS) and acquired (a-LQTS) forms. Drug-induced LQTS is the most common cause of a-LQTS [2].

The congenital LQTS is a life-threatening cardiac arrhythmia syndrome that represents a leading cause of sudden death in the young. The symptomatic patients left without therapy have a high mortality rate, 21% within 1 year from the first syncope. However, with proper treatment, mortality is now $\approx 1\%$ during a 15-year follow-up [3,4].

Acquired LQTS is a disorder of cardiac repolarization most often due to specific drugs, hypokalemia, or hypomagnesemia [5]. Selzer and Wray first reported QT prolongation and ventricular fibrillation as a response to quinidine in 1964; two years later, Dessertenne described torsades de pointes, a polymorphic ventricular tachycardia where QRS complexes twist around an isoelectric line in a sinusoidal fashion in an elderly woman with complete atrioventricular block and syncopal attacks [5]. Torsade de pointes is usually self-limited but may degenerate into ventricular fibrillation. The incidence of acquired long QT syndrome is difficult to be estimated. Although the chances of provoking torsades de pointes by a noncardiac medication are generally lower than antiarrhythmic medications, a number of noncardiovascular drugs have been recently withdrawn from market because of unexpected sudden cardiac deaths associated with prolongation of QT interval and torsades de pointes [6].

The aim of this paper is the mechanisms underlying QT prolongation, risk factors for torsades de pointes (TdP) and the short- and long-term treatment of acquired long QT syndrome.

Results and Discussion

It's known that QT interval on the surface electrocardiogram represents the summation of action potentials in ventricular myocytes. QT prolongation entails action potential prolongation, that results from an increase in inward current (e.g., through sodium or calcium channels) or a decrease in outward current (e.g., through potassium channels). Myocardial repolarization is primarily mediated by efflux of potassium ions. Two subtypes of the delayed rectifier potassium current, IKr (rapid) and IKs (slow), are predominantly responsible for repolarization. The two currents have different activation, inactivation, and deactivation

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characteristics, different sensitivities to blocking drugs, different rate, and catecholamine sensitivity and were later found to be the result of expression of different genes [5]. The hallmark mechanism of acquired LQTS and TdP is the blockade of IKr by specific drugs [7].

There are the multiple clinical risk factors for secondary LQTS development (table 1).

Certain drugs are known to contribute to QT prolongation. Considering that not all agents that prolong the QT interval increase transmural dispersion of repolarization, drugs can be distinguished into the following groups depending on their simultaneous effects on the QT corrected using the Bazett's formula (QTc) interval and on transmural dispersion of repolarization: (1) drugs inducing both QTc prolongation and increased transmural dispersion of repolarization, characterized by a high torsadogenic potential; (2) drugs causing QTc prolongation but with a slight effect on transmural dispersion of repolarization and little, if any, ability to induce TdP; and (3) drugs causing both QTc prolongation and increased TDR below a certain concentration, but inducing TdP once a critical value of transmural dispersion of repolarization is exceeded [8].

Drugs that prolong the QT interval and/or induce Torsades de Pointes in patients with diagnosed or suspected LQTS can be found on the web pages www.torsades.org.

The cornerstone of the management of acquired LQTS includes the identification and discontinuation of any precipitating drug and the aggressive correction of any

metabolic abnormalities, such as hypokalemia or hypomagnesemia. Most of the episodes of torsade de pointes are short-lived and terminate spontaneously. However, prolonged episodes result in hemodynamic compromise and require immediate cardioversion [5].

Short-term treatment of the syndrome focuses on prevention of recurrence of TdP and includes administration of intravenous magnesium sulfate and temporary transvenous cardiac pacing. The mechanism by which magnesium prevents the recurrences of TdP is unclear. Its action is probably mediated through blockage of sodium or calcium currents. Intravenous isoproterenol is rarely needed. Important step in the management of acquired LQTS is withdrawal of offending agents and correction of electrolyte abnormalities [9]. The effectiveness of lidocaine, phenytoin, or atropine even though reported to be beneficial is uncertain [10].

Long-term treatment is rarely required. Conditions that predispose to electrolyte imbalance must be corrected. In cases of sick sinus syndrome or atrioventricular block and bradycardia, permanent pacing may be indicated [5].

Conclusion

Acquired long QT syndrome is an important issue for clinicians and a significant public health problem concerning the large number of drugs with this adverse effect with a potentially fatal outcome, the large number of patients exposed to these drugs, and our inability to predict the risk for a given individual.

Table 1: Risk factors for secondary LQTS formation

	Predictors
1	Female sex
2	Hypokalemia
3	Severe hypomagnesemia
4	Bradycardia
5	Recent conversion from atrial fibrillation
6	Heart failure
7	Left ventricular hypertrophy
8	High drug concentrations or Rapid rate of intravenous infusion with a QT-prolonging drug
9	Ion-channel polymorphisms

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