Re: First International Symposium on Long QT Syndrome on The Internet

Response submitted by Andrew Krahn, MD, FRCPC

Question:

What is the incidence of sudden cardiac death in the young, and how many deaths are related to long QT syndrome?

Answer:

The incidence of sudden death in young patients is mercifully low. Sudden infant death syndrome (SIDS) is a rare cause of "crib death" in the first six months of life. Historically, this has been attributed to predominantly respiratory causes. Recent evidence suggests that a minority of patients (perhaps as many as 3 to 5%) may suffer from QT prolongation and latent or manifest long QT syndrome [1,2]. Of interest, the QT interval shortens in the first six months of life, paralleling the reducing incidence of SIDS.

The next phase of development is associated with a very low incidence of sudden death. There is limited epidemiologic data covering the exact incidence, although information exists that suggests a very low incidence of cardiovascular causes in the absence of obvious structural heart disease. The best estimate of incidence of sudden death between age 1-21 is 3.3/100 000 person years, arising from a study in Newcastle by Wren et al [3] . Several other series have estimated 1.3-4.6/100 000 patient-years [4,5]. In the Wren series, death was attributed to a previously identified condition in 53% of cases, with a cardiovascular cause in 12%. Thirty-two percent of cases were associated with findings first discovered at autopsy, with a cardiovascular cause in 10%. The remaining 15% of cases remained unexplained, potentially representing arrhythmic death. Half of them occurred before the age of two, raising the possibility of a primary respiratory cause (predominantly nocturnal death).

The incidence of sudden death rises, as children become adolescents. To some degree this appears to correlate with increasing physician activity and puberty. Case series of sudden death in athletes suggests a relatively high incidence of unsuspected structural heart disease, including hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and anomalous coronary arteries [6,7](ref). A small proportion of these patients will have previously recognized or a more likely unrecognized substrate for arrhythmia, including conditions such as Wolff Parkinson White syndrome, Brugada's syndrome and Long QT Syndrome.

The incidence of symptoms including sudden death increases with age in all three of the most common forms of Long QT Syndrome [8-10]. In particular, potassium channel mutations causing Long QT Syndrome are most often associated with some form of physical activity or adrenergic stimulation[11]. Long QT 3 is associated with syncope and sudden death at rest or during sleep. Although there are some varying reports in the literature, the lifetime incidence of sudden death from long QT syndrome is in the order of 2 to 5%[12]. The majority of this risk is experienced before the age of twenty, to some degree influenced by genotype. Long QT 1 patients are more likely to be symptomatic earlier in life, with long QT 3 patients manifesting symptoms latest in life. Nonetheless, the incidence of new onset symptoms and sudden death is greatest during adolescence. Although the exact proportion of sudden death that is attributed to long QT syndrome is unknown, it likely represents a small minority of cases of sudden death. Genotyping of patients suffering from unexplained sudden death suggests occasional detection of mutations in the genes known to cause long QT syndrome (ref). Since many patients have presumed mutations in as yet undiscovered genes, some of these may be contributing to childhood and adolescent sudden death that remains unexplained.

Finally, high risk subsets of patients with long QT syndrome clearly exist who may be at increased risk of sudden death. Data from the International Registry would suggest that patients with marked QT prolongation, a family

history of sudden death, previous syncope or resuscitated cardiac arrest are at highest risk, and warrant aggressive preventive measures to prevent sudden death[12].

References:

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