Evaluation of the prevalence of prolonged QT syndrome in children with first unprovoked seizure

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Abstract

Background: The long QT syndrome (LQTS) is a disorder of myocardial repolarization characterized by a prolonged QT interval on the ECG. This syndrome may be congenital or acquired and it can be associated with seizure-like symptoms. ECG is used routinely to diagnose this syndrome.

Materials and Methods: In this cross-sectional study, we evaluated the ECG of children admitted to the emergency room to estimate the prevalence of LQTS in patients with first unprovoked seizure. Patients with underlying causes like fever and those with previous episode of seizure or electrolyte imbalance at time of admission were excluded. First ECG obtained in the emergency room was reviewed and maximum corrected QT (QTc) was determined.

Results: Out of 100 patients (62 boys, 38 girls), only a 6year old boy showed prolonged QTc (0.53) although 21 patients had borderline QTc (0.42-0.46). Most of the patients (58%) presented with non-generalized tonic-clonic seizures. There was no significant difference in the type of seizure and other electrocardiographic parameters between boys and girls.

Conclusion: Patients with seizure and long QT were considerably lower in number in our study in comparison with other studies. This may be due to our case selection as we excluded the children with a previous history of seizure. Moreover, it seems that ECG solely is not valid or sufficiently reliable to identify LQTS, as this cardiac conductive abnormality is a temporary disorder and may occur only at the time of seizure and disappear when patients are admitted in hospital.

Key words: long QT syndrome, seizure, children, emergency room, ECG, QT interval.

Please cite this article as: Katibeh P. et al.
Evaluation of the prevalence of prolonged QT syndrome in children with first unprovoked seizure.
World Family Medicine. 2018; 16(2): 129-132.
DOI: 10.5742/MEWFM.2018.93250

Introduction

Long QT syndrome is a disorder of myocardial repolarization, leading to QT interval prolongation disclosed in electrocardiogram (ECG). This syndrome increases the risk of sudden cardiac arrest and also "Torsade de Pointes", a serious threatening arrhythmia in humans(1,2). Patients are affected congenitally or acquire it due to several reasons, such as electrolyte disturbances or drug interactions(3). The initial symptoms are palpitation, syncope or cardiac arrest in the most disastrous scenario(4,5,6,7), as in the United States congenital long QT syndrome is the main cause of 4000 deaths in children annually (8).

Long QT syndrome is categorized into seven genetic subtypes (LQT1-7) that lead to two distinct phenotypes. One is an autosomal dominant syndrome (Romano ward syndrome) which presents with cardiac manifestations absolutely. The second is an autosomal recessive syndrome (Jervell and Lange-Nielsen syndrome), resulting in neurosensory hearing loss and still more dreadful conditions(7,9). Surprisingly, long QT syndrome may remain obscure, asymptomatic and discovered just after taking incidental ECG or revealed by suspicious sudden death in a family member. In symptomatic patients, it is not uncommon to present with bradycardia (heart rate<60 beats/min) in their first 3 years of life, due to abnormal sodium conduction in the sinoatrial node(10). Also, some external stimulation such as exercise, emotional stress and sudden sleep abruption, swimming, and driving can provoke ventricular arrhythmia in those with long QT syndrome(11).

In spite of the fact that age, gender and genotype can modify the prognosis (Table 1) (13), the clandestine nature of long QT syndrome makes it a potential fatal illness with a remarkable risk of sudden cardiac death, especially for symptomatic cases who have not been treated yet. Overall mortality rate is 20% in the 1st year to 50-60% in the first 10 years, favorably decreasing to 8% in 5 years of age after starting treatment(14,15).

Seizure and long QT syndrome

Occasionally, LQTS manifests with syncope or tonic-clonic seizure-like movements which misleads health-care providers. Thus, identification and management of this complicated group is a major concern, not fully understood yet(13,16,17,18). Pfammatter et al. reported that some cases of LQTS, who presented with falling down, rarely expose obvious QT abnormality in routine ECG after hospital admission and were discovered just by persistent Holter monitoring during exercise(19). Meanwhile, some other reports claim that convulsive disorders may induce QT prolongation in otherwise healthy patients, at least for a transient period of time(20). Hence, one important question is whether ECG is a reliable tool to differentiate LQTS from other common convulsive disorders when patients demonstrate seizure-like movements. Therefore, the purpose of this research was to estimate the number of children with first unprovoked seizure, who exhibited long QT interval in their emergency room ECG. Normal QT interval values are shown in Table 2.

Material and Methods

This cross-sectional study was conducted from 2015 to 2016 on children (1-18 years old) admitted with impression of first unprovoked seizure in the two major and referral pediatric hospitals (Namazi and Dastgheib) Shiraz, Iran. All children with known causes for seizure, such as fever or electrolyte imbalance (hypoglycemia, hypokalemia, hypercalcemia and hypomagnesemia) along with patients with a previous history of convulsive disorders or syndromic or symptomatic epilepsy were excluded from the study.

After admission, ECG was taken in the hospital and in the V5, V6 and II leads, RR and QT intervals were measured to calculate the corrected QT (QTc) interval based on Bazett's formula.

Results

In this study, 100 (62 boys, 38 girls) children with impression of first unprovoked seizure fulfilling inclusion criteria were studied and their QTc were calculated. Seizures in 42 cases were generalized tonic-clonic (GTCS) and in 52 cases they were non-generalized tonic-clonic (NGTCS). The only prolonged QTc was 0.53 detected in a 6 year old boy who presented with NGTCS; however, 21 patients had borderline QTc (0.42-0.46). Differences between boys and girls in ECG parameters or types of seizures were not significant in our study.

Concusion and Dicussion

In Southern Iran, with 100 patients with impression of first unprovoked seizure, one (1%) had long QTc. As expected, there was no significant difference between boys and girls, types of seizure and other ECG parameters among the cases. In research by Davis in 1998, on 126 children who referred to a neurological center, LQTS was diagnosed for 2 patients (1.6%) based on ECG21. In other research by Borzooie et al, also in Iran, out of 273 patients, 32 (11.7%) had long QT syndrome(22). These conflicting results might be due to the selection of cases in different studies. As mentioned before, one of the major exclusion criteria was fever in this study. Febrile convulsion may lead to arrhythmia even in the absence of other factors. In research by Dr Amin et al., fever, alone, has been introduced as a stimulant for ventricular arrhythmia in Brugada syndrome and LQT2(23). Also Burashincov indicated that fever facilitates Torsade de Pointes by prolonging the QT interval(24). Another reason to clarify controversial results was selection of patients with the first episode of seizure and not the chronic, recurrent or complicated ones.

Next to laboratory tests, ECG is almost the only available cardiac evaluation which is implemented routinely on admission in ER. However, many studies questioned ECG's validity and reliability. Kandler et al. pointed out that patients with prolonged QT syndrome usually exhibit ECG abnormality only during the seizure episode(20). Consequently, it is quite possible that ECG shows normal features while most of the patients reach hospital when the seizure is stopped and it is not surprising that some of true

Table.1: Long QT syndrome prognosis QTc: corrected QT interval, LQT: long QT, Sec: Second

High risk (≥50%)	QTc ≥0.50 sec who have LQT1 or LQT2 or (if male) LQT3
Intermediate risk (30 to 49%)	female patients with LQT3 and QTc ≥0.50 sec or patients with QTc <0.50 sec who have LQT3 or (if female) LQT2
Low risk (<30%)	patients with QTc <0.50 sec who have LQT1 or (if male) LQT2

Table.2: Normal value of ECG parameter according to age

AGE	0-7 days	1 wk-1 mo	1 mo-6 mo	6 mo-1 yr	1 yr-5 yr	5-10 yr	10-15 yr	>15 yr
Rate (beats/min)	90-160 (125)	100-175 (140)	110-190 (145)	100-180 (130)	70-160 (110)	65-140 (100)	60-130 (90)	60-100 (80)
QRS axis (degrees)	70-180 (120)	45-160 (100)	10-120 (80)	5-110 (60)	5-110 (60)	5-110 (60)	5-110 (60)	5-110 (60)
PR lead II (msec)	80-150 (100)	80-150 (100)	80-150 (100)	80-150 (100)	80-150 (120)	80-150 (120)	90-180 (140)	100-200 (160)
QRS duration (msec)	40-70 (50)	40-70 (50)	40-70 (50)	40-70 (50)	45-90 (65)	45-90 (65)	50-90 (70)	60-90 (80)
Maximum QTc[†] (msec)	450 max	450 max	450 max	450 max	440 max	440 max	440 max	430 max
QRS V_1 Q (mm)	0	0	0	0	0	0	0	0
R (mm)	5-25 (15)	3-22 (10)	3-20 (10)	2-20 (9)	2-18 (8)	1-15 (5)	1-12 (5)	1-6 (2)
S (mm)	0-22 (7)	0-16 (5)	0-15 (5)	1-20 (6)	1-20 (10)	3-21 (12)	3-22 (11)	3-13 (8)
QRS V_5 Q (mm)	0-1 (0.5)	0-3 (0.5)	0-3 (0.5)	0-3 (0.5)	0-5 (1)	0-5 (1)	0-3 (0.5)	0-2 (0.5)
R (mm)	2-20 (10)	3-25 (12)	5-30 (17)	10-30 (20)	10-35 (23)	13-38 (25)	10-35 (20)	7-21 (13)
S (mm)	2-19 (10)	2-16 (8)	1-16 (8)	1-14 (6)	1-13 (5)	1-11 (4)	1-10 (3)	0-5 (2)
QRS V_6 Q (mm)	0-2 (0.5)	0-2 (0.5)	0-2 (0.5)	0-3 (0.5)	0-4 (1)	0-4 (1)	0-3 (1)	0-2 (0.5)
R (mm)	1-12 (5)	1-17 (7)	3-20 (10)	5-22 (12)	6-22 (14)	8-25 (16)	8-24 (15)	5-18 (10)
S (mm)	0-9 (3)	0-9 (3)	0-9 (3)	0-7 (3)	0-6 (2)	0-4 (2)	0-4 (1)	0-2 (1)
T-wave V_1 (mm)	*0-4 days* = −3 to +4 (0) *4-7 days* = −4 to +2 (−1)	−6 to −1 (−3)	−6 to −1 (−3)	−6 to −1 (−3)	−6 to −1 (−3)	−6 to +2 (−2)	−4 to +3 (−1)	−2 to +2 (+1)

Adapted from references 8-10.
*Values reported as 2nd-98th percentile (mean), except for QTC (maximum value only) and >15 yr data, which report ± 1 SD.
†QTc as corrected by Bazett's formula (QTc = QT ÷ square root RR).

LQTS cases would not be identified by ECG in ER. In Davis et al.'s study, 8 out of 126 children previously diagnosed with LQTS had normal ECG at the time of evaluation. Therefore, they concluded that ECG was not sufficiently appropriate to discover LQTS, as cardiac repolarization is a temporary dynamic phenomenon and QT prolongation exists only in 5-10% of gene carriers at rest(21). Furthermore, Kandler et al., who measured QT interval in two separate occasions (2 hours after seizure and 9 days later), reported that out of 7 patients with prolonged QT interval at first, just one revealed long QT interval after 9 days and proposed that seizure itself might actuate the prolongation of QT interval(20).

However, seizure or syncope sometimes do not represent neurologic disorders and follow cardiac electrical conduction disturbances. In Pfammter's study, 8 patients were treated as convulsive cases for about 5 years when finally cardiac arrhythmia was diagnosed as the main cause of their syncope and seizure(19).

Based on all the above-mentioned points, we have to accept that although electrocardiogram is an available simple and inexpensive tool to assess and monitor electrical activity of the heart in emergency situations, ECG alone is not sufficiently valid and reliable for diagnosing new patients with LQTS. Unfortunately, no other modality has been introduced as a golden standard test up to now, but we suggest genetic studies following serial ECGs or Holter monitoring and cardiologist consult as a reasonable plan to diagnose the disease. Thus it might be reasonable that patients with seizure, especially following physical activity and other stresses, or those with family history of syncope, hearing loss or sudden death should be evaluated more precisely using multimodal approach along with an ECG in the emergency room.

Acknowledgements: The authors would like to thank Shiraz University of Medical Sciences, Shiraz, Iran and also Center for Development of Clinical Research of Nemazee Hospital and Dr. Nasrin Shokrpour for editorial assistance.

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