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Prevalence of prolonged QTc-interval in electrocardiograms of 1 -12 year-old seizure patients

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Abstract *Background:* Children with long QT intervals are prone to life-threatening ventricular arrhythmias which may lead to seizure and syncope and may be misdiagnosed as seizure.
Objective: This study aimed to assess the frequency of long QT intervals in children with and without convulsion.
Method: This study is case-control. ECG tracings were requested for all children aged between one to twelve years who were hospitalized due to convulsion with no underlying etiology and simultaneously for children of the same age and gender who were admitted due to other than seizure as case group. Consequently, QT intervals were measured and compared in the two groups.
Results: If long QT interval was defined to be longer than 0.47 second, no significant difference was noted between two groups. On the other hand, if this interval was defined to be equal to or longer than 0.46 second, long QT intervals are more frequent in convulsive children.
Conclusions: In this study, long QT interval, defined as QT interval ³ 0.46 second, is found more frequently in children with seizure than non-convulsing ones. It is recommended that children with history of seizure without any identifiable causes and that is unresponsive to anticonvulsive drugs should be investigated with ECG.

Key words: Child, Diagnostic Errors, Long QT Syndrome, Seizure

Introduction

Seizures can be caused by primary dysfunction of the central nervous system, or they can be secondary to metabolic disorders or systemic diseases. Differentiation of these cases is necessary, because, in addition to seizure control, the underlying disease should be treated. Prolonged QTc-interval syndrome is often diagnosed in children with recurrent episodes of syncope and frequent seizures, but in most of the cases, the patient's Electrocardiogram (ECG) is considered normal, and the patient is treated with a diagnosis of neurological problems [1]. However, other disorders that mimic the manifestations of epilepsy are resistant to antiepileptic drugs, and their treatment is so different from that of epilepsy [2].

This syndrome often occurs following exercise, fright, or a sudden startle. Some attacks occur during sleep. Patients may initially experience seizures, presyncope, and palpitations [1]. Diagnosis is based on electrocardiographic and clinical criteria. A corrected QT interval greater than 0.47 sec is highly indicative of prolonged QTc-interval syndrome, but QT intervals greater than 0.44 sec is only suggestive[3,4]. Treatment involves administration of beta-blockers and ICD therapy[5, 6]

Early diagnosis and treatment of prolonged QTc-interval syndrome requires diagnostic accuracy and strong suspicion in order to save the children from sudden death[7, 8].

In this study, we conducted electrocardiograms on one to twelve year-old children with seizures in order to assess the frequency of long QT intervals in children with and without convulsions; in dealing with specific cases, we considered therapeutic interventions.

Method

In this case-control study, we assessed 508 hospitalized children at Amirkabir Hospital in Arak, Iran, and divided them into two groups: 1) case (n=254) and control (n=254) groups. The case group included children with seizures of unknown etiology, and the control group included children who had no seizures and no history of seizures. The patients in both groups ranged in age from

one to twelve years and were matched for age and sex. A questionnaire was completed for all patients upon admission, including information about the age and sex of the patient; family history of seizures, cardiac diseases, and sudden death; previous history of syncope; type of delivery; and child and maternal medications (if the child was breastfed). Then, a 12-lead electrocardiogram (ECG) was recorded for each child. QT and RR intervals were measured in the patient's ECG (in the best lead), and QTc was calculated using Bazett's formula. The QT intervals were compared in both groups and evaluated on the basis of length. If we suspected a problem based on the long corrected QT interval or questions in the questionnaire, the patient received a consultation with a cardiologist.

Entry criteria included all children aged one to twelve years who were hospitalized with seizures without a specific cause, and for whom consent was given to participate in the study. Exclusion criteria included patients who were hospitalized due to secondary seizures (e.g., hypocalcemia, meningitis, brain tumor) or if they were likely to have an underlying cause. Patients were also excluded in the case of underlying heart disease or lack of parental cooperation. Statistical analysis of the collected data was performed using SPSS software.

Ethical considerations

This study was approved by the ethics committee of Arak University of Medical Sciences. During the entire study period and in dealing with patients, the study group was committed to the principles of medical ethics set forth by the Ministry of Health and the Declaration of Helsinki.

Results and discussion

In both groups of children in this study, 142 (55.9%) were male and 112 (44.1%) were female. The distribution frequencies of QTc levels in males and females in both groups are shown in Table 1.

Table 1: Distribution frequencies of QTc levels in males and females in both groups

	QTc Interval	female	male	Total
Case	QTc Interval <0.44	78	101	179
	0.44< QTc Interval<0.47	27	33	60
	QTc Interval>0.47	7	8	15
Control	QTc Interval <0.44	79	101	180
	0.44< QTc Interval<0.47	32	35	67
	QTc Interval>0.47	1	4	5

Statistically, there was no significant difference between QTc interval stratified by sex between the two groups ($p>0.05$). When long QT interval was defined as greater than or equal to 0.46 sec, there also was no significant difference between QTc interval stratified by sex in both groups ($p>0.05$; Table 2).

Table 2: Distribution frequencies of QTc levels in case and control groups if QTC≥0.46

	QTc Interval ≥0.46	0.44< QTc Interval <0.46	QTc Interval<0.44
Case	66(13%)	13(2.6%)	175(34.4%)
control	48(9.4%)	27(5.3%)	179(35.2%)
total	114(22.4%)	40(7.9%)	354(69.7%)

In evaluating the QTc levels in the case group, 175 children (34.4%) had QTc levels less than or equal to 0.44 sec, 64 children (12.6%) had QTc levels of 0.44–0.47 sec, and 15 children (3%) had QTc levels greater than 0.47 sec. In the control group, 178 children (35%) had QTc levels less than or equal to 0.44 sec, 71 children (14%) had QTc levels of 0.44–0.47 sec, and five children had QTc levels greater than 0.47 sec (Table 3).

Table 3: Distribution frequencies of QTc levels in case and control groups if QTC>0.47

	QTc Interval >0.47	0.44< QTc Interval <0.47	QTc Interval<0.44
Case	15(3%)	64(12.6%)	175(34.4%)
Control	5(1%)	71(14%)	178(35%)
Total	20(3.9%)	135(26.6%)	353(69.5%)

When prolonged QTc interval was defined as greater than 0.47 sec, 15 children (3%) in the case group and five children (1%) in the control group had a prolonged QTc interval. In this situation, there was no significant difference in frequency of prolonged QT interval between the two groups ($p>0.05$; Table 3). However, when prolonged QTc interval was considered to be greater than or equal to 0.46 sec, 66 children (13%) in the case group and 48 children (9.4%) in the control group had a prolonged QT interval, and there was a statistically significant difference between the two groups ($p<0.05$; Table 2).

Among all 508 children, only three had a QTc greater than or equal to 0.50 sec. In evaluating the history of syncope in both groups, there was no history of syncope in 251 (98.8%) children in the case group and none in 252 (99.2%) children in the control group. Syncope occurred in three (1.2%) children in the case group and two children (0.8%) in the control group; there was no significant difference in history of syncope between the two groups ($p>0.05$).

In evaluating family history of sudden death, there was a history of a father's sudden death and of a brother's sudden death in the case group, and there was a family history of sudden death of second-degree relatives in two children in the control group. There was no significant difference in family history of sudden death between the two groups ($p>0.05$).

In our evaluation of the frequency of prolonged QTc interval in males and females in the two study groups, there was no significant association between sex and QTc levels ($p>0.05$). In our study, most of the children were male and in the age range of 12–48 months. When the frequency of prolonged QTc interval was defined as greater than 0.47 sec, it was equal in both sexes in the two groups. However, when prolonged QTc interval was defined as greater than or equal to 0.46 sec, the frequency of prolonged QTc interval was greater in the convulsive children than in the non-convulsive children. In addition, most of the children with a history of syncope or sudden death in family members had a QTc interval greater than or equal to 0.46 sec.

In the study that Moss and colleagues conducted on 328 families, most children with long QTc who experienced syncope or cardiac arrest were female [9]. In the study of Lukatti and colleagues in 1998, most of the cases were also female. However, clinical presentations of this syndrome had manifested earlier in males [10.]

In a study conducted in the USA in 1993 on 287 patients under the age of 21 years who had been referred with syncope, seizures, and cardiac arrest and whose QTc intervals were greater than 0.44 sec, 9% of the patients presented with cardiac arrest, 26% with syncope, and 10% with seizures[11].

In a study conducted in India in 2006 on a 10-year-old child with congenital deafness and a history of seizures and recurrent syncope, a QTc interval of 0.72 sec was observed after years of investigation. In evaluating the ECGs of the patient's mother and sister, their QTc intervals were 0.54 sec and 0.50 sec, respectively, and they also had asymptomatic prolonged QTc. This 10-year-old child had Jervell and Lange-Nielsen syndrome and had been wrongly treated with anticonvulsant drugs for years [12].

In a study performed in the USA in 2007 on a 15-year-old girl with an 11-year history of seizures, it became clear after realizing the ineffectiveness of anticonvulsant drugs and obtaining an ECG that she had a prolonged QTc interval, which shows that the syndrome is easily confused with seizures in young people [13].

In our study, when prolonged QTc was defined as 0.47 sec, there was no significant statistical difference in frequency of prolonged QTc interval between the two groups, which is not consistent with the mentioned studies. The reason for this difference could be that all the mentioned studies were on people with prolonged QTc syndrome or were conducted on special cases, such as children with uncontrolled seizures or recurrent syncope. The difference could also be due to the fact that prolonged QTc interval is defined by different values in various articles and references, and no constant value has been determined in this field. As such, when QTc is defined as greater than or equal to 0.46 sec in some references, the frequency of prolonged QTc in children with seizures is greater than in children who were referred for reasons other than seizures. In this instance, the result would be consistent with the mentioned studies.

In all of the listed studies, prolonged QTc syndrome was manifested by symptoms of seizures in children; these cases usually are under medical care for years because of episodes of seizures and syncope in childhood and adolescence. For this reason, diagnosis of this syndrome may be delayed, which may result in cardiac arrest or sudden death when the individual is older.

In our study, there was a child in the case group with QTc=0.48 sec and two children in the control group with QTc=0.46 who had family histories of unexplained sudden death in their families. The cause of those sudden death cases could have been due to this syndrome, which is consistent with previous studies.

Conclusions

Because prolonged QTc syndrome can mimic symptoms of a seizure in children, and because these children might be treated with anticonvulsant drugs for years, it is recommended that follow ups and necessary measures, such as requesting ECGs for any seizures that are unexplained or uncontrolled with antiepileptic drugs, should be taken. If this syndrome is suspected, the patient should be referred to a cardiologist; if the syndrome is confirmed, treatment should be initiated for the patient at the discretion of a specialist.

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References

1. Ackerman MJ. Molecular basis of congenital and acquired long QT syndromes. *J Electrocardiol. 2004;37 Suppl:1-6.*
2. Macleod S, Ferrie C, Zuberi SM. Symptoms of narcolepsy in children misinterpreted as epilepsy. *Epileptic Disord. 2005;7(1):13-7.*
3. Hunter JD, Sharma P, Rathi S. Long QT syndrome. Continuing Education in Anaesthesia, *Critical Care & Pain. 2008;8(2):67-70.*
4. Roden DM. Clinical practice. Long-QT syndrome. *N Engl J Med. 2008;358(2):169-76.*
5. Moss AJ, Zareba W, Hall WJ, Schwartz PJ, Crampton RS, Benhorin J, et al. Effectiveness and Limitations of ß-Blocker Therapy in Congenital Long-QT Syndrome. *Circulation. 2000;101(6):616-23.*
6. Zareba W, Moss AJ, Daubert JP, Hall WJ, Robinson JL, Andrews M. Implantable cardioverter defibrillator in high-risk long QT syndrome patients. Journal of cardiovascular *electrophysiology. 2003;14(4):337-41.*
7. Schwartz PJ, Moss AJ, Vincent GM, Crampton RS. Diagnostic criteria for the long QT syndrome. An update. *Circulation. 1993;88 (2):782-4.*
8. Hofbeck M, Ulmer H, Beinder E, Sieber E, Singer H. Prenatal findings in patients with prolonged QT interval in the neonatal period. *Heart. 1997;77(3):198-204.*
9. Moss AJ, Schwartz PJ, Crampton RS, Tzivoni D, Locati EH, MacCluer J, et al. The long QT syndrome. Prospective longitudinal study of 328 families. *Circulation. 1991;84(3):1136-44.*
10. Locati EH, Zareba W, Moss AJ, Schwartz PJ, Vincent GM, Lehmann MH, et al. Age- and sex-related differences in clinical manifestations in patients with congenital long-QT syndrome: findings from the International LQTS Registry. *Circulation. 1998;97(22):2237-44.*
11. Garson A, Dick M, Fournier A, Gillette PC, Hamilton R, Kugler JD, et al. The long QT syndrome in children. An international study of 287 patients. *Circulation. 1993;87 (6):1866-72.*
12. Mondal RK, Karmakar B, Chandra PK, Sarkar UN. Jervell-Lange Nielsen syndrome in a family with the long QT Syndrome (LQTS). *Indian J Pediatr. 2006;73(7):623-5.*
13. Rossenbacker T, Nuyens D, Van Paesschen W, Heidbüchel H. Epilepsy? Video monitoring of long QT syndrome-related aborted sudden death. *Heart Rhythm. 2007;4 (10):1366-7.*