Research Paper

QT Interval Changes in Children With Febrile Convulsion Compared With Healthy

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ABSTRACT

Introduction: Febrile seizure is a temperature-related seizure that affects the QT interval. The purpose of this study was to evaluate the changes in the QT interval caused by febrile convulsion (FC) compared with healthy children.

Methods: This case-control study examined 180 children equally distributed between patients and controls. The study was conducted at the Ali Ebne Abi Talib Hospital in Zahedan City, Iran. The disease was diagnosed and confirmed based on standard definitions of FC. QT interval was measured by ECG and interpreted by a pediatric cardiologist, and collected data were analyzed using SPSS software, version 19 with a 0.05 significant level.

Results: Among the ECG parameters, HR, R in aVL, S in V_3, LVM, QTd, QTc, and QTcd were significantly different in children with FCs compared to their peers. From those who had abnormal QTd, FC children were more frequent which was not significant (χ^2=1.053, P=0.248), while children with FC had significantly more abnormality regarding QTc (χ^2=13.032, P<0.001) and QTcd (χ^2=21.6, P<0.001). In children with FC, those who were less than 12 months had the highest level of HR which was not significant (χ^2=4.59, P=0.101). Similar trends occurred for R in aVL and S in V_3 that were higher in the age group >24 months (P>0.05). Children in the age group of >24 months had significantly had the highest LVM (χ^2=52.674, P<0.001) and the other QT parameters were the same in FC children with different age groups (P>0.05).

Conclusion: It is concluded that dispersion corrected QT, corrected QT, and dispersion QT changed significantly in children with FC in comparison with the healthy children with constant values in children with FC in different age groups.

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Highlights

• Corrected QT, dispersion QT and corrected-dispersion QT changed in children with febrile convulsion.

• Among the children with abnormal dispersion QT, febrile convulsion were not seen more when children with febrile convulsion (FC) were more in abnormality levels of QTc and QTcd.

Plain Language Summary

The study aimed to evaluate changes in electrocardiography parameters in children with febrile convulsion and found positive correlation.

1. Introduction

Febrile seizure (FS) is one of the most common neurological disorders with approximately 2-5% of prevalence during infancy with an observed peak in the 12-18-month age group (Canpolat et al., 2018). Among disorders of FS, febrile convulsion (FC) is highlighted which is defined as elevated body temperature (fever >38°C) free of any severe essential disorders (Chung, 2014; Leung et al., 2018).

Although FC has been reported in all ethnic groups, it has been observed that FC is more frequent in certain groups of people, for instance, Indian people with 5-10%, Turkish people with 9.7%, and Japanese pediatric with 6-9% (Canpolat et al., 2018). The gender proportion is 1.6 to 1.8 for boys to girls (Chung, 2014). Turkish studies showed that the prevalence of FC was about 10% with a recurrence rate of 25-50% (Aydin et al., 2008; Canpolat et al., 2018).

Many studies have reported an association between cardiovascular changes and seizures (Ali et al., 2017), and take into account the activation of the autonomic nervous system (ANS) that is eliminated with seizures (Akalin et al., 2004). An increase in QT indicated severe arrhythmia and unplanned programs in different diseases such as cardiomypathy (CM), MVP, IHD, and RF (Akalin et al., 2004; Murasawa et al., 2008). In diseases such as FC (Leung et al., 2018), epilepsy (Ali et al., 2017), breath holding (BH) (Akalin et al., 2004), diabetes mellitus (DM) (Uysal et al., 2014), celiac disease (CD) (Noori et al., 2018), thalassemia (Noori et al., 2014), and Kawasaki disease (KD) (Motoki et al., 2017), QT prolongation is known as a predictor of eventual mortality. On the other hand, ECG parameters may change due to medications, electrolyte abnormalities, or endocrine diseases. Factors that increase the likelihood of arrhythmia can be directly assessed through ECG findings such as QT abnormalities (Kurl et al., 2012). Considering the heterogeneity of intraventricular myocardial repolarization using surface ECG, ECG parameters are the main strategy to assess FC in children (Ali et al., 2017; Akalin et al., 2004). This study aimed to evaluate changes in dispersion QT and corrected QT in children with febrile convulsion compared to children with fever but without convulsion.

2. Materials and Methods

This case-control study aimed to evaluate the changes in the ECG parameters of children with FC in 2018. For the present study, 90 children with FC were eligible to enter the study and equally shared with 90 controls that were matched in sex and age. The FC children were collected from those who recourse to the neurology clinic due to seizure complaints. After FC confirmation by a neurologist and considering the exclusion criteria, if the patients were eligible, they were referred to the pediatric cardiologist for ECG examinations. FC was confirmed by the condition of a body temperature of more than 38°C (100.4°F) and aged between 6 to 60 months. In this sense, healthy children were selected among those who came to the hospital for routine checkups with fever and without any diseases.

Exclusion criteria

The following criteria were considered to exclude the participants from the study: Complex febrile seizures, perinatal injury, developmental abnormalities, neurological deficiencies, epilepsy, CNS infection, meningitis, encephalitis, epilepsy-induced syndrome, underlying cardiovascular disease, and structural disorders. Consumption of antipsychotics, antiarrhythmic drugs, antibiotics, and drugs for trauma and all the laboratory measures such as electrolyte disturbance that affect ECG were excluded from the study.

ECG measurement

ECG was performed in a supine position in a quiet place for 10 minutes and the results were recorded simultaneously at a paper speed of 25 mm/s and a voltage of 10 mm/mv. For ECG measures, the following definitions were considered. The QT interval started from Q and continued to the end of T. Its scale is milliseconds measured three times for every lead and the mean of these three consecutive beats was considered for the study. The maximum and minimum duration of the QT wave were measured by standard ECG and the difference between this max and min was defined as dispersion QT. Bazett's Equation (Equation 1) was applied to measure QTc, and then QTcd was measured as the difference between the long and short duration of QTc (Noori et al., 2019a).

1. $(QTc=QT/\sqrt{RR})$

Left ventricular mass by ECG calculated by the Equations 2 and 3 for boys and girls, respectively:

2. $LVM\ (g)=0.026\ (RaVL+SV_3)+1.25\ weight+34.4$

3. $LVM\ (g)=0.020\ (RaVL+SV_3)+1.12\ weight+36.2$ (Noori et al., 2019b).

Statistical analysis

SPSS software, version 20 (released by IBM Corp. in 2011) was used for data analysis. To check the normality of the data, the Kolmogorov-Smirnov test was applied. All quantitative data had free distribution, and the unpaired Mann-Whitney U test was applied for the comparisons and the chi-square (χ^2) analysis was used for the categorical variables. The value considered for the significance level was 0.05.

3. Results

Normality test showed that all the numerical data had free distribution. Table 1 showed that the gender distribution was similar in groups of the participants (χ^2=1.429, P=0.232). The ECG findings such as HR (P<0.001), R in aVL (P=0.007), S in V_3 (P<0.001), LVM by ECG (P<0.001), dispersion QT (P<0.001), corrected QT (P<0.001), and corrected dispersion QT (P<0.001) varied significantly in children with FC contrasted to their counterparts (Table 2). As shown in Table 3, among FC children, only 6.7% had QTd >50 compared to controls with 3.3% QTd >50. This trend showed a non-significant difference (χ^2=1.053, P=0.248). QTc and QTcd as two important ECG parameters had significant percentages of abnormality, and the abnormality rate of QTc and QTcd was 35.6% compared to 13.3% in controls (χ^2=13.032, P<0.001) and 40% compared to 10% in controls (χ^2=21.6, P<0.001) respectively. Table 4 showed that heart rate was the highest level in the FC children aged less than 12 months which was not significant (χ^2=4.59, P=0.101). R in aVL and S in V_3 was higher in the age group of >24 months which was not significant (P>0.05). LVM had the highest value in children aged more than 24 months (χ^2=52.674, P<0.001). Table 4 also showed that all the QT parameters were the same in FC children with different age groups (P>0.05).

4. Discussion

This examination assessed electrocardiography findings in children with FC and controls. The results showed that R in aVL, S in V_3, LVM, dispersion QT, corrected QT, and corrected dispersion QT were significantly different in FC children. From the individuals who had ab-

Table 1. Sex distribution in FC and healthy children

Groups		No. (%)		
Statistics		Control	Febrile Convulsion	Total
Sex	Girls	46(51.10)	38(42.20)	84(46.67)
	Boys	44(48.90)	52(57.80)	96(53.33)
Total		90(100)	90(100)	180(100)
Chi-square		1.429		
P		0.232		

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Table 2. Mann-Whitney U test to compare electrocardiography findings between febrile convulsion and healthy children

Findings	Participants	Mean±SD	Mean Rank	MWU	P
Age (m)	Healthy	2.3±0.82	97.82	3391.5	0.058
	FC	2.13±1.06	83.18		
Weight (kg)	Healthy	14.69±8.79	112.35	2083.5	<0.001
	FC	11.01±2.64	68.65		
Height (cm)	Healthy	93.88±15.26	114.89	1854.5	<0.001
	FC	81.27±10.88	66.11		
QT	Healthy	0.31±0.03	88.23	3845.5	0.555
	FC	0.31±0.03	92.77		
HR	Healthy	108.78±26.01	74.17	2580	<0.001
	FC	125.79±25.38	106.83		
R in aVL	Healthy	0.24±0.16	80.27	3129.5	0.007
	FC	0.32±0.25	100.73		
S in V_3	Healthy	0.64±0.37	77.02	2836.5	<0.001
	FC	0.84±0.44	103.98		
LVM	Healthy	52.85±10.87	111.6	2151	<0.001
	FC	48.53±3.18	69.4		
Dispersion QT	Healthy	0.03±0.01	66.33	1875	<0.001
	FC	0.04±0.01	114.67		
Corrected QT	Healthy	0.41±0.04	73.71	2538.5	<0.001
	FC	0.44±0.05	107.29		
Corrected dispersion QT	Healthy	0.03±0.02	64.81	1737.5	<0.001
	FC	0.05±0.02	116.19		

Abbreviations: MWU: Mann-Whitney U; FC: Febrile convulsion; SD: Standard deviation; HR: Heart rate.

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normal QTd, FC children were more frequent but not significant. At the point of the anomaly regarding corrected QT and corrected dispersion QT, children with FC were more, and those who were <12 months had higher but non-significant values compared to other age groups. R in aVL and S in V_3 was higher in the age >24 months. LVM had the most noteworthy value in the age >24 months and the wide range of various QT parameters were similar in FC children of all ages.

Perhaps the most well-known reason for pediatric seizure is FC and the prospect that ANS brokenness is the essential anomaly in the pathophysiology of FC (Chung, 2014). (Kandler et al., 2005) showed that 7 of 30 pediatric patients had QTc prolongation during a postictal. Another investigation by (Brotherstone et al., 2010) showed that children with right transient projection seizures, right fleeting subclinical seizures, and general tonic-clonic seizures had an increment in corrected QT in excess of 60 ms contrasted with other seizure types.

(El Amrousy et al., 2017) led an examination on the status of secondary epileptics to FS and detailed QTs changes in the initial six hours after convulsion and they found shortening of the QT. (Sadrnia et al., 2013) brought about a critical contrast in delayed QT in mem-

Table 3. The distribution of participants in the abnormality of different types of QT

Electrocardiography Findings	Status	No. (%) Participants Control	FC	Total	χ^2	P
Dispersion QT	<50	87(96.7)	84(93.3)	171(95.0)	1.053	0.248
	>50 (Abnormality)	3(3.3)	6(6.7)	9(5.0)		
Corrected QT	<450	78(86.7)	58(64.4)	136(75.6)	13.032	<0.001
	>450 (Abnormality)	12(13.3)	32(35.6)	44(24.4)		
Corrected dispersion QT	<60	81(90)	54(60)	135(75)	21.6	<0.001
	>60 (Abnormality)	9(10)	36(40)	45(25)		
Total		90(100)	90(100)	180(100)		

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bers to the extent that three children with seizures and two liberated from seizures had a past history of syncope as per their folks' reports.

A little expansion in QTc during epileptic seizures was seen in (Brotherstone et al., 2010) with changes in delayed QTc past ordinary cutoff points in any event during self-settling seizures. They also announced an unexpected demise because of ventricular tachycardia during epileptic seizures within the sight of delayed cardiovascular repolarization.

Numerous investigations, for example, (Hwang et al., 2015) revealed a significant effect of epilepsy on electroencephalography abnormality. (Ravindran et al., 2016) assessed the connection between EEG and ECG and uncovered that autonomic yield to the heart is fundamentally adjusted most noticeably during the ictal stage in patients with epilepsy. (Canpolat et al., 2018) found a significant relationship between the first EEG and the hazard of epilepsy, and 89.3% of those with first epilepsy had neurotic EEG with no relationship between definite EEG and the hazard of epilepsy. A population-based study confirmed that drawn-out guess is acceptable in many patients with febrile scenes and about 92.6% of the patients treated with a decent conclusion of FC were mitigated appropriately and totally. (Canpolat et al., 2018) presumed that the commonness of FC in their general public is close to devolved nations. They inferred that the primary driver of intermittent FC was a background marked by FC in the youngster and family members. In an investigation acted in southern Iran, 100 patients with first unjustifiable seizures were considered and it was found that 1% had long corrected QT prolongation with no contrast between sexes, sorts of seizure, and other ECG findings (Katibeh et al., 2018). These clashing outcomes may be because of the determination of cases in various examinations. As referenced previously, one of the significant prohibition measures was fever in this examination. An FC may prompt arrhythmia even without different factors as Amin et al. revealed that fever alone can be presented as an energizer for ventricular arrhythmia (Amin et al., 2010). Additionally, (Burashincov et al., 2008) demonstrated that fever works with polymorphic ventricular tachycardia by QT prolongation. Another motivation to explain disputable outcomes was the choice of patients with the main scene of seizure but liberated from any ongoing, repetitive, and inconvenience. Along with research facility tests, electrocardiography is practically the lone accessible heart assessment that is executed consistently for admission to the trauma center with a solid obscurity in legitimacy and unwavering quality. Sometimes, when the kids are in treatment with antidepressant sedates, the QT assessment should be considered more carefully on account of the referenced medications' impact on QT spans (Zemrak & Kenna, 2008). In this respect, Krishnan & Krishnamurthy, 2013 explained this issue by keeping away from the frustration of these medications in contrasting epilepsy and non-epileptic children for repetitive seizures which was an exclusion criterion in the current examination. A positive and significant association between corrected QT and the age of the children with FC has been reported by (Krishnan & Krishnamurthy, 2013). They found that corrected QT increased with age when we found dissimilar results showing that corrected

Table 4. Kruskal-Wallis test to compare electrocardiography findings between FC children with different age groups

Findings	Age (m)	Mean±SD	Mean Rank	χ^2	P
HR	<12	133.83±18.05	55.89	4.59	0.101
	12_24	126.67±24.34	45.77		
	>24	120.36±29.11	39.52		
R in aVL	<12	0.29±0.13	48.22	0.615	0.735
	12_24	0.32±0.29	43.15		
	>24	0.34±0.26	46.79		
S in V_3	<12	0.86±0.67	40.94	0.993	0.609
	12_24	0.83±0.38	45.09		
	>24	0.86±0.36	48.47		
LVM	<12	46±1.86	21.44	52.674	<0.001
	12_24	47.22±2.24	35.1		
	>24	51.45±2.41	70.91		
QT	<12	0.3±0.03	35.42	3.417	0.181
	12_24	0.31±0.03	47.67		
	>24	0.31±0.03	48.44		
Dispersion QT	<12	0.04±0.01	49.56	0.655	0.721
	12_24	0.04±0.01	44.26		
	>24	0.04±0.01	44.76		
Corrected QT	<12	0.44±0.03	43.33	0.274	0.872
	12_24	0.44±0.05	45.06		
	>24	0.44±0.05	47.2		
Corrected dispersion QT	<12	0.06±0.02	55.72	3.529	0.171
	12_24	0.05±0.02	42.17		
	>24	0.05±0.02	43.86		

SD: Standard deviation; HR: Heart rate.

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QT did not change with FC children. Considering the above-mentioned materials and the present study results, it is observed and confirmed that one of the reasons for QT prolongation was FC disease in children suggesting electrocardiography performance for the children who come to the hospital due to seizures.

Study limitations

The principal restriction of this examination was the absence of legitimate partnership by members particularly controls that caused a long-time information assortment.

5. Conclusion

The study concluded a significant change in corrected QT, dispersion, QT and corrected-dispersion QT in FC pediatric population. When these parameters did not change with age groups. Among children with abnormal QTd, FC children were more visited yet not huge when children with FC were more in abnormality levels of QTc and QTcd. To proceed with a recognized program in FC pa-tients, there is a need to evaluate ECG parameters adjust-ments particularly QT intervals.

Ethical Considerations

Compliance with ethical guidelines

The present study was approved by the Ethics Committee of Zahedan University of Medical Sciences (No.: 2569), and the consent form was taken from the participants' parents.

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Authors' contributions

Conceptualization and study design: Noor Mohammad Noori; Data acquisition: Noor Mohammad Noori and Ali Khajeh; Data analysis and drafting the manuscript: Alireza Teimouri; Interpretation and final approval: All authors.

Conflict of interest

The authors declared no conflict of interest.

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