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Title: QT Interval Changes in Children With Febrile Convulsion Comparing With Healthy

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Abstract

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

Method

This case-control study considered the distribution of 180 children equally shared between patients and controls. The study was conducted at the "Ali Ebne Abi Talib" Hospital in Zahedan, Iran. The disease diagnosed and confirmed based on standard definitions of febrile convulsion. QT interval measured by ECG and interpreted by a pediatric cardiologist and collected data were analyzed with SPSS 19 considering 0.05 as significant error.

Results

Among the ECG parameters, HR, R in aVL, S in V₃, LVM, QTd, QTc and QTcd were significantly different in children with febrile convulsion compared to the peers. From those who had abnormal QTd, FC children were more frequented but not significant (CHI SQUARE=1.053, $p=0.248$), when children with FC were more in abnormality regarding QTc (CHI SQUARE=13.032, $p<0.001$) and QTcd (CHI SQUARE=21.6, $P<0.001$) significantly. In children with FC, those who were aged less than 12 months, had the highest level of HR but not significant (CHI SQUARE=4.59, $p=0.101$). Similar trends occurred for R in aVL and S in V₃ that were higher in the age group >24 months ($p>0.05$). LVM had the highest value in the age group of >24 months significantly (CHI SQUARE= 52.674, $P<0.001$) and the other QT parameters were same in Fc children with different age groups ($P>0.05$).

Conclusion

From the study concluded that dispersion corrected QT, corrected QT and dispersion QT changed significantly in children with febrile convulsion in comparing with the healthy children but with constant values in children with FC in different age groups.

Keywords: ECG, Febrile seizures, Pediatric

Introduction

febrile seizures (FS) is one of the most common neurological disorder with approximately 2-5% of prevalence during infancy with an observed peak in the 12-18-month age group (1). Among disorders of FS, febrile convulsion (FC) is highlighted which are defined as associated with elevated body temperature (fever $> 38^{\circ}\text{C}$), but free of any severe essential disorders (2, 3).

Although it has been reported in all ethnic groups, it has been observed that certain groups of people are more frequented; for instance, Indian people with 5-10% , Turkish people with 9.7% and Japanese pediatric with 6-9% (1), with the proportion gender is 1.6 to 1.8 for boys to girls (2). Turkish studies showed that the prevalence of FC was about 10% with the recurrence rate of 25-50% (4, 1).

Many studies have reported an association between cardiovascular changes and seizures (5), and take into account the activation of the autonomic nervous system (ANS) that eliminated with seizures (6). An increase in QT indicated with severe arrhythmia and unplanned programs in different disease such as CM, MVP, IHD, and RF (6,7). In diseases such as FC (3), Epilepsy (5), Breath Holding (BH) (6), Diabetes Mellitus (DM) (8), Celiac Disease(CD) (9), Thalassemia (10) and Kawasaki Disease (KD) (11), QT prolongation 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 (12). Considering the heterogeneity of intraventricular myocardial repolarization using surface ECG, ECG parameters are the main strategy used to assess FC in children (5,6). The purpose of this study was to evaluate changes in dispersion QT and corrected QT in children with febrile convulsion compared to children with fever but without convulsion.

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 collected from those who recourse to the neurology clinic due to seizures' complain. After FC confirmation by a neurologist and considering the exclusion criteria, if the patients were eligible, they referred to the pediatric cardiologist for ECG examinations. In patients FC confirmed by condition of body temperature 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 checkup with fever and without any diseases.

Exclusion criteria

The following criteria 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 effect on ECG were excluded from the study.

Ethics approval

The present study approved by ethics committee of ZaUMS and numbered as 2569 and then after approval the consent from taken from the participants' parents.

ECG measurement

ECG performed on supine position in a quiet place in 10 minutes and the results recorded simultaneously at a paper speed of 25mm / 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 and measured three times for every lead and the mean of these three consecutive beats considered for the study. Max and min duration of the QT wave were measured by standard ECG and the difference between this max and min defined as dispersion QT. Bazett's formula; ($QT_c = QT / \sqrt{RR}$) applied to measure QT_c , and then QT_{cd} measured as the difference between the long and short duration of QT_c (13). Left ventricular mass by ECG calculated by following formulae for boys and girls respectively; $LVM (g) = 0.026 (RaVL + SV_3) + 1.25 \text{ weight} + 34.4$ and $LVM (g) = 0.020 (RaVL + SV_3) + 1.12 \text{ weight} + 36.2$ (14)).

Statistical analysis

For the data analysis SPSS version 20.0 software (released by IBM Corp. in 2011. IBM SPSS Statistics for Windows, version 20.0. Armonk, NY: IBM Corp) were used and 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 used for the categorical variables. The value considered for the significance level is 0.05.

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 ($CHI \text{ SQUARE}=1.429$, $p=0.232$). The ECG findings such as HR ($P<0.001$), R in aVL ($p=0.007$), S in V3 ($p<0.001$), LVM by ECG ($p<0.001$), and dispersion QT ($p<0.001$), corrected QT ($p<0.001$) and corrected dispersion QT ($p<0.001$) were warried significantly in children with FC contrasted their counterparts (Table 2). From the table 3 observed that from FC children

only 6.7% had QTd > 50 compared to controls that 3.3% had QTd > 50. This trend showed a non-significant difference (CHI SQUARE =1.053, p=0.248). QTc and QTcd as two important ECG parameters had significant percentages of abnormality such that abnormality rate of QTc and QTcd were 35.6% compared to 13.3% in controls (CHI SQUARE=13.032, p<0.001) and 40.00% compared to 10.00% in controls (CHI SQUARE=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 but not significant (CHI SQUARE=4.59, p=0.101). R in aVL and S in V₃ were higher in the age group of >24 months but not significant (p>0.05). LVM had the highest value in children aged more than >24 months (CHI SQUARE= 52.674, P<0.001). From the table also resulted that all the QT parameters were same in Fc children with different age groups (P>0.05).

Table1: Sex distribution in FC and Healthy children

Groups		Control		Febrile Convulsion		Total	
Statistics		n	%	n	%	n	%
Sex	Girls	46	51.10%	38	42.20%	84	46.67%
	boys	44	48.90%	52	57.80%	96	53.33%
Total		90	100.00%	90	100.00%	180	100%
CHI SQUARE		1.429					
P value		0.232					

Table 2 Mann–Whitney U test to compare Electrocardiography findings between FC and healthy children

Findings	Participants	Mean(SD)	Mean Rank	MUW	P value
Age	Healthy	2.3(0.82)	97.82	3391.5	0.058
	FC	2.13(1.06)	83.18		
Weight	Healthy	14.69(8.79)	112.35	2083.5	<0.001
	FC	11.01(2.64)	68.65		
Height	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		

M W.U: Mann-Whitney U.

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

Electrocardiography Findings	Status	Statistics	participants		Total	CHI SQUARE	P value
			Control	FC			
Dispersion QT	<50	Frequency	87	84	171	1.053	0.248
		Percent	96.7%	93.3%	95.0%		
	>50 (Abnormality)	Frequency	3	6	9		
		Percent	3.3%	6.7%	5.0%		
Corrected QT	<450	Frequency	78	58	136	13.032	<0.001
		Percent	86.7%	64.4%	75.6%		
	>450 (Abnormality)	Frequency	12	32	44		
		Percent	13.3%	35.6%	24.4%		
CorrectedDispersion QT	<60	Frequency	81	54	135	21.6	<0.001
		Percent	90.0%	60.0%	75.0%		
	>60 (Abnormality)	Frequency	9	36	45		
		Percent	10.0%	40.0%	25.0%		
Total		Frequency	Frequency	90	180		
		Percent	Percent	100.0%	100.0%		

Table 4: Kruskal-Wallis Test to compare Electrocardiography findings between FC children with different age groups

Findings	Age (months)	Mean(SD)	Mean Rank	CHI SQUARE	P value
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		
CorrectedDispersion 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		

Discussion

The examination assessed electrocardiography findings in children with FC and controls. This came about that, R in aVL, S in V₃, LVM, dispersion QT, corrected QT and corrected dispersion QT were different significantly in FC children. From the individuals who had abnormal QTd, FC children were more frequented but not significant. At the point of anomaly regarding corrected QT and corrected dispersion QT, children with FC were more and those who were <12 months, had higher values but not significant compared to other age groups. R in aVL and S in V₃ were higher in the age >24 months yet was same. LVM had the most noteworthy worth in the age >24 months essentially and the wide range of various QT parameters were similar in FC children in all age.

Perhaps the most well-known reasons for pediatric seizure is FC and the prospect that ANS brokenness is the essential anomaly in the pathophysiology of FC (2). Kandler et al., (15) saw that 7 of 30 pediatric patients had QTc prolongation during a postictal. In another investigation by Brotherstone et al., (16) came about that children with right transient projection seizures, right fleeting subclinical seizures, and general tonic-clonic seizures had an increment in corrected QT of in excess of 60 ms contrasted with other seizure types.

El Amrousy et al., (17) led an examination on status of secondary epilepticus to FS and detailed QTs changes in the initial six hours after convulsion and they found shortening of the QT. Sadrnia et al., (18) brought about a critical contrast in delayed QT in members to such an extent that three children with seizure and two liberated from seizure had a past history of syncope as per their folks' reports.

A little expansion in QTc during epileptic seizures saw in the Brotherstone et al., (16) with change in delayed QTc past ordinary cutoff points in any event, during self-settling seizures. They likewise 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. (19) revealed a significant effect of epilepsy on electroencephalography abnormality. Regarding, Ravindran et al., (20) 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., (1) found a significant relationship between first EEG and hazard of epilepsy to such an extent that in those with first epilepsy 89.3% had neurotic EEG when they discovered no relationship between definite EEG and hazard of epilepsy. A population based study confirmed that drawn out guess is acceptable

in many patients with febrile seizures to such an extent that about 92.6% of the patients treated with a decent conclusion of FC were mitigated appropriately and totally. Canpolat et al., (1) presumed that the commonness of FC in their general public is near evolved nations. They likewise 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 with first unjustifiable seizures considered and found 1% had long corrected QT prolongation with no contrast between sexes, sorts of seizure and other ECG findings (21). 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. A FC may prompt arrhythmia even without different factors to such an extent that Amin et al., has revealed, fever alone can be presented as an energizer for ventricular arrhythmia (22). Additionally, Burashincovet al.,(23) 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 however liberated from any ongoing, repetitive and inconvenience. Alongside research facility tests, electrocardiography likewise is practically the lone accessible heart assessment that is executed consistently for admission to the trauma center however with a solid obscure in legitimacy and unwavering quality. Sometimes, when the kids are in treatment with antidepressants sedates, the QT assessment should be in more thought on account of the referenced medications impact on QT spans (24). In this respects, Krishnan et al. (25) explained this issue by keeping away from the frustrating of these medications in contrasting epilepsy and non-epileptic children for seizure repetitive which is in the current examination this issue was in an exclusion criterion. A positive and a significant association between corrected QT and age of the children with FC has been reported by Krishnan et al. (25). They found that corrected QT increased with age when we found dissimilar results such that that corrected QT did not changewith FC children. Considering the mentioned above materials and the present study results, observed and confirmed that one of the reason for QT prolongation was FC disease in children and suggested electrocardiography performance for the children who come to the hospital due to seizures.

Study Limitation

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

Conclusion

The study concluded a significant change in correctedQT, dispersion QTand corrected-dispersion QT in FC pediatric population. When these did not change with age groups. From the children who had abnormalQTd, 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 patients, there is a need to evaluate ECG parameters adjustments particularly QT intervals.

Conflict of interest:

The authors would like to declare for any conflict of interests.

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