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ELECTROCARDIOGRAPHY CHANGES IN CHILDREN WITH FEBRILE CONVULSION, BREATH-HOLDING COMPARED TO CONTROLS

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Contribution
NMN conceived the idea and designed the study. Data collection and manuscript writing was done by NMN, AK, ESS, and AT. All the authors contributed equally to the submitted manuscript.

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ABSTRACT

Objective: Cardiovascular changes are related to some of epilepsy disorders such as seizures and breath holding. The study objective was to evaluate ECG findings in breath-holding and febrile convulsion compared to healthy individuals.

Methodology: This Cross-sectional study was conducted on 270 children of 90 with febrile convulsion, 90 with breath-holding patients and 90 healthy children in 2019. Electrocardiography parameters of; QT interval, dispersion QT, corrected QT and dispersion QTc measured for participants. Consent form was asked to be signed by the parents before the study execution. Data analysis done by SPSS 20.0 considering 0.05 as significant error.

Results: Females were 46(51.1%), 38(42.2%) and 35(38.9%) in control, febrile convulsion and breath holding, respectively. QTc was normal in 97.8%, 76.7% and 71.1% of controls, febrile convulsion and breath holding respectively. A significant association observed between QTc measures in different groups ($p<0.001$). QTd was normal in 100.00%, 98.9% and 96.7% of controls, febrile convulsion and breath holding respectively with a non-significant association in groups of participants ($p=0.196$). QTcd was normal in 95.6%, 72.2% and 85.6% of controls, febrile convulsion and breath holding respectively with a significant association ($p<0.001$).

Conclusion: Concluded that QTc was higher in breath-holding compared to febrile convulsion. QTcd was higher in febrile convulsion compared to breath-holding spells. Both were higher than controls QTd were higher significantly in the febrile convulsion compared to children with breath-holding spells. The results of the study suggested performing ECG for children who suffered from seizures or breath- holding spells to control their cardiac dysrhythmia.

Keywords: Electrocardiography, Breath holding, Febrile convulsion, Children

INTRODUCTION

Cardiovascular changes have a link to seizures[1] and breath holding spells (BHs).[2] QT dispersion (QTd) defined as interval between longest and the shortest QT.[3,4] Prolonging of QT intervals show a high risk of dysrhythmia and sudden death in various illnesses such as; cardiomyopathies, mitral valve prolapses, ischemic coronary heart diseases and end stage renal failure.[3] And noted as a predictor of child mortality due to various diseases[6] such as; diabetes mellitus,[7] celiac,[3] thalassemia,[4] epilepsy,[1] breath holding,[5] febrile seizure,[5] QT intervals also change in general population due to medications, electrolyte abnormalities, or endocrine disease.[8]

BHs are well described phenomenon known to occur mostly in children aged 6 to 18 months even later in childhood, up to 4 years of age with 5% due to crying.[9] Cyanotic and pallid are types of BHs such that sometimes, some children have both in their lives. The mechanism of BHs is unknown and still is controversial but expressed that cerebral anoxia, anemia and genetic have impact effects.[10]

A seizure is a sudden, uncontrolled electrical disturbance in the brain and occasionally occurred after losing consciousness; and then, return to normal status.[2] In this regards, febrile convulsions (FC) or febrile seizures (FS) that has been described as an event occurring during fever in children elder than one month without history and free of CNS infection, and without specific causes such as electrolyte imbalance, metabolic disorder, intoxication or trauma by ILAE.[1] FS occurring in children aged 6 months to 5 years with fever greater than 38°C (100.4°F), without intracranial cause symptom and without a history of an afebrile seizure.[7,11]

In another side, FS has been defined as common neurologic disorder in children that affecting 2–5% of children peaked in the age of 12 -18 months.[7] Although FS is seen in all ethnic groups, but it is more frequent in Asian regions such as; India with 5–10% and Japan with 6–9%[7] and Middle East regions such as; 9.7% to 25–50% in Turkey.[12]

The present study aimed to assess QT findings variation in children with breath-holding spells and febrile convulsion compared to healthy ones.

METHODOLOGY

This cross sectional study was conducted on children with FC or with breath holding comparing with healthy group in the pediatric neurology clinics of Zahedan University of Medical Sciences (ZaUMS) Hospitals in 2019. During the year of 2019, 101 children with BHs and 121 children with FC referred to the pediatric clinic of neurology. After considering exclusion criteria, from these children 90 and 96 referred to the unit of pediatric cardiology respectively. For having a similar size in patients and controls, the sample size of 270, 90 in each group considered for the study.

BHs diagnosed based on the criteria of; reported history of BHs by the parents (three or more spells in 1 month), and having the clinical sequences of provocation followed by crying to a point of consciousness. The BHs participants collected from those who referred to the clinics with complain of cyanotic attacks and/or fainting or by observation of the typical attacks during an examination by pediatric specialists.

The exclusion criteria for this group of patients were; epilepsy history, electrolyte imbalances, hypoglycemia, iron deficiency, impaired kidney function tests, abnormal neurological findings during examination, receiving any medications that all criteria have significant effect on QT intervals.

The children with FC collected from those who were referred to the clinics due to complain of seizure. Febrile convulsion was defined as convulsion based on the mentioned definition by ILAE with the exclusion criteria of; abnormal laboratory affecting on ECG such as calcium, potassium, magnesium. Any medications of anti-psychotics, anti-arrhythmia, and antibiotics and free of any underlying cardiovascular disease, trauma, meningitis, encephalitis, seizure-inducing syndromes, and structural disorders.

Healthy children matched in frequency and gender with the patients and selected randomly from those who came to the clinics to have a checkup routine after considering same exclusion criteria.

Electrocardiogram (ECG) changes was detected with an electrocardiogram by the Saadat device made in Iran initially from 30 minutes to 2 hours after seizure. ECG in standard scheme was obtained. Once the participants had rested for 10 minutes in a supine position in a quiet room, all 12 ECG leads were simultaneously recorded at a paper speed of 25mm/s and a voltage of 10mm/mV.

From the 12 lead of electrocardiogram that performed, at least 8 leads selected and from each lead, three complex of QT calculated. In final from these 24 calculated QT, the average considered for the study. QT interval was accepted as the distance from the beginning of the Q wave to the end of the T wave. In each lead, the duration from the beginning of the Q wave to the end of the T wave was calculated in milliseconds, the average was taken (QT average) for three consecutive beats. The maximum and minimum duration of the QT wave was selected from these 24 QT measures. The difference between maximum and minimum duration was defined as QTd.

The average QTc was calculated using the same QT interval measured using the Bazett formula (QTc¼ QT/ √RR); among all derivations, the difference between the longest and shortest QTc was calculated (QTcd).[13,14] To calculate left ventricular mass in ECG we used the following formulas: LV mass (g) =0·026 (RaVL+SV3) + 1·25 Weight + 34·4 for boys, and 0·020 (RaVL+SV3) + 1·12 Weight + 36·2 for girls.[15,16] The QT parameters of QTd, QTc and QTcd were normal when were higher than 0.05, 0.45 and 0.06 second respectively.[17] The mean of Heart rate calculated of three consecutive ventricular heart rates in lead II. Consent form was asked to be signed from the parents. The study coded 2569 and approved by ethical committee of the ZaUMS.

Data analysis performed by SPSS 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows). For the frequency and percentages, Chi-square test applied for the association and for quantities variables, first normality test applied for diagnosis of variables distribution that founded all had free distribution. To find the differences in ECG findings in pairwise comparisons, unpaired Mann-Whitney U-test applied. The error P<0.05 was considered as significant level.

RESULTS

Gender distribution and abnormality of ECG parameters in Febrile Convulsion, Breath Holding, and Controls are presented in Table 1. The gender distributed similarly in groups of participants (p=0.233). Table 1 showed that QTc was normal in 97.8%, 76.7% and 71.1% of controls, febrile convulsion and breath holding respectively with significant association (p<0.001). QTd was normal in 100.00%, 98.9% and 96.7% of controls, febrile convulsion and breath holding respectively with a non-significant association (p=0.196). QTcd was normal in 95.6%, 72.2% and 85.6% of controls, febrile convulsion and breath holding respectively with a significant association (p<0.001).

Table 1: Gender distribution and abnormality of ECG parameters in Febrile Convulsion, Breath Holding, and Controls

	Healthy	Febrile Convulsion	Breath Holding	P-value
N	**90**	**90**	**90**	-
Sex				
Female	51.1% (46)	42.2% (38)	38.9% (35)	0.233
Male	48.9% (44)	57.8% (52)	61.1% (55)	
QTc				
<0.45	97.8% (88)	76.7% (69)	71.1% (64)	<0.001
≥0.45	2.2% (2)	23.3% (21)	28.9% (26)	
QTd				
<0.05	100% (90)	98.9% (89)	96.7% (87)	0.196
≥0.05	0% (0)	1.1% (1)	3.3% (3)	
QTcd				
<0.06	95.6% (86)	72.2% (65)	85.6% (77)	<0.001
≥0.06	4.4% (4)	27.8% (25)	14.4% (13)	

Age (p=0.074), QTd (p=0.127), QTc min (p=0.630), QTc max (p=0.337) and QTcd (p=0.073) were similar when comparison performed between febrile and controls. When weight (p<0.001) and height (p<0.001) were lower in breath holding children. Weight (p=0.065), height (p=0.438), QTc min (p=0.528) and QTcd (p=0.596) were same in BHs and FC children. But QTd were higher significantly in the febrile convulsion children than children who had BHs. In this regards, the ECG parameters of QT

min, QT max and QTc max were higher in the children with BHs disorder (Table 2).

Table 2: Demographics and ECG parameters comparison among Health Control (CN), Febrile Convulsion (FC), and Breath-Holding Spells (BH) groups

	Mean ± SD	P-value		
		CN	FC	BH
Age				
CN	2.29±0.84	-	0.074	0.118
FC	2.13±1.06	0.074	-	0.784
BH	2.2±1.36	0.118	0.784	-
Weight				
CN	14.61±8.84	-	<0.001	<0.001
FC	11.01±2.64	<0.001	-	0.065
BH	10.39±3.22	<0.001	0.065	-
Height				
CN	93.54±15.56	-	<0.001	<0.001
FC	81.27±10.88	<0.001	-	0.438
BH	82.69±10.86	<0.001	0.438	-
QT min				
CN	0.29±0.03	-	0.006	0.461
FC	0.27±0.04	0.006	-	<0.001
BH	0.29±0.03	0.461	<0.001	-
QT max				
CN	0.31±0.03	-	0.006	0.002
FC	0.3±0.04	0.006	-	<0.001
BH	0.33±0.03	0.002	<0.001	-
RR interval				
CN	0.57±0.11	-	0.001	0.936
FC	0.51±0.13	0.001	-	<0.001
BH	0.57±0.09	0.936	<0.001	-
Heart rate				
CN	109.33±26.35	-	<0.001	0.984
FC	125.79±25.38	<0.001	-	<0.001
BH	108.74±19.27	0.984	<0.001	-
S in V1				
CN	0.71±0.36	-	0.007	<0.001
FC	0.58±0.36	0.007	-	<0.001
BH	0.37±0.22	<0.001	<0.001	-
R in V5				
CN	1.01±0.44	-	0.898	<0.001
FC	2.29±11.92	0.898	-	0.001
BH	0.79±0.33	<0.001	0.001	-
R in aVL				
CN	0.24±0.16	-	0.007	<0.001
FC	0.32±0.25	0.007	-	<0.001
BH	0.44±0.22	<0.001	<0.001	-
S in V3				
CN	0.64±0.37	-	<0.001	0.004
FC	0.84±0.44	<0.001	-	<0.001
BH	0.5±0.32	0.004	<0.001	-
LVM by ECG				
CN	52.77±10.92	-	<0.001	<0.001
FC	48.53±3.18	<0.001	-	0.043
BH	47.35±6.19	<0.001	0.043	-
QTd				
CN	0.02±0.01	-	0.127	<0.001
FC	0.03±0.02	0.127	-	0.015
BH	0.03±0.01	<0.001	0.015	-
QTc max				
CN	0.42±0.04	-	0.337	0.001
FC	0.42±0.04	0.337	-	0.025
BH	0.43±0.03	0.001	0.025	-
QTc min				
CN	0.39±0.03	-	0.63	0.914
FC	0.38±0.04	0.63	-	0.528
BH	0.39±0.03	0.914	0.528	-
QTcd				
CN	0.03±0.02	-	0.073	<0.001
FC	0.04±0.03	0.073	-	0.596
BH	0.05±0.02	<0.001	0.596	-

P-values are based on Mann–Whitney U test

DISCUSSION

From the present study resulted that QTc was abnormal in 2.2%, 23.3% and 28.9% and QTcd was abnormal in 4.4%, 27.8% and 14.4% in healthy individuals, FC and BHs in the order given.Also resulted that QTd, QTc min, QTc max and QTcd were similar in groups of FC and controls. QT min and QTc min were similar in BHs and in healthy individuals. QTc min and QTcd were same in BH and FC children. But QTd were higher significantly in the FC compared to children with BH. And QT min, QT max and QTc max were higher in the children with BHs. Olsen et al.[18] showed that in children with BHs, the QT intervals parameters did not change compared to controls. Akalın et al.[19] concluded that QT, QTc were similar in BHs patients and in healthy individuals. But QTd and QTcd were significantly lower in healthy ones compared to BHs children.

Noori et al.[20] conducted a study on children to evaluate electrocardiography findings in BHs compared to in healthy individuals. They found that QT max, QTd, QTc max, and QTcd were different in patients compared to healthy individuals significantly similar to the present study findings. Amoozgar et al.[21] reported that QTcd was higher in BHs compared to healthy individuals when QTd was similar. Therefore, in comparing with our results, it seems that there is a confusing of using the ECG parameters for assessing cardiac involvements in BHs patients because of contradiction in reports.

Noori et al.[17] evaluated electrocardiography findings in FC compared to healthy individuals and found that QTc, QTd and QTcd were higher in FC children significantly compared to healthy children. They also found that QT min and QT max did not changed in FC children. Tomoum et al.[22] concluded that a higher QTd in BHs patients compared to healthy individuals. They also observed that during BHs attacks the bradycardia had longer time and more observations of dysrhythmia during cyanotic spells in patients with BHs. These results are importance in clinical status and may led to the effective autonomic dysfunction in nervous system. The link between these findings and dysrhythmia need to be clarified. The knowledge and awareness about ion channel disorders causing paroxysmal symptoms are increasing in various systems due to impaired electrical activity. Previously thoughts of BHs were; being self-limited, benign and resolving spontaneously.

The complications and prolonged QTd revealed more investigations about arrhythmia and ANS dysfunctions in BHs. Kandler et al.[23] showed 23% QTc prolongation in FC within two hours after seizures. Sadrnia et al.[24] resulted a significant prolongation QT in patients with seizure compared to healthy individuals. Brotherstone et al.[25] showed a mild or a short increase in QTc during seizures when El Amrousy[26] found 55% of the patients with convulsion had ECG changes in epileptic seizures during the first six hours. From their study also resulted that, the most frequent abnormalities in ECG were conduction abnormalities, ischemic change, and arrhythmias. The shortening of the QT interval that detected in El Amrousy et al.[26] can be induced by catecholamine release, acidosis, and hyperkalemia which are very common during or shortly after seizures. Yilmaz et al.[10] considered two groups of children with BHs and FC. They observed similar values of QTc in the groups. They also received to the conclusion that in BHs, QTc were similar in cyanotic and pallid types of BHs. In this regards, the present study received to an opposite direction.

Overall, the studies that above mentioned, showed that both BHs and FC are causes of long QT. Some of ECG parameters such as QTd and QTc were different among these two types of diseases such that QTd were higher in the FC compared to BHs and QT and QTc were higher in BHs compared to FC. The electrocardiography parameters need to be assessed for cardiac dysrhythmia that increases the life-threatening particularly in BHs[22] and FCs.[23]

Limitations

The study was limited in design and generalizability as it was done in a single center.

CONCLUSION

From the present study concluded that QTc prolonged in breath-holding spells more than febrile convulsion as well more that healthy individuals. QTcd and QTd were prolonged more in febrile convulsion than breath-holding spells and also than healthy individuals. The results of the study suggest an ECG performance for children who suffered from seizures or breath- holding spells to control their cardiac dysrhythmia.

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