

EVALUATING QT DISPERSION IN CHILDREN WITH SYNCOPE ATTACKS BASED ON BLOOD CRITERIA

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Contribution

AHM conceived, designed and did statistical analysis. MHA and AMS did data collection and manuscript writing. MS and SR did review and final approval of manuscript. All Authors contributed equally.

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ABSTRACT

Introduction: The aim of this study was to evaluate the QT dispersion in children with syncope.

Methodology: This was a case control study performed on 50 children with syncope attacks (case group) referred to the Clinic of Shahid Beheshti Hospital in Kashan during 2014 and healthy children (control group) referred to the center for causes such as a cold or developmental examination. After explaining the project to the parents, data was obtained from the case and control group. Then; using Chi-square, Mann-Whitney, Kolmogorov-Smirnov, Levene's, Kruskal-Wall statistical tests, the data was analyzed.

Results: Total of, 100 children took part in the study, the participants were divided into two groups of case (n=50) and control (n=50). Among the studied children, a total of 46 of them (46%) were boys and the rest were girls. The mean age ranges of children in the case and control groups (absence of syncope attacks) were 7.73 ± 2.33 and 8.09 ± 2.31 years, respectively ($p=0.440$). There was a significant difference between them in terms of each of the 4 parameters ($p<0.001$), and the value of indices in the control group was significantly less than that of the patient group.

Conclusion: According to the results of the study, precise ECG examining in children suspected of syncope attacks can be helpful in confirming the incidence of syncope.

Key Words: Syncope, QT interval, QTd dispersion, QTcd dispersion

INTRODUCTION

Syncope is a common disease including about 1-2% of ED visits.^{1,2} However, the etiology of most attacks is unknown.³⁻⁷ Recently, using Head-up tilt test (HUT) to diagnose the cases with unknown etiologies has led to decreased incidence of syncope. Cardiovascular diseases are the main causes of syncope in adults.^{8,9} Adolescents and children with syncope attacks, neurological diseases account for 50-66% of cases; in other words, NMS (Neurally-mediated syncope) is the most common type in adolescents and children.⁹ Less than 50% of the syncope cases occur in children due to ventricular tachycardia.¹⁰ Some studies have shown that it is age-dependent.¹¹ Among other etiologies, cardiac reason is associated with high degrees of mortality.¹² Therefore, electrocardiogram (ECG) is a good tool for early diagnoses the attacks caused by heart problems. The cardiac causes being detected by ECG include arrhythmias and acute coronary syndrome (ACS). There are many fulfilled studies in this regard that examine the morphology of QRS to determine the prognosis of the attacks in the affected patients.¹³ ECG parameters increasing the mortality rate in patients with cardiovascular diseases include QRS interval, QRS-T angle and QTC (Corrected QT Innerved), QTC dispersion, and heart rate changes.¹⁴⁻²¹ Factors increasing the chance of arrhythmias can be directly evaluated by ECG and by measuring changes in QT intervals between different QT dispersions. QTd can be obtained by determining the time difference between QTmax and QTmin (QTmin-QTmax=QTd). QTd is a reflection of the heterogeneity of cardiac repolarization, and its increase indicates the potential for ventricular arrhythmias and sudden cardiac death.²²⁻²⁵ QT is one of the factors that has been evaluated as a predictor of mortality in various diseases, including diabetes mellitus, congestive heart failure (CHF).²⁷⁻²⁹ Unfortunately, few studies are carried out to determine the relationship between QT and syncope attacks. A study performed by Jha.OP et al. on children with syncope, ADHD, and epilepsy demonstrated that the prevalence rate of prolonged QT interval in patients with epilepsy, syncope attacks and ADHD was 14%, 4% and 2%; respectively. The aforementioned study emphasized that ECG should be routinely performed on patients with epilepsy and syncope to recognize the etiology and to adopt preventive measures for the children.³⁰ Another study performed by Judy fulliu et al. on 1648 patients with prolonged QT aimed to investigate the risk factors for syncope incidence and the results showed that an increase greater than 500 ms in QTC could be considered as a predictive factor in the diagnosis of syncope for the first time at the age less than 20 years. This study revealed that during childhood (0-12 years), the attack is more likely common in males than females, but female gender is subjected to syncope attacks for subsequent attacks.³¹ Nancy Colman et al. also conducted a study on 32 patients with prolonged QT interval and 69 patients with vasovagal shock, all of whom

was younger than 40 years of age, and the results revealed that having a family history of syncope and sudden death due to cardiovascular diseases was more common in patients with prolonged QT interval and, on the other hand, standing posture, as a risk factor for syncope, was more frequently found in patients with vasovagal shock.³²

QT dispersion can be regarded as a predictive factor for syncope in individuals not having the history of syncope; but also have a role in determining the prognosis of patients with syncope attacks. There are lack of studies on the QT dispersion in children with syncopal attacks, the present study attempted to investigate QT dispersion in children with syncope attacks in Kashan, Iran.

METHODOLOGY

This was a case control study performed from 1st January to 31st December 2014. Children having a syncope attack and referred to Shahid Beheshti Clinic in Kashan for treatment and follow up were included using consecutive sampling. The inclusion criteria included the occurrence of syncope attack, age range between 3 months to 15 years and Hb levels between the 5% to 95%. Exclusion criteria included infants less than 3 months of age and more than 15 years old, abnormal Hb levels, height and weight less than 5% and more than 95%, a disease or drug use leading to the acquired and secondary increase in the QT interval, as well as any conditions leading to decreased consciousness level e.g. epilepsy, dizziness, hypoglycemia, head trauma, coma and shock. The syncope was defined as a sudden onset of attacks, short duration and rapid and continuous recovery of the attack. Out of the children referred to the clinic for a routine visit, healthy children were selected and were matched with the case group in terms of age and gender. ECG was also taken from the participants. The control and case groups were compared regarding the effects of QT intervals on the incidence of the attacks. After obtaining the parents' consent, explaining the project for them and obtaining written informed consent, the children of both case and control groups were taken part in the study. Secondly, they were analyzed using t-test, Kolmogorov-Smirnov, Mann-Whitney U, Levene's, Kruskal-Wallis and Chi-square.

RESULTS

Total 100 children were included with 50 each in case and control groups. About 54% of the children in the case and control groups were males respectively (Table 1). The statistical analysis based on Chi square test showed that there was no significant difference between two groups in terms of gender distribution ($p=0.545$). Mean age ranges in children in case and control groups were 7.73 and 8.09 years (Table 2). The statistical analysis based on Independent t-test showed that there was no significant difference between two groups in terms of age distribution

(p=0.440).

Mean hemoglobin levels in children in case and control groups were 11.84 and 11.79 mg/dl respectively (Table 3). The statistical analysis based on Independent t-test showed that there was no significant difference between the groups in terms of distribution of hemoglobin levels (p=0.849).

Mean PR interval dispersions in children in case and control groups were 137.80 and 134.80 ms respectively (Table 4). The statistical analysis based on Mann-Whitney U test showed that there was no significant difference between the groups in terms of PR interval dispersion (p=0.466).

Table 1: The Distribution of the Case and Control Groups Regarding Gender

Gender	Control (Healthy)		Case (Syncope)		P value
	n	%	n	%	
Male	20	40.0%	23	46.0%	0.545
Female	30	60.0%	27	54.0%	
Sum	50	100.0%	50	100.0%	

P*Chi square test

Table 2: Age of study population (n=100)

Age	Group		P value
	Healthy	Syncope	
Mean	8.09	7.73	0.440
Standard Deviation	2.31	2.33	
Median	8.00	7.75	
Mode	8.00	10.00	

P*Independent t test

Table 3: The Distribution of the Case and Control Groups in Terms of Hemoglobin Levels age of study population (n=100)

Hb levels	Group		P value
	Healthy	Syncope	
Mean	11.79	11.84	0.849
Standard Deviation	1.42	1.19	
Median	11.75	11.90	
Mode	11.00	11.00	

P*Independent t test Hb:hemoglobin

Table 4: The Distribution of th Case and Control Groups in Terms of PR Distance (n=100)

PR	Group		P value
	Healthy	Syncope	
Mean	134.80	137.80	0.466
Standard Deviation	19.51	14.61	
Median	140.00	140.00	
Mode	160.00	140.00	

P*Mann-Whitney test

There was a significance between the groups in terms of QTcd levels even after matching with all variables such as age, gender, BMI, PR intervals and base hemoglobin levels, and these variables could have influences on this relationship (p<0.225).

DISCUSSION

Syncope is a sudden decrease in the level of consciousness and muscle strength, followed by spontaneous healing that is caused by brain impairment and accounts for 2% of children's visits to the emergency department. It is more common at the age of 15 to 19 years and almost 50% of

adolescents experience at least one syncope attack. The incidence is gender dependent and is more common among females than males.³³ The aim of the present study was to investigate the QT interval dispersion in children with syncope attack (case group) and also to compare it with healthy children (control group). The mean age of children in the case group was 7.73 ± 2.33 years old and the number of females was 27 (54%). In other words; like previous conducted studies in this literature, there was a gender tendency in favor of girls. There was no significant difference between children in the control and case groups in terms of age and gender. The results of comparing the case and control groups showed that factors such as height,

weight, Hb levels and blood pressure had no effect on the prolongation of QT dispersion and the onset of syncope attack. However, a study carried out by Srivastava D et al. showed that the anthropometric characteristics of patients with severe and moderate nutritional disturbances had effects on the normal values of QT interval and its dispersion, and led to prolonged QT intervals.³⁴ Another study accomplished by Aklinf et al. investigated the role of Hb levels and Iron deficiency anemia on QTd and the onset of breath-holding spells. The results suggested that these factors had no effects on QT dispersion and the onset of breath-holding spells.³⁵ However, some studies such as one conducted by KocakG et al., believed that Iron deficiency anemia was associated with decreased oxygen transport capacity of and the onset of breath-holding spells using a mechanism of action on the metabolism of catecholamine and the function of neurotransmitters, and the reduction of myocardial oxygenation was associated with a prolongation of the QT intervals.³⁶ On the other hand, since reduced brain oxygen supply is one of the main mechanisms for the occurrence of syncope, iron deficiency anemia and the resulting caused damage can cause syncope attack by the same mechanism. None of the studied children in the present study suffered from nutritional disturbances such as shortness of height, low weight, or anemia; therefore, there was no difference between the groups in terms of the effect of these characteristics on the QT interval and dispersion. QT dispersion is a simple and non-invasive method for assessing the risk of ventricular arrhythmia and sudden death. Increased QT dispersion is a symptom of ventricular non-homogenous repolarization in myocardium which causes rhythm disturbances.³⁷ The QT dispersion indicates the difference in action potentials in different areas of the myocardium. A region with prolonged repolarization is resistant to electrical conductivity and causes the occurrence of a reentry phenomenon.^{35,37} Normal values of QT dispersion in adults are between 25-50, which are longer in patients with long QT syndrome and may reach 150-200ms. It is accepted that QT dispersion of greater than 80-90ms is associated with an increased risk of dysrhythmia.³⁵ There are some problems with the standardization of QT dispersion in children. Vialle et al. performed a study on the values of QT dispersion with arrhythmia in children.³ However, the values obtained in the present study were greater than the ones obtained by Vialle. Firstly, the reason was that there was a significant difference between individuals in measuring QT and QTd values. Secondly, none of the patients had no proved arrhythmia, increased QT and QTd values in patients with non-cardiac syncope (nervous syncope).³⁶ Although its value is higher than the normal values, its increase is far less than the values that are associated with arrhythmia. A study carried out by Movahedian et al. on QT dispersion in children with breath-holding spells in Kashan University of Medical Sciences showed that The values were consistent with the ones

obtained in our study, which could be indicative of the effects of the differences between the genetic characteristics of patients and the effects on QT interval and its dispersion; therefore, performing such studies in each region necessitates using a control group to compare the values with the case one having normal values being consistent with the genetic characteristics of the same region.³⁸ In the current study, patients suffered from syncope attacks were compared with the control group. Although the obtained values were not consistent with the study accomplished by Vialle, there was a significant difference between them.

In addition to the differences between individuals in measuring QT values and its distribution, the amount of the values is also affected by sinus arrhythmia and a significant difference is observed after correcting the QT value based on the heart rate and using Bazett's Formula in people with such arrhythmias. For example, Tutar et al. do not recommend using QTd in children with breath-holding spells, since they believe that respiratory sinus arrhythmia is more prevalent in this group of patients, and therefore different values may be appeared in the corrected ones.³⁹ In the present study, the comparison of QT dispersion values in both case and control groups showed that QT, QTc, QTd and QTcd values in the case group were much higher than those in the control group; that is, by measuring the above values in children's ECG, one can predicts whether syncope attack would happen in the future or not. The results obtained from the studies investigating the association between QT dispersion, cardiac arrhythmias and sudden death showed that the higher the numerical value of the dispersion, the more likely the risk of arrhythmias and sudden death, and prolonged QT dispersion is more predictive than the prolonged QT in this literature.⁴⁰ Autonomic nervous system dysfunction is mainly associated with numerous non-cardiac syncope attacks in children.³³ In the current study, the participants were visited by pediatric heart subspecialists collaborating in the project concerning diseases caused by cardiac structure deformities and dysfunctions. By conducting echocardiography, the authorities found that none of the patients had heart diseases. Increases in parasympathetic tone and decreases in the sympathetic tone are associated with prolongation of QTc values, but there is a controversy over its effect on QTd values.⁴¹ It has been evident that the disruption of the autonomic nervous system is associated with increased QTd in diabetics and patients with primary autonomic disorders.²⁶ Therefore, Akalin et al., investigated changes in QT and QTcd levels in patients with breath-holding spells and conclude that if QT and QTc levels are not increased in the patient at risk of breath-holding spells, the increased QTd interval cannot be attributed to autonomic dysfunction.³⁵ Similarly, if there are changes in QT and QTd intervals in ECG of children with a syncope attack(s), we should seek causes with a lower incidence of syncope and, but, with a higher risk. Attempts were made in a study that was performed on

patients with aortic stenosis, to predict the occurrence of syncope attacks, complications of aortic stenosis, by measuring the QT dispersion. It was also shown that the maximum QTc and QTc dispersion in patients with stenosis and those with complicated aortic stenosis were equal to 477 ± 49 and 60 ± 13 ms and 493 ± 48 ms and 68 ± 12 ms, respectively. This suggests that QTc dispersion can predict the occurrence of the syncope attack in patients with aortic valve stenosis.⁴² In our study, the case group subjects had significantly more QT dispersion than the control group. Another study investigated the prognostic effect of QT dispersion on the occurrence of syncope in patients with Prinzmetal angina. In patients with variant angina, temporary and reversible coronary artery spasms can cause syncope and even ventricular arrhythmia and sudden death. The present study also showed that QT dispersion was higher in the group that experienced the syncope attack, while there was no clinical, biochemical or angiographic differences between the two groups of patients. Patients with syncope attack underwent echocardiography in our study, and it was evident that those affected by syncope attack are healthy in terms of cardiac structure. Obviously, most individuals with cardiac structural abnormalities usually refer with other symptoms such as heart palpitations, dyspnea, cyanosis, etc. Therefore, we should not neglect patients who refer with the syncope history, but have paraclinical and clinical examinations. Attempts should also be made to ensure that the QT dispersion is measured on their 12 Lead ECG, which also has a complementary role in the diagnosis of syncope and can also predict future attacks. However, it has been shown in some previous studies that QT dispersion is prolonged at the time of the syncope attack and after a long time, and normalized after some time.⁴³ However, in our study, all children were referred several hours and days after the onset of syncope, and suffered from increased QT dispersion at the same time. The reason is that QT dispersion is an approximate measure of total abnormalities during cardiac repolarization period and is affected by factors such as measurement error, even type of food consumed and day/night cycle, as well as genetics and physiology; therefore the complementary methods should be used for quantifying repolarization abnormalities such as T-wave analysis, T-wave morphology, etc.⁴⁴

CONCLUSION

Performing the electrocardiography and examining the QT interval and other related indexes in children with syncope attack is an important method to confirm the diagnosis and predict the incidence of subsequent attacks in such way that the prolongation of the QT interval, and especially the increased QT dispersion, should be carefully measured and documented in all of these children.

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