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ORIGINAL ARTICLE

Electrocardiographic Changes in Type-1 Diabetes Mellitus Children with Diabetic Ketoacidosis Presenting to Tertiary care Hospital, Karachi

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ABSTRACT

Introduction: Cardiac arrhythmias and arrest have been described in children with diabetic ketoacidosis and generally have been presumed to be caused by electrolyte abnormalities. The rationale of this study was to assess the role and importance of ECG monitoring, as a simple, quick, non-invasive and readily available tool in the diagnosis and confirmation of hypokalemia and hyperkalemia in patients with DKA in the Emergency Department
Objective: To Assess the Frequency of electrocardiographic changes in Type-1 diabetes mellitus children with diabetic ketoacidosis presenting to tertiary care hospital, Karachi.
Materials and Methods: This retrospective cross sectional study was carried out at the department of pediatric medicine, NICH Karachi. At the time of presentation, the standard 12-lead ECG was recorded by a single pediatric cardiologist having more than 2 years of experience, QT and RR intervals were measured. Three separate measurements were obtained from each ECG, and the mean of these measurements was used as the value for QTC. QTC of at least 0.45s (450ms) was considered as prolonged QTC. QTD was also assessed at the same time and QTD>50 ms was considered as prolonged QTD.
Results: One hundred cases of T1DM with DKA were included in this study. Average age of children was 7.9 ±3.5 years (Min – Max = 0.5 – 14 years), male to female ratio was 1: 0.96. Prolong QTc and QTd interval was observed in (56%) and (38%) children respectively, Mean (±SD) QTc and QTd interval was 449.4 ±36.6 mc and 39.3 ±16.1 mc respectively. While ECG changes were found in (58%) cases. Association between ECG changes and the cases with higher RBS (>350 mg/dl) was statistically significant 81 (81%) cases with ECG changes had higher RBS (p<0.0001) while ECG changes were statistically similar in both age groups and gender (p-values > 0.05).
Conclusion: The frequency of ECG changes was higher in T1DM children with diabetic ketoacidosis. ECG changes was significantly associated with higher RBS (>350 mg/dl).
Key words: T1DM, Diabetic Ketoacidosis, ECG, QTc, QTd

INTRODUCTION

Diabetic ketoacidosis (DKA), which is an acute complication of type 1 diabetes, is characterized by hyperglycemia, metabolic acidosis, and ketonemia. Diabetic ketoacidosis develops as a result of insulin deficiency and increased epinephrine, glucagon, cortisol, and growth hormone. The cardiovascular complications of diabetic ketoacidosis have been known for a long time. Cardiovascular complications including cardiac arrhythmia, acute myocardial infarction, and cardiac arrest may be observed during diabetic ketoacidosis, and this leads to mortality with a rate of 2–10%[1,2].

Arrhythmia and cardiac arrest have also been described during DKA in children. Prolongation of the QTc interval is an important electrocardiographic (ECG) finding, which is observed frequently in DKA and leads to a risk of sudden death. It is thought that it generally develops secondary to electrolyte imbalance as with the other cardiac complications of diabetic ketoacidosis.

The incidence of DKA in the US stays rise, and it accounted for around 140,000 hospitalizations in 2009 and 168,000 hospitalizations in 2014[3].

Studying ECG changes in diabetic ketoacidosis is an essential tool for improving the management and outcome of DKA patients[4].

It is reported that hypokalemia associated with diabetic ketoacidosis had risky clinical condition especially in comatose patients who need Potassium a repletion and intravenous insulin with correction of other electrolyte disturbances. This study showed a significant association between prolonged QT interval in ECG of diabetic ketoacidosis patients and hypokalemia (p=0.002).This finding is consistent with results of Aygün et al[5]. Although the incidence of DKA in Iraq is more common in girls, the severity of the condition is more in boys[6].

Prolongation of QT interval is a serious condition that provides substrate for the development of potentially life-threatening arrhythmias torsade de pointes7. Previous studies supported the association of other ketotic conditions with QTc prolongation and deaths in patients receiving ketogenic diets[8,9].

The rationale of this study was to assess the role and importance of ECG monitoring, as a simple, quick, non-invasive and readily available tool in the diagnosis and confirmation of hypokalemia and hyperkalemia in patients with DKA in the Emergency Department.

MATERIAL AND METHODS:

This retrospective cross sectional study was carried out at the department of pediatric medicine, NICH Karachi, from

December 2016 to June 2017. The estimated sample size of this study was 97 ≅ 100 consecutive cases; sample size was calculated by using WHO calculator with prevalence of prolonged QTC was 53.3%10, 95% CI and 10% margin of error. The inclusion criteria was children with T1DM (HbA1C > 6.5%) presenting with diabetic ketoacidosis, 0.5 - 14 years of age and either gender. While cases with history of hypothyroidism or hyperthyroidism, with congenital or rheumatic heart diseases, systolic left ventricular dysfunction and children taking medications like sodium channel blockers, calcium channel blockers were excluded from the study. Unreliable identification of the end of the T wave in the ECG was also excluded from the study.

Presence of hyperglycemia (blood glucose >11 mmol/L or=200 mg/dL), Venous Ph <7.3 OR BICARBONATE <15mmol/L, Ketonemia (presence of ketone bodies in blood) and ketonuria (presence of ketone bodies in Urine) was considered as Diabetic Ketoacidosis.

Prior to conduct the study, ethical approval was required from the institutional review board (IRB) of the institute. Informed consent was obtained from the parents of the eligible children after explaining the purpose, risk procedure and benefits from the study. At the time of presentation, the standard 12-lead ECG was recorded by a single pediatric cardiologist having more than 2 years of experience and masked to patient's clinical laboratory data, QT and RR intervals were measured. QT interval was measured from the onset of the QRS complex to the end of the T wave. The end of QT interval was defined as the intersection of a tangent to the steepest down slope of the dominant repolarization wave with the so electric line. Lead Two was used preferentially for QTC measurement. Three separate measurements was obtained from each ECG, and the mean of these measurements was used as the value for QTC. QTC of at least 0.45s (450ms) by using Bazett's Formula ($QTC=\sqrt{\frac{QT}{R}}R$) was considered as prolonged QTC. QTD was also assessed at the same time and QTD>50 ms was considered as prolonged QTD. All of these information along with the baseline demographics like age, gender, height, weight and RBS was noted in the Performa attached as annexure.

Data entry and analysis was done on IBM (SPSS) version 21 for windows. Frequencies and percentages was presented for qualitative variables like gender, prolonged QTC, QTD and ECG changes. Mean and standard deviation was calculated age of the patients, height, weight, Random Blood Sugar (RBS), QTC and QTD. Effect modifiers like age, gender, RBS, height and weight was dealt through stratification to see the effect of these on the outcome (ECG changes). Post stratification chi square test/fisher exact test was applied, using level of significance of 0.05.

RESULTS

Hundred diagnosed cases of T1DM presented with DKA were analyzed in this study. Average age of children was 7.9 ±3.5 years (Min – Max = 0.5 – 14 years), majority of cases 58% had age >7 years. There were 51 (51%) male and 49 (49%) female (M: F = 1: 0.96). out of 100 cases, 54 (54%) had height > 25 cm, mean (±SD) height was 124 ±21 cm. Fifty two (52%) children presented with ≤ 25 kg weight, mean (±SD) weight was 23.6 ±6.7 kg. majority of cases 52 (52%) were presented with >350 mg/dl of RBS, mean (±SD) RBS was 356.2 ±78.8 mg/dl. Mean (±SD) serum potassium was 4.3 (±0.50) mmol/L, majority of cases 53 (53%) were presented with >4 mmol/L of potassium.

Prolong QTc and QTd interval was observed in 56 (56%) and 38 (38%) children respectively, Mean (±SD) QTc and QTd interval was 449.4 ±36.6 mc and 39.3 ±16.1 mc respectively. While ECG changes were found in 58 (58%) cases. Table-2

Stratification of ECG changes was done according to age, gender, height, weight and RBS in Table-3. Association between ECG changes and the cases with higher RBS (>350 mg/dl) was statistically significant 81 (81%) cases with ECG changes had higher RBS (p<0.0001) while ECG changes were statistically similar in both age groups and gender. ECG changes were also similar in height, weight and serum potassium level (p-values > 0.05).

Table 1: Demographic characteristics of children (n = 100).

		Frequencies	%age
Gender (M: F = 1: 0.96)	Male	51	51
	Female	49	49
Age (Years) Mean ±SD = 7.9 ±3.5	≤ 7	42	42
	> 7	58	58
Height (cm) Mean ±SD = 124 ±21	≤ 125	46	46
	>125	54	54
Weight (kg) Mean ±SD = 23.6 ±6.7	≤ 25	52	52
	>25	48	48
RBS (mg/dl) Mean ±SD = 356.2 ±78.8	≤ 350	48	48
	>350	52	52
Potassium concentration (mmol/l) Mean ±SD = 4.3±0.50 mmol/L	≤4	47	47
	>4	53	53

Table-2: Prevalence Prolong QTc, QTd and ECG changes (n = 100)

		Frequencies	%age
Prolong QTc Mean ±SD = 449.4 ±36.6 mc	Yes	56	56
	No	44	44
Prolong QTd Mean ±SD = 39.3 ±16.1 mc	Yes	38	38
	No	62	62
ECG Changes	Yes	58	58
	No	42	42

Table: Comparison of ECG Changes with respect to Gender, Age, Height, Weight and RBS (n = 100)

		ECG Changes		P-values
		Yes	No	
Gender	Male	29 (50%)	22 (52.4%)	0.81
	Female	29 (50%)	20 (47.6%)	
Age (Years)	≤ 7	24 (41.4%)	18 (42.9%)	0.06
	> 7	34 (58.6%)	24 (57.1%)	
Height (cm)	≤ 125	25 (43.1%)	21 (50%)	0.5
	>125	33 (56.9%)	21 (50%)	
Weight (kg)	≤ 25	29 (50%)	23 (54.8%)	0.64
	>25	29 (50%)	19 (45.2%)	
RBS (mg/dl)	≤ 350	11 (19%)	37 (88.1%)	<0.0001
	>350	47 (81%)	5 (11.9%)	
Potassium concentration (mmol/l)	≤4	23 (39.7%)	24 (57.1%)	0.084
	>4	35 (60.3%)	18 (42.9%)	

DISCUSSION

Diabetic ketoacidosis (DKA) is a dangerous complication of DM that with a significant mortality in spite of intensive latest therapy with electrolyte and fluid replacement, acidosis correction, insulin administration and controlling the precipitating factors. A rapid and often quick drop in the serum electrolyte level can occur in DKA after initiation of therapy. The ECG is a most valued and easily available

indicator of such changes, however not a substitute for the serum electrolyte determinations, and may be used to make reliable decisions in the management of DKA.5 A previous study has reported a prolongation of QTc in children receiving ketogenic dietand in other conditions associated with ketosis in the absence of electrolyte[11, 12].

Studying ECG changes in diabetic ketoacidosis is an essential tool for improving the management and outcome of DKA patients.4 In this study, ECG changes were found in 58% of children while prolong QTc interval was found in 56% children and prolong QTd in 38% children. A study from USA reported 53.3% had prolonged QTc and 63.3% had prolonged QTd in type-1 diabetic children with DKA.10 Mean (±SD) QTc and QTd interval was 449.4 ±36.6 mc and 39.3 ±16.1 mc respectively. Same study reported the similar ean QTc values of patients during DKA 450 ±89 ms but higher mean QTd 48.77 +6.36 ms.10 Association between ECG changes and the cases with higher RBS (>350 mg/dl) was statistically significant 81% cases with ECG changes had higher RBS (p<0.0001). Patients had no electrolyte disturbances or hypoglycemia that could account for QTc prolongation, so the role of ketoacidosis in causing such prolongation and delayed cardiac repolarization was suggested.

Many studies have been conducted in relation with the presence and importance of QTc prolongation in diabetes[13-15]. QTc prolongation may be observed in children with long-term diabetes in the absence of ketoacidosis. Diabetic autonomic neuropathy may affect many organs including the cardiovascular system. Cardiac autonomic neuropathy (CAN) consist of sympathetic and parasympathetic dysfunction and it is known to lead to sudden death in adults. QTc interval has been used to demonstrate Cardiac autonomic neuropathy in adults rather than prolonged ventricular depolarization and repolarization[16]. Marthur et al[17]. conducted a study with 50 asymptomatic adult patients with diabetes in 2006 and found findings of Cardiac autonomic neuropathy in 19 patients; QTc prolongation was found in 15 of these patients.

CONCLUSION

In conclusion, prolonged QTc occurs frequently during DKA and is correlated with ketosis and hyperglycemia. ECG and cardiac monitoring of children during DKA should be strictly followed.

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