Electrocardiographic changes in chronic hemodialysis children at Sohag university hospital.

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Abstract: Background: Cardiovascular disease is the leading cause of mortality among patients on chronic hemodialysis (HD). 30% of the deaths in these patients are due to cardiac arrest, death of unknown cause or cardiac arrhythmia. The increasing time of ventricular depolarization and repolarization, measured by QT interval duration on the electrocardiogram (ECG) at rest, has emerged as a predictor of complex ventricular arrhythmias. **Objectives:** To determine ECG alterations in chronic (HD) children before and after HD. **Design:** Cross sectional study**. Setting:** Pediatric HD unit of Sohag University Hospital, Sohag, 2016. **Methods:** after obtaining consents from all patients less than 18 years on dialysis, they were submitted to the examination of a 12-lead ECG: heart rate, QRS duration, QRS amplitude, T-wave amplitude and QT interval was measured 10 min pre and post-HD, and QT interval was corrected for heart rate using Bazett's formula. Children were monitored during dialysis session by 3 leads ECG to detect any sustained arrhythmia. **Main outcome measures**: 12-lead electrocardiogram. **Results:** 20 patients on regular HD were included in the study. 75% of them were females; the average age was 12.9 (3.7) years old and 55% of all patients had QTc prolongation before dialysis. No significant QTc prolongation occurred after dialysis. HD leaded to a significant increase in the QRS explained by the decrease of the extracellular fluid and blood volume and hence a decrease of the cardiac preload. HD also decrease of the T-wave amplitude explained by potassium decrease during HD. PVCs observed in the ECG of 3 children after dialysis. No sustained arrhythmias occurred to our patients during dialysis sessions. **Conclusion**: children on chronic HD had high frequency of abnormal ECG findings, especially prolonged QTc interval. **Limitation:** the studied cohort was small that may weaken the statistical power of the study.

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Key words: ECG, cardiac, hemodialysis.

1- Introduction

Cardiovascular complications are a major cause of morbidity and mortality in adult patients with end-stage renal disease (ESRD). In particular, cardiac arrhythmias are well known life-threatening events [1, 2]. Although 5-year survival is ≥90% in pediatric patients on hemodialysis (HD) or after renal transplantation, cardiovascular complications are, together with infections, the main causes of death [3, 4].

Pediatric and adult patients with ESRD are subjected to the same metabolic and volume load changes that may alter cardiac function. However, the cardiovascular impact of HD may be different in the pediatric population. In children, the cardiovascular system is rarely affected by primary cardiovascular or systemic disease, such as long-standing atherosclerosis or diabetes mellitus, and children often undergo prompt renal transplantation [3]. Thus, volume and electrolyte shifts rather than myocardial abnormalities may cause arrhythmias in pediatric HD patients. The increasing time of ventricular depolarization and repolarization, measured non-invasively by measuring the QT interval on the electrocardiogram at rest, has emerged as a predictor of complex ventricular arrhythmias, a major cause of sudden cardiac death.

In everyday clinical practice, different methods of surface ECG are being studied for their ability to predict either the occurrence of these ventricular arrhythmias or their clinical relevance [5, 6]. In the conventional ECG, the prolonged QT interval has been reported to be associated with arrhythmogenesis in a number of cardiac disorders [7].

The factors contributory to cardiac abnormalities include anemia, hypertension, volume overload, uremic cardiomyopathy, electrolyte imbalance, hyperlipidemia, and arteriovenous fistula.

2- Patients and methods:

Study design:

Cross sectional hospital based study that was conducted in the pediatric HD unit in Sohag University hospital. The Hospital is a tertiary health institution, located in the south zone of the country. All children under 18 years who met criteria for diagnosis of chronic renal failure and were on HD for more than 6 months and had given informed consent

were included in the study. We excluded from the study, patients who did not give consent. Also we excluded patients with overt cardiac disease or cardiomyopathy in the preceding six months prior to diagnosis of CKD. The study protocol was approved by the Research Ethics Board of our institution.

Hemodialysis: All patients underwent two or three HD sessions per week of 3–3.5 h using a polysulfone dialyzer. The dialysate was bicarbonate buffered and contained (for each liter of diluted solution) 103 m.ml sodium, 17.5 m.ml calcium, and 2 m.ml potassium, the latter adapted to the plasma concentrate.

Data collection:

For all the patients enrolled in the study checklist that included the needed data was filled by the investigator. The checklist included data of the patients concerning age, sex, duration of HD, measurement of weight and systolic blood pressure before and after the session. Two blood samples were collected from the patients one hour before the dialysis and one hour after dialysis. They were analyzed for serum creatinine, serum (Na, k and ionized Ca) and blood gases and the results were documented in the checklist. All patients had 2-D and M-mode echocardiographic examinations in accordance with the American Society of Echocardiography standards.

ECG: 12 leads ECG were performed to all children with CKD on regular HD 10 min pre and post-HD using (Fukuda Denshi CardiMax ECG device model FCP-7101 with a 25 mm/s paper speed, gain 10 mm/mV). Location of chest electrodes was not changed before and after HD. The electrocardiograms were reviewed through the creation of descriptive reports and determination of the following variables: heart rate, QRS duration, QRS amplitude was measured by summation of the amplitude of S wave in V1 and R wave in V6 as an indicator of left ventricular voltage [8], T-wave amplitude was measured in lead II. The QT interval was measured from the onset of the QRS complex to the end of the T wave, defined by the return of the terminal T wave to the isoelectric T-P baseline. When U waves were present, the end of the T wave was taken as the nadir between the T and U waves. Then QT interval was corrected for heart rate using Bazett's formula [9, 10].Interpretation of every ECG paper was done using specific centile tables for normal values of ECG waves and intervals according to age [11].ECG was examined for any abnormal rhythm (ectopics ,supraventricular or ventricular tachycardia) . Children were monitored during dialysis session by 3 leads ECG monitor to detect any sustained arrhythmia.

Data analysis:

Data processing, grouping and analysis were done using statistical Package of Social Scvience version 16 (SPSS). The data were assessed as regard to the distribution using the *Shapiro-Wilk* normality test. Paired sample T test was used to assess differences between quantitative variables, and when appropriate, the *Mann-Whitney* test was used. Values of $p< 0.05$ were considered statistically significant.

3-Results:

20 children having chronic renal failure attending HD unit of Sohag University Hospital approved participating in the study. Their age ranged from 4.5 years to 18 years and 75% of them were females. Table (1) shows clinical data of the studded 20 children with renal failure on chronic hemodialysis. The mean age was 12.9 years while the mean duration of hemodialysis was 3.4 years. As regard systolic blood pressure 37.8% of the patients had high blood pressure while 17.4% of them have sinus tachycardia.

Table (1): clinical data of the studied 20 children on chronic hemodialysis:

Age Mean & SD	12.9 (± 3.7) years
Sex Male percent	5 (25%)
Duration of dialysis Mean &SD	3.4 (±2,4) years
Weight Mean & SD Weight loss after dialysis & P value	29.8 (± 7.5) Kg1.5 Kg& (0.0000)
SBP- Mean & SD-Percent of children with High SBP	124 (15)11 (47.8%)
Heart rate-Mean & SD-Percent of children having sinus tachycardia	100 (18.9)4 (17.4%)
Causes of renal failure- Cystic kidney diseases- Chronic interstitial nephritis- Bilateral reflux uropathy- Pyelonephritis- Focal segmental glomerulosclerosis- Obstructive uropathy- not known	4332314

Table (2) represents change in serum creatinine, electrolytes and blood gases before and after dialysis. There was very high statistically significant difference between pre and post dialysis levels of serum creatinine, PH and Hco3 (P value= 0.000). Reduction of the mean of serum K from 5.12 to 3.94 is found with high statistically significant difference (*P* value=0.01). Table (3) represents ECG changes before and after dialysis. No statistically significant QTc prolongation occurred after dialysis. HD leads to a significant increase in the QRS and decrease of the T-wave amplitude. One patient had 2nd degree heart block followed by junctional escape beat before dialysis and3 children had PVCs in the ECG

performed for them after dialysis. No sustained arrhythmias occurred to our patients during dialysis sessions. Figure (1) shows mean R+S before and after dialysis. Figure (2) shows T wave amplitude before and after hemodialysis. Echocardiography was done for all patients and 18 (90%) of them showed echocardiographic features of uremic cardiomyopathy.

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Table (2) laboratory changes in serum creatinine, electrolytes and blood gases before and after dialysis:

	Mean Before dialysis	**Mean After dialysis**	***P* value**
Serum creatinine	7.03	2.18	0.000
K	5.12	3.94	0.01
Na	140	135	0.057
Ionized Ca	1.33	1.32	0.492
pH	7.34	7.41	0.000
PCO_2	37.30	37.15	0.867
HCO_3	19.91	25.44	0.000

Table (3): ECG changes before and after dialysis:

Factor	Before dialysis	After dialysis	*P* value
RR (ms)	611.8	596.8	0.940
PR (ms)	141.5	136.4	0.167
QRS (ms)	96.1	98.5	0.771
QTC (ms)	461.7	459.1	0.845
AXIS (o)	61	58	0.459
RV6 (mv)	1.85	1.96	0.355
SV1 (mv)	0.99	1.37	0.000
RV6+SV1(mv)	2.85	3.34	0.01
T wave (mv)	2.8	1.8	0.014

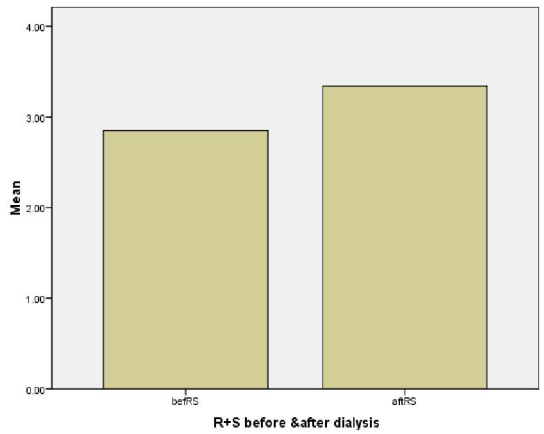

Figure (1): Mean R+S before and after dialysis:

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One patient had 2nd degree heart block followed by junctional escape beat before dialysis and3 children had PVCs in the ECG performed for them after dialysis. No sustained arrhythmias occurred to our patients during dialysis sessions.

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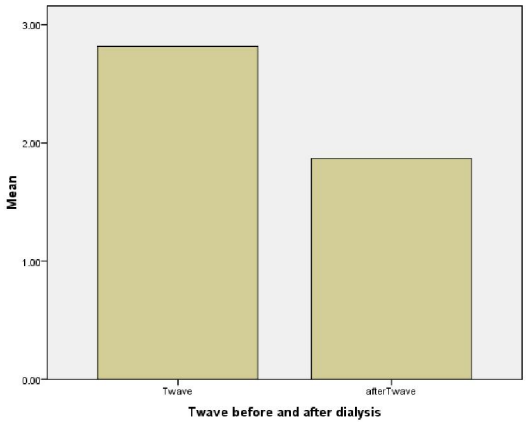

Figure (2): T wave amplitude before and after hemodialysis

4- Discussion

Mortality in patients on maintenance dialysis is high and predominantly due to cardiovascular causes. The high prevalence of anemia, hyperparathyroidism and hypertension among chronic dialysis children together with, fluid overload and metabolic abnormalities such as metabolic acidosis and dyskalemia lead to an increased risk of clinically significant arrhythmia .The mechanisms of arrhythmias in ESRD patients are extremely complex. The compromised myocardium (alteration in myocardial function and structure secondary to uremia), the impact of HD on electrolyte equilibrium (fluctuating levels of potassium, ionized calcium or sodium), on body fluid composition, tissue hydration or adrenergic activation are associated with considerable effects on the excitability of the cardiac cells and on arrhythmias [(1)].

Hemodynamic alterations induced by dialysis, metabolic alterations, derangements and the molecular level of the current alterations in the L-type calcium channels of the heart are a number of factors that have been implicated in the genesis of arrhythmias in renal failure patients who are receiving long-term hemodialysis [(4)].

Age-specific mortality rates for children treated with dialysis and kidney transplantation are approximately 30 times higher than those in healthy children [(2)].

A retrospective cohort study of pediatric ESRD patients studied the long-term mortality data for Canadian pediatric ESRD patients treated in Canada between 1992 and 2007 using data from a national organ failure registry within a universal health care system. Overall, 10-year survival for the entire cohort was 86%. The most important risk factors for mortality were dialysis as the RRT modality and age less than 1 year of age at the start of RRT. They found that Cardiac deaths constituted 27.4% of all known causes of death and they concluded that further evaluation is necessary to elucidate factors that may be associated with increased risk of death in this population[(3)].

75% of our patients were females, this disagree with most adult researches that found that fewer women than men were being treated with dialysis for end-stage renal disease and concluded that the large discrepancies in sex-specific hemodialysis prevalence by country and age group are likely explained by factors beyond biology [(12)].

In our study more than half of our patients had prolonged QTc interval before starting haemodialysis that was not correlated with their serum calcium level and can be explained by the high prevalence of uremic cardiomyopathy in these patients and that was present in the echocardiography of most of our patients. The link between LVH and prolonged QT interval has previously been demonstrated by other authors in cross-sectional studies conducting echocardiograms and electrocardiograms simultaneously [(13, 14).] A lengthening of the QT interval corrected for heart rate (QTc) predisposes to torsade de pointes ventricular tachycardia, which can degenerate into ventricular fibrillation[(1)].

In contrast with QTcbehaviour and with data from the literature, in this young HD population without ischemic cardiac disease**,** in our study we found no statistically significant increase in QTc duration during the session of haemodialysis. No sustained arrhythmias occurred to our patients during dialysis sessions and premature ventricular contractions were the main arrhythmia occurred to them after dialysis.

In the intradialytic period, in which changes in the concentrations of calcium, potassium, magnesium, and bicarbonate due to hemodialysis may induce disturbances in the cardiac electrical conduction. Genovesi *et al.*(22), using dialysates with different concentrations of calcium (K^+ of 2 and 3 mmol/L; Ca^{2+} of 1.25, 1.5, or 1.75 mmol/L), observed QTc> 440 ms in 56% of the patients in which the dialysate contained the lower concentrations of calcium and potassium, and only 18% of the patients in which dialysate was prescribed with higher concentrations of these ions. Similar results were found by Di Iorio *et al.* [(15),] as the QTc interval was significantly more prolonged in patients with dialysate that contained the lowest concentrations of calcium and potassium and the highest concentrations of bicarbonate.

The increase in QTc duration during the session of haemodialysisin adults was linked to that: the HD causes sudden shifts in volume and electrolytes within a short time that alters the physiological milieu. This leads to reduced coronary artery oxygen delivery while increasing myocardial oxygen demand during

HD [16]. Theso called 'oxidative stress' [17]. This HD-induced 'silent ischemia' leads to increased myocardial vulnerability to serious Arrhythmias[18]. The arrhythmogenic effect of dialysis was also studied by Berta *et al*. [19] who concluded that the metabolic changes during dialysis treatment can lead to considerable risk of cardiac arrhythmias.

In the present study with 20 HD children we found that HD is associated with a significant change in QRS and T wave amplitude. Analysis of the current results shows that dialysis leads to a significant increase of the QRS amplitude (P=0.01).

The fact that the decrease of patient's blood volume and intra-cellular liquid is a leading cause to increase in QRS amplitude has been discussed in Simov. [20]. QRS amplitude increase after HD has also been shown in previous studies[21, 6]. Where it was related to the extracellular water and blood volume loss. The mechanism involved is most probably change of electrical resistance of the tissues surrounding the heart caused by loss of interstitial fluid.

The decrease in T-wave amplitude is explained by potassium (K) decrease during HD [7].

5-Conclusion

Prolonged QT interval is a highly prevalent condition in children with CKD undergoing hemodialysis, and is one of the known pathophysiological mechanisms of sudden death in this population. No significant QTc prolongation occurred in our children after dialysis and no sustained arrhythmias occurred for them during dialysis. PVCs were the main arrhythmia occurred in our patients. HD is associated with a significant increase in QRS amplitude and decrease in T wave amplitude. The etio-pathogenesis and future significance of these changes is not thoroughly explained and requires further investigation. New studies need to be outlined to confirm these results.

6-Recommendations

Nephrologists must pay attention to identify patients with prolongation of the QT interval and the associated clinical and laboratory conditions, such as structural changes of the heart, and the prescription of drugs that induce QT interval prolongation, particularly in patients already presenting an extended QT interval. It is important to attempt a reduction of the development of structural cardiac disease, particularly LVH which predisposes the patient to both arrhythmias, to optimize the dialysis procedure in terms of hemodynamic stability and electrolyte shifts.

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