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Original Article

Internal Medicine Section

Effect of Haemodialysis on QTc in Newly Diagnosed Chronic Kidney Disease Patients

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ABSTRACT

Introduction: Cardiovascular disease and mortality is twice as common in patients with Chronic Kidney Disease (CKD) compared to the general population. The QT interval which depicts ventricular repolarisation, is a crude non-invasive marker of susceptibility to ventricular arrhythmias. Effects of haemodialysis on corrected QT (QTc) interval in newly diagnosed CKD patients is undocumented till date.

Aim: To assess the effect of haemodialysis on QTc in patients with newly diagnosed CKD.

Materials and Methods: This was a prospective cohort study of 50 newly diagnosed CKD patients admitted for their first session of haemodialysis in the Departments of General Medicine and Nephrology, at Bapuji Hospital between October and November 2019. ECGs were recorded before the first and after the third session of haemodialysis. Serum electrolytes (sodium, potassium, chloride, phosphorous and calcium), blood sugar and haemoglobin levels before haemodialysis were recorded. QT interval was calculated and corrected using Bazett's and Framingham's methods. Descriptive statistics, simple and multiple linear regression were used for analysis using Microsoft® Excel.

Results: The mean predialysis QTc was 0.434 seconds and postdialysis QTc was 0.477 seconds. QTc prolongation was observed in 44 (88%) patients (mean=0.042 seconds). The QTc prolongation correlated positively with postdialysis QTc (p=0.00001, Framingham; p=0.0009, Bazett) (R_{Bazett}=0.61 and $R_{Framingham}$=0.74).

Conclusion: Substantial QTc prolongation after three sessions of haemodialysis screens a population that has a greater risk of adverse cardiovascular events. This warrants vigilant cardiac monitoring in patients on haemodialysis.

Keywords: Arrhythmia, Chronic renal failure, Dys-electrolytemia, QT interval, QT prolongation

INTRODUCTION

Cardiovascular disease is twice as common in patients with CKD compared to the general population [1]. The most frequent line of treatment for patients with dysfunctional kidneys is haemodialysis. However, the socio-economic burden due to haemodialysis and its complications is dramatic [2].

Lindner A et al., were the first to point out the higher incidence of cardiovascular morbidity in patients undergoing haemodialysis [3]. The incidence of sudden cardiac death is more common in patients undergoing dialysis, usually triggered by a ventricular arrhythmia. The QT interval on the Electrocardiogram (ECG) is a reflection of the ventricular repolarisation. The relationship between glomerular filtration rate, risks of sudden death from cardiovascular events is nonlinear [4]. Nonetheless, the QT interval is a crude and non-invasive marker of susceptibility to ventricular arrhythmias.

No study was found documenting the effects of haemodialysis in patients with newly diagnosed CKD in the literature. Thus, the objective of this study was to investigate the changes occurring in the QT interval in patients who, for the first time, would undergo haemodialysis thereby contributing to a probable increased risk of cardiac arrhythmias and sudden cardiac death.

MATERIALS AND METHODS

This was a prospective cohort hospital-based study of in patients admitted in the departments of General Medicine and Nephrology, Bapuji Hospital, Davangere between October and November 2019. The study was commenced after obtaining Institutional Ethical Committee clearance (IEC-91) and after taking informed written consent of the participants.

Inclusion criteria: Fifty patients who were newly diagnosed with CKD according to Kidney Disease Improving Global Outcomes 2012 criteria [5] i.e., GFR <60 mL/min/1.73m^2, albuminuria (<30 mg/g, 30-300 mg/g, >300 mg/g) and electrolyte abnormalities as mentioned were enrolled into the study.

Exclusion criteria: The study excluded patients on regular haemodialysis, on medications prolonging the QT interval (antiarrhythmics, ondansetron, fluoroquinolones, macrolides, antipsychotics) and cardiovascular rhythm abnormalities (long QT syndrome, bundle branch block, implanted artificial pacemaker).

The normal values of serum electrolytes are: serum sodium=135-148 mEq/L, serum potassium=3.5-5.3 mEq/L, serum chloride 98-107 mEq/L, serum calcium=8.5-10.5 mEq/L, serum phosphorous=1.12-1.45 mEq/L.

The enrolled patients were investigated for serum electrolytes (sodium, potassium, chloride, phosphorous and calcium), blood sugar and haemoglobin levels. A 12-lead ECG, at 10 mm/mV and 25 mm/s, was performed fifteen minutes before the first session of haemodialysis. All patients underwent three bicarbonate based haemodialysis sessions using polysulfone capillaries. All the patients underwent three continuous sessions on 3 consecutive days. This procedure was same for all 50 patients. A repeat ECG was recorded 30 minutes after the completion of the third session of haemodialysis.

The QT interval, duration from the beginning of the Q wave till the end of the T wave, was calculated in lead II by two observers who were not blinded to each other, defined in accordance to the threshold method [6].

The corrections for heart rate were made following two methods: Bazett (QTc =QT/√RR) and the Framingham {QTc=QT+0.154(1-RR)} [7].

STATISTICAL ANALYSIS

Descriptive statistics was employed to present the demographic data of the patients. Simple and multiple linear regression was

performed in order to look for statistical correlations using Microsoft® Excel for Mac, version 16.31.

RESULTS

The mean age of the population was 51.6±2.9 years. The sample size consisted of 26 females and 24 males. There were 24 patients aged between 18-60 years [Table/Fig-1].

Age	Female	Male	Total
18-60	12	12	24
>60 years	14	12	26
Total	26	24	50

[Table/Fig-1]: Age and gender of patients.
Mean age of sample=51.6±2.9 years

Mean haemoglobin levels of the patients were 8.86±1.86 g/dL. Thirty six patients out of 50 were anaemic.

Patients hailed from four different districts/talukas and 14 were from (Harapanahalli Districts of Karnataka, India) [Table/Fig-2].

Place	No. of individuals
Davangere	11
Harihar	12
Harapanahalli	14
Chitradurga	13

[Table/Fig-2]: Geographic distribution of patients.

There were 26 females and 24 males. Except for two, all patients had an imbalance in their electrolyte levels measured before their first haemodialysis session. Hyponatremia was observed in 30 patients, hyperkalemia was observed in 34 patients, hyperchloremia was observed in 26 patients, hypocalcaemia was observed in 38 patients, hyperphosphatemia was observed in 42 patients and 16 patients had random blood sugar>200 mg/dL [Table/Fig-3].

Metabolic disturbance	No. of individuals
Hyponatremia	30
Hyperkalemia	34
Hyperchloremia	26
Hypocalcaemia	38
Hyperphosphatemia	42
RBS>200 mg/dL	16

[Table/Fig-3]: Metabolic disturbances seen in individuals.

The mean predialysis QTc was 0.434 seconds and the mean postdialysis QTc was 0.477 seconds. QTc prolongation was observed in 44 patients. The mean duration of QTc prolongation was 0.042 seconds (Bazett) and 0.032 seconds (Framingham) [Table/Fig-4].

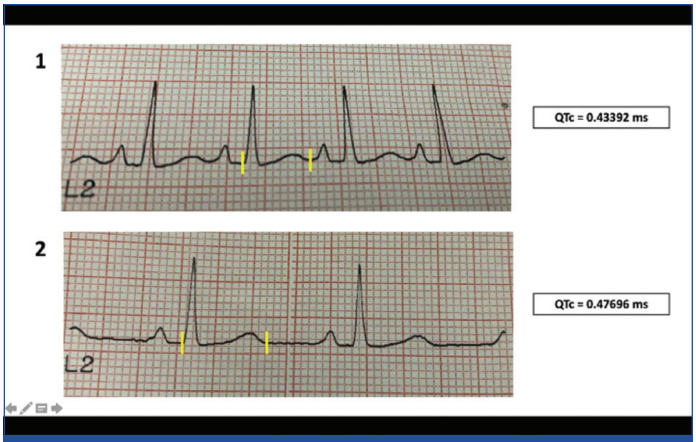
On linear regression analysis, it was observed that the QTc prolongation correlated positively with postdialysis QTc (p=0.00001, Framingham; p=0.0009, Bazett). The r value for Bazett was 0.61 and r value for Framingham was 0.74. A positive correlation was found between QTc prolongation and predialysis QTc only for Framingham but not for Bazett (p=0.01, Framingham) [Table/Fig-5].

DISCUSSION

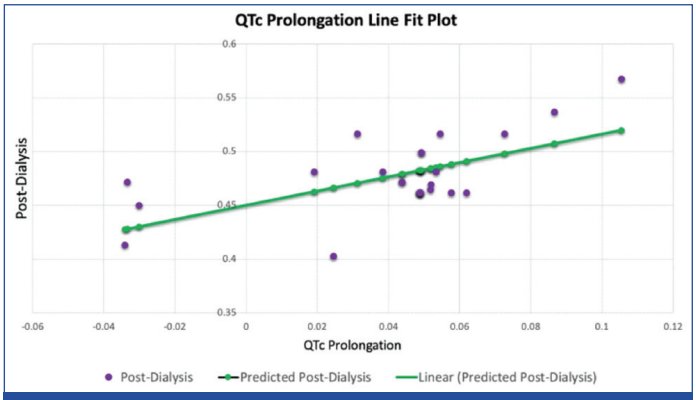
There was a significant observable prolongation of QTc interval as early as after three sessions of haemodialysis. This may be due to the imbalance in electrolyte levels [8,9].

Khosoosi Niaki MR et al., concluded that intra-dialytic arrhythmias are mainly caused by electrolyte imbalance, particularly calcium and potassium [10]. However, electrolyte levels after three sessions of haemodialysis could not be analysed due to economic constraints.

The QTc prolongation was substantially larger in those patients with longer postdialysis QTc. This clearly identifies a section of



[Table/Fig-4]: An illustration of QTc prolongation.



[Table/Fig-5]: Line fit plot showing the strength of correlation between QT_c prolongation and Post dialysis QT_c. Note: 20 data points in this plot as data overlapped.

the population that is more susceptible to adverse cardiovascular events. These patients develop the risk of ventricular arrhythmias and sudden cardiac death much earlier in their course of maintenance haemodialysis, although the predialysis QTc interval was not on the higher side. This is the novel observation made in this study.

In patients with CKD, QT interval may be prolonged due to calcium and potassium channel remodelling of the heart due to ischaemic heart disease, left ventricular hypertrophy, hypertension, heart failure and exposure to proarrhythmic drugs. Rapid shift of electrolytes across the membrane, occurring during haemodialysis also hampers the ventricular repolarisation and prolongs the QT interval. However, in this study, patients who were included were newly diagnosed with CKD with no known cardiovascular abnormalities [11].

In a study conducted by Matsumoto Y et al., a clear imbalance of fluid and electrolytes lead to sudden arrhythmia and cardiac death during dialysis. An increase in the sugar levels in the night was another major risk factor observed in their study [12]. In this study, hyponatremia, hyperkalemia, hypocalcaemia and hyperphosphatemia were observed. In comparison to their study, only 16 patients in this study had an RBS of >200 mg/dL.

In a study conducted by Malhis M et al., QTc interval prolongation was observed as an excellent marker which showed CKD patients on regular maintenance haemodialysis are more prone to ventricular arrhythmias [13]. In comparison, this cohort in the present study consisted of newly diagnosed CKD patients who had never undergone haemodialysis before.

Covic A et al., concluded that ionised calcium levels before dialysis and calcium levels after dialysis were crucial factors affecting QTc. This correlated with the findings in the present study which consisted of hypocalcaemia being observed in 38 patients. Calcium is well known to have significant effects on left ventricular activity, electrical activity and arterial compliance. Dialysate calcium levels should be decided after a full cardiology evaluation [14].

Limitation(s)

A small sample size was the major limitation of this study. Future studies must correlate the effect of different types of dialysate fluids to draw a comparison of the effects. Postdialysis and serial electrolyte monitoring should be conducted. However, in this study electrolyte levels after three sessions of haemodialysis could not be performed due to economic constraints.

CONCLUSION(S)

Substantial prolongation of the QTc interval occurring after three sessions of haemodialysis identifies a population that is at a greater risk of adverse cardiovascular events. This group of people are more susceptible to arrhythmias and sudden cardiac death. Therefore, regular monitoring of cardiac rhythm is warranted. Early and watchful monitoring of ECGs of all patients undergoing haemodialysis, from the beginning is recommended to define this cohort.

Declaration

This topic was presented as a paper presentation in January 2020 at APICON 2020 in Agra as part of the Annual Conference of The Association of Physicians of India. This manuscript has not been published elsewhere. The abstract of this manuscript has been published in Journal of the Association of Physicians of India (JAPI).

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