Original Article

Variation in QTc Interval and QT Dispersion Before and After Dialysis among Patients on Thrice Weekly Hemodialysis - Multi Centered Study

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ABSTRACT

Objective: In this study, we intended to measure variation in QT, QTc interval and dispersion before and after hemodialysis in patients of ESRD on MHD. We also tried to check its relationship with various biochemical parameters.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Dialysis centers of SughraShafi Hospital, Narowal and Sir Ganga Ram hospital, Lahore during July 2019.

Materials and Methods: Sixty eight patients of ESRD booked for thrice weekly MHD were enrolled in this study. Baseline characteristics of the all patients recorded. Measurement of QT, QTc and QTD are made on 12 leads ECGs during pre and post dialysis period and compared with the values of serum electrolytes and other dialysis related variables recorded at the time of ECG.

Results: Male to female ratio was 1.9:1, with mean age of 47 years. QTc and QTD were prolonged in 100% and 53% of patients pre-dialysis and prolonged further among 75% and 66% of patients during post dialysis respectively. Serum potassium, magnesium levels, LVH, and serum bicarbonate appeared to be the main determinants of QTD pre and post dialysis.

Conclusion: This study showed that QTcmax and QT dispersion are elevated in hemodialysis patients, and rose further during post-dialysis period. Significant association seen with changes in serum potassium, magnesium, changes in acid-base status and presence of LVH.

Key Words: ESRD: end stage renal disease, MHD: maintenance hemodialysis, QTD: QT dispersion, QTc, corrected QT interval, LVH: left ventricular hypertrophy, ECG: electrocardiography.

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INTRODUCTION

It is true that patients on maintainanance dialysis are still having increase risk of death in spite of significant improvement in techniques of dialysis. In United States, the annual mortality rate among dialysis patients in the year of 2008 was 200 deaths per 1000 patient-years[1]. Major cause of death among these patients was related to the underlying cardiac diseases, accounting for 40% of all cause mortality[1].

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Another study showed that 50% of the patients suffering from end stage renal disease died due to cardiovascular event[2]. Arrhythmias and sudden cardiac arrest (SCA) are the most common cardiac events according to the United States Renal Data System (USRDS) database[1]. In hemodialysis patients, arrhythmias lead to almost 64% of deaths[3] while coronary artery diseases (CAD) accounted for almost 20% of deaths. These mortality figures are considerably higher compared to normal population.

What is causing sudden death among dialysis patients is still unknown. However, multiple causes leading to irregularities between myocardial depolarization and repolarization have been identified[4]. It has been proposed that, QT dispersion can directly measure the changes in myocardial repolarization[5]. QT dispersion measured on 12 lead electrocardiogram by subtracting duration of shortest QT interval from longest QT interval. A QT dispersion above 80 ms is considered as abormal and it reflects that repolarization process in myocardial tissue is not in synchrony[6]. Abnormal QT dispersion can predispose to life threatening arrhythmias and sudden cardiac death[7,8]. It has been

studied that QT interval can be affected by multiple factors involved in active dialysis sessione.g, coronary artery disease, left ventricular hypertrophy[9,10], rapid electrolyte shift, hyperkalemia, and increase dialysis vintage[11-15].

Fewer previous studies are available showing the variable effect of changing electrolyte concentration on QTc and QTD during hemodialysis[16,17]but none of the local study is available up to date. Furthermore, assessmemt of QT interval can provide us with a simple, easy to perform, cheap and fast test to diagnose changes in myocardial action potential. The main objective was to assesschangesin QT, corrected QT (QTc) interval and QT, QTc interval dispersion pre and post hemodialysis in patients on MHD. We also tried to checkrelationship between variousbiochemical parameters with changes in QT interval.

MATERIALS AND METHODS

Seventy one patients with ESRD undergoing regular HD three times a week, 3-4 hours per session from dialysis centers of SughraShafi Hospital, Narowal and Sir Ganga Ram hospital, Lahore, were enrolled in this cross sectional study during July 2019.

Inclusion criteria: The subjects were patients with end stage renal disease on maintenance hemodialysis three times per week above 15 year of age.

Exclusion Criteria:Patients having ECGs with Un-measurable T waves, Atrial fibrillation, Bundle branch block, Pacemaker andPatients taking drugs that affect the QT interval e.g quinidine, procainamide, digoxin, tricyclic & tetracyclic antidepressant were excluded from study.

Data collection procedure:

Patients were enrolled in this study after getting informed written consent. All data regarding their age, gender, cause of end stage renal disease, associated comorbidities, and duration of renal replacement therapy was recorded. Vital signs and ECG was recorded before and after dialysis along with serum electrolytes including serum sodium, potassium, calcium, magnesium, bicarbonate levels. Furthermore serum creatinine and urea levels were checked both pre and post dialysis. Ultrafiltration volume was assessed, and the ultrafiltration rate was calculated. Patient were weighed before and after dialysis. Dialysis of all patients was done with the same dialysate, constituting Na/Ca/K/Mg/Cl/acetate/Hco3-
138/1.25/2.0/0.75/107.5/5.0/35.0 mmol/l, glucose 5.5mmol/l, total osmolarity 294.5mosm/l.

Patient underwent 12 lead electrocardiograms immediately before and after single hemodialysis session under similar conditions. Position of Chest leads was fixed by marking with marker to avoid position change. All ECGs were coded and analyzed manually by first observer. Later on these findings were confirmed by a second blind observer, an experienced cardiologist, to confirm changes. The QT interval was labelled as the distance between start of Q wave to end of T wave. The end of T wave was marked by a tangent intersecting to limb of T wave with the isoelectric line. In case if U wave was seen then QT interval was measured till the notch between T and U wave. If in any lead end of T wave is not clear, that was excluded from study. Mean value of QT was calculated from three successive QT readings. The Bazett's formula was applied to the maximum QT interval value to get corrected QT for heart rate. The QT dispersion was calculated by the difference between maximum and minimum QT interval in same ECG. Later on corrected QT dispersion was calculated. Abnormal value for QTc interval and QT dispersion were considered if found greater than 440ms and 65ms respectively.

Statistical analysis:

Data analysis was done with the help of SPSS 21. All categorical variables were presented in frequencies and percentage form. All quantitative variables described in mean and standard deviation form. Paired t-test was used for paired samples (pre and post-dialysis) to determine statistical significance. Pearson'stest was used to look for correlations between variables. Significant differences in proportions were assessed by the chi-square test. P values <0.05 was considered significant.

RESULTS

We studied 71 patients enrolled in dialysis center of Sir Ganga Ram Hospital, Lahore. Three of them were excluded from study and rest of 68 patient's data was entered for analysis.The major characteristics of patients are shown in table # 1A and 1B. The mean values of serum markers before and after dialysis are shown in table # 2. The mean QT interval duration and QTD values, before and after dialysis, are shown in table#3. Both the QTc interval duration and QTD showed marked variability after hemodialysis. In all patients QTc was found abnormal (>440ms) even in pre-hemodialysis period and increased further in post-hemodialysis period in 51 patients and decreased in 14 patients and remain almost unchanged in 3 patients.

QTD was found abnormal (>65ms) in 36 patients and normal in 32 patients pre-hemodialysis, while post hemodialysis it was abnormal in 51 patients and remain normal in 17 patients. QTD increased post-hemodialysis in 45 patients and decreased in 14 patients and remain almost unchanged in 9 patients. Table # 4 is showing percentage of patients having prolonged QTD in post dialysis period from different categories.

Serum potassium, magnesium levels and presence of LVH appeared to be the main determinants of QTD duration pre-dialysis, while serum bicarbonate was appeared to be the main determinants of QTD duration post-dialysis. While no relationship was observed with

age, gender, mean body weight, blood pressure, changes in serum calcium, albumin, sodium, creatinine, urea and blood sugar level,or with presence or absence of hypertension, diabetes, IHD, or with any specific medications.

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Table No.1A: Baseline characteristics of patients

Characteristics	Frequency (percentage)
Male	44 (64)
Female	24 (36)
Known IHD	16 (23.5)
Hypertension	61(89.7)
Diabetics	32(47)
Current smoker	5(7.4)
Past smoker	18(26.4)

Table No.1B: Baseline characteristics of patients

Characteristics	Frequency (percentage ± SD)
Age (years)	47.2 (13.3)
BMI	24.6 (6.9)
Duration of RRT(years)	4 (2.3)
Ultrafiltration volume(ml)	2406.8 (666.5)

Table No.2: The result of measured variable before and after hemodialysis

	Before hemodialysis (Mean ± SD)	After hemodialysis (Mean + SD)
Serum sodium(meq/L)	141.4 (6.5)	142.7 (5.9)
Serum potassium(meq/L)	5.0 (0.9)	3.6 (1.0)
Serum magnesium(meqlL)	2.1 (0.6)	1.6 (0.4)
Serum calcium(mg/dl)	8.0 (1.0)	8.6 (0.6)
Serum Bicarbonate(mg/dl)	12.6 (4.6)	17.7 (3.5)
Serum urea(mg/dl)	108.9 (29.6)	37.8 (15.4)
Serum Creatinine (mg/dl)	8.2 (2.4)	3.3 (1.2)
Blood sugar level(mg/dl)	157.3 (82.1)	139.7 (51.6)
Serum Albumin(g/dl)	3.9 (0.43)	4.3 (0.5)
Blood pressure (mmHg) Systolic Diastolic	153.9 (21) 77.9 (12)	144.5 (22.8) 73.7 (13.8)
Heart rate (beats/min)	83.4 (13.3)	87.8 (14)
Weight (Kg)	68.4 (19.5)	66.1 (19.3)

Table No.3: Mean values of QTc interval duration and QTD before and after hemodialysis (msec)

	Before hemodialysis	After hemodialysis
QTc interval max	538.7 (49.1)	574.2 (62)
QTD	77.03 (40.7)	107.5 (53.1)
QTcD	89.3 (44.2)	126.5 (56.7)

Table No.4: Percentage of patients having Post dialysis prolonged QTD

Diabetic	35.5%
Non-diabetic	39.7%
Hypertensive	67.6%
Non-hypertensive	7.4%
IHD	19.1%
Non-IHD	55.4%
LVH by Framingham criteria	39.7%
Non-LVH	35.3%

DISCUSSION

This study showed that QTc and QTc dispersion are higher in hemodialysis patients, and rose significantly in post-dialysis period. Similar results are seen in different previous studies[18,19]. On the other hand, a study done by Covic et al demonstrated that hemodialysis lead to the prolongation of corrected QT interval but no effect seen on corrected QTD in patients with end stage renal disease[17]. Such higher levels of QT

dispersion are seen following acute myocardial infarction when patients are at highest risk of potentially fatal ventricular arrhythmias[20]. Therefore, these results suggest that patients on dialysis are at higher risk of ventricular arrhythmias, especially in the immediate post-dialysis period. Holter monitoring has also documented increased incidence of ventricular arrhythmias among hemodialysis patients[21].

As we already know that, the QT interval is influenced by changes in serum electrolytes, cations and anions. So, we attempted to check the effect of these variables on changes in QTc dispersion. In our study, serum potassium and magnesium were main determinants of QTD interval in pre-dialysis period with p-value of <0.05. On the other hand, serum bicarbonate was an independent predictor of the QT dispersion during immediate post-dialysis period. However, rest of the plasma variable didn't show any significant relationship with QTc dispersion. However, in previous studies inverse relationship seen between QTc dispersion and serum potassium and serum calcium levels, but no correlation found with serum magnesium levels and serum bicarbonate levels[17,22,23,24]. This can be due to the fact that the serum bicarbonate level could be influenced by the bicarbonate-based dialysate fluid in our study. So, additional studies are therefore needed with direct measurement of PH and varied composition of bicarbonate in dialysate, to determine this association in more detail.

Another factor which was found significant determinant of increased QT dispersion was presence of LVH by voltage criteria. There is high prevalence of LVH in dialysis dependent patient as seen in previous studies[10,25] and confirmed in this study by voltage criteria.

The main limitations in our study were small sample size and varying composition of bicarbonate based dialysate solution. Therefore, further studies are needed with larger sample size and standardized dialysate solution to mask its effect on results.

CONCLUSION

This study showed that QTcmax and QT dispersion are elevated in hemodialysis patients, and rose further during post-dialysis period. We found significant association with changes in serum potassium and magnesium, changes in acid-base status and presence of LVH. As this elevated QTc dispersion is linked to increase risk of malignant ventricular arrhythmia, therefore, In future, QT dispersion may prove a novel target for monitoring of hemodialysis patients to reduce mortality and risk of sudden death.

Author's Contribution:

Concept & Design of Study:	Shahid Anwar
Drafting:	Alvina Zanib
Data Analysis:	Shehzad Tawab
Revisiting Critically:	Shahid Anwar, Alvina Zanib
Final Approval of version:	Shahid Anwar

Conflict of Interest: The study has no conflict of interest to declare by any author.

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