Original Article

Changes in QT interval before and after hemodialysis

Mohammad Reza Khosoosi Niaki (MD) [1]
Mehrdad Saravi (MD) [*1]
Farshid Oliaee (MD) [2]
Roghayeh Akbari (MD) [2]
Sepideh Noorkhomami (MD) [3]
Seyed Hassan Bozorgi Rad (BSc) [4]
Kobra Fallahpoor (BSc) [4]
Mir Saeed Ramezani (MD) [3]

1- Department of Cardiology, Babol University of Medical Sciences, Babol, Iran.
2- Department of Internal Medicine, Babol University of Medical Sciences, Babol, Iran.
3- Babol University of Medical Sciences, Babol, Iran
4- Shahid Beheshti Hospital, Babol University of Medical Sciences, Babol, Iran

*** Correspondence:** Mehrdad Saravi, Department of Cardiology, Babol University of Medical Sciences, Babol, Iran.
Postal Code: 47135-434

E-mail: msaravi1967@aol.com
Tel: 0098 111 2196633
Fax: 0098 111 2198833

Received: 18 July 2012
Revised: 13 Nov 2012
Accepted: 20 Nov 2012

Abstract

Background: Cardiovascular mortality and morbidity are high in chronic renal failure (CRF) patients. Increased dispersion of QT intervals is known to predispose to ventricular arrhythmias and sudden cardiac death. This study was conducted to assess the effect of hemodialysis (HD) on corrected QT (QTc) intervals and their dispersions (QTd) in chronic hemodialyzed patients.

Methods: Fifty-eight patients (mean age 54.2±15.8 years) with chronic renal disease on chronic hemodialysis (HD) were assessed by standard examination including blood pressure, body weight, heart rate, 12–lead electrocardiography and laboratory tests like electrolytes (Na^+, K^+, Ca^{++}, phosphate), urea, and creatinine 30 minutes before and after HD. The QT intervals and QTc QTc= QT $\sqrt{R\text{-}R}$ (in milli seconds [ms]) for each lead were measured manually by one observer using calipers. The difference between the maximum and the minimum of QT interval was noted as QT dispersion (QT d).

Results: The mean of pre and post dialysis R-R intervals was 859.22±96.85 ms and 870.43±91.45 ms, respectively ($p>0.05$). The mean of corrected QT_{cmax} intervals increased significantly from 423.45±24.10 to 454.41±30.25 ms ($p<0.05$). The mean of QT dispersions and the corrected QT interval dispersions changed from 51.56±12.45 to 63.21±14.43 ms ($p<0.05$) from 59.40±13.58 to 68.33±14.55 ms ($p<0.05$), respectively. The changes in serum potassium and calcium levels were related with QT interval prolongation.

Conclusion: QT and QTc interval and dispersion increase in HD patients. Prolonged QT interval indices had relation with K^+ and Ca^{++} ions before but not after HD.

Keywords: Chronic renal disease, Hemodialysis, QT interval, Arrhythmia

Caspian J Intern Med 2013; 4(1): 590-594

Cardiovascular diseases represent the main causes of death (especially sudden cardiac death) in patients affected by renal failure and chronic hemodialysis (1, 2). The reasons for great incidences of arrhythmia and death are complex and multifactorial (3). Dialytic treatment per se can be considered as an arrhythmogenic stimulus, moreover, uremic patients are characterized by a pro-arrhythmic substrate because of the high prevalence of ischaemic heart disease, left ventricular hypertrophy and autonomic neuropathy, myocardial dysfunction, changes in electrolyte concentration like calcium and potassium (1, 4-8). Among the noninvasive techniques which can be useful for predicting the patients at risk for sudden death is the measurement of QT interval changes with 12-lead surface electrocardiogram (9).

QT dispersion (QTd) defined as maximum QT interval minus minimum QT interval for a given set of electrocardiogram lead, was proposed as an approximation for repolarization abnormalities and measured for regional heterogeneity of myocardial refractoriness (10, 11). Prognostic value of QTd was evaluated in patients with end stage renal disease patients requiring hemodialysis and in patients with diabetes mellitus (12). The purpose of this study was to assess the effect of hemodialysis (HD) on QT and corrected QT (QTc) intervals and dispersion.

Methods

Sixty-two patients with chronic renal disease (mean age 54.2±15.8 years) attending a routine midweek HD session were enrolled in this study. All patients were receiving thrice weekly bicarbonate based HD sessions lasting between 3.5 and 4 hours, using polysulfone capillaries and bicarbonate dialysate containing 138 Na^+, 2.0 K^+, 1.75 Ca^{++}, and 0.5 Mg^{++} mmol/l. The duration of HD therapy ranged from 14 to 126 months (mean 31±20 months). All HD sessions were uncomplicated.

The exclusion criteria were patients with pacemaker, bundle branch block, atrial fibrillation, unmeasurable T waves, antiarrhythmic drugs that lengthen the QT interval. Informed consent was obtained from all the participants. The study was approved by Babol University of Medical Sciences. Thirty minutes before and after HD, the body weight and 12-leads standard ECG were recorded using a Mortara instrument ELI 250, sequence 02010, (USA) electrocardiograph at paper speed of 25 mm/s and 50 mm/s and 10 mm/mV, 0.05-40 Hz, and a blood specimen was drawn to measure plasma electrolytes, hemoglobin (Hb) and hematocrit (Ht).

In addition to the fluid volume removed (FVR) by HD, the estimated fluid volume loss (FVL) was calculated by subtracting 500 cc from the FVR to account for the patients' oral intake during HD. The ECGs were performed with the patients lying comfortably in the supine position and to ensure reproducibility of the ECGs before and after HD, and the V1-V6 leads were obtained from fixed chest landmarks made, using a skin marker. The QT intervals for each lead were measured manually with a caliper by one observer from the onset of the QRS complex to the end of the T wave. When T waves were inverted, the end was taken at the point where the trace returned to the T-P baseline.

However, when U waves were present, the end of the T wave was taken as the nadir between the T and U waves. If the end of the T wave was not clear in a particular lead then it was excluded from analysis. Each QT interval was corrected for heart rate using Bazett's formula: QTc= QT $\sqrt{R-R}$ (ms), where QTc is the corrected QT interval. QT and QTc dispersions were defined as differences between the minimal and maximal QT and QTc values in each of the 12-leads. To evaluate intraobserver variability in QTc interval and QTd measurements, the ECGs of 20 patients, chosen randomly, were analyzed by a single observer on 2 different occasions. There were no significant differences in QTc interval (412±28 ms vs. 411±31 ms) between the two readings. For greater accuracy, all measurements were performed after scanning the documents and evaluating them with software of Picasa 3.

Statistical analysis: Statistical analysis was performed using SPSS version 16. The means and standard deviations (SD) of all variables were calculated. The relationship of the mean of differences between intervals and dispersions in groups (pre-HD and post-HD) and differences among subgroups (ischemic heart disease, hypertension, gender, and diabetes) were analyzed using ANOVA. Analysis employed the student's t-test for paired data to determine the significance of differences. Univariate correlation coefficients were examined to assess the effects of electrolyte, BP changes, and QT dispersion, $p<0.05$ was considered statistically significant.

Results

The mean age of these 58 patients (29 males, 29 females) was 54.2±15.8 years. Hypertension, diabetes mellitus and glomerulonephritis were seen in 19, 16 and 11 cases, respectively. Obstructive, polycystic renal disease, vesico-uretral reflux and unknown etiology were seen in 2, 3, 1 and 6 cases respectively. The mean kilogram weight loss during hemodialysis, ultrafiltration, ultrafiltration rate (UFR) and hemodialisis Coefficent (KT/V) were 3.02±1.1kg, 2.5±0.7, 0.63±0.06 and 1.25±0.19, respectively. There were no significant differences between the RR intervals (859±97 ms pre-HD vs. 870±91 ms post-HD; $p>0.05$). The maximal QT interval had no significant change from 453±21.23 to 464±26.29 ms ($p>0.05$). The QTc dispersion increases from 59.40±13.58 ms before HD (QTc max=433.45±24.10 ms, QTc min=382.1±21.1 ms) to 68.33±14.55 ms after HD (QTc max=464.41±30.25 ms, QTc min=398.3±25.9 ms). Due to hemodialysis, the mean of serum potassium levels decreased from 5.09±0.7 to 3.96±0.54 mML and the mean of phosphate levels from 6.42±1.39 to 4.37±1.08 mg/L ($p<0.05$), and the mean of calcium levels decreased from 7.34±0.9 to 7.72±0.6 ($p<0.05$). Whereas, the mean of serum sodium levels increased insignificantly from 138.80±1.81 to 139.03±2.41 mML (table 1). In multiple regression analysis, where the changes in calcium, phosphate, sodium, potassium, magnesium, creatinin, urea, age, sex, ejection fraction, and diastolic blood pressure were independent variables, no correlations could be found between any of

them and change in QTc-d after HD. But in fact, potassium and calcium plasma levels appeared to be the main determinants of QTc duration pre-dialysis. After HD, changes in serum sodium and ionized calcium were seen but they were not significant. As a result of the comparison of different subgroups in multiple regression analysis, it was found that the increase of QTc and QTcd intervals after HD was independent of gender and hypertension. However, the QTc, QTd, and QTcd intervals were significantly increased in the pre and post HD in diabetic patients (table 2).

Table 1. The results of the measured variables before and after hemodialysis

Variable	Pre-HD (Mean±SD)	Post-HD (Mean±SD)	p-value
Sodium (mM/L)	138.79±1.81	139.03±2.41	0.295
Potassium (mM/L)	5.09±0.70	3.96±0.54	0.000
Calcium (mg/L)	7.34±0.90	7.72±0.60	0.001
Phosphate (mg/L)	6.42±1.39	4.37±1.08	0.000
Magnesium (mg/L)	2.04±0.15	1.96±0.14	0.000
Hemoglobin (g/dL)	9.51±1.62	10.01±1.98	0.024
Hematocrit (%)	29.90±4.81	31.43±4.90	0.001
Urea (g/l)	59.88±9.50	21.97±4.81	0.000
Creatinin (mg/dl)	5.44±1.22	2.58±0.72	0.000
Systolic BP(mmHg)	146.38±22.08	144.40±22.69	0.037
Diastolic BP(mmHg)	90.26±6.58	87.07±6.35	0.000
Heart rate(beat/min)	81±11	83± 10	0.454
QT msec	408.13±15.35	453.30±14.30	0.035
QT max (msec)	453±21.23	464±26.9	0.343
QTc (msec)	394.13±12.45	443.15±19.20	0.018
QT cmax (msec)	433.45±24.10	464.41±30.25	0.000
QTd (ms)	51.56±12.45	63.21±14.43	0.04
QTcd (ms)	59.40±13.58	68.33±14.55	0.016
R-R (ms)	859.22±96.85	870.43±91.45	0.151

Table 2. The result of QTc interval and QTc dispersion in subgroups of study patients

	QTc Interval (ms)		QTc Dispersion (ms)	
Subgroup	Pre-HD (Mean±SD)	Post-HD (Mean±SD)	Pre-HD (Mean±SD)	Post-HD (Mean±SD)
Male (N=29)	395±21	411±26	41±10	59±14
Female (N=29)	410±22	426±27	45±15	64±15
Hypertensive(N=19)	439±19	449±27	49±14	61±13
Nonhypertensive(N=39)	425±21	438±23	44±11	58±15
Diabetes(N=16)	433±20	458±24	45±10	63±18
Non diabetes (N=42)	412±22	432±28	39±13	49±13

Discussion

There is a significant bidirectional association between chronic renal disease (CRD) and cardiovascular disease; CRD is an independent risk factor for cardiovascular disease and cardiovascular disease is a risk factor for CRD. Recent evidence similarly suggests that there are close relationships between arrhythmias and CRD (13). Ventricular arrhythmias

are frequently observed in patients undergoing hemodialysis. One of the most important pathogenetic elements involved in the onset of intra-dialytic arrhythmias is the alteration in electrolytes concentration, particularly calcium and potassium (1). In our patients, the levels of potassium and calcium were the main determinant of QTc before hemodialysis.

Abnormal and high risk range of QTc dispersion was 65 msec (5). Our study like the result of others study showed an increase of QTc dispersion post hemodialysis which might increase the risk of lethal ventricular arrhythmias (14). Because QT dispersion reflects a non-homogeneous recovery of ventricular excitability, the results suggest that dialysis patients may be at higher risk of reentrant arrhythmias, and that this risk rises in the immediate post dialysis period. The incidence of ventricular arrhythmias among HD patients has been shown to be elevated, which may be life threatening (15, 16).

Although their predictive power for mortality in the HD population has not yet been shown. The factors influencing QTc interval dispersion are the large amount of or rapid potassium removal, low calcium dialysate, intracellular magnesium overload, rapid bicarbonate gain and also patient with acute myocardial infarct, presence of ischemic heart disease, left ventricular hypertrophy in HD patients (5). In our study, the patients with diabetes mellitus had significantly longer QTc intervals and greater QTc dispersion in the pre and post HD, so this group of patients might be at higher risk for ventricular fibrillation and sudden cardiac death (SCD).

In diabetics, cardiac autonomic neuropathy is well known and is associated with QT prolongation and increased ventricular arrhythmogenicity, and is associated with the structural and functional properties of the myocardium (17). We conclude that QT indices increased in patients with chronic renal disease requiring HD. The prolongation of these parameters may be a further non-invasive marker of susceptibility to ventricular arrhythmias.

Acknowledgments

We thank to the nurses of the Dialysis Ward of Shahid Beheshti Hospital for cooperation.

Funding: self funded.
Conflict of interest: None declared.

References

1. Buemi M, Coppolini G, Bolignano D, et al. Arrhythmias and hemodialysis: role of potassium and new diagnostic tools. Ren Fail 2009; 31: 75-80.
2. Sniderman AD, Solhpour A, Alam A, Williams K, Sloand JA. Cardiovascular death in dialysis patients: lessons we can learn from AURORA. Clin J Am Soc Nephrol 2010; 5: 335-40.
3. Covic A, Diaconita M, Gusbeth-Tatomir P, et al. Haemodialysis increases QT(c) interval but not QT(c) dispersion in ESRD patients without manifest cardiac disease. Nephrol Dial Transplant 2002; 17: 2170-7.
4. Voroneanu L, Covic A. Arrhythmias in hemodialysis patients. J Nephrol 2009; 22: 716-25.
5. Wu VC, Lin LY, Wu KD. QT interval dispersion in dialysis patients Nephrology (Carlton) 2005; 10: 109-12.
6. Herzog CA, Mangrum JA, Passman R. sudden cardiac death and dialysis patients Seminars in Dialysis. Semin Dial 2008; 21: 300-7.
7. Cobo Sánchez JL, Alconero Camarero AR, Casaus Perez M, et al. Hyperkalaemia and haemodialysis patients: eletrocardiographic changes. J Ren Care 2007; 33: 124-9.
8. Drighil A, Madias JE, El Mosalami H, et al. Determinants of augmentation of ECG QRS complexes and R waves in patients after hemodialysis. Ann Noninvasive Electrocardiol 2007; 12: 111-20.
9. Crişu D. Sudden death and ventricular arrhythmias risk stratification after myocardial infarction. Rev Med Chir Soc Med Nat Iasi 2010; 114: 13-9. [In Romanian]
10. Di Iorio B. Relevance of QT dispersion in haemodialysis patients. Nephrol Dial Transplant 2010; 25: 1357-9.
11. Murasawa T, Sakai Y, Sakai S, et al. QT dispersion increases during hemodialysis procedures in patients undergoing maintenance dialysis: association with an RA system and holter electrocardiogram. Nihon Jinzo Gakkai Shi 2008; 50: 481-7. [In Japanese]
12. Garadah TS, Kassab S, Mahdi N, Abu-Taleb A, Jamsheer A. QTc Interval and QT Dispersion in Patients with Thalassemia Major: Electrocardiographic (EKG) and Echocardiographic Evaluation. Clin Med Insights Cardiol 2010; 4: 31-7.
13. Watanabe H, Watanabe T, Sasaki S, et al. Close bidirectional relationship between chronic kidney disease and atrial fibrillation: the Niigata preventive medicine study. Am Heart J 2009; 158: 629-36.

14. Malhis M, Al-Bitar S, Farhood S, Zaiat KA. Changes in QT intervals in patients with end-stage renal disease before and after hemodialysis. Saudi J Kidney Dis Transpl 2010; 21: 460-5.
15. Zareba W. Dispersion of repolarization: Time to move beyond QT dispersion. Ann Noninvasive Electrocardiol 2000; 5: 373-81.
16. Zabel M, Portnoy S, Franz MR. Electrocardiographic indexes of dispersion of ventricular repolarization: An isolated heart validation study. J Am Coll Cardiol 1995; 25: 746-52.
17. Voulgari C, Moyssakis I, Perrea D, et al. The association between the spatial QRS-T angle with cardiac autonomic neuropathy in subjects with Type 2 diabetes mellitus. Diabet Med 2010; 27: 1420-9