The Comparison of Four Different Dialysates on QT Dispersion and Arrhythmias in Hemodialysis Patients

Hemodiyaliz Hastalarında Dört Farklı Diyalizat Kullanımının QT Dispersiyonu ve Aritmiler Üzerine Etkisi

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ABSTRACT

OBJECTIVES: Sudden cardiac death (SCD) is common in patients with end-stage renal disease receiving hemodialysis. SCD may be caused by electrolyte imbalance or malignant arrhythmias in hemodialysis patients. We aimed to evaluate the effects of four different dialysates on QT dispersion and arrhythmia.

MATERIAL and METHODS: Twenty-one patients receiving hemodialysis were enrolled. Four different dialysates were used and twelve-lead ECG measurements were recorded to determine QTc and QTc dispersion. Holter ECG was performed to assess arrhythmia.

RESULTS: In group 1 (1.0 K +, 1.5 Ca++), predialytic and postdialytic QTc dispersion measurements were 52.3±11.7 and 59.2± 13.1 msec respectively and this is statistically significant (p=0.007). In group 2 (2.0 K +, 1.5 Ca++), group 3 (1.0K +, 1.75Ca++), and in group 4 (2.0 K +, 1.75Ca++), QTc dispersion measurements were 53.5±14.4 and 53.2± 15.0 msec, 53.5±14.4 and 53.2±15.0 msec, 50.8±12.0 and 52.2±13.3 msec, 51.3±12.2 and 52.1±12.3 msec, respectively, and these were not statistically significant.

CONCLUSION: In group 1, patients had higher QTc dispersion. There was no statistically significant difference regarding QTc dispersion among the four groups. We also could not find an increased rate of arrhythmias in the groups. These results suggest that there may be other causative risk factors that can affect QT dispersion and arrhythmias in hemodialysis patients.

KEY WORDS: Hemodialysis, QT dispersion, Arrhythmia

ÖZ

AMAÇ: Ani kardiyak ölüm (AKÖ) hemodiyaliz hastalarında sık görülen bir durumdur. Günümüzde AKÖ nedenleri genellikle elektrolit imbalansına ve malign aritmilere ikincil olarak gelişmektedir. Bu nedenle çalışmamızda dört farklı eletrolit içeriğine sahip diyalizatın, QTc dispersiyonu ve intradiyalitik aritmi üzerine etkisini araştırmayı amaçladık.

GEREÇ ve YÖNTEMLER: Çalışmamızda 21 hemodiyaliz hastasında bir hafta arayla dört farklı diyalizat kullanılarak diyaliz öncesi ve sonrasında 12 derivasyonlu EKG çekilerek ve intradiyalitik Holter EKG kaydedilmek suretiyle QTc dispersiyonu ve aritmi gelişimi değerlendirildi.

SONUÇLAR: Hastalar kullanılan diyalizatın elektrolit içeriğine göre 4 farklı gruba ayrıldılar. Grup 1'de (mM/L olarak 1,0 K^+, 1,5 Ca^{++}) prediyalitik ve postdialitik QTc ölçümleri sırasıyla 52,3±11.7 and 59,2± 13,1 msn saptandı (p=0,007). Grup 2 (2,0 K^+, 1,5 Ca^{++}), grup 3 1,0 K^+, 1,75 Ca^{++}) ve grup 4 (2,0 K^+, 1,75 Ca^{++}), QTc ölçümleri sırasıyla 53,5±14,4 ve 53,2±15,0 msn, 53,5±14,4 ve 53,2± 15,0 msn, 50,8±12.,0 ve 52,2± 13.3 msn, 51,3±12,2 ve 52,1± 12,3 msn olarak tespit edildi.

TARTIŞMA: Düşük potasyum ve kalsiyum içeriğine sahip diyalizatla hemodiyalize alınan grup 1'de diyaliz sonrası QTc dispersiyonu daha yüksek bulundu. 4 grup arasında QTc dispersiyonu açısından fark yoktu. Supraventriküler ve ventriküler aritmi riski artışı tespit edilmedi. Bu sonuçlar bize hemodiyaliz hastalarında QTc dispersiyonu ve intradiyalitik aritmi üzerine sadece diyalizat elektrolit içeriğinin değil, başka faktörlerin de etkili olabileceğini düşündürmektedir.

ANAHTAR SÖZCÜKLER: Hemodiyaliz, QT dispersiyonu, Aritmiler

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INTRODUCTION

Cardiovascular complications including coronary artery disease, congestive heart failure and sudden cardiac death (SCD) constitute a high percentage of mortality in patients with end-stage renal disease (ESRD) receiving renal replacement therapy (1-2). Although the mechanisms responsible for the increased risk of SCD could be attributed to electrolyte imbalance or malignant arrhythmias in hemodialysis (HD) patients (3), the whole scenario is not clear because of complex characteristics of ventricular myocardium physiology. The prolonged QT interval has been reported to be associated with arrhythmogenesis in many cardiac diseases (4-5). QT dispersion, that is calculated by subtraction of the maximum QT interval from the minimum QT interval on standard 12-lead electrocardiogram (ECG), predicts mortality both in patients with high risk of CVD (3-4) and in ESRD patients receiving HD (6-7). In the literature there are conflicting results about the effects of different dialysate solutions on QT dispersion in different studies (6-9). However, to date, none of the studies compared different dialysates effect on QT dispersion and arrhythmias in ESRD patients **in the same study**. Therefore, we aimed to evaluate the effects of four different dialysate solutions on QT dispersion and intradialytic arrhythmias assessing by ECG in the pre and post dialysis period and by holter monitoring in the intradialytic period, respectively.

MATERIALS and METHODS

PATIENTS

This study was designed as a prospective study including maintenance hemodialysis patients from Hemodialysis Unit of Selcuk University Meram School of Medicine, Konya, Turkey. The hemodialysis modality included conventional 4-hour hemodialysis thrice a week with 1.6 m^2 hemophan dialysers (Bellco 1608). A 250 ml/min (range 200-300 ml/min) of mean blood flow and 500 ml/min dialysate flow rate were obtained during hemodialysis sessions. Of the 36 patients, 4 refused to participate, 3 were excluded because of congestive heart failure, 5 had bundle branch block and 3 had atrial fibrillation. The remaining 21 patients (16 women, 5 men, mean age 42.9±16.9 years, mean HD time 39±32 months) receiving HD thrice a week. The causes of chronic kidney disease were as follows: chronic glomerulonephritis (n=11), autosomal dominant polycystic kidney disease (n=3), obstructive uropathy (n=2), amyloidosis (n=1), chronic pyelonephritis (n=1) and unknown etiology (n=3).

Four different dialysates with standard bicarbonate were used for only one session and all of the patients received each dialysate solution separately. There was one week between the sessions. The ingredients of the solutions were as follows: solution 1 containing (in mMol/L) 140 Na^+, 1.0 K^+, 1.5 Ca^{++},0.5 Mg^{++} 110 Cl^-, 33 HCO_3^-; solution 2 containing (in mMol/L) 140 Na^+, 2.0 K^+, 1.5 Ca^{++}, 0.5 Mg^{++} 110 Cl^-, 33 HCO_3^- ; solution 3 containing (in mMol/L) 140 Na^+, 1.0 K^+, 1.75 Ca^{++}, 0.5 Mg^{++}, 110 Cl^-, 33 HCO_3^-; and solution 4 containing (in mMol/L) 140 Na^+, 2.0 K^+, 1.75 Ca^{++}, 0.5 Mg^{++}, 110 Cl^-, 33 HCO_3^-. During hemodialysis sessions, no drug therapy was administered except isotonic NaCl for washing the tubes and heparin sodium for anticoagulation. Serum creatinine, blood urea nitrogen, serum Na^+, Ca^{++}, Mg^{++} and phosphorus were studied before and after hemodialysis.

Methods of Measurement of QT/QTc Interval, and QT / QTc Dispersion

Twelve-lead ECG measurements of the patients were recorded at 10 mm/mv and 50 mm/s (using a Hewlett-Packard page writer 200i) after a five-minute resting period in the supine position. Measurements of QT and QTc intervals were obtained fifteen minutes before and after HD sessions. For the analysis of the QT interval, the 12-lead ECG was scanned and enlarged by a factor of two. Three consecutive cardiac cycles were measured and the average of these numbers were obtained. The QT intervals for each lead were measured manually with calipers by two blinded observers. The QT interval was measured from the onset of the QRS complex to the end of the T wave. If the T wave could not be defined, the ECG was not included in the analysis and the recording was performed again. When the U wave was determined, the end of the T wave was taken as a nadir between the T and U waves. Each QT interval value was corrected for patient heart rate using Bazett's formula: $QTc = QT/\sqrt{RR}$ (ms) (10).

QT dispersion was calculated by subtraction of the maximum QT interval from the minimum QT interval on standard 12-lead ECG (11). Interobserver variability was 12% for the measurements of QT dispersion.

Holter Monitoring

Holter ECG monitoring was recorded for 4 hours during hemodialysis to assess supraventricular or ventricular arrhythmias by HolterWin-P-V Ver 5.40.

Statistical Analysis

Data were expressed as mean ± SD. Wilcoxon Signed Ranks has been used for comparisons. In addition, Friedman test was used for multiple calculations. Post Hoc Bonferroni corrected Wilcoxon Signed Ranks was used for comparison of significant variables. $p < 0.05$ was considered significant. Statistical analysis was performed by using SPSS ver. 11.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

The demographic and laboratory features of the patients are shown in Table I. The course of various laboratory parameters in predialysis and postdialysis periods in patients dialyzed by various dialysates are provided in Table II. In group 1 (dialysate containing (in mMol/L), 1.0 K^+, 1.5 Ca^{++}); during hemodialysis serum potassium levels were decreased from 4.9±0.7 to

3.9±0.5 mEq/L (p<0.0001), phosphorus levels from 4,4±1.0 to 3.1±0.9 mg/dL (p<0.0001) and magnesium levels from 2.7±0.5 to 2.5±0.8 mg/dL (p=0.021), whereas calcium levels were increased to 8.5±1.0 to 9.6±1.0 mg/dL (p=0.001). Predialytic and postdialytic QTc dispersion measurements were 52.3±11.7 and 59.2± 13.1 msec, and these were statistically significant (p=0.007). However predialytic and postdialytic QTc intervals were 580±34 and 588±38 msec, respectively and there was no statistically significant difference.

In group 2 (dialysate containing (in mMol/L), 2.0 K^+, 1.5 Ca^{++}); during hemodialysis serum potassium levels were decreased from 4.9±0.6 to 4.1±0.4 mEq/L (p<0.0001), phosphorus levels from 4,2±1.0 to 2.9±0.8 mg/dL (p<0.0001) and magnesium levels from 2.5±0.6 to 2.2±0.5 mg/dL (p=0.019), whereas calcium levels were increased to 8,8±1.1 to 9.7±1.2 mg/dL (p=0.008). Predialytic and postdialytic QTc dispersion measurements were 53.5±14.4 and 53.2± 15.0 msec, respectively, and these are not statistically significant. Predialytic and postdialytic QTc intervals were 585±26 and 579±40 msec, respectively and there was no statistically significant difference.

In group 3 (dialysate containing (in mMol/L), 1.0 K^+, 1.75 Ca^{++}); during hemodialysis serum potassium levels were decreased from 5.0±0.6 to 3.9±0.4 mEq/L (p<0.0001), phosphorus levels from 4.5±1.4 to 3.7±1.3 mg/dL (p=0.035) and magnesium levels from 2.8±0.7 to 2.6±0.8 mg/dL (p=NS). Serum calcium levels were increased to 9.8±1.5 to 11.1±0.8 mg/dL (p=0.004). Predialytic and postdialytic QTc dispersion measurements were 50.8±12.0 and 52.2± 13.3 msec, respectively, and these are not statistically significant. Predialytic and postdialytic QTc intervals were 581±37.7 and 586±33.5 msec, respectively and there was no statistically significant difference.

In group 4 (dialysate containing (in mMol/L), 2.0 K^+, 1.75 Ca^{++}); during hemodialysis serum potassium levels were decreased from 5.0±0.6 to 4.1±0.6 mEq/L (p<0.0001), phosphorus levels from 5.1±1.6 to 3.0±1.0 mg/dL (p<0.001) and magnesium levels from 2.7±0.9 to 2.5±0.9 mg/dL (p=0.005) whereas serum calcium levels were increased to 9.6±1.1 to 11.0±1.1 mg/dL (p<0.001). Predialytic and postdialytic QTc dispersion measurements were 51.3±12.2 and 52.1± 12.3 msec, respectively, that is not statistically significant. However predialytic and postdialytic QTc intervals were 573.6±33.5 and 583.4±29.4 msec, respectively and there results were statistically significant (p=0.04).

Table I: The demographic and laboratory features of the patients.

Parameters	Hemodialysis Patients (n=21)
Age (year)	42.9±16.9
Male/Female (n)	16/5
Dialysis Vintage (month)	39.3±32.7
SBP (mmHg)	128±21
DBP (mmHg)	77±10
Kt/v	2,1±0,6
Hemoglobin (g/dl)	10.9 ± 1.56
Calcium (mg/dl)	8,8±0,5
Phosphorus (mg/dl)	4,6±1,3
iPTH (pg/ml)	181±52
Total Cholesterol (mg/dl)	156±39
Triglyseride (mg/dl)	154±23
Albumin (g/dl)	3,9±0,3

DISCUSSION

In the present study, we examined the effects of four different dialysates comprising varying potassium and calcium content on arrhytmogenesis during hemodialysis in ESRD patients. In group 1, patients receiving hemodialysis with low potassium and calcium containing dialysate had higher QTc dispersion than the other patients in other groups in the postdialytic period. However, there was no statistically significant difference regarding QTc dispersion among the four groups. We also could not find an increased rate of arrhythmia including ventricular extrabeats and supraventricular tachyarrhythmias by assessment with Holter monitoring in the intradialytic period in any group that was enrolled in the study.

Our results in terms of QTc dispersion were not consistent with findings of previous studies (6,7). Morris et al. (6) showed that QTc max and QTc dispersion were significantly higher in HD patients when compared with healthy subjects. These high scores increase in the postdialysis period. However, in this study they did not mention the composition of the dialyste used in HD patients and the absolute changes in electrolyte values during dialysis did not correlate with the changes in QT dispersion. Therefore, Morris et al. concluded that the changes in QTc dispersion could be attributed to other factors rather than changes in electrolyte compositions (6).

The other study regarding QTc dispersion in HD patients receiving bicarbonate dialysate containing (in mM) 135 Na^+, 2.0 K^+, 1.5 Ca^{++}, and 1.0 Mg^{++}, also demonstrated that QTc and QTC dispersion was increased in postdialysis period (7). The dialysate used in this study was similar with our study group 2 except Na^+ and Mg^{++} composition (Table II). However, we could not find a statistically significant difference regarding QTc when comparing the predialysis and postdialysis periods.

The relationship between QT dispersion and arrhythmogenesis in ESRD patients remains unclear. There are several factors including uremic autonomic neuropathy (12), ventricular dilation and fibrosis secondary to increased PTH levels (13),

Table II: Various laboratory parameters in the predialysis and postdialysis periods in patients dialyzed by various dialysates.

	Group 1 (1.0 K^+, 1.5 Ca^{++})	Group 2 (2.0 K^+, 1.5 Ca^{++})	Group 3 (1.0 K^+, 1.75 Ca^{++})	Group 4 (2.0 K^+, 1.75 Ca^{++})	p-value
Urea (mg/dL)					
Predialysis	126±26	122±23	127±23	126±29	NS
Postdialysis	50±25	43±19	43±15	41±15	NS
Creatinine (mg/dL)					
Predialysis	6.2±1.6	6.9±2.3	5.9±0.9	6.2±1.2	NS
Postdialysis	3.0±1.4	2.9±1.3	2.8±1.2	2.4±0.7	NS
Potassium (mEq/L)					
Predialysis	4.9±0.7	4.9±0.6	5.0±0.6	5.0±0.6	NS
Postdialysis	3.9±0.5	4.1±0.4	3.9±0.4	4.1±0.6	NS
Calcium (mg/dL)					
Predialysis	8.5±1.0[a]	8.8±1.1[b]	9.8±1.5	9.6±1.1	0.0001
Postdialysis	9.6±1.0[c]	9.7±1.2[d]	11.1±0.8	11.0±1.1	0.0001
Magnesium (mg/dL)					
Predialysis	2.7±0.5	2.5±0.6	2.8±0.7	2.7±0.9	
Postdialysis	2.5±0.8	2.2±0.5	2.6±0.8	2.5±0.9	NS
Phosphorus (mg/dL)					
Predialysis	4.4±1.0	4.2±1.0	4.5±1.4	5.1±1.6	NS
Postdialysis	3.1±0.9	2.9±0.8	3.7±1.4[e]	3.0±1.0	0.010
SBP (mmHg)					
Predialysis	133±23	126±20	73±13	76±15	NS
Postdialysis	75±11	72±12	72±12	73±10	NS
DBP (mmHg)					
Predialysis	78±8.9	76±9.8	73±13.2	76±14.7	NS
Postdialysis	75±11.1	72±12.1	72±12.1	73±9.8	NS
QTc dispersion (msn)					
Predialysis	52.3±11.7	53.5±14.4	50.8±12.0	51.3±12.2	NS
Postdialysis	59.2±13.1	53.2±15.0	52.2±13.3	52.1±12.3	NS
Weight (kg)					
Predialysis	59.8±15.3	60.1±15.3	60.4±14.5	60.3±14.7	NS
Postdialysis	57.8±14.8	58.2±14.7	58.6±14.4	58.6±14.6	NS
Ultrafiltration (L/4 hr)	1.97±1.1	1.91±1.1	1.84±1.0	1.76±1.0	NS
Total VEB (beat/4hr)	24.2±55.2	10±26.9	39.6±105.2	3.0±10.4	NS
Total SVT (beat/4hr)	14.3±37.9	20.1±60.9	71.7±296.6	33.9±123.3	NS
Total arrhythmia (%)	0.22±0.3	0.22±0.4	0.84±2.1	0.21±0.6	NS

NS; Not significant, **VEB;** ventricular extrabeat, **SVT;** supraventricular tacchyarrhythmia
a; predialysis Ca level in group 1 was statistically significant when compared with group 3 and 4 (p= 0.0001),
b; predialysis Ca level in group 2 was statistically significant when compared with group 3 (p= 0.0001),
c; postdialysis Ca level in group 1 was statistically significant when compared with group 3 and 4 (p= 0.0001),
d; postdialysis Ca level in group 2 was statistically significant when compared with group 3 and 4 (p= 0.0001),
e; postdialysis phosphorus level in group 3 was statistically significant when compared with group 2 and 4 (p= 0.0001).

impaired cardiac performance (14), serum K^+ ,Mg^{++} and Ca^{++} levels (15-17), and rapid correction of metabolic acidosis (18) that can influence the occurrence of arrhythmogenesis in ESRD patients.

There are some limitations that deserve mention in our study. First, the number of ESRD patients enrolled in our study was relatively small. Second, single four-hour hemodialysis sessions may have missed out some extrabeats that can influence the results. Nonetheless, we demonstrated that there were no difference about ectopic beats during dialysis sessions with four different dialysates. Third, manual determination of QTc is prone to error. However, ECG recordings were evaluated by two blinded experienced cardiologists to avoid bias.

In conclusion, the increased risk of arrhythmias depends on multiple abnormalities in ESRD patients. The changes of electrolyte composition during HD could not explain the whole scenario of arrhtyhmias seen in HD patients. Despite the easy way of measurement of QTc and QT dispersion, these measurements are not sufficient to assess the clinical arrhythmia risk stratification in uremic patients. Additional experimental and clinical studies are needed to clarify the etiopathogenesis of arrhythmias.

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