IJMS
Vol 34, No 1, March 2009

Original Article

The Effect of the Type of Hemodialysis Buffer on the QTc Interval in Patients on Chronic Hemodialysis

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Abstract

Background: Identifying the sources of variation in QTc measurements is important for preventing arrhythmias during and after hemodialysis. The present study was designed to determine the correlation between the type of hemodialysis buffer and the changes in QTc interval in patients on chronic hemodialysis.

Methods: Fifty-nine patients on chronic hemodialysis who referred in winter 2007 to hemodialysis centers of Ghaem and Hashemi Nejad hospitals, in Mashhad, Iran, were divided into two groups according to their last dialysate buffer: acetate or bicarbonate. Electrocardiography, arterial blood gas parameters, serum K^+, Na^+, ionized calcium, and albumin levels were measured prior to and after hemodialysis in all patients.

Results: All arterial blood gas parameters and serum electrolytes concentrations were increased except K^+ levels that were significantly decreased with hemodialysis. PCO_2 and QTc intervals were slightly increased in all patients, however this increase was not statistically significant. We found that the type of dialysate affected the QTc interval, HCO_3, base excess, base excess of extra cellular fluid, and base buffer changes with no effect on ionized calcium, pH, PCO_2, and serum albumin concentration. QTc interval was prolonged by using bicarbonate and shortened by using acetate dialysate buffer. We found no correlation between the variations of QTc interval and serum electrolytes or arterial blood gas parameters in either group.

Conclusion: Bicarbonate buffer use in hemodialysis prolonged QTc interval and acetate buffer shortened it. This effect is independent of serum electrolytes and pH changes during hemodialysis. The effect of bicarbonate buffer is probably due to more tolerability of ultra filtration, more effective edema reduction and augmented body electro-conductivity.
Iran J Med Sci 2009; 34(1): 29-35.

Keywords ● Chronic ● hemodialysis ● dialysate buffer

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Submitted: 8 April 2008
Revised: 2 November 2008
Accepted: 25 December 2008

Introduction

The risk of ventricular arrhythmias is known to increase during hemodialysis, however, the cause of this phenomenon has remained undetermined. Measurement of QTc and QTc dispersion is a simple bedside method

that can be used for analyzing ventricular repolarization during hemodialysis.[1]

Identifying the sources of variation in QTc measurements, most likely cardiac in origin, is critical in establishing the credibility and reliability of QTc changes that are used in defining and assessing cardiac risk.[2]

QT changes reflect heterogeneity of cardiac repolarization[1]. Hemodialysis is an intermittent procedure accompanied by significant shifts of fluid and electrolytes concentrations. The effects of the type of dialysate buffer on the QTc changes either directly or indirectly through fluid and electrolyte shift have been reported only in few studies. We seized the rare opportunity occurred by dialysate buffer change from acetate to bicarbonate in two hemodialysis centers to evaluate the effects of hemodialysis buffer type on the arterial blood gas (ABG) parameters and on the changes of QTc interval in patients on chronic hemodialysis.

Patients and Methods

Seventy-nine patients on chronic hemodialysis who were dialyzed three times per week during winter 2007 in hemodialysis centers of Ghaem and Hashemi Nejad hospitals, in Mashhad, Iran, were evaluated for entering the present study. The patients who excluded from the study were: patients with inadequate hemodialysis (urea reduction ratio less than 60%), patients taking antiarrhythmic drugs that affect the QTc interval, and patients with interventricular conduction defect or bundle branch block that prolong Qc interval. Urea reduction ratio (URR) was calculated as follows: 1 minus post hemodialysis urea/pre hemodialysis urea. To homogenize two study groups for demographic data and eliminate bias due to unequal proportion, 10 additional patients with diabetes mellitus with a history of ischemic heart diseases or hypertension and duration of hemodialysis less than 8 weeks were also excluded from the two groups (Data not shown). The remaining 59 patients who enrolled into the study consisted of 28 females and 31 males including 10 diabetic patients, 34 in bicarbonate group and 25 in acetate group. There was a discrepancy in gender distribution in two groups in favor of female in acetate group. Homogenization was not possible, because all the patients were going to be dialyzed by bicarbonate buffer (figure 1).

The mean age of patients was 49.6 ± 15.57 years. The mean duration of hemodialysis was 37 ± 30.85 months. The patients were divided into two groups based on the type of dialysate buffer used for the last hemodialysis session. We decided to measure QTc interval because it is easy to measure and does not require patient cooperation.[3] All the paraclinical tests including electrocardiography (ECG), ABG, and blood biochemistry for ionized calcium and serum albumin were taken prior to and within 20 minutes after termination of the hemodialysis process. Serum K^+ and Na^+ concentrations were measured by flame photometric method (SeacFP-20 Radim group company, Italy). Ionized calcium was measured by ion selective method (Cobas121 Roche Company Germany). Serum urea and albumin levels were measured by bromocresol green method.[3] Calcium and phosphor were measured spectrophotometrically by enzymatic method (Lyasis, Italy). All ABG parameters were

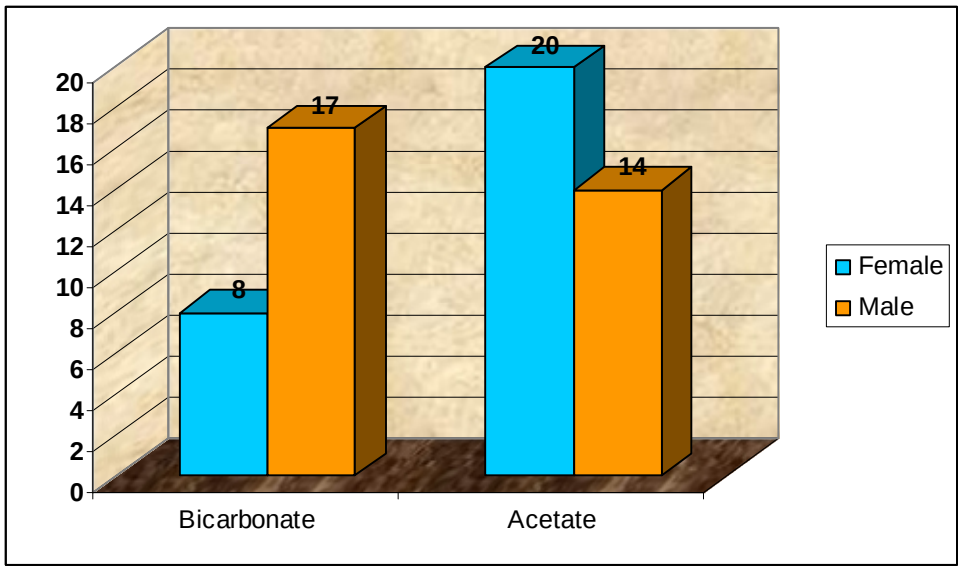

Figure 1: The comparative chart for gender and type of buffer

measured by AVL 995 ABG equipment (AVL995 ABG equipment. AVL9 USA) All patients were hemodialyzed using Feresnius 4008(f Feresnius Germany) hemodialysis machines using polysulfone hemodialysis filters with dialysate fluid concentration of K^+ = 2 mmol/lit, Na^+ = 135 mmol/lit, Ca^{++} = 1.25 mmol/lit, chloride = 111 mmol/lit, and bicarbonate =35 mEq/l for bicarbonate dialysis. QT intervals were measured manually by three different observers using an ECG ruler, and data entered into SPSS version 15. QT intervals were corrected by the root of RR interval according to Bazet's formula (QTc=QT/√R-R). Corrected QT intervals obtained by three observers were compared by ANOVA and did not show any significant differences. The mean of the three QTc interval measurements was analyzed.

Finally, the effect of dialysate buffer type (acetate or bicarbonate) on QTc intervals, serum ionized calcium, and ABG parameters was assessed by one–way ANOVA or by Kruskall-Wallis test as appropriate. Statistical analysis was performed by using paired-samples *t* test or Wilcoxon signed ranks test to compare variables before and after hemodialysis. Regression models were employed to study the correlation between QTc interval changes, and electrolytes concentrations and ABG parameters changes in the two groups.

Results

Descriptive statistics for study variables in all the patients, before and after hemodialysis, are shown in table 1. All of the parameters increased except serum K^+ concentration that decreased significantly with hemodialysis. PCO2 and QTc interval were also increased in all patients but not to a significant level. Obtained results according to the buffer type are shown in table 2. Serum K^+ concentration significantly reduced in both groups. All of the variables increased after hemodialysis in acetate group, except QTc interval which decreased. The same analysis in bicarbonate group showed somehow different results (table 2). In this group, all parameters increased significantly except serum K^+ concentration. The increment in PCO2 was not significant (P = 0.192).

The results of QTc intervals and the changes of laboratory parameters prior to and after hemodialysis are shown in table 3. The type of dialysate affected QTc interval, HCO_3, base excess, base excess of extra cellular fluid, and base buffer while ionized calcium concentration, pH, PCO_2, and serum albumin level remained unchanged. Correlations between the changes of QTc interval and ABG parameters, ionized calcium, and serum albumin level following hemodialysis are shown in table 4.

There was a negative correlation between

Table 1: Overall QTc and laboratory findings of patients in pre-dialysis and post-dialysis phases.

	Before dialysis (mean ± SD)	After dialysis (mean ± SD)	P value*
QTc (ms)	463 ± 57	467 ± 45	0.575
iCa (mg/dl)	2.44 ± 0.84	2.68 ± 1.14	0.013
K^+ (mEq/l)	5.3 ±0.56	3.36 ±0.41	0.021
Albumin (gr/dl)	4.43 ± 0.49	4.69 ± 0.83	0.006
pH	7.29 ± 0.07	7.35 ± 0.11	0.006
PCO2 (mm Hg)	34.06 ± 7.03	38.35 ± 15.78	0.202**
HCO3 (mEq/l)	16.32 ± 3.61	19.69 ± 4.26	<0.001
BE (mEq/l)	-8.79 ± 4.46	-4.74 ± 4.33	<0.001
BE ECF (mEq/l)	-9.01 ± 4.14	-4.96 ± 4.31	<0.001
BB (mEq/l)	38.96 ± 4.32	43.18 ± 4.37	<0.001

*Paired *t* test **Wilcoxon Signed Ranks test, iCa=ionized calcium, Pco2=pressure of dioxide carbon (Co2) gas, HCO3=Bicarbonate, BE=base excess, BE ECF= base excess of extra cellular fluid, BB=Base Buffer

Table 2: QTc and laboratory findings of patients in predialysis and postdialysis phases in both acetate and bicarbonate groups.

	Acetate			Bicarbonate		
	Before dialysis	After dialysis	P value*	Before dialysis	After dialysis	P value*
QTc	481 ± 73	465 ± 42	0.297	449 ± 38	469 ± 48	0.020
iCa	2.26 ± 0.86	2.48 ± 1.09	0.097	2.58 ± 0.81	2.85 ± 1.17	0.067
K^+	5.21±0.10	4.88±0.21	***0.025***	5.4±0.18	5.05±0.36	0.015
Albumin	4.37 ± 0.48	4.55 ± 0.79	0.228	4.48 ± 0.49	4.79 ± 0.86	0.011
PH	7.29 ± 0.08	7.32 ± 0.08	0.277	7.29 ± 0.07	7.37 ± 0.12	0.011
PCO2	32.74 ± 5.59	34.00 ± 8.67	0.515	35.58 ± 7.43	41.33 ± 19.28	0.192**
HCO3	15.63 ± 3.48	16.99 ± 3.09	0.163	16.80 ±3.68	21.58 ±3.97	<0.001
BE	-9.02 ± 4.84	-7.40 ± 3.69	0.218	-8.64 ± 4.26	-2.93 ± 3.80	<0.001
BE ECF	-9.56 ± 4.19	-7.83 ± 3.46	0.146	-8.64 ± 4.12	-3.00 ±3.72	<0.001
BB	38.52 ± 4.47	40.49 ± 3.71	0.134	39.26 ± 4.26	45.00 ±3.84	<0.001

*Paired *t* test **Wilcoxon Signed Ranks test, iCa=ionized calcium, Pco2=pressure of dioxide carbon (Co2) gas, HCO3=Bicarbonate, BE=base excess, BE ECF= base excess of extra cellular fluid, BB=Base Buffer

Table 3: Changes in QTc and laboratory parameters in predialysis and postdialysis phases in both acetate and bicarbonate groups.

	Acetate (mean ± SD)	Bicarbonate (mean ± SD)	P value*
QTc	16 ± 69	-19 ± 42	0.029
iCa	0.22 ± 0.61	0.26 ± 0.75	0.821
Albumin	0.18 ± 0.69	0.31 ± 0.65	0.475
PH	0.03 ± 0.12	0.08 ± 0.16	0.228
PCO2	1.27 ± 8.75	5.75 ± 19.35	0.621**
HCO3	1.36 ± 4.29	4.77 ± 3.95	0.005
BE	1.62 ± 5.83	5.71 ± 4.89	0.009
BE ECF	1.72 ± 5.23	5.64 ± 4.34	0.005
BB	1.96 ± 5.75	5.74 ± 4.92	0.014

* Independent samples *t* test ** Mann-Whitney test, iCa=ionized calcium, Pco2=pressure of dioxide carbon (Co2) gas, HCO3=Bicarbonate, BE=base excess, BE ECF= base excess of extra cellular fluid, BB=Base Buffer

Table 4: Correlation between QTc changes and the changes of ABG parameters, ionized calcium and albumin following hemodialysis.

	Overall		Acetate		Bicarbonate	
	Pearson r	P value*	Pearson r	P value*	Pearson r	P value*
iCa Changes	-0.017	0.914	0.003	0.990	-0.075	0.721
K^+ Changes	-0.370	0.146	-0.298	0.284	-0.348	0.198
Albumin Changes	-0.210	0.156	-0.129	0.600	-0.431	0.022
pH Changes	-0.308	0.047	-0.356	0.161	-0.366	0.072
PCO2 Changes	0.165	0.292	0.149	0.568	0.174	0.396
HCO3 Changes	-0.131	0.407	-0.331	0.195	-0.134	0.522
BE Changes	-0.189	0.225	-0.271	0.292	-0.274	0.176
BE ECF Changes	-0.202	0.194	-0.376	0.137	-0.225	0.27
BB Changes	-0.244	0.114	-0.392	0.120	-0.272	0.179

*Correlation is significant at the 0.05 level (2-tailed).

overall changes of ABG parameters and overall QTc variations, except for PCO_2 that its changes were in positive correlation with QTc interval variations. There was also a significant negative correlation between pH changes and QTc interval variations in both bicarbonate and acetate groups. Correlation between QTc changes and ionized calcium was positive in acetate group and negative in bicarbonate group. This finding is in conflict with the fact that QTc decreased in acetate group and increased in bicarbonate group; neither of these correlations reached a significant level.

In summary, there was a significant difference regarding the effect of dialysate buffer type on QTc changes: QTc interval was prolonged by bicarbonate and was shortened by acetate buffer. There was no correlation between ABG parameters and electrolytes (K^+, Na^+, and ionized calcium) and the changes of QTc interval in the two groups. We found a negative correlation between the overall changes of QTc and serum albumin that was significant only in bicarbonate group.

Discussion

The increments in all ABG and electrolyte variables in acetate group, except K^+, were remarkable, however, have not reached to a statistically significant level. This might be due to the small sample size of the study in acetate group. Since all the patients were going to be dialyzed by bicarbonate buffer it was not possible to add subjects to the acetate group. We found a significant increase in all ABG parameters except PCO_2 only in bicarbonate group; Ca^{++} was also increased in this group. Increase in ABG parameters and calcium with bicarbonate buffer are also reported by other authors.[4,5] The possible explanation for different changes in QTc interval in the two groups might be due to unequal gender distribution with more female patients in acetate group (P = 0.038). However, one-way ANOVA found no gender or age effect on overall and two groups QTc changes. This finding rules out the possibility of gender effect. Although some authors have reported more prolongation of QTc interval in female patients.[6]

There was an overall negative correlation between potassium and QTc changes in both groups, which was not statistically significant and did not explain QTc shortening in acetate group. Regarding the effect of electrolytes changes on QTc changes with hemodialysis, Howse et al.[7] have also reported no significant correlation between the changes in QTc dispersion and the changes in measured serum ions during dialysis. Covic et al.[8] noticed that hemodialysis resulted in increase in QTc interval but not in the QTc dispersion in patients with end stage renal disease (ESRD). These authors

also found no effect of electrolytes on QTc. These results are consistent with our findings.

Our study found an interesting negative correlation between serum albumin level and QTc changes that was statistically significant in bicarbonate group. As explained earlier, we found that serum albumin level and pH significantly and ionized calcium increased (although not significant) in bicarbonate group. In fact, according to accepted physiologic principals, increment in ionized calcium must result in QTc shortening and increment in pH –due to prolongation of the repolarization phase– should be correlated positively with QTc interval changes. Therefore, unexpected correlation between iCa, pH variations, and QTc changes (its decrement in acetate group and its increment in bicarbonate group) could be explained in two ways. First, changes in QTc interval in the two groups are independent to ionized calcium, potassium, and pH changes. Second, the increment in QTc interval in bicarbonate group could be the result of measurement errors originated from the decrease in the amplitude of T waves in these patients as proposed by others.[9] When the magnitude of T wave amplitude reduction was compared before and after hemodialysis, a significant reduction was found at the end of hemodialysis (P value<0.001). However, there was no significant difference between the two groups (P value=0. 798) in this regard. One possible explanation for significant negative correlation between QTc and serum albumin changes in bicarbonate group might be related to the role of albumin as a negative acute phase reactant. In patients with malnutrition who simultaneously have more cardiovascular risk factors and, consequently, have hypoalbuminemia, there is lesser increment in serum albumin with hemodialysis. Therefore, less increment in albumin is associated with more QTc prolongation, showing more severe overall underlying cardiovascular co-morbidity. There are also reports showing more QTc prolongation in malnourished patients with severe hypoalbumenia.[10] The significant negative correlation between QTc and albumin changes in bicarbonate group may also reflect more volume contraction in bicarbonate group due to more tolerability of weight reduction in this group. It may also show better demonstration of the changes of ECG with bicarbonate buffer because of better edema reduction and increment in body electroconductivity.

Comparing the weight reduction in the two groups, the present study found more weight reduction in bicarbonate group. Others have also reported more tolerability of ultra filtration with bicarbonate.[11] Madias has proposed the same mechanism of edema reduction and augmented body electro-conductivity for QTc prolongation with hemodialysis.[12]

The effect of buffer lasts throughout the entire dialysis session, whereas the membrane effect is most pronounced within the first hour of the procedure. This corresponds to the period when there is the greatest activation of the complement system.[13] The mechanism of QT changes in patients with end-stage renal failure during hemodialysis is a matter of speculation. In general, these changes depend partly on the autonomic tone and abnormal ventricular structure and metabolism.[14] Increased dispersion of refractoriness may be due to the regional differences of ventricular wall stress (mechanoelectrical or contraction-excitation feedback) caused by ventricular dilation and fibrosis, e.g., in chronic heart failure. Myocyte hypertrophy may cause a lengthening of action potential duration. Increased interstitial fibrosis may be associated with reduced action potential amplitude and membrane potential and therefore shortened action potential.[15] As seen in patients with cardiac failure, the myocardial fibrosis, especially Parathormone level (PTH)-dependent, intermyocardiocytic fibrosis,[16] and probably the myocardial calcification may also influence the homogeneity of ventricular repolarization that might lead to increased QTc in uremic patients. QT and QTc abnormalities in uremic patients may be partly due to autonomic failure caused by uremic autonomic neuropathy.[16,17] Impaired cardiac performance and impaired potassium, calcium, and/or phosphate metabolism could be major contributors to the pathogenesis of arrhythmias in uremic patients receiving hemodialysis. Contributing factors based on the publications in this field are as follow: 1) The differences between the serum and intracellular potassium, or rapid decrease of serum potassium,[17,18] 2) Changes in serum calcium and magnesium level,[19] 3) Decrease in the circulatory volume,[20] 4) Fast correction of metabolic acidosis,[21] 5) Increased PTH levels,[22] and 6) Increased free fatty acid level.[22,23]

There is also a lack of consensus regarding the mechanisms underlying the acute changes in QTc and QT dispersion (QTd) with dialysis. It seems logical that shifts in plasma electrolytes particularly potassium and calcium would be the main cause. However, this rationale is not always seen in the published literature.[13-23] The degree of reduction and the absolute end dialysis plasma concentrations of potassium, calcium, magnesium, and pH have all been linked to lengthening QTc, QTd, and an

increase in arrhythmias. Whereas some authors have not found such associations, our results are in concordance with some others.[6-8]

Conclusion

Bicarbonate buffer use in hemodialysis prolonged QTc interval and acetate buffer shortened it. This effect is independent of serum electrolytes and pH changes during hemodialysis. This effect may be due to more tolerability of ultra filtration, more effective edema reduction and augmented body electro-conductivity by bicarbonate buffer that is reflected in more prolonged QTc interval measurement in the body surface by ECG monitoring.

Acknowledgment

Authors thank Drs. Afsin Azhir and Maryam Tagavi for helpful review of the article and Zohreh Mahmoodi, Niloofar Barakati, and Aida Kashani for assistance with manuscript preparation.

Conflict of Interest: None declared

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