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Haemodialysis Alters the Index of Cardiac-Electrophysiological Balance

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ABSTRACT

Objective: To study electrocardiographic changes during haemodialysis and determine the relationship between electrolyte alterations and acid-base balance.

Study Design: Cross-sectional analytical study.

Place and Duration of Study: Haemodialysis Unit, Combined Military Hospital, Peshawar Pakistan, from Jun to Jul 2022.

Methodology: Adult patients with end-stage renal disease on maintenance hemodialysis were selected by convenience sampling. Exclusion criteria included current hospitalization, chest pain during haemodialysis, intra-dialytic hypotension, atrial fibrillation, pericardial effusion, shortening of haemodialysis sessions and unwillingness to participate in the study. Twelve lead electrocardiograms were recorded immediately before the start and end of haemodialysis sessions. At the same time, serum urea, creatinine, potassium, calcium and phosphate were measured. Bicarbonate levels were assessed by venous blood gas analysis. In addition, measurements for heart rate and durations of the PR interval, QRS complex, QT interval and corrected QT interval reported by ECG machine software were recorded.

Results: There were 35 patients with a mean age of 48.69±11.39 years. Duration of QRS complex increased from 92.83±9.98 to 100.00± 17.94 seconds after haemodialysis (p=0.017). Changes in other parameters were insignificant. QT/QRS and QTc/QRS ratios reduced by 0.27±0.62 and 0.31±0.62 after haemodialysis (p=0.014 and 0.005, respectively). Changes in none of the biochemical parameters during haemodialysis could predict the reduction in QT/QRS or QTc/QRS ratios.

Conclusion: The reduction in the index of cardiac electrophysiological balance during hemodialysis was not related to intradialytic changes in different electrolytes or base content.

Keywords: Cardiac arrhythmia, Electrocardiography, End-stage renal disease.

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INTRODUCTION

Haemodialysis (HD) is one of Pakistan's most prevalent forms of renal replacement therapies. Patients with the end-stage renal disease require this long-term treatment two to three times a week to sustain life. HD is useful for removing uraemic toxins and is also required to maintain a near-to-natural fluid, electrolyte and acid-base status in these individuals.[1] Many changes would occur in the internal milieu during these four hours of sessions.

Patients with the end-stage renal disease generally die of cardiovascular complications. This is because they have accelerated atherosclerosis attributable to multiple traditional risk factors. However, death may occur more importantly due to malignant ventricular arrhythmias. Resting electrocar-diographic changes in such patients could predict myocardial infarction, heart failure, stroke and sudden cardiac death.[2,3]

Among HD-dependent patients, the length of QT interval on ECG is associated with an increased risk of ventricular arrhythmias.[2] The index of cardiac electrophysiological balance (iCEB) is a relatively newer parameter, calculated as the ratio of QT interval to QRS duration. It is non-invasive and very easy to calculate. It gives us greater information about ventricular arrhythmias risk than QT interval alone.[4] An increase in iCEB is predictive of torsades de pointes, whereas a decrease is associated with non-torsades de points mediated ventricular tachycardia or fibrillation.[5,6]

This study was carried out to study changes in ECG during HD and determine the relationship between electrolyte alterations and acid-base balance. The results would help better understand the risk of arrhythmias in our HD-dependent patients and formulate strategies to reduce this risk.

METHODOLOGY

This cross-sectional analytical study was carried out at the HD Unit of Combined Military Hospital, Peshawar Pakistan, from June to July 2022. Approval from the Ethics Review Committee for Medical and Biomedical Research of the hospital was obtained (Reference No. 00226/22 dated 23 May 2022). The

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sample size was calculated using a calculator by the University of California San Francisco, taking a confidence level of 95%, a margin of error of 5%, and reported change in iCEB of 0.560±0.160 seconds.[6] The estimated sample size came out to be three patients. This number was very small, so we increased it to 35. Patient selection was carried out via consecutive sampling technique.

Inclusion Criteria: Adult patients undergoing maintenance HD for end-stage renal disease for at least three months were included in the study.

Exclusion Criteria: Hospitalized patients, chest pain during HD sessions, intra-dialytic hypotension, atrial fibrillation, pericardial effusion, shortening of HD sessions as per the patients' wish were excluded from the study.

Written consent was also obtained from all participants. All patients had 12 lead electrocardiograms recorded in a supine position immediately before the start of the HD session. Kenz 305 ECG machine was used for this purpose. At the same time, blood samples were collected from the arterial port of the blood tube lining using the standard protocol for measurement of serum urea, creatinine, potassium, calcium and phosphate. Venous blood gas analysis was also done to assess whole blood bicarbonate levels. HD was carried for three and a half hours on Fresenius F4008 machines. Consistency in HD prescription was ensured by the universal use of Fresenius F8 HPS dialysers, 17G arteriovenous fistula needles and a uniform blood flow rate of 300ml/min and dialysate flow rate of 500ml/min. Ultrafiltration volumes were, however, different in all patients, depending on inter-dialytic weight gain. The dialysate composition was: bicarbonate 27mmol/L, potassium 2.0mmol/L, calcium 1.25mmol/L, magnesium 0.75mmol/L and sodium 138mmol/L. Twelve lead ECGs were repeated 5-minutes before finishing the HD session. At the end of the session, blood sampling was carried out again, and all the investigations done before the start of HD were repeated. Measurements for heart rate and durations of the PR interval, QRS complex, QT interval and QT interval corrected by Bazett's formula (QTcB) were reported by the software of the ECG machine and were noted down as such.

Data analysis was done using Statistical Package for the social sciences (SPSS) version 24.00. All quantitative variables were described as mean± standard deviation. Different biochemical parameters before and after HD were compared using paired samples t-test. QT/QRS and QTc/QRS ratios were calculated, and the values for these variables before and after HD sessions were compared using paired samples t-test. The relationship of changes in these two ratios with different biochemical parameters was examined using linear regression analysis. All variables with $p<0.250$ on univariate analysis were included in multiple linear regression models. The $p\leq0.05$ was considered significant for all statistical analyses.

RESULTS

This study was carried out on 35 patients with a mean age of 48.69±11.39 years. There were 23(65.71%) male and 12(34.29%) female patients. Out of them, 24(68.57%) were on two times a weekly HD schedule, whereas 11(31.43%) had HD three times a week. The Median HD vintage was 24(12-36) months. Different ECG parameters recorded before and after HD sessions are shown in Table-I. There was a statistical reduction in QT/ QRS and QTc/QRS ratios after HD, the mean changes being 0.27±0.62 and 0.31±0.62, respectively. Levels of different biochemical parameters before and after HD are compared in Table-II. However, changes in none of the biochemical parameters studied could predict a reduction in QT/QRS or QTc/QRS ratio during HD. As shown in Table-III, none of the biochemical parameters had a statistically significant p-value for the QT/QRS ratio reduction. The same was the case for using these parameters to guess the change in QTc/QRS ratio, as shown in Table-IV.

Table-I. Comparison of ECG parameters before and after hemodialysis sessions (n=35)

Parameter	Pre-Dialysis (n=35)	Post-Dialysis (n=35)	*p*-value
Heart Rate(/min)	75.51±11.67	77.29±15.00	0.289
PR Interval (msec)	157.46±24.70	158.51±25.79	0.764
QRS complex (msec)	92.83± 9.98	100.00±17.94	0.017
QT Interval (msec)	394.26±43.54	392.97±55.48	0.865
QTc Interval (msec)	442.46±27.68	441.11±48.05	0.864
QT/QRS ratio	4.28±0.56	4.01±0.68	0.014
QTc/QRS ratio	4.81±0.51	4.50±0.67	0.005

DISCUSSION

This study has provided an interesting insight into the electrocardiographic changes occurring acutely during haemodialysis. There is a decrease in iCEB during this period, something that could increase the vulnerability towards malignant ventricular arrhythmias. Moreover, this change is primarily because of the prolongation of the QRS complex since the change

in QT or QTcB intervals during haemodialysis was insignificant. All biochemical parameters changed by the end of haemodialysis, except serum calcium. None of these could predict a reduction in iCEB.[7]

Table-II: Comparison of Biochemical Parameters before and after Haemodialysis (n=35)

Parameter	Pre-Dialysis (n=35)	Post-Dialysis (n=35)	*p*-value
Serum Urea (mmol/l)	14.88±6.00	4.91±2.34	<0.001
Serum Creatinine (µmol/l)	648.63±234.04	211.51±126.46	<0.001
Serum Sodium (mmol/l)	139.04±5.38	142.09±5.11	0.010
Serum Potassium (mmol/l)	4.18±0.93	3.33±0.70	<0.001
Serum Calcium (mmol/l)	2.65±0.99	2.55±0.38	0.605
Serum Phosphate (mmol/l)	0.94±0.75	0.52±0.60	0.005
Serum Bicarbonate (mmol/l)	19.83±3.53	22.63±3.35	0.001

ECGs were done immediately before the end of HD sessions when the physiological cardiac stress related to changes in fluid, electrolytes, and acid-base balance was at its peak.[8,9] The pro-arrhythmic risk in HD-dependent patients is heightened during the first six hours following dialysis sessions when the internal milieu changes in response to readjustments through transcellular shifts.[10,11] It would have been interesting to note how the dynamic ECG changes behave during this period, but we should have followed up on our outdoor patients for this long as they would have faced logistic issues. We recorded the measurements for different waves and intervals as reported by the software of the ECG machine rather than interpreting them manually. This approach was expected to reduce the analysis time and, thus, the burden on physicians.[12] However, we did our best to minimize the bias by excluding patients with atrial fibrillation or other arrhythmias and repeating ECGs with significant background noise. Serum sodium levels before and after hemodialysis have been reported in the results of this study. However, they were not included in the regression models since they are not known to affect the length of any of the ECG waves or intervals.

QT dispersion, the difference between the maximum and minimum QT intervals on a standard ECG, reflects hetero-genicity in ventricular repolarization. It is widely accepted as a mark of increased ventricular arrhythmias and sudden cardiac death risk.[13] This has been studied extensively amongst patients with end-stage renal disease on maintenance HD.[14] Whereas the QT dispersion looks at ventricular repolarization, another new non-invasive marker of arrhythmogenic risk reflects the balance between depolarization and repolarization. This marker, iCEB, is a reflection of the cardiac wavelength λ. Therefore, it is better at estimating the risk of arrhythmias since it looks at both ventricular depolarization and repolarization.[15] For this reason, we looked at iCEB rather than QT or QTc dispersion in this study.

We need an adequate explanation for the lack of association between variations in iCEB with changes in different laboratory parameters. We did not measure serum magnesium levels in our patients before and after HD sessions due to limited resources. Afshinnia

Table-III: Relationship of Biochemical Parameters with Change in QT Ratio (n=35)

Factors	Univariate Logistic Regression			Multivariate Logistic Regression		
	p- value	Unadjusted OR	95% CI for UOR	*p*- value	Adjusted OR	95% CI for AOR
Serum Urea	0.574	0.011	(-0.028, 0.049)	-	-	-
Serum Creatinine	0.231	0.001	(0.000, 0.002)	0.458	0.000	(-0.001, 0.002)
Serum Potassium	0.751	0.028	(-0.150, 0.206)	-	-	-
Serum Calcium	0.166	0.125	(-0.054, 0.303)	0.311	0.098	(-0.096, 0.292)
Serum Phosphate	0.432	0.104	(-0.162, 0.369)	-	-	-
Serum Bicarbonate	0.569	0.014	(-0.034, 0.061)	-	-	-

Table-IV: Relationship of Biochemical Parameters with Change in QTcB Ratio

Factors	Univariate logistic regression			Multivariate logistic regression		
	p-value	Unadjusted OR	95% CI for UOR	*p*-value	Adjusted OR	95% CI for AOR
Serum Urea	0.599	0.010	(-0.028, 0.048)	-	-	-
Serum Creatinine	0.361	0.000	(-0.001, 0.002)	-	-	-
Serum Potassium	0.894	-0.012	(-0.188, 0.165)	-	-	-
Serum Calcium	0.168	0.123	(-0.054, 0.300)	0.168	0.123	(-0.054, 0.300)
Serum Phosphate	0.372	0.117	(-0.145, 0.379)	-	-	-
Serum Bicarbonate	0.495	0.016	(-0.031, 0.063)	-	-	-

et al. have shown that variations in dialysate magnesium levels during HD do not influence QT interval dispersion in hemodynamically stable patients.[16] On the other hand, in a study done on 25 HD-dependent patients, Taner *et al.* reported an inverse relationship between QT interval and serum magnesium levels. In contrast, changes in serum potassium and calcium levels were not contributory.[17]

There are a few other limitations of this study as well. We did not record data on left ventricular systolic function or coronary artery disease in our patients, as most of them did not have complete information documented in medical records. Amongst two hundred patients with no clinical evidence of cardiac disease, Sohal *et al.* found that both the QTc interval and QTc dispersion increased after a single session of HD.[18] Howse et al. showed that patients with angina, a history of myocardial infarction of percutaneous coronary intervention has longer QTc intervals and QTc dispersion. However, this was not statistically different from patients without ischaemic heart disease.[8] Arrhythmogenic tendency is higher amongst patients with heart failure or coronary artery disease, and how this could have affected the results of our study is not obvious. Among HD-dependent patients, longer QTc intervals are associated with thicker left posterior ventricular walls as the utmost marker of mortality.[19] However, we did have any such echocardiographic information available for our patients.

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CONCLUSION

The index of cardiac electrophysiological balance decreased during HD, thereby increasing the risk of malignant ventricular arrhythmias. However, this was unrelated to intradialytic changes in different electrolytes or base content.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

ARA & TK: Conception, study design, drafting the manuscript, approval of the final version to be published.

FAS & ST: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

SA & MQ: Critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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