Abstract

Hyperkalaemia is a commonly encountered problem in dialysis patients with end-stage renal disease (ESRD) this might lead to increase corrected QT (QTc) duration which could have serous consequences. The aim of this study is to assess the effect of serum electrolyte imbalance mainly Potassium causing ECG changes such as QTc during haemodialysis (HD). Prospectively, eighteen haemodialysis patients with ESRD had ECG and serum electrolyte tested before and after HD. The ECG parameters were measured manually, the QT interval was corrected to the heart rate, the data were calculated and analysed with SPSS 17 software.

There were significant effects of HD on serum electrolytes and some ECG parameters; the pre-HD K\textsuperscript{+} was 5.24±0.87 mmol/L and post-HD was 3.93±0.69 mmol/L (P 0.007) and pre-HD Ca\textsuperscript{++} was 1.98±0.17 mmol/L and post-HD was 2.22±0.15 mmol/L (P 0.003). QTc interval pre-HD 431.3 ± 32.1 ms and post-HD was 443.5 ± 32.4 ms (P 0.002). T wave pre-HD 4.33±1.89 mm and post-HD was 3.18±1.11 mm (P0.045). An abnormally prolonged QTc (>440 ms) was measured in 27.7% of cases pre-HD and was recorded in 38.9% of cases in post-HD.

There was correlation between pre-HD K\textsuperscript{+} and pre-HD QTc interval (r 0.699, P 0.001), and negative influence of the net change of K\textsuperscript{+} on the amplitude difference of T wave during haemodialysis (r -0.422, P 05). No other influence of serum electrolyte imbalance on ECG changes was noted. Significant changes in serum electrolyte changes and ECG parameters during haemodialysis. There was limited association between serum electrolyte and ECG parameter changes during haemodialysis.

Tأثير اختلال توازن أملاح الدم على تخطيط القلب لمرضى الكلى في نهاية مرحلة المرض قبل وبعد غسيل الكلى

الخلاصة

زيادة البوتاسيوم في الدم مشكلة شائعة الوجود لدى مرضى غسيل الكلى (الديليزا) على وجه الخصوص مع نهاية مرحلة المرض ESRD، والذي قد يكون لها عواقب وخيمة على QT (و هذا قد يؤدي إلى زيادة في فترة QT). ESRD، وقد كان الهدف من هذه الدراسة هو قياس تأثير اختلال توازن أملاح مصل الدم وخصوصا البوتاسيوم الذي يسبب تغييرات في Tخطيط القلب مثل QT. خلاصاً، و بعد عملية غسيل الكلى ESRD، تأثير اختلال توازن أملاح مصل الدم وخصوصا البوتاسيوم الذي يسبب تغييرات في Tخطيط القلب مثل QT. Premier Medical Journal of Babylon- Vol. 8 - No. 2 - 2011 - مجلة بابل الطبية - العدد الثامن - العدد الثاني -
Potassium (K⁺) is the principle and most important intracellular cation. It is mainly regulated by the kidneys and excess potassium is excreted in urine and to a lesser extent from intestine. It plays an important role in maintaining the electrical potential across the cellular membrane and its blood level affects all types of neuromuscular activities. An alteration in the serum level of potassium may present with cardiovascular and/or neuromuscular signs and symptoms. of these cardiovascular complications are cardiac arrhythmias[1,2].

Hyperkalaemia (serum K⁺> 5 mmol/L) is a relatively common finding in patients with end-stage renal disease (ESRD). Severe Hyperkalaemia might occur in 10 -19% of haemodialysis (HD) patients [1, 2]. It has been shown by several studies that a sudden shift and decrease in serum K⁺ causes arrhythmia especially in patients undergoing dialysis [3-6].

Sudden death is not uncommon among dialysis patients and the annual death rate for these patients is 230 per 1000 patient per year, ischemic heart disease and rapid electrolyte shift are the most common causes during dialysis sessions [7]. HD has been reported to determine an increase in QTc interval [8] which is a risk factors that predispose to severe ventricular arrhythmias and sudden death [9,10].

The aim of this study was to evaluate the pre and post dialysis serum electrolyte mainly potassium level and any associated ECG changes in patients with ESRD and without obvious cardiac disease.

Patients and Methods

In this prospective study, 18 patients were recruited, all with ESRD and undergoing haemodialysis treatment three times per week for a minimum duration of at least 6 months. The mean duration for sessions of the dialysis was 3 hours. The patients were normally treated with a bicarbonate dialysate which contained the following electrolyte concentration: K⁺, 2.0 mmol/L; Mg²⁺, 1.0 mmol/L; Ca²⁺, 1.75 mmol/L; Na⁺, 135 mmol/ and HCO3 32 mmol/L. Blood flow rate was 250-300 ml/minute with a dialysate flow of 500 ml/min. The patients were dialysed using Polysulfone-based dialysis membrane (Haemodialysis
Apparatus Fresenius Medical Care 4008 B) in Merjan hospital 1 in Babylon, Iraq.

Patients with ischemic heart disease (according to detailed medical history and ECG findings), ECG changes of atrial fibrillation, left ventricular hypertrophy or left bundle branch block (LBBB) and those on anti-arrhythmic medication were excluded from the study.

Blood samples were obtained from each patient just before the haemodialysis session and 10 minutes after the session for measurements of serum level of $K^+$ and $Ca^{2+}$ as well as serum level of urea and creatinine as described in the dialysis outcomes quality initiative guidelines[11]. In addition, a standard 12-leads ECG recorded before dialysis and 20 minutes after the dialysis in supine position. Kenz Cardio 302 three channel ECG machine was used for all patients. Potassium and the rest of the electrolyte were analysed and detected by flame photometry method by using SEAC model FLP20, Italy.

The patients were followed for at least 6 months (6 -14 months) to record any adverse outcomes.

**Electrocardiograms (ECG)**

The interpretation of ECG was performed by measuring the amplitude of the T and R waves, QT and R-R intervals. All QT intervals were corrected for heart rate (QTc) by dividing the QT interval to the square root of the R–R interval (Bazett’s formula; QTc = QT/√(R-R)). The ECG readings were measured manually after magnification according to Higham and Campbell [12] recommendation. All the ECGs were reviewed and interpreted by a single cardiology consultant based at Merjan hospital.

**Statistical analysis**

SPSS (Statistical Program for social sciences version 17 SPSS Inc, Chicago, Illinois) was used for statistical analysis. Results were expressed as mean ± standard deviation. Paired t-test was used to analyse differences between before and after dialysis measurements and Pearson’s test and multi-variant regression analysis were used to look for correlations between variables.

**Results**

The baseline characteristics of the subjects are shown in (Table 1). Majority of the patients were male (77.7%). The median age in the study population was 47 (range: 28–63) years. The most prevalent underlying kidney disease was chronic glomerulonephritis (38.8%) and around 22.2% had an unknown aetiology and to a lesser extent had pyelonephritis, polycystic kidney and nephrocalcinosis 39 %, and 44.5% of the patients were smokers. The median duration of HD was 13 (range: 6 – 64) months.
Table 1: Demographic characteristics of the study population and the causes for ESRD

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Gender (M/F)</td>
<td>14/4</td>
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</tr>
<tr>
<td>Age (median)</td>
<td>47(range: 28–63) years</td>
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<tr>
<td>Smokers</td>
<td>8</td>
<td>44.5%</td>
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<tr>
<td>Duration of HD</td>
<td>13(range:28-64)months</td>
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Causes for ESRD

<table>
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<tr>
<th>Causes of ESRD</th>
<th>Number</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Chronic Glomerulonephritis</td>
<td>7</td>
<td>38.8%</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>3</td>
<td>16.7%</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>3</td>
<td>16.7%</td>
</tr>
<tr>
<td>Nephrocalcinosis</td>
<td>1</td>
<td>5.6%</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>4</td>
<td>22.2%</td>
</tr>
</tbody>
</table>

There were significant effects of HD on serum electrolytes mainly K⁺ and Ca²⁺ and ECG parameters when examined by t test (Table 2); the serum K⁺ decreased (P 0.007) and serum Ca²⁺ increased (P0.003). The analysis of serum K⁺ results revealed the pre-dialysis mean level was 5.24±0.87 mmol/L and abnormally hyperkalaemia > 5.5 mmol/L was recorded in 33.3% of cases pre-HD but was 3.93±0.69 mmol/L post-HD. Similarly, the dialysis session had shown increased QTc intervals (P 0.002) and decreased T amplitude (P 0.045) but it had less effect on R-R interval or R amplitude. An abnormally prolonged QTc (>440 ms) was measured in 27.7% of cases pre-HD and was recorded in 38.9% of cases post-HD.

Bi-varient Pearson’s analysis revealed that serum K⁺ level appeared to be the main determinant of QTc duration pre-HD (r 0.699, P 0.001) but showed no influence on R or T waves amplitude (r -0.088, P 0.729 and r -0.149, P0.554 respectively). Pre-HD Ca²⁺ has no significant effect on the pre-HD QTc interval (r 0.083, P 0.743). There was no influence of post-HD serum K⁺ and Ca²⁺ on the changes in post-HD QTc interval (r.532, P 0.152 and r 0.136, P.059).  

Table 2: Effects of HD on serum electrolytes mainly K⁺ and Ca²⁺ and ECG parameters

<table>
<thead>
<tr>
<th></th>
<th>Pre-HD</th>
<th>Post-HD</th>
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4
However, the net change (pre-HD - post-HD difference) of the T amplitude had negative correlation with the net change of serum K\(^+\) (\(r = -0.422\), \(P < 0.05\)) i.e. patients with limited decline in the serum K\(^+\) following dialysis have higher change in the amplitude of their T wave (Figure 1).

No significant correlation was observed between QTc or QTc net changes and basal blood pressure or variations in systolic and diastolic arterial pressures or the age of patients during dialysis.

When a linear multiple regression analysis for the absolute or net change values of QTc interval and T amplitude was performed in the pooled data of serum electrolyte (K\(^+\), Ca\(^{2+}\)), there was no significant relation between these ECG

<table>
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<tr>
<td>QT interval (ms)</td>
<td>371.2 ± 43.1</td>
<td>370.3 ± 43.9</td>
<td>0.006</td>
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<td>QTc interval (ms)</td>
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<td>0.002</td>
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<tr>
<td>R-R interval (ms)</td>
<td>747.3 ± 153.5</td>
<td>834.8 ± 84.1</td>
<td>NS</td>
</tr>
<tr>
<td>T amplitude (mm)</td>
<td>4.33±1.89</td>
<td>3.18±1.11</td>
<td>0.045</td>
</tr>
<tr>
<td>R amplitude (mm)</td>
<td>9.01 ± 2.9</td>
<td>9.7±2.5</td>
<td>NS</td>
</tr>
<tr>
<td>sBP (mmHg)</td>
<td>130.8 ± 9.8</td>
<td>124.2 ± 6.6</td>
<td>NS</td>
</tr>
<tr>
<td>dBP (mmHg)</td>
<td>77.7±8.7</td>
<td>72.7±7.2</td>
<td>NS</td>
</tr>
<tr>
<td>K(^+) (mmol/L)</td>
<td>5.24±0.87</td>
<td>3.93±0.69</td>
<td>0.007</td>
</tr>
<tr>
<td>Ca(^{2+}) (mmol/L)</td>
<td>1.98±0.17</td>
<td>2.22±0.15</td>
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**Figure 1** The correlation between the net change of K\(^+\) and the T wave amplitude during haemodialysis.
changes and serum electrolyte variables (Figure 2).

During follow-up of the patients, there were three deaths (16.6 %). One of these patients died following emergency laparotomy for peritonitis following a perforated appendix. Unfortunately he developed septicemia and died of multi-organ failure. The second patient developed severe pneumonia and died from sepsis and respiratory failure. The third patient suffered a sudden death at home within 24 hours following his routine HD. She was 55 years old with no other previous risk factor (cardiac or respiratory disease).

Figure 2 The correlation between the pre-HD K+ and pre-HD QTc intervals.

Discussion
In this study we examined the change of electrolyte mainly K⁺ during haemodialysis in patients with ESRD. These patients usually present with hyperkalemia.

Hyperkalemia reduces the resting membrane potential, slows the conduction velocity and increases the rate of repolarization [13,14]. Hypokalemia on the other hand increases the resting membrane potential, and increases the duration of action potential and refractory period, which are potentially arrhythmogenic [15].

All these changes are the signs of membrane instability and cardiac arrest or ventricular fibrillation may follow and thus this situation usually requires careful and prompt management [16]. During haemodialysis there is quick shift of serum K⁺ which leads to hypokalemia and this might lead to the ECG changes [8]. The main change is increase of the QTc interval which is a marker of the ventricular repolarization and its prolongation has been associated with increased risk of sudden death in both pathological [9, 17, 18] and healthy[19] populations. There are several studies which address the analysis of QT interval; this is often significantly changed by the end of the dialysis treatment. Nevertheless, these studies do not show same effects of haemodialysis on QTc interval. In some studies, the QTc interval increased during the dialysis session [20-26]. In other studies the QTc interval did not change, or decrease or show a variable response [5, 8, 27-34]. Discrepancies between these studies may be attributed to population selection, methods of QT measurement and variables related to the dialysis technique [35].

In our study the main significant ECG changes are the increase of QTc duration and decrease the amplitude of the T wave. These findings are compatible with a study done by Tarif et al [16]. There was significant correlation between these ECG changes (i.e. QTc) and serum K⁺ level before haemodialysis but this relation could not be found at the end of haemodialysis. Therefore, we could not prove any significant association between all these variables after dialysis.

The most important influencing factor on the serum K⁺ level during haemodialysis is the concentration of K⁺ in the dialysate as well as the duration of dialysis, type of the dialyzer and blood flow rate. Therefore, using standardised dialysate for all patients without considering the electrolyte values before the haemodialysis might have serious effect. It is appropriate for the dialysate to be tailored for each patient.

The Mortality rate of patients undergoing haemodialysis is high [36]. It has been shown that most of these sudden deaths do not occur during the dialysis session [37] but in the following hours [38]. Accordingly, it is very difficult to obtain an ECG tracing able to reveal the cause of sudden death [39]. In our study, it had not been identified the aetiology of death of the third patient who passed away within 24 hours following dialysis.

Conclusion

There were significant changes in ECG parameters and serum electrolytes during haemodialysis. However, there was no obvious influence of serum electrolytes (K⁺ and Ca²⁺) on the ECGs in patient with
ESRD, apart from the net change of serum K⁺ on the amplitude T wave difference, during haemodialysis. More evaluation with larger sample to see the effect of electrolyte on ECG changes might be required.

Acknowledgements

Many thanks to all in the renal department and to Dr M.A.M Alwash (cardiology consultant) at Marjan Hospital for their help and support.

References


