ORIGINAL ARTICLE

Changes in the corrected QT interval and corrected QT dispersion during haemodialysis

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The link between increased QT dispersion and cardiac death in subjects with diabetes and arterial disease is well recognised. Corrected QT dispersion was studied in subjects with end stage renal failure on haemodialysis. Thirty one stable, chronic subjects on haemodialysis had 12-lead electrocardiograms (ECGs) taken before and after a single haemodialysis session. The QT interval was measured manually in each and the corrected QT and corrected QT dispersion calculated. Serum concentrations of potassium, calcium, and magnesium were measured at the same time as ECG acquisition. Corrected QT dispersion increased from a mean (SEM) 90.6 (5.8) to 117.7 (10.2) ms (p=0.002). Serum potassium and magnesium decreased from 5.0 (0.14) to 3.5 (0.09) mmol/l and 0.95 (0.04) to 0.89 (0.09) mmol/l respectively, while serum calcium increased from 2.56 (0.04) to 2.77 (0.04) mmol/l. Intradialytic weight fell by a mean of 2.1 kg. There was no significant correlation between the change in QTc dispersion and the changes in measured serum anions or the subjects' weight during dialysis. Corrected QT dispersion was higher in subjects on haemodialysis than previously suggested normal values, and was significantly increased by haemodialysis. This reflects increased inhomogeneous ventricular repolarisation, which may lead to an increased risk of arrhythmias and sudden death. Studies looking at QT dispersion in subjects on dialysis should standardise the timing of ECG recordings taken with respect to dialysis.

Cardiovascular disease is a major cause of mortality and morbidity among subjects on haemodialysis. Cardiovascular death is responsible for up to 50% of deaths among subjects on dialysis.[1] Cardiac arrhythmias are frequent among the haemodialysis population, particularly during and immediately after a dialysis session.[2–5] These arrhythmias may be caused by the rapid changes in intracellular and extracellular electrolytes during the dialysis session, in hearts that are susceptible due to both myocardial ischaemia and intramyocardiocytic fibrosis.[6 7] A reliable way of predicting subjects at risk of ventricular arrhythmias would be an extremely useful tool for the dialysis physician.

Recently, dispersion of the QT interval has emerged as an important predictor of ventricular arrhythmias. The QT dispersion is simply the difference between the shortest and longest QT interval on a standard surface 12-lead electrocardiograph.[8] This is a non-invasive measurement of myocardial repolarisation inhomogeneity and hence predisposition to re-entry arrhythmias.[9] A QT dispersion above 80 ms reflects a loss of synchronisation in the repolarisation process.[10] In clinical studies, a wide QT dispersion has been shown to be a risk factor for cardiac arrhythmia after myocardial infarction,[11] congestive cardiac failure,[12] peripheral vascular disease,[13] and drug induced arrhythmiogenicity.[14] It has also been shown that a wide QT dispersion can narrow when congestive cardiac failure is treated with enalapril[15] and after successful thrombolysis for acute myocardial infarction.[16]

We speculated that QT dispersion might also predict ventricular arrhythmias in subjects on dialysis. However, as the QT interval is partially influenced by the concentrations of the dialysable cations, calcium, magnesium and potassium, and may also be influenced by cardiac filling pressures,[17] it is likely that both the QT interval and QT dispersion are altered during a haemodialysis session. To test this hypothesis, we measured QT dispersion in 34 stable chronic uraemic subjects, before and after an uncomplicated haemodialysis session.

SUBJECTS AND METHODS

Patients

Thirty four subjects with end stage renal failure, attending for routine midweek haemodialysis, were invited to participate in the study. All subjects were receiving thrice weekly bicarbonate based haemodialysis sessions lasting between three and four and a half hours. All subjects were dialysed using a flat plate dialyser incorporating a low density polyethylene membrane (Gambro, UK). The presence of a permanent cardiac pacemaker or atrial fibrillation at the time of the study were treated as exclusion criteria. Verbal consent was obtained in all cases after an explanation of the study.

Before the haemodialysis session, the subject was weighed and a standard 12-lead electrocardiogram (ECG) recorded. Blood was taken for measurement of plasma electrolytes. At the end of haemodialysis blood was again taken and electrolytes measured as described in the dialysis outcomes quality initiative guidelines.[18] A further 12-lead ECG was immediately recorded, and the subject reweighed. All dialysis sessions were uncomplicated.

Electrocardiograms

QT intervals were measured manually in each ECG lead after photocopier enlargement. This was done in line with the recommendations of Higham and Campbell.[8] The start of the QT interval was measured from the beginning of the QRS complex. The end of the QT interval was measured at the return to the TP baseline, or, when a U wave was present, at the nadir between the T wave and the U wave. In order to allow for changes in heart rate during dialysis, all QT intervals were corrected for heart rate by dividing by the square root of the R–R interval (Bazett's formula). The mean QTc interval was calculated as the arithmetic means of QTc intervals measurable on a single ECG. The QTc dispersion was calculated as the maximum QTc minus the minimum QTc. In instances where the QTc was not measurable in every lead, the QTc dispersion was adjusted by dividing it by the square root of the number of leads with unanalysable QT intervals. If the

Table 1 Baseline characteristics of subjects

Characteristic	Frequency
Male/female	18/13
Age* (years)	59.6 (13.6)
Known IHD†	13
Hypertension	28
Diabetic	2
Current smokers	5
Medication	
Atenolol	4
Calcium antagonist	14
Passium channel modulator	2
Doxazosin	7
Aodarone	3
Digoxin	2‡

*Mean (SD); †ischaemic heart disease (IHD) was defined as a definite history of angina, myocardial infarction, or coronary artery revasculisation procedure; ‡in both cases used as a positive inotrope in patients in sinus rhythm.

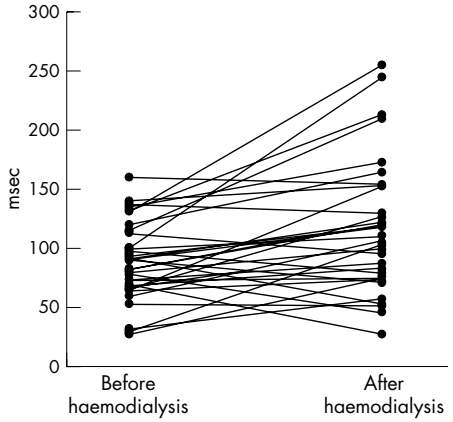

Figure 1 Changes in QTc dispersion before and after an uncomplicated haemodialysis session; p = 0.002 by Student's *t* test.

Table 2 Abnormalaties of the ECG before haemodialysis defined using standard criteria

Abormality	No
Voltage criteria for left ventricular hypertrophy	13
Q waves consistent with anterior myocardial infarction	1
Q waves consistent with inferior myocardial infarction	2
Flattening/inversion of T waves in V4–6	8
First degree heart block	2
Left bundle branch block	1
Left anterior fasicular block	1

Table 4 Corrected QT intervals and QTc dispersions, before and after dialysis in subjects with and without ischaemic heart disease (IHD)

Haemodialysis session	IHD	No IHD
Before		
QTc	450 (6.1)	438 (8.2)
QTc dispersion	85.5 (8.2)	97.6 (7.9)
After		
QTc	454 (9.1)	445 (12.9)
QTc dispersion	119.9 (15.7)	116.1 (13.7)

Differences between those with and without IHD were not significant.

QT interval was measurable in less than 10 leads, the ECG was excluded.

Two researchers (MH and SS) undertook these measurements. Interobserver variation was undertaken in 15 randomly selected ECGs. The coefficient of agreement was 13%, which is comparable to other studies.[19 20]

Statistical analysis

Results were expressed as mean (SEM) unless otherwise stated. Student's *t* test was used to analyse differences between before and after dialysis measurements and Pearson's test was used to look for correlations between variables.

RESULTS

Thirty one of 34 pairs of ECGs were judged interpretable. The characteristics of the subjects are shown in table 1. Baseline abnormalities, defined by standard criteria,[21] of the ECG are described in table 2. The results of the changes in measured variables are shown in table 3. The change in the mean QTc interval was not significant being 443 (5.5) before dialysis and 449 (7.5) ms after dialysis. The mean QTc dispersion increased from 90.6 (5.8) to 117.7 (10.2). This increase was significant (fig 1).

As expected dialysis resulted in a significant change in serum potassium, calcium bicarbonate, urea, and body weight (table 3). As serum electrolyte concentrations and mechanical loading of the heart influence the QT interval we attempted to correlate these changes with the changes in the ECG intervals measured. The change in QTc and QTc dispersion did not correlate with changes in the measured plasma electrolytes, calcium, magnesium, potassium or bicarbonate, or the changes in subjects' weight, all of which decreased during haemodialysis.

The data for patients with and without ischaemic heart disease are shown in table 4. Ischaemic heart disease was defined as a definite history of myocardial infarction, angina, or cardiac revascularisation procedure. As can be seen, subjects with pre-existing ischaemic heart disease had marginally longer QTc intervals and greater QTc dispersion but these results did not reach significance. There was no correlation between the age of the patient and either the absolute values or changes in the QTc intervals or the QTc dispersion.

Table 3 Changes measured variables before and after haemodialysis

Variable	Before haemodialysis (n=31)	After haemodialysis (n=31)	p Value*
Potassium (mmol/l)	5.0 (0.14)	3.5 (0.1)	<0.001
Calcium (mmol/l)	2.56 (0.04)	2.77 (0.04)	<0.001
Magnesium (mmol/l)	0.95 (0.04)	0.89 (0.09)	0.052
Bicarbonate (mmol/l)	23.1 (0.68)	27.9 (0.65)	<0.001
Urea (mmol/l)	24.8 (1.07)	10.3 (0.54)	<0.001
Weight (kg)	67.7 (2.4)	65.6 (1.8)	<0.001
QTc (ms)	443 (5.5)	449 (7.5)	0.434
QTc dispersion (ms)	90.6 (5.8)	117.7 (10.2)	0.002

*Measurement of significance before and after dialysis using Student's *t* test.

Similarly, there were no significance differences in the ECG intervals measured and subjects' sex, presence or absence of hypertension, or with any medications (data not illustrated).

DISCUSSION

Holter monitoring has shown that the incidence of ventricular arrhythmias among haemodialysis patients is high.[22] These may be life threatening, although their predictive power for mortality in the haemodialysis population has not yet been shown.[23]

Until recently, the only non-invasive way of assessing ventricular repolarisation was the measurement of the QT interval in a single lead. While this was useful in the diagnosis of the hereditary long QT syndromes,[24] its application in other areas was less fruitful. This may have in part been due to fact that there was no standardisation for measurement of the QT interval.[25]

The novel approach of QT dispersion appears to be a powerful way of predicting both ventricular arrhythmias and sudden cardiac death in a variety of clinical situations.[12] However, before applying this technique to haemodialysis patients, we thought it necessary to investigate the effect of dialysis itself on QTc dispersion. We used a validated manual method of measuring QTc dispersion. Although automated systems exist, these have not been shown to be superior.

We have shown that in our haemodialysis population mean QTc dispersion is 90.6 (5.8) ms. This is prolonged when compared with controls in other studies that typically quote mean QT dispersion in the range 20–30 ms.[26 27] In a study of patients with acute myocardial infarction the mean QTc was 56 ms and those who suffered ventricular fibrillation it was 88 ms.[26] The QTc dispersion was increased further after a haemodialysis session. These findings confirm other studies.[19 20 28] This increase in QTc dispersion may reflect an increase in regional inhomogeneity of myocardial repolarisation and predispose to arrhythmias.

The cause of the increase in QTc dispersion is unclear. As the QT interval is influenced by changes in plasma cations, we attempted to correlate changes in QTc dispersion with these variables. No such correlations were found. Studies specifically designed to measure the changes in QT dispersion and plasma concentrations of dialysable drugs and cations may reveal the mechanism of the changes in these intervals during a dialysis session. Unmeasured factors such as neurohumoral mechanisms,[29] which contribute to the complex nature of the QT intervals, may play an important part. Rombola *et al* found that there was a greater fall in intraerthyrocytic potassium concentration during dialysis in patients with an arrhythmic tendency compared with those without such a tendency.[30]

The change in QTc dispersion during haemodialysis makes it imperative that when this interval is used in clinical studies, the point during the dialysis cycle at which it is measured must be defined and standardised. Studies in non-dialysis patients have used retrospective ECGs to measure QTc dispersion.[13] Unless the timing of the ECG in relationship to the dialysis session is known, studies of this type cannot be carried out in dialysis patients. If the results of QT dispersion, measured, this way could be correlated with mortality rates of patients on renal replacement therapy then this would of great importance.

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