



ORIGINAL ARTICLE

A simple modification of dialysate potassium: its impact on plasma potassium concentrations and the electrocardiogram

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ABSTRACT

Background. Sudden death is frequent in haemodialysis (HD) patients. Both hyperkalaemia and change of plasma potassium (K) concentrations induced by HD could explain this. The impact of increasing dialysate K by 1 mEq/L on plasma K concentrations and electrocardiogram (ECG) results before and after HD sessions was studied.

Methods. Patients with pre-dialysis K >5.5 mEq/L were excluded. ECG and K measurements were obtained before and after the first session of the week for 2 weeks. Then, K in the dialysate was increased (from 1 or 3 to 2 or 4 mEq/L, respectively). Blood and ECG measurements were repeated after 2 weeks of this change.

Results. Twenty-seven prevalent HD patients were included. As expected, a significant decrease in K concentrations was observed after the dialysis session, but this decrease was significantly lower after the switch to an increased dialysate K. The pre-dialysis K concentrations were not different after changing, but post-dialysis K concentrations were higher after switching ($P < 0.0001$), with a lower incidence of post-dialysis hypokalaemia. Regarding ECG, before switching, the QT interval (QT) dispersion increased during the session, whereas no difference was observed after switching. One week after switching, post-dialysis QT dispersion [38 (34–42) ms] was lower than post-dialysis QT dispersion 2 weeks and 1 week before switching [42 (38–57) ms, $P = 0.0004$; and 40 (35–50) ms, $P = 0.0002$].

Conclusions. A simple increase of 1 mEq/L of K in the dialysate is associated with a lower risk of hypokalaemia and a lower QT dispersion after the dialysis session. Further study is needed to determine if such a strategy is associated with a lower risk of sudden death.

Keywords: arrhythmia, haemodialysis, potassium

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INTRODUCTION

Chronic haemodialysis (HD) patients are at higher risk of cardiovascular mortality [1–3], sudden death being the largest contributor [3–18]. Ventricular hypertrophy, anaemia, heart failure or ischaemic heart disease and electrolyte variations are all potential substrates for arrhythmia and sudden death [4, 12, 13, 16–19]. Abnormalities of potassium (K) before and after dialysis session, and rapid changes in K concentrations during the dialysis session have been suggested as a potential cause of arrhythmia [5, 7, 12, 13, 20–22]. Hyperkalaemia before dialysis session is frequent, dangerous and increases morbidity and mortality [7, 17, 18, 22–30]. Additional data also suggest that pre-dialysis hypokalaemia, although less frequent, could be associated with higher mortality [11, 13, 22, 25, 27, 30–32]. The risk of post-dialysis hypokalaemia is much less well studied and thus its prevalence is not precisely known [11, 31, 33]. Recent data from an observational cohort of 3967 Japanese patients showed that post-dialysis hypokalaemia (defined as K concentration <3.5 mEq/L) was seen in half of the patients; almost all of the patients in that study were dialysed with a dialysate K of 2 mEq/L [31]. Several authors have suggested that such hypokalaemia induced by dialysis could trigger arrhythmias, and especially ventricular arrhythmias [5, 21]. The excess occurrence of arrhythmia and sudden death in the first hours after the dialysis session has been described and would be consistent with the role for post-dialysis hypokalaemia [4–7, 13–15, 17, 34, 35]. In addition, there may be a higher risk of mortality and sudden death in dialysis patients treated with low dialysate K [4, 8, 9, 12–15, 17, 18, 25, 28–30, 36, 37]. These observations suggest the utility of switching from low K dialysate to higher K dialysate [4, 12, 13, 15, 18, 22, 28, 30]. However, most data supporting this hypothesis are derived from purely observational cohorts. Moreover, results from observational studies comparing mortality according to K dialysate are not uniform, and some authors showed no association between low K dialysate and mortality [17, 24, 30, 36, 38, 39]. A recent observational Japanese study showed significant association between post-dialysis K concentration and mortality, but the association was lost after adjustment for pre-dialysis K concentration [31]. The present study sought to examine the impact of increasing dialysate K both on plasma K concentrations and electrocardiographic results in HD patients.

MATERIALS AND METHODS

The current prospective study was performed in the department of dialysis at the University Hospital of Liège, Belgium. In November 2017, nephrologists responsible for the dialysis unit decided to switch the central distribution of dialysate to higher dialysate K, i.e. from a dialysate concentration of 1 mEq/L (K1) to 2 mEq/L (K2), or from 3 mEq/L (K3) to 4 mEq/L (K4). The patients with the following characteristics were included in the study: age >18 years old, dialysis vintage of at least 3 months and ability to understand and sign the informed consent. The patients with the following characteristics were excluded: dialysate K other than K1 or K3 at the first day of the dialysis week, pre-dialysis K concentration >5.5 mEq/L in one of the last four blood tests (routinely sampled the first dialysis day of the week, every 2 weeks in our centre) in patients dialysed with K1, patients with a non-sinus rhythm at the time of inclusion and patients haemodialysed less or more than three times a week. Two weeks before the dialysate K increases, a resting electrocardiogram (ECG) was done on the first dialysis day of the week just before starting dialysis session and, for practical reasons,

the ECG was repeated within 10 min before the end of the same dialysis session. At the same time as ECG, blood samples were drawn for measurement of K, sodium (Na), ionized calcium (Ca^{++}), bicarbonates and total magnesium (Mg). All the measurements (ECG and blood samples, both before and after dialysis session) were then repeated during 1 and 2 weeks after switching to higher dialysate K, and as before, on the first dialysis day of the dialysis week. During the study period of 4 weeks (two before and two after switching to higher dialysate K), the dialysate K was modified with no other change in Na, Ca^{++} , bicarbonates or Mg prescriptions (dialysate or *per os*). At the time of the study, only sodium polystyrene sulphonate (Kayexalate) was prescribed in our centre, and prescription was not modified during the study period. In the same view, therapies with potential impact on K (like renin–angiotensin–aldosterone inhibitors or diuretics) or ECG results (like β -blockers) were not modified.

Both plasma Na and K were measured by indirect potentiometry, Mg by colorimetry (xylidyl blue) and bicarbonates by an enzymatic method. All these measurements were made on Cobas 8000 (Roche Diagnostics, Mannheim, Germany). Ionized Ca^{++} was measured by specific electrode on Rapidlab (Siemens Healthineers, Erlangen, Germany). All measurements were done in the same laboratory (Department of Clinical Chemistry, University of Liège) accredited for the ISO 15189 Guideline. ECG was performed with a classical 12-lead ECG, the AT 10 Plus (Schiller AG, Baar, Switzerland). Basal echocardiographic data were obtained from electronic medical records in 1 year prior to the study. The protocol of the study was approved by the Ethics Committee of our institution 'Comité d'éthique hospitalo-facultaire universitaire de Liège' (number B707201627193). The study was in accordance with the ethical standards of the Declaration of Helsinki, and signed written consent was obtained from each patient.

Statistical analysis

Each patient acts as his own control. Data are expressed as mean \pm SD when distribution was normal and as median with interquartile range (quartile 1–3) when not. Normality was assessed by the Shapiro–Wilk test. Accordingly, the paired samples t-test or the Wilcoxon was considered. Because the sample is relatively small and the distribution of K concentrations was not systematically normal (notably after dialysis session), all concentrations of K are expressed as median with interquartile range (quartiles 1–3) in comparison analyses. Head-to-head comparisons were performed for data before and after the dialysis sessions by Wilcoxon test, and a difference was considered as significant when $P < 0.05$. Then pre-dialysis K concentrations before switching (during 2 weeks) were compared with pre-dialysis concentrations after switching (during 2 weeks) using repeated measures analysis of variance (ANOVA). The same type of comparison was then obtained for post-dialysis concentrations. Finally, the percentages of hyperkalaemia before dialysis and of hypokalaemia after dialysis were compared before and after switching, by McNemar test. Hyperkalaemia was defined as a K concentration >5.1 (the normal upper value in our laboratory) or >5.5 mEq/L (the upper value frequently considered in many observational studies). Hypokalaemia was defined as K concentration <3.5 (the normal lower value in our laboratory) or <3.0 mEq/L (a value that could be considered as severe hypokalaemia). All concentrations presented here were those obtained on the first day of the dialysis week (Monday or Tuesday). Regarding ECG data, the following analyses were considered

and analysed in the same way as kalaemia (before and after the dialysis session, then before and after the switching of dialysate, Wilcoxon test and repeated measures ANOVA, respectively): heart rate (HR), PQ interval (PQ), QRS duration (QRS), QT interval (QT), corrected QT (cQT) interval and dispersion of cQT. All variables are expressed in ms, except HR which is in beats per minute (b.p.m.). cQT was calculated with the Bazett formula [16, 40], and cQT dispersion was defined as the difference between the maximum and minimum QT interval of the 12-lead ECG [41]. All ECG studies were read by the same observer (F.K.). In analyses where we considered four results for each patient (results from 2 weeks and 1 week before and after switching to higher K dialysate), we used $P < 0.05/6 = 0.0083$ to claim statistical significance according to Bonferroni correction in pairwise analyses. All analyses and calculations were performed using MedCalc (Mariakerke, Belgium).

RESULTS

Study population

When the decision to switch to higher K dialysate was made, 76 patients were chronically haemodialysed in our department. Among them, 49 were not considered in the further analysis because they were already treated with dialysate K2 ($n = 15$) or K4 ($n = 1$), they were < 18 years old ($n = 1$), their dialysis vintage was < 3 months ($n = 1$), they were unable to understand the informed consent (not speaking French or English or demented, $n = 3$) or they were dialysed more ($n = 1$) or less ($n = 1$) than three times a week. Finally, 13 patients were excluded because of persistent hyperkalaemia unless using a low K1 dialysate prescription. One additional patient was finally excluded due to problem with arteriovenous fistula (unpredictable single- or two-needle dialysis). Among eligible patients ($n = 39$), 12 refused to participate, leaving 27 patients (five women) with complete data for final analysis.

Mean (SD) age was 62.9 ± 15.3 years old. Clinical and biological characteristics of the population are summarized in Table 1. Native kidney disease is diabetic nephropathy ($n = 8$), glomerulonephritis ($n = 6$), hypertensive nephropathy ($n = 2$), autosomal dominant polycystic kidney disease ($n = 3$), toxic nephropathy ($n = 1$), rhabdomyolysis ($n = 1$), chronic pyelonephritis ($n = 1$) and unknown ($n = 5$). Among the 27 patients, 6 had a history of cardiac arrhythmia. Two of them were treated by acenocoumarol and β -blockers, one by amiodarone and one by amiodarone and β -blocker.

Effect on plasma K

Before changing the dialysate K, a significant decrease in K concentrations was observed after the dialysis session: from 4.45 (4.11–4.85) to 3.10 (2.82–3.50) mEq/L ($P < 0.0001$) 2 weeks before switching and from 4.55 (4.20–4.95) to 3.34 (2.81–3.66) mEq/L ($P < 0.0001$) 1 week before switching. After changing to a higher dialysate K, the decrease in plasma K concentration after dialysis remained highly significant: from 4.59 (4.35–4.80) to 3.77 (3.26–4.07) mEq/L ($P < 0.0001$) 1 week after switching and from 4.80 (4.58–5.12) to 3.70 (3.36–4.25) mEq/L ($P < 0.0001$) 2 weeks after switching. However, the decrease observed in K concentration during dialysis was significantly lower after switching to higher dialysate K: -0.89 (-1.37 to -0.39) mEq/L 1 week after and -1.14 (-1.30 to -0.67) mEq/L 2 weeks after, versus -1.66 (-1.96 to -0.75) mEq/L 2 weeks before and -1.34 (-1.64 to -0.88) mEq/L 1 week before (all comparisons between before versus

Table 1. Clinical and biological characteristics of the participants ($n = 27$)

Age, years	62.9 \pm 15.3
Dry weight, kg	77.3 \pm 19.1
Dialysis vintage, years	2.31 (1.11–4.67)
Residual renal function (> 200 mL), %	67
Dialysis time per session, min	240 (210–240)
Haemodiafiltration, %	59
Diabetes, %	30
Inter-dialytic weight gain, the first week, kg	2.3 \pm 1.5
Cardiologic history	
History of heart failure, %	4
History of cardiac hypertrophy, %	56
History of cardiac arrhythmia, %	22
History of atrial fibrillation, %	11
Left ventricular ejection fraction, %	65 (51–70)
Left ventricular end-diastolic diameter, mm	50 \pm 6
Left atrium dilatation, %	70
Dialysate composition	
Sodium, mEq/L	140 (138–140)
Potassium, %	
K1	55
K3	44
Calcium, %	
1.25 mEq/L	11
1.5 mEq/L	89
Bicarbonate, mEq/L	35 (31–37)
Biological variables	
Plasma sodium	139.6 \pm 2.8
Plasma potassium	4.50 \pm 0.50
	4.45 (4.11–4.85)
Plasma ionized calcium	1.17 (1.15–1.24)
Plasma bicarbonates	22.5 (20.8–23.8)
Plasma magnesium	0.84 \pm 0.11
Treatment, %	
Potassium chelators	8
RAAS inhibitors	26
Magnesium <i>per os</i>	19
Bicarbonates <i>per os</i>	4
Calcium <i>per os</i>	100
Diuretics <i>per os</i>	48
β -blockers <i>per os</i>	48
12-lead ECG variables	
Heart rhythm, b.p.m.	71 \pm 12
PQ, ms	176 (157–193)
QRS, ms	94 (86–111)
QT, ms	412 \pm 41
cQT, ms	445 \pm 35
QTc dispersion, ms	38 (31–50)

All plasma concentrations and ECG parameters are those obtained on the first dialysis day of the week, during the first week of the study (before switching). RAAS, renin–angiotensin–aldosterone system.

after switching are significant $P < 0.05$). The pre-dialysis K concentrations during the 4-week period were compared by repeated measures of ANOVA. Pairwise comparisons showed slightly higher concentrations 2 weeks after switching, compared with concentrations before switching, but the difference did not reach statistical significance ($P > 0.0125$). Regarding post-dialysis K concentrations, significant higher concentrations ($P < 0.0001$) were observed after switching to higher K dialysate (Table 2 and Figure 1).

Before switching, the percentage of post-dialysis K concentrations < 3.5 and 3 mEq/L was 71 and 38%, respectively. After

Table 2. Impact of switching to higher K dialysate on different biological variables

Variables	Before switching				After switching				Pairwise comparison ^a	Pairwise comparison ^b
	Pre-dialysis results		Post-dialysis results		Pre-dialysis results		Post-dialysis results			
	2 weeks before	1 week before	2 weeks before	1 week before	1 week after	2 weeks after	1 week after	2 weeks after		
K (mEq/L)	4.45 (4.11–4.85)	4.55 (4.20–4.95)	3.10 (2.82–3.50)	3.34 (2.81–3.68)	4.61 (4.35–4.81)	4.80 (4.60–5.10)	3.77 (3.26–4.07)	3.70 (3.36–4.25)	NS	P < 0.0001 for all comparisons
Na (mEq/L)	140.0 (137.5–141.8)	140.0 (138–142)	139.0 (137.0–141.8)	139.0 (137–140)	139 (136–140)	140.0 (138–140.8)	139.0 (136.3–140)	139.0 (137.0–140.0)	P = 0.0006 between 2 weeks before and 1 week after	NS
Ca ⁺⁺ (mEq/L)	1.17 (1.15–1.24)	1.18 (1.12–1.21)	1.21 (1.16–1.28)	1.24 (1.17–1.28)	1.20 (1.13–1.25)	1.19 (1.13–1.28)	1.21 (1.19–1.31)	1.24 (1.17–1.29)	NS	NS
Bicarbonates (mEq/L)	22.5 (20.8–23.8)	22.3 (21.5–23.7)	27.6 (26.2–29.7)	27.9 (25.7–29.7)	21.8 (19.8–23.3)	21.6 (20.8–23.7)	27.3 (25.4–28.6)	27.4 (26.1–29.1)	NS	NS
Mg (mEq/L)	0.84 (0.76–0.89)	0.83 (0.79–0.93)	0.77 (0.71–0.78)	0.75 (0.72–0.77)	0.85 (0.79–0.91)	0.86 (0.82–0.96)	0.78 (0.73–0.81)	0.78 (0.75–0.79)	NS	NS

^aP-values for comparison of pre-dialysis concentrations before and after switching.
^bP-values for comparison of post-dialysis concentrations before and after switching.
NS, not significant.

switching to higher K dialysate, this percentage was 35 and 6%, respectively, a significant decrease for both ($P < 0.0001$). Regarding the risk of pre-dialysis hyperkalaemia, we observed a percentage of pre-dialysis K concentration >5.1 and 5.5 mEq/L of 11 and 6%, respectively, before the switch. After switching to higher K dialysate, the percentages were 17 and 7%, respectively. These percentages were not significantly different before and after the switch to higher K dialysate.

Effect on other electrolytes

In Table 2, we compared the impact of switching to higher K dialysate on other biological variables (comparison of pre-dialysis values before versus after switching and comparison of post-dialysis values before versus after switching). For other biological variables considered, we did not find any impact of the change in dialysate K, especially after the dialysis session.

Effect on ECG results

Pre- and post-dialysis variables were analysed by Wilcoxon test four times (2 weeks before, 1 week before, 1 week after and 2 weeks after switching to higher dialysate K). The following variables did not change during the dialysis sessions for the 4 weeks: HR, PQ and QT (Figure 2). QRS values increased during the dialysis session 2 weeks before the switch [94 (86–111) to 98 (90–122) ms; $P = 0.0068$], 1 week before switching [90 (83–102) to 96 (90–124) ms; $P = 0.0416$] and 2 weeks after switching [94 (84–111) to 98 (87–119) ms; $P = 0.0078$]. cQT increased during dialysis 2 weeks before switching [446 (415–466) to 459 (433–483) ms; $P = 0.0436$] and 2 weeks after switching [432 (417–464) to 459 (431–502) ms; $P = 0.0025$]. Two weeks or 1 week before switching, the QT dispersion increased during the dialysis session from 38 (31–50) to 42 (38–57) ($P = 0.005$) and from 38 (32–50) to 40 (35–50) ($P = 0.0001$), respectively, whereas no difference was observed after switching (Figure 2). Then, evolution of pre-dialysis ECG results was compared by repeated measures ANOVA before and after changing to higher dialysate K. Pairwise comparisons did not show any difference in pre-dialysis ECG results for HR, PQ, QRS, QT, cQT and QT dispersion. The same results were observed in post-dialysis ECG results, except for QT dispersion. Indeed, 1 week after switching to higher dialysate K, post-dialysis QT dispersion [38 (34–42) ms] was lower than post-dialysis QT dispersion 2 weeks and 1 week before switching [42 (38–57) ms, $P = 0.0004$; and 40 (35–50) ms, $P = 0.0002$, respectively]. Two weeks after switching to higher dialysate K, post-dialysis QT dispersion [38 (35–44) ms] was not different than post-dialysis QT dispersion 2 weeks and 1 week before switching [42 (38–57) ms, $P = 0.0169$; and 40 (35–50) ms, $P = 0.1026$, respectively] (Figure 3).

DISCUSSION

The present study shows the impact of switching from lower to higher dialysate K in 27 HD patients. As expected, we found that dialysis sessions caused a significant decrease of plasma K concentrations. The increase in dialysate K was associated with a lesser decrease in plasma K concentrations [12, 13, 28, 30, 42–46], and accordingly with a much lower prevalence of post-dialysis hypokalaemia, including severe hypokalaemia (plasma K <3.0 mEq/L in 6 versus 38% of cases). The higher post-dialysis K concentrations observed with higher dialysate K was accompanied by only a modest and non-significant increase in pre-dialysis plasma K concentrations (and a non-significant higher

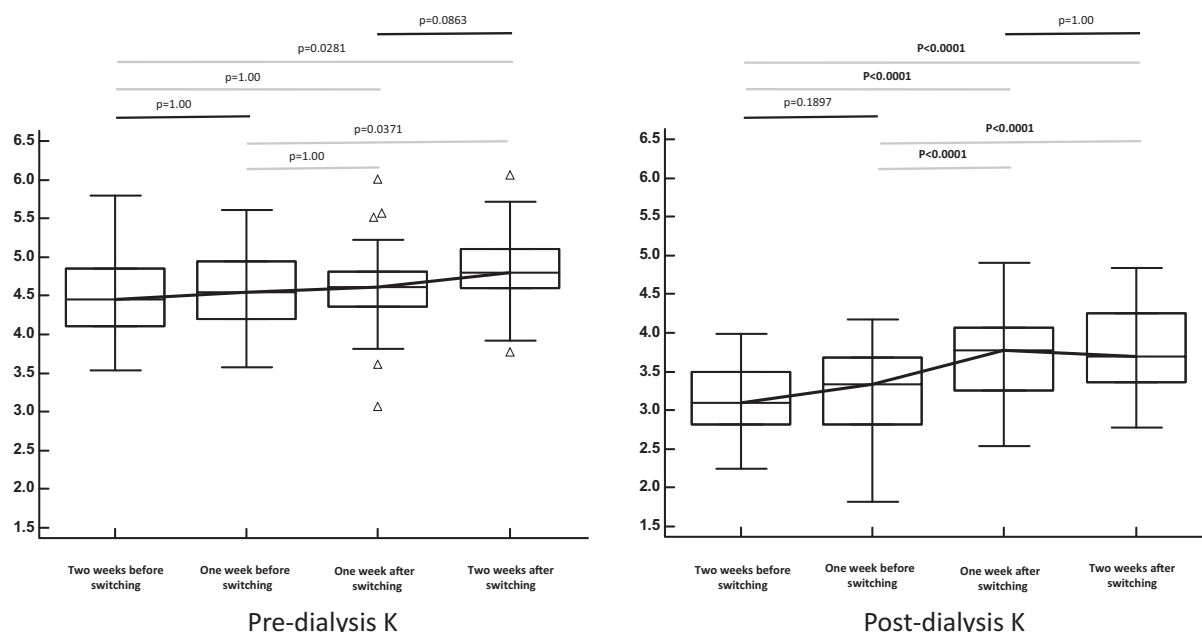


FIGURE 1: Evolution of K concentrations by repeated measures ANOVA before and after switching to higher K dialysate. Comparison of (A) pre-dialysis concentrations and (B) post-dialysis concentrations. In box-and-whisker plots, the central box represents the values from the lower to upper quartile (25th–75th percentile), the middle line represents the median and a line extends from the minimum to the maximum value, excluding ‘outside’ values, which are displayed as separate points (open triangle). Pairwise comparison: significant P-value at 0.0083 (bold results are significant). Grey line represents pairwise comparison between a timing before and after switching, and black line when comparison between timing both before or after switching.

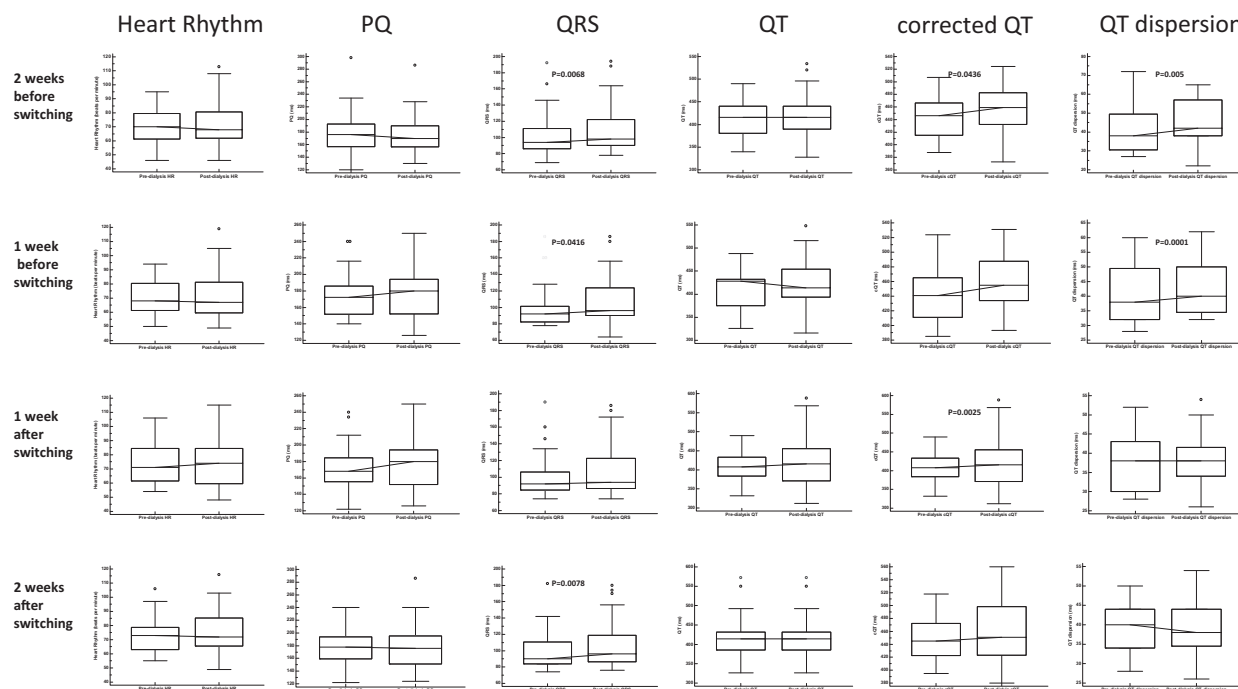


FIGURE 2: Comparison of pre- and post-dialysis electrocardiographic variables. Comparison 1 and 2 weeks before switching (upper figures) and 1 and 2 weeks after switching (lower figures). In box-and-whisker plots, the central box represents the values from the lower to upper quartile (25th–75th percentile), the middle line represents the median and a line extends from the minimum to the maximum value, excluding ‘outside’ values, which are displayed as separate points (open triangle). Only significant results are shown in bold ($P < 0.05$).

prevalence of hyperkalaemia). In parallel with variations of K concentrations, we also observed that QT dispersion after the dialysis session was significantly lower after the switch to higher K dialysate. QT interval reflects the total ventricular

recovery time, and QT dispersion is a direct measure of regional heterogeneity of myocardial repolarization. QT dispersion is associated with a higher risk of mortality and arrhythmia both in the cardiac [47–49] and dialysis populations [19, 50–53].

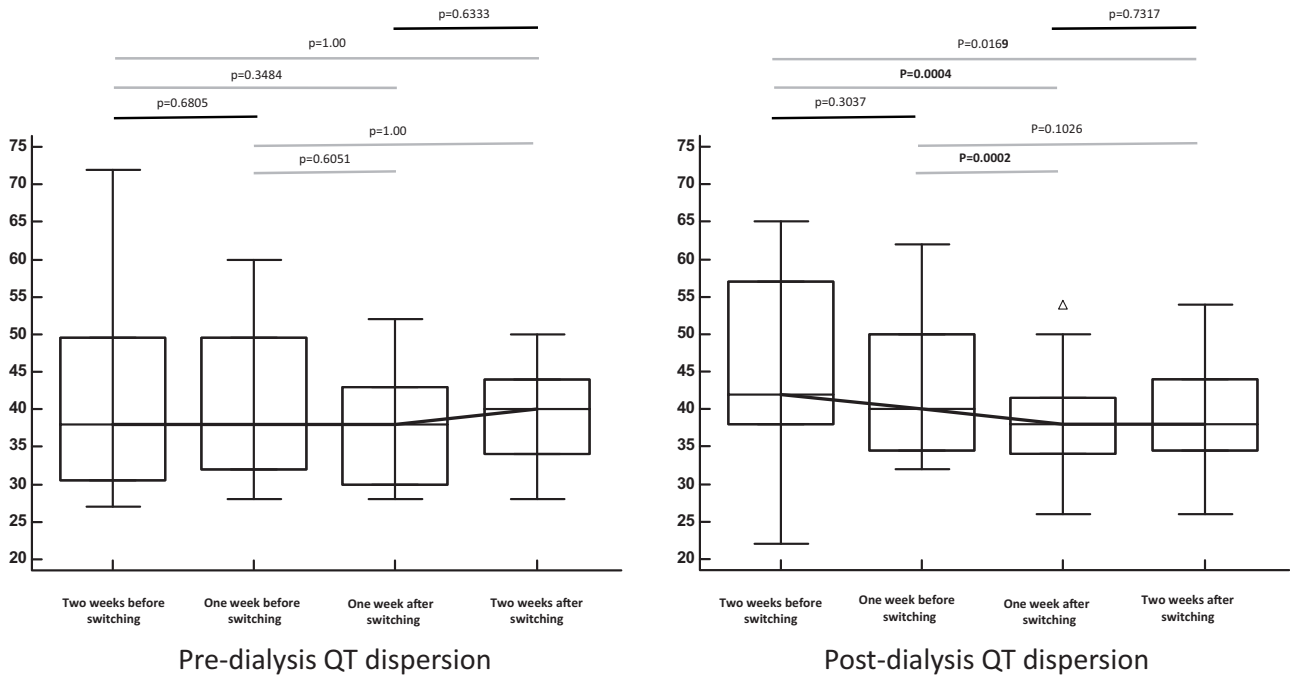


FIGURE 3: Evolution of QT dispersion concentrations by repeated measures ANOVA before and after switching to higher K dialysate. Comparison of (A) pre-dialysis QT dispersion (in milliseconds) and (B) post-dialysis QT dispersion. In box-and-whisker plots, the central box represents the values from the lower to upper quartile (25th–75th percentile), the middle line represents the median and a line extends from the minimum to the maximum value, excluding ‘outside’ values, which are displayed as separate points (open triangle). Pairwise comparison: significant P-value at 0.0083 (bold results are significant). Grey line represents pairwise comparison between a timing before and after switching, and black line when comparison between timing both before or after switching.

The decrease of K concentrations during the dialysis session was expected [12–14, 28, 30, 42, 43, 54, 55]. Also, data from large cohorts suggested that patients who were treated with lower K dialysate had a larger decrease in K concentrations during the dialysis session and, logically a higher risk of hypokalaemia [43]. However, in these studies, a substantial variability in post-dialysis K concentrations was observed, even in groups treated with the same K dialysate [43]. In our study, the patient was his own control, and such data are rare in the literature. With this design, we confirm that a dialysis session with a higher dialysate K is associated with a lower decrease in K level and a lower risk of post-dialysis hypokalaemia. The price to pay in terms of pre-dialysis potential hyperkalaemia seems acceptable.

Several authors have also studied the impact of a dialysis session on ECGs. Results from these observational studies are quite variable, even if most authors showed a modification of QTc length and/or QT dispersion [20, 54, 56–62]. The role of K or K changes on these ECG modifications has only been suggested by few authors who found associations between modification of plasma K during the dialysis and the incidence of QT abnormalities [54, 57, 58, 62]. Compared with these studies, our results are straightforward because they were obtained in the same patient after a single intervention, i.e. an increase of K in the dialysate. Few studies on the impact of modifying K dialysate concentrations are available. In 1980, Morrison *et al.* [21] suggested that a higher K concentration in the dialysate (from 2 to 3.5 mEq/L) could be beneficial to decrease ventricular ectopy as shown by 24-h Holter monitoring, but it was shown in only four patients. In 1996, Redaelli *et al.* [46] compared dialysis with constant K concentration in the dialysate (mean concentration of 2.31 mEq/L) with a K concentration in the dialysate varying according to the change of plasma K during the dialysis session in 36 patients who were their own control. In the variable K arm

of the study, the K concentration in the dialysate was 1.5 mEq/L less than that in the plasma and then diminished progressively until it reached a concentration of 2.5 mEq/L at the end of the dialysis session. They showed that premature ventricular complexes detected by Holter monitoring were less frequent during and after the dialysis with ‘adapted K dialysate concentration’ or ‘K profile’. QTc and QT dispersion were not considered in that study. These interesting results were, however, not confirmed in a study with a similar design in 30 patients [63]. In 2005, Buemi *et al.* [42] studied 28 patients haemodialysed with K2 dialysate versus a K concentration in the dialysate that was 1 mEq/L less than the concentration in the plasma and then diminished progressively until it reached K2 at the end of the dialysis session. They showed that the dialysis with the dialysate K profile had beneficial effect on QT parameters. In 2008, Muñoz *et al.* studied 12 patients considered at high risk of arrhythmia and compared 3 weeks of dialysis with a constant K concentration in the dialysate with 3 weeks of dialysis with K dialysate concentration that varied during the session, being higher at the beginning and lower at the end. They observed a beneficial effect on the cQT values after dialysis, but no effect on QT dispersion [45]. We confirmed and extended the results of these studies. We confirmed the same positive consequences on ECG variables, but contrary to previous studies, our intervention was simpler, being an increase of dialysate K by 1 mEq/L, and did not require the monitoring of plasma K concentration before (and during) every dialysis session. We note that similar beneficial effects on QT parameters were observed in studies switching patients from HD to haemodiafiltration [55] or from low to high calcium dialysate [64].

Our study must be read in the light of its limitations. First, the increase in dialysate K was used only in patients without severe pre-dialysis hyperkalaemia. Secondly, our study was

short-term, i.e. only for a 4-week period. It could be argued that a steady-state in K is possibly not reached after 2 weeks. Therefore, we retrospectively analysed the three pre-dialysis plasma K concentrations obtained directly after the end of the current study (K concentration is determined every 2 weeks in our centre). Dialysate K was not modified during this period of time (dialysate K similar to dialysate after switching). These three pre-dialysis plasma K concentrations were not different (all $P > 0.0083$) from those observed before and after switching [4.79 (4.49–5.07), 4.89 (4.40–5.22), 4.83 (4.52–5.29)]. Moreover, 3 months after the switch, patients were re-analysed. Among the 27 patients, 2 died and 2 were transplanted. Among the 23 remaining, the dialysate K remained stable in all, except three patients who moved from K4 to K2 prescription. Thirdly, for practical reasons, we measured plasma K and performed the ECG just before the end of the dialysis. It is known from kinetic studies that a post-dialysis rebound occurs after dialysis because of rapid redistribution of intracellular K [12–14, 43]. If such a rebound is sufficient to be associated with a concomitant, then improvement in QT dispersion is actually not known. Also, we admit that QT dispersion is a surrogate marker for cardiac arrhythmia and mortality [16, 18, 30, 65]. Lastly, our study remains limited to 27 patients and our results should be confirmed in a larger sample.

These clinical data support the switch to higher K dialysate. Indeed, such a single and simple switch to higher K concentration (from K3 to K4 or K1 to K2) is accompanied by a lower prevalence of severe post-dialysis hypokalaemia, to a higher post-dialysis concentration of K and to lower QT dispersion on ECG obtained after the dialysis session. The price to pay for such a strategy seems to be only a modest increase in pre-dialysis K concentrations. Further studies are needed to test if the beneficial short-term effect of switching to higher K dialysate both on K concentration and ECG results is also confirmed in long-term studies with hard clinical outcomes.

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CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. *Am J Kidney Dis* 1998; 32: S112–S119
2. Brown JH, Hunt LP, Vites NP et al. Comparative mortality from cardiovascular disease in patients with chronic renal failure. *Nephrol Dial Transplant* 1994; 9: 1136–1142
3. Herzog CA. Cardiac arrest in dialysis patients: approaches to alter an abysmal outcome. *Kidney Int Suppl* 2003; 63: S197–S200
4. Makar MS, Pun PH. Sudden cardiac death among hemodialysis patients. *Am J Kidney Dis* 2017; 69: 684–695
5. Bleyer AJ, Hartman J, Brannon PC et al. Characteristics of sudden death in hemodialysis patients. *Kidney Int* 2006; 69: 2268–2273
6. Charytan DM, Foley R, McCullough PA et al. Arrhythmia and sudden death in hemodialysis patients: protocol and baseline characteristics of the monitoring in dialysis study. *Clin J Am Soc Nephrol* 2016; 11: 721–734
7. Genovesi S, Valsecchi MG, Rossi E et al. Sudden death and associated factors in a historical cohort of chronic haemodialysis patients. *Nephrol Dial Transplant* 2009; 24: 2529–2536
8. Jadoul M, Thumma J, Fuller DS et al. Modifiable practices associated with sudden death among hemodialysis patients in the dialysis outcomes and practice patterns study. *Clin J Am Soc Nephrol* 2012; 7: 765–774
9. Karnik JA, Young BS, Lew NL et al. Cardiac arrest and sudden death in dialysis units. *Kidney Int* 2001; 60: 350–357
10. Ramesh S, Zalucky A, Hemmelgarn BR et al. Incidence of sudden cardiac death in adults with end-stage renal disease: a systematic review and meta-analysis. *BMC Nephrol* 2016; 17: 78
11. Sacher F, Jesel L, Borni-Duval C et al. Cardiac rhythm disturbances in hemodialysis patients. *JACC Clin Electrophysiol* 2018; 4: 397–408
12. Hung AM, Hakim RM. Dialysate and serum potassium in hemodialysis. *Am J Kidney Dis* 2015; 66: 125–132
13. Labriola L, Jadoul M. Sailing between Scylla and Charybdis: the high serum K-low dialysate K quandary. *Semin Dial* 2014; 27: 463–471
14. Lee J, Mendelssohn DC. Optimizing dialysate potassium. *Hemodial Int* 2016; 20: 573–579
15. Thornley-Brown D, Saha M. Dialysate content and risk of sudden cardiac death. *Curr Opin Nephrol Hypertens* 2015; 24: 557–562
16. Shamseddin MK, Parfrey PS. Sudden cardiac death in chronic kidney disease: epidemiology and prevention. *Nat Rev Nephrol* 2011; 7: 145–154
17. Rhee CM, Chou JA, Kalantar-Zadeh K. Dialysis prescription and sudden death. *Semin Nephrol* 2018; 38: 570–581
18. Weisberg LS, Racho J-S. The safety of low-potassium dialysis. *Semin Dial* 2010; 23: 556–560
19. Beaubien ER, Pylypchuk GB, Akhtar J et al. Value of corrected QT interval dispersion in identifying patients initiating dialysis at increased risk of total and cardiovascular mortality. *Am J Kidney Dis* 2002; 39: 834–842
20. Cupisti A, Galetta F, Morelli E et al. Effect of hemodialysis on the dispersion of the QTc interval. *Nephron* 1998; 78: 429–432
21. Morrison G, Michelson EL, Brown S et al. Mechanism and prevention of cardiac arrhythmias in chronic hemodialysis patients. *Kidney Int* 1980; 17: 811–819
22. Wanner C, Herzog CA, Turakhia MP et al. Chronic kidney disease and arrhythmias: highlights from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int* 2018; 94: 231–234
23. Brunelli SM, Du Mond C, Oestreicher N et al. Serum potassium and short-term clinical outcomes among hemodialysis patients: impact of the long interdialytic interval. *Am J Kidney Dis* 2017; 70: 21–29
24. Karaboyas A, Zee J, Brunelli SM et al. Dialysate potassium, serum potassium, mortality, and arrhythmia events in hemodialysis: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Am J Kidney Dis* 2017; 69: 266–277
25. Kovesdy CP, Regidor DL, Mehrotra R et al. Serum and dialysate potassium concentrations and survival in hemodialysis patients. *Clin J Am Soc Nephrol* 2007; 2: 999–1007
26. Yusuf AA, Hu Y, Singh B et al. Serum potassium levels and mortality in hemodialysis patients: a retrospective cohort study. *Am J Nephrol* 2016; 44: 179–186
27. Hoppe LK, Muhlack DC, Koenig W et al. Association of abnormal serum potassium levels with arrhythmias and

- cardiovascular mortality: a systematic review and meta-analysis of observational studies. *Cardiovasc Drugs Ther* 2018; 32: 197–212
28. Moledina D, Geller D. Is low dialysate potassium ever indicated in outpatient hemodialysis? *Semin Dial* 2014; 27: 263–265
 29. Pun PH, Lehrich RW, Honeycutt EF et al. Modifiable risk factors associated with sudden cardiac arrest within hemodialysis clinics. *Kidney Int* 2011; 79: 218–227
 30. Pun PH. Dialysate potassium concentration: should mass balance trump electrophysiology? *Semin Dial* 2018; 31: 569–575
 31. Ohnishi T, Kimachi M, Fukuma S et al. Postdialysis hypokalemia and all-cause mortality in patients undergoing maintenance hemodialysis. *Clin J Am Soc Nephrol* 2019; 14: 873–881
 32. Lee S, Kang E, Yoo KD et al. Lower serum potassium associated with increased mortality in dialysis patients: a nationwide prospective observational cohort study in Korea. *PLoS One* 2017; 12: e0171842
 33. Abuelo JG. Low dialysate potassium concentration: an over-rated risk factor for cardiac arrhythmia? *Semin Dial* 2015; 28: 266–275
 34. Fotheringham J, Fogarty DG, El Nahas M et al. The mortality and hospitalization rates associated with the long interdialytic gap in thrice-weekly hemodialysis patients. *Kidney Int* 2015; 88: 569–575
 35. Roy-Chaudhury P, Tumlin JA, Koplan BA et al. Primary outcomes of the Monitoring in Dialysis Study indicate that clinically significant arrhythmias are common in hemodialysis patients and related to dialytic cycle. *Kidney Int* 2018; 93: 941–951
 36. Al-Ghamdi G, Hemmelgarn B, Klarenbach S et al. Dialysate potassium and risk of death in chronic hemodialysis patients. *J Nephrol* 2010; 23: 33–40
 37. Ferrey A, You AS, Kovesdy CP et al. Dialysate potassium and mortality in a prospective hemodialysis cohort. *Am J Nephrol* 2018; 47: 415–423
 38. Brunelli SM, Spiegel DM, Du Mond C et al. Serum-to-dialysate potassium gradient and its association with short-term outcomes in hemodialysis patients. *Nephrol Dial Transplant* 2018; 33: 1207–1214
 39. Huang C-W, Lee M-J, Lee P-T et al. Low potassium dialysate as a protective factor of sudden cardiac death in hemodialysis patients with hyperkalemia. *PLoS One* 2015; 10: e0139886
 40. Bazzet HC. An analysis of time relations of electrocardiograms. *Heart* 1920; 7: 353–367
 41. Day CP, McComb JM, Campbell RW. QT dispersion: an indication of arrhythmia risk in patients with long QT intervals. *Br Heart J* 1990; 63: 342–344
 42. Buemi M, Aloisi E, Coppolino G et al. The effect of two different protocols of potassium haemodiafiltration on QT dispersion. *Nephrol Dial Transplant* 2005; 20: 1148–1154
 43. Agar BU, Culleton BF, Fluck R et al. Potassium kinetics during hemodialysis. *Hemodial Int* 2015; 19: 23–32
 44. Hou S, McElroy PA, Nootens J et al. Safety and efficacy of low-potassium dialysate. *Am J Kidney Dis* 1989; 13: 137–143
 45. Muñoz RI, Montenegro J, Salcedo A et al. Effect of acetate-free biofiltration with a potassium-profiled dialysate on the control of cardiac arrhythmias in patients at risk: a pilot study. *Hemodialysis Int* 2008; 12: 108–113
 46. Redaelli B, Locatelli F, Limido D et al. Effect of a new model of hemodialysis potassium removal on the control of ventricular arrhythmias. *Kidney Int* 1996; 50: 609–617
 47. Darbar D, Luck J, Davidson N et al. Sensitivity and specificity of QTc dispersion for identification of risk of cardiac death in patients with peripheral vascular disease. *BMJ* 1996; 312: 874–879
 48. Elming H, Holm E, Jun L et al. The prognostic value of the QT interval and QT interval dispersion in all-cause and cardiac mortality and morbidity in a population of Danish citizens. *Eur Heart J* 1998; 19: 1391–1400
 49. Schouten EG, Dekker JM, Meppelink P et al. QT interval prolongation predicts cardiovascular mortality in an apparently healthy population. *Circulation* 1991; 84: 1516–1523
 50. Guney M, Ozkok A, Caliskan Y et al. QT dispersion predicts mortality and correlates with both coronary artery calcification and atherosclerosis in hemodialysis patients. *Int Urol Nephrol* 2014; 46: 599–605
 51. Wang CL, Lee WL, Wu MJ et al. Increased QTc dispersion and mortality in uremic patients with acute myocardial infarction. *Am J Kidney Dis* 2002; 39: 539–548
 52. Nakamura S, Ogata C, Aihara N et al. QTc dispersion in haemodialysis patients with cardiac complications. *Nephrology* 2005; 10: 113–118
 53. Wu V-C, Lin L-Y, Wu K-D. QT interval dispersion in dialysis patients. *Nephrology (Carlton)* 2005; 10: 109–112
 54. Alabd MA, El-Hammady W, Shawky A et al. QT interval and QT dispersion in patients undergoing hemodialysis: revisiting the old theory. *Nephron Extra* 2011; 1: 1–8
 55. Barta K, Czifra Á, Kun C et al. Hemodiafiltration beneficially affects QT interval duration and dispersion compared to hemodialysis. *Clin Exp Nephrol* 2014; 18: 952–959
 56. Covic A, Diaconita M, Gusbeth-Tatomir P et al. Haemodialysis increases QTc interval but not QTc dispersion in ESRD patients without manifest cardiac disease. *Nephrol Dial Transplant* 2002; 17: 2170–2177
 57. Cupisti A, Galetta F, Caprioli R et al. Potassium removal increases the QTc interval dispersion during hemodialysis. *Nephron* 1999; 82: 122–126
 58. Floccari F, Aloisi E, Nostro L et al. QTc interval and QTc dispersion during haemodiafiltration. *Nephrology* 2004; 9: 335–340
 59. Kalantzi K, Gouva C, Letsas KP et al. The impact of hemodialysis on the dispersion of ventricular repolarization. *Pacing Clin Electrophysiol* 2013; 36: 322–327
 60. Lorincz I, Matyus J, Zilahi Z et al. QT dispersion in patients with end-stage renal failure and during hemodialysis. *J Am Soc Nephrol* 1999; 10: 1297–1302
 61. Morris ST, Galiatsou E, Stewart GA et al. QT dispersion before and after hemodialysis. *J Am Soc Nephrol* 1999; 10: 160–163
 62. Yetkin E, Ileri M, Tandogan I et al. Increased QT interval dispersion after hemodialysis: role of peridialytic electrolyte gradients. *Angiology* 2000; 51: 499–504
 63. Santoro A, Mancini E, London G et al. Patients with complex arrhythmias during and after haemodialysis suffer from different regimens of potassium removal. *Nephrol Dial Transplant* 2007; 23: 1415–1421
 64. Näppi SE, Virtanen VK, Saha HH et al. QTc dispersion increases during hemodialysis with low-calcium dialysate. *Kidney Int* 2000; 57: 2117–2122
 65. Lin CY, Lin LY, Chen PC. Analysis of T-wave morphology from the 12-lead electrocardiogram for prediction of long-term prognosis in patients initiating haemodialysis. *Nephrol Dial Transplant* 2007; 22: 2645–2652