Increased P Wave Dispersion and Maximum P Wave Duration after Hemodialysis

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Background: Atrial fibrillation is a frequent arrhythmia in patients undergoing hemodialysis. The consequences of hemodialysis on P wave durations and P wave dispersion have not been fully understood. The objective of this study was to study the effect of dialysis on P wave maximum (P_{max}), P wave minimum (P_{min}), and P wave dispersion (P_d).

Methods: We studied P_{max}, P_{min}, and P_d in 32 patients (17 men and 15 women, mean age 54 ± 18 years) with chronic renal failure undergoing hemodialysis. The difference between maximum and minimum P wave duration was calculated and defined as P wave dispersion ($P_d = P_{max} - P_{min}$).

Results: There was a significant increase in P_{max} at the end of dialysis compared to the beginning (98 ± 13 ms vs. 125 ± 12 ms, $P < 0.001$). P_{min} did not show any significant change (71 ± 11 ms vs. 73 ± 10 ms, $P = 0.42$). P_d was significantly increased at the end of dialysis (27 ± 9 ms vs. 52 ± 11 ms, $P < 0.001$). There was a negative correlation between serum potassium, magnesium, phosphate, blood urea nitrogen, and creatinin at the end of dialysis and P_{max} and P_d, respectively ($P < 0.05$). A weak positive correlation was found between serum calcium, bicarbonate at the end of dialysis and P_{max} and P_d ($P < 0.05$).

Conclusion: Hemodialysis ends with significant increase in P wave maximum duration and P wave dispersion, which might be responsible for the increased occurrence of atrial fibrillation in these groups of patients.

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The prevalence of atrial fibrillation (AF) in patients with chronic renal insufficiency on the hemodialysis program is three times more common than in the general population. AF has been shown to increase the mortality (23% with AF vs. 6% in sinus rhythm) and morbidity of these patients on hemodialysis. Approximately one in three hemodialysis patients with AF had thromboembolic complications within 1 year of follow-up.[1] Risk factors for AF may be more common in dialysis patients including age, cardiac enlargement, and abnormal calcium–phosphorous metabolism.[1–4] Hemodialysis was also associated with a significantly higher risk of AF than peritoneal dialysis.[5] The majority of the arrhythmia episodes during hemodialysis have been reported to occur between the third and fourth hours of hemodialysis.[6]

There are some electrophysiologic abnormalities detected in the atria prone to fibrillation. Intraatrial and interatrial conduction times tend to be prolonged in addition to inhomogeneous propagation of sinus impulses. Previously, these conditions have been assessed by simple electrocardiographic markers, including maximum P wave duration (P_{max}) and P wave dispersion (P_d).[7–15] However, the effect of hemodialysis on these P wave parameters has not been widely examined.

The purpose of our study was to evaluate the effects of hemodialysis on P wave durations and P wave dispersion.

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METHODS

Study Population

Thirty-two nondiabetic patients (17 males, mean age 54 ± 18 years, range 23–85) with end-stage renal failure were selected. The study population had no impulse generation or conduction defect or previous episode of AF. All the patients were in sinus rhythm during the study period. The underlying causes for chronic renal failure were chronic glomerulonephritis (n = 16), hypertensive nephropathy (n = 9), and chronic tubulointerstitial nephropathy (n = 7). Prior to hemodialysis two-dimensional and M-mode echocardiographic examinations were performed with Hewlett-Packard 2000 system with a 2.5 MHz transducer. Left atrial dimensions and left ventricular ejection fraction were measured from parasternal long-axis view as suggested by the American Society of Echocardiography. Treatment modalities taken by patients were as follows: in three (9%) patients digitalis, in two (6%) patients nitrates, in three (9%) patients α-blockers, in eleven (34%) patients angiotension-converting enzyme (ACE) inhibitors, in eight (25%) patients calcium antagonists, in nine (28%) patients β-blockers, and in five (16%) patients angiotensin receptor antagonists.

Hemodialysis sessions were carried out in standard settings (4008-B, Fresenius Medical Care, Germany), F 5 and F 7 HPS polysulfone (Fresenius Medical Care, AG.D-61343 Bad Hamburg, Germany) for 3.5–4 hours, three times per week. Bicarbonate dialysate fluids contained 140 mMol/L sodium, 2.0 mMol/L potassium, 1.5 mMol/L calcium, and 1.0 mMol/L magnesium. During the sessions no drugs were administered, except for isotonic NaCl and sodium heparin. Maintenance therapy consisting of digitalis, nitrates, α-blockers, ACE inhibitors, calcium antagonists, angiotensin receptor antagonists, and beta-blockers remained unchanged. Sodium, potassium, calcium, phosphate, and magnesium levels were measured before and after the hemodialysis session. Blood urea nitrogen and creatinine were also determined.

Electrocardiographic Analysis

All subjects underwent 12-lead ECG recording after a 20-minute resting period in supine position at a paper speed of 50 mm/s and 2 mV/cm before the hemodialysis session. After the session another 12-lead ECG was recorded. The P wave duration was measured manually in all simultaneously recorded 12 leads of the surface ECG by two of the investigators unaware of the study hypothesis. In each lead the mean values for the three complexes were calculated. For greater accuracy, the measurements were performed with calipers and magnifying lens, as described by previous investigators.[7–9] The onset of the P wave was defined as the point of first visible upward departure from baseline for positive waveforms, and as the point of first downward departure from baseline for negative waveforms. The return to the baseline was considered to be the end of the P wave. The P_{max} measured in any of the 12 leads of the surface ECG was used as the longest atrial conduction time. The difference between the maximum (P_{max}) and minimum P wave duration (P_{min}) was calculated and defined as P wave dispersion ($P_d = P_{max} - P_{min}$).[15] The average values of P_{max} and P_d obtained from two investigators were used for a comparison of the pre- and postdialytic period. Intraobserver and interobserver coefficients of variation (SD of differences between two observations divided by the mean value and expressed as percent) were found to be 2.9% and 3.1% for P_{max}, 3.4% and 3.6%, respectively for P_d.

Statistical Analysis

All data were expressed as mean ± SD. Statistical analysis was carried out using a paired Student's *t*-test for continuous variables with the Statistical Package for Windows version 8.0 (SPSS Inc, Chicago, IL). Correlations were analyzed with the Pearson's correlation coefficient. A P value < 0.05 was considered statistically significant.

RESULTS

Demographic variables have been shown in Table 1. Mean left ventricular ejection fraction was 58 ± 9% and left atrial diameter was 41.0 ± 3.2 mm. P wave maximum duration increased significantly after the hemodialysis session compared to predialysis values (98 ± 13 ms vs. 125 ± 12 ms, $P < 0.001$). However, P wave minimum duration did not show any significant difference between pre- and postdialysis values (71 ± 11 ms vs. 73 ± 10 ms, $P = 0.42$). P wave dispersion increased significantly after hemodialysis compared to predialysis values (27 ± 9 ms vs. 52 ±11 ms, $P < 0.001$) (Fig. 1). None of our patients developed AF during or after the hemodialysis session.

Table 1. Clinical and Echocardiographic Data of the Study Population

Mean age (years)	54 ± 18
Sex (male/female)	17/15
Average time of dialysis (months)	22.0 ± 28.1
Ultrafiltration ratio (mL/h)	546.6 ± 168.9
Systolic blood pressure (mmHg)	127 ± 21
Diastolic blood pressure (mmHg)	83 ± 12
Ischemic heart disease n (%)	4 (13)
Hypertension n (%)	17 (53)
Left ventricular ejection fraction (%)	58 ± 9
Left atrial diameter (mm)	41.0 ± 3.2

During the sessions, serum sodium did not show a significant change. Serum potassium decreased significantly (5.3 ± 1.1 mMol/L to 3.9 ± 0.8 mMol/L, $P < 0.001$) after hemodialysis compared to predialysis values. Calcium concentration at the end of the dialysis showed significantly higher values compared to the predialysis values (2.31 ± 0.21 mMol/L vs. 2.58 ± 0.23 mMol/L, $P < 0.01$). Magnesium concentration at the end of dialysis showed a significantly lower value compared to the predialysis value (0.86 ± 0.23 mMol/L vs. 0.74 ± 0.2, $P < 0.001$). Phosphate levels decreased by the end of dialysis (2.38 ± 0.4 mMol/L vs. 1.61 ± 0.3 mMol/L, $P < 0.001$) (Table 2).

There was a negative correlation between serum potassium, magnesium, phosphate, blood urea nitrogen, creatinin at the end of dialysis and P_{max} and $P_{d,}$ respectively ($P < 0.05$). A weak positive correlation was found between serum calcium, bicarbonate at the end of dialysis and P_{max} and P_d ($P < 0.05$).

DISCUSSION

Atrial fibrillation is a highly prevalent arrhythmia in patients with chronic renal insufficiency on hemodialysis, which is also observed during the dialysis sessions.[5–6] In our study, we have demonstrated significant increases in P wave maximum duration and P wave dispersion after hemodialysis compared to the predialysis period. Thus, the hemodialysis session ends with an increase in atrial conduction time and dispersion of atrial refractoriness, which might lead to the occurrence of AF mostly toward the end of sessions.

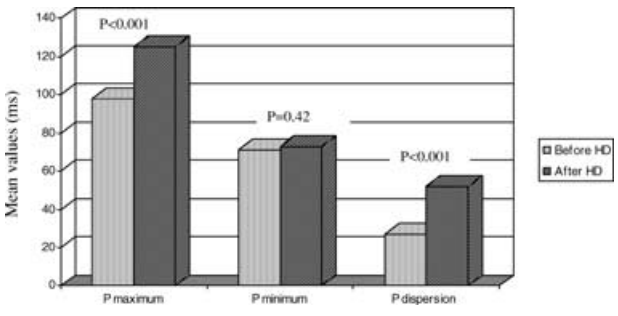

Figure 1. Mean values of P wave durations and P dispersion (HD = hemodialysis).

Ansari, Manis, and Feinfeld[3] studied retrospectively the frequency of atrial arrhythmias over 3 years in 106 patients on hemodialysis. Ten patients suffered from atrial arrhythmias, three of them had AF. Except one of them, all were recorded between 3 and 4 hours of hemodialysis. Paroxysmal AF that occurs during hemodialysis has also been reported to stop spontaneously without therapeutic intervention 2–3 hours after the dialysis session.[6] Our findings also showed significant change of P_d and P_{max} at the end of session compared to the beginning. Though none of our patients developed atrial arrhythmia during or after the sessions, repeated sessions might have a cumulative role on atrial electrical remodeling after a prolonged period on dialysis.

Hemodialysis itself through changes in electrolyte levels might create a milieu relatively arrhythmogenic in chronic renal failure patients. When dialyzed "against" a potassium concentration of 2 mEq/L, these patients become relatively hypokalemic during the last 2 hours of a standard 4-hour treatment during which AF commonly occurs.[16] Hypokalemia is considered to be an accepted risk factor for both ventricular and supraventricular arrhythmias.[17] This has been shown in patients with prolonged diuretic therapy,[18] and hypokalemia may actually be a serious problem in patients with an acute myocardial infarction,[19] or with a failing heart.[20] In our study, we have also seen a significant decrease in the potassium level at the end of dialysis that is negatively correlated with P_{max} and P_d. Korzets, Ori, and Herman recommended performing dialysis "against" a dialysis potassium concentration of 3 mEq/L for the patients with a history of AF detected during the sessions.

P wave dispersion is derived from a common 12-lead ECG and is used as a marker of the inter-lead variation in P wave duration measurements calculated in all the 12 leads simultaneously recorded.[7–8,13] P wave dispersion has been used for the prediction of paroxysmal AF in patients with

Table 2. Serum Electrolytes Before and After Hemodialysis

	Before Hemodialysis	After Hemodialysis	P Value
Heart rate (bpm)	82 ± 15	84 ± 11	0.62
Sodium (mMol/L)	138 ± 3.2	137 ± 2.9	0.81
Potassium (mMol/L)	5.3 ± 1.1	3.9 ± 0.8	<0.001
Magnesium (mMol/L)	0.86 ± 0.23	0.74 ± 0.2	<0.001
Calcium (mMol/L)	2.31 ± 0.21	2.58 ± 0.23	<0.01
Phosphate (mMol/L)	2.38 ± 0.4	1.61 ± 0.3	<0.001
Bicarbonate (mMol/L)	21 ± 4	26 ± 5	<0.001
Blood urea nitrogen (mMol/L)	27.3 ± 3.8	15.9 ± 2.1	<0.001
Serum creatinin (μMol/L)	910 ± 183	426 ± 92	<0.001

lone AF,[7–8] patients undergoing coronary artery bypass surgery,[9] patients with hypertension,[10] hypertrophic cardiomyopathy,[11] and chronic obstructive pulmonary disease.[12] Dilaveris et al.[14] also found maximum P wave duration as a predictor of frequently relapsing AF.

Szabo et al.[15] also studied the effect of hemodialysis on P wave duration and P_d. They found that P_{max} and P_d increase significantly after the hemodialysis session. However, when they subgrouped the patients according to left atrial diameter, P_d increased significantly after hemodialysis only in those with left atrial diameter greater than 45 mm. P_{max} did not significantly change after hemodialysis in both of these groups. Compared to Szabo's group of patients, our patient group had a relatively smaller left atrial diameter (mean 4.1 ± 3.2 mm), though we have demonstrated significant increase both in P_{max} and P_d after hemodialysis.This difference in left atrial diameters might be due to differences in the severity of underlying heart and renal disease and duration of hemodialysis. Ischemic heart disease (64% vs. 13%) and hypertension (82% vs. 53%) were more prevalent in Szabo's patients than in our study population. In addition, Szabo's patients were under maintenance hemodialysis for a longer period of time compared to our study population (54 ± 34 months vs. 22.0 ± 28.1 months, respectively). Though P wave duration, which is thought to be an accepted indicator of interatrial conduction disturbance, was found to be independent of an increase in atrial size,[21] Ansari, Manis, and Feinfeld,[3] in their retrospective study reported that left atrial enlargement is an important risk factor for the development of AF. Probably, hemodialysis sessions together with left atrial enlargement occurring in time alter the susceptibility of atria to develop AF.

The effect of supplemental magnesium on P_d were studied by Dagdelen et al. in a group of patients undergoing coronary artery bypass surgery and supplemental magnesium was found to decrease P_d and the incidence of postoperative AF.[22] However, in a recent study supplemental magnesium was not found to be effective in the prevention of postoperative AF.[23] In our study, there was significant decrease in magnesium levels at the end of dialysis. Though we found a weak correlation between postdialytic serum magnesium concentrations and P_{max} and P_d, intradialytic magnesium supplementation may help in ameliorating AF in these patients, which has been shown to decrease P_d after coronary artery bypass surgery.

Atrial fibrillation is a highly prevalent arrhythmia in patients with chronic renal insufficiency on the dialysis program.[1] The prevalence was estimated as 13.6% and was directly related to age, being present in 16.4% of the patients >64 years of age and in more than a third of those >74 years of age. These were >3 times the prevalence observed in the general population in whom arrhythmia has been quantified as 4.7% or 5.9% of those individuals ≥65 years of age. Abbott et al. found age ≥71 years, extremes of predialysis blood pressure (both high and low), dialysis modality (hemodialysis vs. peritoneal dialysis), and digoxin use associated with AF in chronic dialysis patients. Atrial fibrillation in patients on hemodialysis was also found to be associated with a greater thromboembolic impact than that in the general population.[1]

Study Limitations

In our study, P wave duration was measured manually and for greater accuracy, measurements were performed with calipers and magnifying lens,

as described by previous investigators.[7,9] However, Dilavers et al.,[24] comparing three different methods for the manual measurement of P wave duration, namely (1) by cursor on a high-resolution computer screen (on screen), (2) by calipers and a magnifying glass (on paper), and (3) by a high-resolution digitizing board (on board), have found that intraobserver and interobserver relative errors were significantly different among the three methods; the lowest errors were associated with the on-screen measurement. Therefore, also in our study on-screen measurements would have yielded much fewer intraobserver and interobserver relative errors.

CONCLUSION

Chronic renal failure patients harboring well-established risk factors for AF in the general population might be under greater risk than their counterparts induced by the hemodialysis itself and/or the ionic imbalance. Our findings showed significant increase in atrial conduction time and dispersion of atrial refractoriness at the end of dialysis, which possibly reflects the increased susceptibility of dialysis patients to AF.

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