The Egyptian Journal of Hospital Medicine (July 2022) Vol. 88, Page 3802-3807

The Impact of Low Sodium Dialysate on Different Echocardiographic Parameters in Prevalent Hemodialysis Patients

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ABSTRACT

Background: About one-fifth of the adult population has end-stage renal disease **(**ESRD), which is associated with an elevated risk of illness and death. To remove excess sodium from the body, hemodialysis treatments using dialysate sodium (D-NA) with a concentration of 120 mEq/L have been utilized for decades. Higher D-Na (around140 mEq/L) has been employed for dialysis hemodynamic stability over time.

Objective: To determine the impact of decreased dialysate Na (equal to or less than 135 mEq/L) on cardiac functions and different echocardiographic parameters in prevalent hemodialysis patients.

Patients and Methods: At Rod Elfarag Hospital's Dialysis Unit, 45 patients on regular hemodialysis underwent a 6-month prospective study.

Results: This study found a significant difference between baseline and six-month lab results in terms of hemoglobin, WBCs, platelets and Ht/URR as well as serum albumin and Ca/Na/phosphorus and BNP ($p < 0.001$). We discovered a highly statistically significant variation in PR interval, QRS duration, and QT interval between the baseline and follow-up ECGs after six months ($p < 0.001$). There was high statistically significant difference between baseline echocardiography and after 6 months echocardiography as regard left atrium diameter, ejection fraction (EF%), diastolic blood pressure (DBP) and systolic BP ($p < 0.001$).

Conclusion: Our results showed that the PR interval, QRS duration, and QT interval at baseline were all statistically significantly different from those after six months of treatment. DBP couldn't be lowered in this short time frame at all. This strategy's impact should be investigated in depth over an extended period of time.

Keywords: Echocardiographic Parameters, Low Sodium Dialysate, Prevalent Hemodialysis.

INTRODUCTION

ESRD affects around 15% of the adult population, resulting in an increase in both morbidity and mortality rates **(1).**

Dialysate sodium (D-NA) in the range of 120 mEq/L was traditionally used in hemodialysis treatments to remove excess sodium from the body. Higher D-Na (around 140 mEq/L) has been employed for dialysis hemodynamic stability over time **(2).**

People who are diagnosed with renal failure undergoing HD are unable to restrict their Na intake, resulting in considerable saline overflow between dialyses. Dialysate Na concentrations are a significant contributor to Na overload. As a result of increased left ventricular (LV) filling pressure and Na intake or dialysate, large changes in circulatory volume have been shown to significantly affect transmitral flow. It's been shown that noninvasive Doppler echocardiography is an effective way to check the diastolic function of the left ventricle, with distinctive variations in the transmitral Doppler flow as a result of inadequate filling of the left ventricle. No matter if the EF is normal or low, diastolic dysfunction is linked to aberrant mechanical processes of the myocardium and includes diminished filling and delayed LV relaxation **(3).**

When sodium is loaded into the body either by excessive dietary intake or through excessive diffusion through the dialysis dialysate, both blood pressure and intra-dialytic weight gain (IDWG) are exacerbated, according to research. The hardening of the vascular endothelium is possibly a mechanism by which an increase in plasma [Na^+] can cause hypertension without extracellular fluid (ECF) volume **(4).**

Dialysis fluid [Na^+] is associated with less thirst, a lower IDWG, a smaller ECF volume, and lower BP in a variety of observational and small clinical trials. In order to maintain their dry weight within the time constraints of their dialysis session, patients with large fluid gains (interdialytic weight increase) are subjected to high urine full report (UFR). Higher mortality rates as well as morbidity usually associate higher values of UFR and IDWG **(5).**

To boost results, a "volume first" approach must be adopted. Excessive sodium intake has been linked to water retention and an increase in blood pressure, therefore cutting back on salt intake is essential. Dialysis patients are encouraged to minimize their IDWG by limiting their oral sodium intake **(6).**

Sodium is eliminated nearly exclusively by dialysis when remaining renal function diminishes. Ultrafiltration uses convection to remove sodium from the water. Diffusion, in which sodium moves down its concentration gradient from blood to dialysate or vice versa, also influences sodium balance during dialysis. This process is influenced by a number of variables **(7).**

Due to sodium diffusion from dialysate to serum when D-Na is greater than serum sodium (S-Na),

Received: 04/04/2022
Accepted: 01/06/2022

the post dialysis serum sodium concentration will be greater than the predialysis concentration. Increased IDWG results from both increased blood pressure and a consequent increase in thirst [8].

Lowering D-Na has a number of other benefits, including lower pulmonary artery pressure, lower inferior vena cava diameter, enhanced left ventricular diastolic characteristics, reduced left ventricular systolic diameter, reduced tricuspid regurgitation as well as regression of left ventricular hypertrophy [8].

Reduced arterial stiffness, as evaluated by pulse wave velocity, has been reported as an increase in vascular endothelial performance [9]. Thickness of the brachial artery wall is considered a marker of improved endothelial function [1].

Cardiac risk factors are prevalent in patients with end-stage renal disease (ESRD). The severity and extent of cardiovascular problems in patients with end-stage renal disease cannot be explained by standard CV risk factors alone. ESRD patients' mortality can be better explained by a combination of endothelial dysfunction (asymmetric dimethyl arginine), inflammatory biomarkers (CRP), and myocardiopathy (BNP), which has been shown to boost explanatory power by about twenty percent. Furthermore, recent research have demonstrated that cardiac troponin T, BNP, NT-proBNP, and high-sensitivity CRP are strongly linked to one another, demonstrating a complicated interaction between inflammation, cardiac biomarkers, malnutrition, as well as over hydration in dialysis patients [10].

The aim of the present study was to determine the impact of decreased dialysate Na (equal to or less than 135 mEq/L) on cardiac functions and different echocardiographic parameters in prevalent hemodialysis patients.

PATIENTS AND METHODS

For six months, 45 patients on routine hemodialysis at Rod Elfarag Hospital's Dialysis Unit participated in a prospective cohort research. HD Regimen: 3 sessions/week, bicarbonate-containing dialysate and heparin anticoagulation.

Exclusion Criteria:

Heart failure, IHD, malignancy, active auto-immune disease, history of pulmonary embolism, Hb level <8 gm/dl, hypotension (BP<100/60) and hyponatremia (<130) meq

Study Procedures:

All patients were subjected to: Full history taking including medical co-morbidities, etiology of renal failure, regimen of HD, duration on dialysis and complications related to HD, and clinical examination. Venous samples were taken for (just before the session of the midweek): Complete blood picture, serum urea (pre-dialysis and post-dialysis), serum albumin, serum electrolytes (Ca^{++}, PO_4, Na^{+}) alkaline phosphatase and PTH, BNP, 12-lead surface ECG, echocardiography: left atrium diameter, EF%, diastolic, pressure: transmitral flow, T-wave Doppler and systolic pressure: 2D, M mode.

After Six months of maintained low dialysate sodium in hemodialysis sessions: the patients were re-evaluated clinically; the second venous samples were taken for the same laboratory investigations and echocardiography and ECG.

To conduct transthoracic echocardiographic exams, a single skilled heart doctor used an advanced Philips machine (Philips IE33; Philips, Eindhoven, The Netherlands).

Ethical consent:

An approval of the study was obtained from Ain Shams University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test.

Qualitative data were represented as frequencies and relative percentages. Quantitative data were expressed as mean ± SD (Standard deviation) and range and were compared by paired samples t-test. P value < 0.05 was considered significant.

RESULTS

This table shows the demographic data of the studied patients (Table 1).

Table (1): Demographic data of studied patients

Demographic data	Cases	
Age (years)		
Range.	35.0 – 52.0	
Mean ± SD.	43.87 ± 5.0	
Gender		
	No.	%
Male	27	60.0
Female	18	40.0
BMI (kg/m²)		
Range.	22.0 – 29.9	
Mean ± SD.	25.67 ± 2.29	

This table shows that among the studied cases there were 55.6% with hypertension (Table 2).

Table (2): Co-morbidities among studied cases

Cases		
Co-morbidities		
	No.	**%**
Hypertension	25	55.6
Diabetes mellitus	11	24.4
Hepatitis C virus	2	4.4

There was a significant difference between baseline and six-month lab results in terms of hemoglobin, WBCs, platelets and Ht/URR as well as serum albumin and Ca/Na/phosphorus and BNP (Table 3).

Table (3): Comparison between baseline lab investigation and after 6 months

Lab investigation	Baseline (n = 45)	6 months (n = 45)	P
Hb (gm/dl)			
Mean ± SD.	9.89 ± 0.8	10.25 ± 0.84	0.04*
Hematocrit (%)			
Mean ± SD.	33.52 ± 3	35.97 ± 3.08	<0.001*
Urea Reduction Ratio URR (%)			
Mean ± SD.	68.81 ± 3.87	67.77 ± 4.02	<0.001*
Serum Albumin (mg/dL)			
Mean ± SD.	3.87 ± 0.68	3.65 ± 0.31	0.027*
Ca (mg/dL)			
Mean ± SD.	9 ± 1.22	8.16 ± 1.33	<0.001*
Phosphorus (mg/dL)			
Mean ± SD.	5.79 ± 1.41	5.27 ± 1.43	<0.001*
Na (mEq/L)			
Mean ± SD.	137.56 ± 3.75	136.04 ± 3.4	0.047*
BNP (pg/ml)			
Mean ± SD.	88.2 ± 5.15	79.76 ± 7.26	<0.001*

*: Statistically significant, HB: hemoglobin, BNP: B-type natriuretic peptide

It's clear from this table that there was a statistically significant difference between periods when it came to PR intervals and when it came to QRS duration and QT intervals (Table 4).

Table (4): Comparison between baseline ECG and after 6 months

ECG	Baseline (n = 45)	6 months (n = 45)	P
PR interval (ms)			
Mean ± SD.	0.2 ± 0.03	0.17 ± 0.03	<0.001*
QRS duration (ms)			
Mean ± SD.	0.14 ± 0.04	0.12 ± 0.03	0.008*
QT interval (ms)			
Mean ± SD.	0.44 ± 0.04	0.42 ± 0.03	0.0087*

*: Statistically significant

In this table, statistically significant differences in left atrium diameter and diastolic BP can be seen, as well as statistically significant differences in EF percentage and systolic BP between different periods (Table 5).

Table (5): Comparison between baseline echocardiography and after 6 months

Echocardiography	Baseline (n = 45)	6 months (n = 45)	P
Left atrium diameter (mm)			
Mean ± SD.	38.62 ± 4.69	37.72 ± 4.72	<0.001*
EF%			
Mean ± SD.	65.8 ± 3.41	63.77 ± 2.96	0.003*
Systolic BP(mm/Hg)			
Mean ± SD.	142.89 ± 29.67	130.22 ± 24.17	0.028*
Diastolic BP (mm/Hg)			
Mean ± SD.	83.56 ± 10.9	78.44 ± 10.86	<0.001*

*: Statistically significant, EF: emptying fraction

This table shows that there was negative correlation between BNP with Na (Table 6 and Figure 1).

Table (6): Correlation between BNP and Na after 6 months

BNP		
	r	P
Na	-0.306	0.041

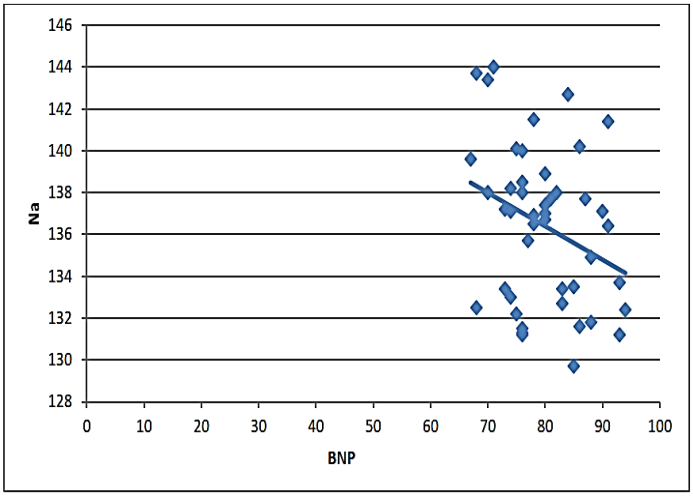

Fig (1): Correlation between BNP and Na after 6 months

DISCUSSION

Mortality and morbidity rates are greater among dialysis patients. During the long inter-dialytic interval (LII), a period of 68 hours without hemodialysis (HD) in which patients having traditional HD therapy three times a week are subjected, there is an elevated

risk of hospital admissions and cardiovascular issues**.** Toxins and acids, as well as electrolytes such as potassium, are likely to have accumulated throughout this time period. As a side effect, a greater degree of hemodynamic instability and electrolyte instability are observed during the first HD session following the LII **(11).**

Patients on dialysis who have a 24-hour urine output more than 200 millilitres (mL) are less likely to suffer from complications and death than those who do not have any residual renal function (RRF). The greater sodium and water excretion of RRF patients results in reduced interdialytic weight gain (IDWG) and better blood pressure (BP) values. Additionally, they have superior control over their serum bicarbonate, phosphate as well potassium levels. A superior metabolic and hemodynamic profile is predicted in dialysis patients with RRF during the LII due to their improved ability to drain electrolytes, acids, and fluids compared to those without RRF. Dialysis patients with RRF **(11).**

Few studies have compared patients with and without RRF in terms of blood electrolyte levels, acid-base status (pH and PCO_2), and hydration balance, particularly during the LII period of the disease. We recognize that acquiring these data is crucial because it can stimulate behaviors targeted at preserving RRF, as well as promote therapeutic techniques to limit the LII's detrimental effects on the population of patients without RRF **(12).**

Extracellular volume (ECV) increases in chronic renal failure (CRF), even if overload isn't visible because of edema. Sedentary patients with advanced CRF are more vulnerable to hyponatremia. Even with a normal sodium consumption that is quite low, hypertension nevertheless develops. As CRF advances, this unusual sensitivity to sodium burden becomes more pronounced. A saline surplus develops between dialysis sessions in patients with renal insufficiency and hemodialysis (HD) **(13).**

Dialysate sodium content is a critical factor in sodium overload. There will be a drop in extracellular sodium concentration if sodium is being removed diffusively, as occurs with low dialysate sodium concentrations. Dialysis patients may benefit from a higher dialysate sodium concentration, but this may come at the expense of increased inter-dialytic weight gain (IDWG) and hypertension **(14).**

Dialysate sodium concentrations should aim to strike a balance between sodium removal and blood volume preservation in order to achieve appropriate dialysate sodium concentrations. Hypertension and left ventricular hypertrophy in HD patients are primarily caused by the accumulation of water and sodium. Thus, the elimination of sodium and water during HD is critical to improving HD patients' cardiovascular risk profile. The dialysate sodium concentration can be manipulated in HD patients to enhance water and sodium control. The diffusive elimination of sodium may be increased by lowering the dialysate's sodium concentration, which may reduce IDWG and thirst **(15).**

Dialysate Na overload is caused in part by an increase in the concentration of Na. As a result of increased left ventricular (LV) filling pressure and Na intake or dialysate, large changes in circulatory volume have been shown to significantly affect transmitral flow. Indices based on Doppler measurements. It's been shown that noninvasive Doppler echocardiography is an effective way to check the diastolic function of the left ventricle, with distinctive variations in the transmitral Doppler flow as a result of inadequate filling of the left ventricle. No matter if the EF is normal or low, diastolic dysfunction is linked to aberrant mechanical processes of the myocardium and includes diminished filling and delayed LV relaxation **(8).**

The aim of the present study was to determine the impact of decreased dialysate Na (equal to or less than 135 mEq/L) on cardiac functions and different echocardiographic parameters in prevalent hemodialysis patients. At Rod Elfarag Hospital's dialysis unit, 45 patients on regular hemodialysis underwent a 6-month prospective study.

In our population, the mean age of studied patients was 43.87 (±5 SD) with range (35-52) years. Among the studied patients there were 27 (60%) males and 18 (40%) females and mean BMI of studied group was 25.67 (±2.29 SD) with range (22-29.9). Slightly similar to our results, **Akyol *et al.*** **(8)** results that showed that the mean of age of studied patients was 48.6 (± 3.1 SD) and there were 31 (63.27%) males and 18 (36.73%) females, **Aybal Kutlugün *et al.*** **(16)** results that showed that the mean age of studied patients was 48.4 (± 17.8 SD), there were 17 (56.7%) males and 13 (43.3%) females and **Amoako *et al.*** **(17)** who reported that males were in the majority (64.5%), females were (35.5%) with the mean age was 43.86 ± 17.84 (range 18 - 85) years. **Jacobs *et al.*** **(10)** reported results that were slightly similar to our results as regard gender 30 (68.18%) were males, 14 (31.81%) were females while they reported mean of age was higher than our results (66 ±10.50 SD years).

In contrast to our results, **MacRae *et al.*** **(18)** found that males accounted for 36.4% while females were 63.6% and mean age was 74.9 years, which was higher than our results and **Afshinnia *et al.*** **(19)** showed that there were 16 females (72.7%) and 6 males (27.3%) and the mean (SD) age was 53.7 (18.0) years, which was higher than our results.

In our patients, as regard co-morbidities, there were 25 (55.6%) with hypertension, 11 (22.4%) with diabetes and 2 (4.4%) with hepatitis. Higher than our results was found by **Lee *et al.*** **(20)** who reported that there were 66.4% with hypertension, 33.2% with diabetes and 3.1% with liver disease, **Aybal Kutlugün *et al.*** **(16)** who found that there were 8 (26.7%) with diabetes, 9 (30%) with CVD and 3 (10%) with hepatitis, **Akyol *et al.*** **(8)** who showed that there were 16 (32.6%) with diabetes, but results according to hypertension

were lower than our results as they reported that there were only 12 (24.5%) with hypertension and **MacRae *et al.*** [18] found that there were 71.2% with hypertension and 26.3% with diabetes.

This study found a significant difference between baseline and six-month lab results in terms of hemoglobin, WBCs, Platelets and Ht/URR as well as serum albumin and Ca/Na/phosphorus and BNP. **Akyol *et al.*** [8] agreed with our results in reporting that a highly statistically significant variation in BNP levels was found between the initial lab examination and that conducted six months later ($p < 0.001$) and disagreed with our results in reporting that, baseline and follow-up lab investigations after 6 months for serum Na showed no statistically significant differences. ($p= 0.714$). **Lee *et al.*** [21] disagreed with us in reporting that, serum Na levels were not statistically different between the baseline and follow-up tests six months later ($p= 0.764$), potassium ($p= 0.642$) and calcium levels ($p= 0.352$) measured after HD and agreed with us in reporting that the mean Hb of these two groups differed significantly from one another. ($p <0.001$) and significant differences between these two groups were found in mean Ht ($p= 0.017$).

While, **Roberts *et al.*** [22] found that Dialysis patients with cardiovascular conditions have the highest B-type natriuretic peptide levels, which are substantial predictors of death. **Mostafa *et al.*** [23] reported that after the dialysis session, BNP levels dropped significantly (Pre- dialysis HD was 374 ±412 pg/dl vs. HD after; 273 ±321 pg/dl, $p < 0.001$). Sixty-three percent of patients saw a decrease in BNP of at least 20% following the HD session, compared to just 36.7% who showed no change. And, **Marshall *et al.*** [24] showed that after a year of monitoring, a sodium dialysate concentration of 135 mmol/L had no effect on the left ventricular mass index compared to the control, despite considerable decreases in plasma B-type natriuretic peptide concentrations at six and twelve months.

Furthermore, **Afshinnia *et al.*** [19] performed research on the impact of different dialysate magnesium concentrations on QTc dispersion in hemodialysis patients and found that serum potassium and magnesium levels decreased significantly in both low and normal magnesium dialysate groups ($p < 0.001$). Bicarbonate levels continued to rise, but salt and calcium levels did not alter ($p < 0.001$).

In our population, based on the ECGs taken at baseline and six months later, we discovered a substantial difference in the PR interval, the QRS duration and the QT interval. **Astan *et al.*** [25] agreed with our results in reporting that pre-hemodialysis and post-hemodialysis patients differed significantly in terms of QRS length and QT interval ($p < 0.001$) but disagreed with our results in reporting that pre-hemodialysis and post-hemodialysis patients differed significantly in terms of QRS length and QT interval, according to statistical analysis ($p= 0.58$). **Lee *et al.*** [21] agreed with us in reporting that sudden cardiac death (SCD) patients' QRS durations were substantially longer than those of survivors in pre-HD ECG (100.6 ± 14.9 vs. 92.6 ± 14.0 ms, $p = 0.015$) and disagreed with us in reporting that other characteristics, such as the PR and QT intervals, did not differ significantly between the two groups.

In agreement with our results, **Morales *et al.*** [26] reported that the QRS length was much longer at both 25 Hz and 40 Hz filters (from 98 ± 11 to 106 ± 16 ms and from 97 ± 12 s to 102 ± 13 ms, respectively, $P<0.001$). And, **Afshinnia *et al.*** [19] found that there was a substantial rise in the mean QTc for both groups of dialysis patients who were given different concentrations of magnesium ($p \leq 0.049$). After dialysis, the QTcd was reduced in the low magnesium bath group and grew in the normal magnesium bath group, but the difference was not statistically significant in any of the two groups.

We found substantial differences in left atrial diameter, EF percentage, diastolic and systolic blood pressure in our patients' baseline and follow-up echocardiograms after six months. In contrast to our results, **Akyol *et al.*** [8] research found no statistically significant difference in left atrium diameter between baseline and follow-up echocardiography at 6 months ($p= 0.843$), EF% ($p= 0.811$) and diastolic BP ($p= 0.634$). For systolic blood pressure, the change between baseline echocardiography and after six months echocardiography was statistically significant ($p < 0.05$).

In agreement to our results, **Lee *et al.*** [21] found that both before and after HD, the EF in the SCD group was considerably lower than in the survivor group (pre-HD TTE: 54.8 ± 12.4 vs. 59.4 ± 11.3, $p = 0.037$; post-HD TTE: 46 ± 11.8 vs. 58.4 ± 11.6, $p < 0.001$).

While, **Sayarlioglu *et al.*** [27] reported that lower sodium dialysate treatments reduced LVSD, TR, PAP, and IVCD in terms of echocardiographic measures (p was 0.002, 0.04, 0.013, and < 0.01, respectively). Comparing pre- and post-dialysis BP, as well as post-dialysis systolic BP and IDWG to baseline, we found that all three variables were statistically lower (p was < 0.01, 0.011, 0.022, and < 0.01, respectively and **Marshall *et al.*** [24] reported that dialysate sodium concentration of 135 mmol/L was found to have no effect on the left ventricular mass index over the course of 12 months of follow-up, despite large decreases in interdialytic weight growth and extracellular fluid volume.

Mostafa *et al.* [23] agreed with us that dialysis had a considerable impact on reducing left atrial dilatation (before 3.06 ±0.5 mm vs. after 2.73 ±0.4 mm, $p < 0.001$) and disagreed with us in reporting that, pre- and post-HD studies showed no significant alterations in the systolic function measured by FS percent and EF percent (FS% ($p = 1$) and EF% ($p = 0.699$)).

Afshinnia *et al.* [19] found that in both groups of dialysis patients, a substantial drop in systolic and diastolic blood pressure was observed post-dialysis

compared to the pre-dialysis levels of blood pressure ($p < 0.001$).

CONCLUSION

Based on the patient's pre-dialysis sodium levels, dialysate sodium concentration could be reduced to lower the SBP and lower the volume stress on the heart. DBP could not be decreased within this short time frame. A large and in-depth examination of the impact of this strategy is necessary.

Conflict of interest: The authors declare no conflict of interest.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution: Authors contributed equally in the study.

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