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Effect of Blood and Fistula Flow Rates on Dialysis Adequacy, Phosphate Removal and Cardiac Function in Hemodialysis Patients

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ABSTRACT

Background: dialysis adequacy refers to the delivery of a dose of dialysis considered high enough to promote an optimal long term outcome. Quantification of the dialysis dose is an essential element because the adequacy has a profound effect on patient morbidity and mortality. **Aim of the study**: assessment the effect of blood and fistula flow rates on dialysis adequacy, phosphate removal and cardiac function in hemodialysis patients. **Patients and Methods**: this study was conducted on eighty patients with regular hemodialysis (HD) selected from Al-Azhar University Hemodialysis Unite in New Damietta. The studied patients were divided into two main groups according to blood flow rate (BFR) as follows: Group A 40 patients on BFR 250 mL/min and Group B 40 patients on BFR 350 mL/min. **Results:** there was statistically significant decrease of pre dialysis phosphate in group A in comparison to group B. There was statistically significant increase of KT/V, UUR and PRR in group B in comparison to group A. Arteriovenous fistula (AVF) Qa had negative correlation with TAPSE while it had positive correlation to all echocardiography findings except EF and heart rate (HR), kt/V and URR in group A. AVF Qa had positive correlation to all echocardiography findings except (EF, HR and TAPSE), kt/V, URR and PRP in group B

Conclusion: increasing of blood and fistula flow rates are effective in increasing dialysis adequacy and phosphate reduction ration and it is more evident where using high-flux hemodialysis.

Keywords: Hemodialysis; Arteriovenous Fistula.

INTRODUCTION

Dialysis adequacy refers to the delivery of a dose of dialysis considered high enough to promote an optimal long term outcome [(1)].

Urea reduction ratio (URR) is a method of measuring adequate dialysis that correlates with patient outcome [(1)]. **Rafik *et al.*** [(2)] found that the most common marker to quantify dialysis adequacy is Kt/V index**. Basile *et al.***[(3)] suggested that patients at greater risk for the development of high output cardiac failure are those with Qa ≥ 2000 ml/min.

To achieve an adequate Kt/V, many factors could be optimized as follows: dialyzer size and characteristics, dialysis time, dialysis frequency, dialysate flow rate, and blood flow rate (BFR). However, the use of some of these methods is not always possible due to clinical intolerance and economic constraints [(4)].

Quantification of the dialysis dose is an essential element in the management of chronic hemodialytic treatment because the adequacy of the dose has a profound effect on patient morbidity and mortality [(5)]. **Roozitalab *et al.*** [(6)] found that failure to reach the target Kt/V could have multiple reasons, including inability to provide the prescribed BFR due to inefficient access, error in estimating dry weight, inaccurate dialyzer specified clearance, clotting in the dialyzer, shorter dialysis sessions and in appropriate dialyzer selection**.**

AIM OF THE STUDY

Assessment the effect of blood and fistula flow rates on dialysis adequacy, phosphate removal and cardiac function in hemodialysis patients.

PATIENTS AND METHODS

1. Study Design: This study was conducted on eighty (80) patients with regular hemodialysis (HD) selected from Al-Azhar University Hemodialysis Unite in New Damietta during periods from Oct. 2018 to Jul 2019. The studied patients were divided into two (2) main groups according to blood flow rate (BFR) as follows: Group A: Forty (40) patients on BFR 250 mL/min and Group B: Forty (40) patients on BFR 350 mL/min

2. Ethical Aspects

The study protocol was accepted by the local Ethics and Research Committee, and consent was signed by the patients.

3. *Exclusion criteria:*

Patients with duration of HD therapy of less than three months and patients with central venous line.

4. Inclusion Criteria:

Patients with duration of HD therapy of at least three months, three dialysis sessions per week; 4 hours each, Fresenius 4008S, bicarbonate buffer and age of patients ranged from 20 to 70 years

5. Study Protocol:

All patients underwent history taking, clinical examination, arteriovenous fistula examination, laboratory investigations included, renal function tests: serum creatinine, blood urea, parathyroid hormone (PTH) by full automated analyzer, serum sodium, potassium, calcium, and phosphorus by full automated chemistry analyzer.

Radiological investigation: A) Echocardiography: Each patient underwent echocardiography performed by

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the Cardiology Unit using SEQUOIA C256 (SIEMENS) echocardiograph machine.

The following parameters were recorded for every patient: Left ventricle hypertrophy (LVH): Concentric or eccentric, left ventricle dilatation, ejection fraction (EF), left ventricle diastolic dysfunction, pulmonary pressures and wall motion abnormalities; valvular heart disease

B) Doppler ultrasound: Colour flow Doppler provides accurate imaging and flow volume measurement of vascular access in hemodialysis. Doppler ultrasound became the standard of care for evaluation of AVF dysfunction and is essential in the preoperative evaluation for access placement. Fistulae were scanned with a linear array transducer, longitudinally and transversely. All vascular flow measurements were done by a single experienced user using a dedicated vascular probe (4-10 MHz 10L-Linear Probe, GE medical systems).

Parameters of hemodialysis adequacy:

Measurement of urea reduction ratio: Urea reduction ratio is measured as follows:

- URR = $\frac{(C0-Ct)}{C0}$ X100%. Co: urea concentration at the start of the dialysis session, Ct: urea concentration at the end of the dialysis

Calculation of phosphate reduction ratio:

- PRR = $\frac{(C0-Ct)}{C0}$ X100%. Co: pre-dialysis serum phosphate level, Ct: post-dialysis serum phosphate level

Equilibrated Kt/V formula:

- Daugirdas: kt/v=-In ($\frac{postBUN}{preBUN-.03}$) + (4-3.5× $\frac{postBUN}{preBUN}$) × $\frac{UF}{weight}$)

K is the effective clearance of urea, t is the duration of the session, and V is the volume of urea distribution, UF: Ultrafiltration (weight loss), weight: postdialysis weight (dry weight).

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:
  - Probability (P-value)
  - P-value <0.05 was considered significant.
  - P-value <0.001 was considered as highly significant.
  - P-value >0.05 was considered insignificant.

RESULTS

There was statistically significant decrease of pre dialysis phosphate in group A in comparison to group B (Table 1).

Table (1): Comparison between group A and group B as regards laboratory investigations

	Group A (No.=40)		Group B (No.=40)		Independent test
	Mean	SD	Mean	SD	P value
Calcium	8.31	0.51	8.37	0.52	>0.05
Phosphate (Mg/dl) (pre dialysis)	6.25	0.60	7.63	1.12	<0.001
Phosphate (Mg/dl) (post dialysis)	3.29	0.45	2.97	0.21	<0.001
Potassium (mmol/L)	5.43	0.54	5.43	0.54	>0.05
Sodium	138.75	4.51	138.75	4.51	>0.05
Creatinine (mg/dl)	5.29	0.81	5.31	0.84	>0.05
PTH	47.20	2.50	51.68	4.32	>0.05
BUN (pre dialysis)	114.05	15.35	121.70	16.23	0.033
BUN (post dialysis)	33.08	4.60	24.38	3.87	<0.001
WBCs	5.83	1.76	5.90	1.70	>0.05
HB	9.29	1.38	9.36	1.35	>0.05
PLT	205.63	6.10	204.88	6.72	>0.05

Table (2): Comparison between group A and group B as regards KT/V, UUR and PRP

	Group A (No.=40)		Group B (No.=40)		Independent test
	Mean	SD	Mean	SD	P value
Kt /V (Daugirdas)	1.41	0.07	1.84	0.13	<0.001
URR	70.89	1.76	79.54	2.75	<0.001
PRR	47.46	4.83	60.46	5.66	<0.001

There was statistically significant increase of KT/V, UUR and PRR in group B in comparison to group A (Table 2). There was statistically significant increase in Kt/V (1.45± 0.05) P < 0.001 and URR (72.08 ± 1.28) P < 0.001 and PRR (47.70 ± 4.17) P < 0.023 in high flux in comparison to low flux Kt/V (1.35± 0.05) URR (69.31± 0.83) PRR (44.14± 5.72) in group A.

Table (3): Comparison between group A and group B as regards echocardiography and AVF Qa data

	Group A (No.=40)		Group B (No.=40)		Independent test
	Mean	**SD**	**Mean**	**SD**	**P value**
LVEDD (cm)	5.00	0.37	5.70	0.35	<0.001
LVESD (cm)	3.17	0.33	3.92	0.41	<0.001
LVEDV (ml/m2)	59.62	11.47	93.37	10.61	<0.001
IVSd (cm)	1.10	0.11	1.29	0.09	<0.001
PWd (cm)	1.10	0.09	1.30	0.09	<0.001
LVESV (ml/m2)	24.66	4.79	37.05	5.81	<0.001
EF	61.76	4.23	56.23	2.70	<0.001
LV mass (g)	168.48	41.68	326.67	59.95	<0.001
BSA (m2)	1.80	0.17	1.99	0.17	<0.001
LV mass index (g/m2)	109.91	32.53	190.75	42.41	<0.001
RWT	0.47	0.04	0.44	0.04	<0.001
LA volume (ml/m2)	32.63	11.50	52.56	8.65	<0.001
SV (ml)	106.73	28.03	172.99	28.55	<0.001
HR (bpm)	80.55	5.50	87.83	3.29	<0.001
CO (ml/min)	8.62	2.43	14.93	2.47	<0.001
SPAP (mm Hg)	29.21	5.31	38.57	3.87	<0.001
TAPSE (cm)	2.60	1.07	1.82	0.24	<0.001
LVOTd (cm)	2.64	0.22	2.89	0.20	<0.001
LVOT area (cm2)	5.22	0.78	7.25	0.75	<0.001
LVOT VTI (cm)	19.45	3.10	26.60	3.06	<0.001
AVF Qa ml/min	996.90	296.73	2370.78	487.92	<0.001

In group B, there was statistically significant increase in LVEDD, LVESD, LVEDV, LVESV, BSA, SV, LVM, LVMI, CO, and LA volume in comparison to group A (Table 3).

Table (4): Correlation between AVF Qa as regards echocardiography

	AVF Qa ml/min	
	r	**P value**
LVEDD (cm)	0.910	<0.001
LVESD (cm)	0.978	<0.001
LVEDV (ml/m2)	0.991	<0.001
IVSd (cm)	0.863	<0.001
PWd (cm)	0.969	<0.001
LVESV (ml/m2)	0.937	<0.001
EF	-0.200	>0.05
LV mass (g)	0.914	<0.001
BSA (m2)	0.820	<0.001
LV mass index (g/m2)	0.985	<0.001
RWT	-0.860	<0.001
LA volume (ml/m2)	0.981	<0.001
SV (ml)	0.995	<0.001
HR (bpm)	0.174	>0.05
CO (ml/min)	0.943	<0.001
SPAP (mm Hg)	0.980	<0.001
TAPSE (cm)	-0.273	<0.001
LVOTd (cm)	0.967	<0.001
LVOT area (cm2)	0.993	<0.001
LVOT VTI (cm)	0.996	<0.001
Kt /V (Daugirdas)	0.315	0.048
URR	0.349	0.027
PRR	0.620	0.012

AVF Qa had significant negative correlation with TAPSE while it had significant positive correlation to all echocardiography findings except EF and HR (Table 4).

DISCUSSION

In our study, we found that there was statistically significant increase in KT/V, URR and PRR in group B in comparison to group A. In addition there was statistically significant increase in pre dialysis phosphate and BUN in group B in comparison to group A but there was statistically significant decrease in post dialysis phosphate and BUN in group B in comparison to group A.

These findings are in agreement with **Borzou *et al.*** [(7)] who found that increasing the BFR can increase the dialysis efficiency. Nevertheless, attention should be given to factors such as patients' tolerance, hemodynamic status, using suitable filter according to patients' weight, and suitable BFR. In addition **Rafik *et al.*** [(2)] showed that Kt/V Daugirdas was ≥1.4 in 73% of cases with a BFR of 250 mL/min and in 100% of cases with a BFR of 350 mL/min. Several observational studies have examined the relationship between BFR and dialysis dose. **Chang *et al.*** [(8)] also showed that BFR was positively correlated with spKt/V ($\beta = 0.108$, $P = 0.001$) and odds ratio of patients with BFR <250 mL/min to have inadequate dialysis dose (spKt/V ≤1.2) was 1.5 (95% CI, 1.03 to 2.20; $P = 0.036$).

In addition **Cigarran *et al.*** [(9)] found that usage of more efficient dialyzers, increasing the BFR, increasing dialysate flow rate and increasing dialysis duration can all increase delivery of HD. On the other hand **Gutzwiller *et al.*** [(10)] assessed the effectiveness of increasing BFR on clearance of potassium and phosphate with dialysis and showed that increasing the BFR was effective in increasing clearance of potassium but was not effective in phosphorus clearance. This discrepancy could possibly be due to a longer follow-up of their study, during which a number of intervening factors, including life style modification, diet, nutrition and efficacy of dialysis prescription.

In our study there was statistically significant increase in Kt/V, URR and PRR in high flux in comparison to low flux Kt/V, URR, and PRR in group A. In addition there was statistically significant increase in Kt/V, URR, and PRR in high flux in comparison to low flux Kt/V, URR, and PRR in group B. These findings are in agreement with **Rafik *et al.*** [(2)] who showed that increasing BFR is effective in increasing dialysis dose and PRR during high-flux HD. Another study reported by **Yuehong *et al.*** [(11)] showed that the high-flux FX60 dialyzer significantly alleviated HD patients' renal anemia, hyperphosphatemia and hypertension even within three-year study periods. This study suggests that high-flux HD might provide better hypertension control, improve anemia and decrease phosphate levels compared to low-flux HD. **Khodayar *et al.*** [(12)] showed a significantly higher quality of life in patients with high flux dialyzers than those treated with low flux dialyzer.

In our study we found a positive correlation between fistula flow rate and LVEDD, LVESD, LVEDV, LVESV, BSA, SV, LVM, LVMI, CO, LA volume with normal EF. These findings are in agreement with **Mohamed *et al.*** [(13)] who showed that HFA was associated with a significant dilatation of left cardiac chambers (LA and LV) along with a relatively lower ejection fraction and a higher SPAP, compared to subjects with a non-HFA. In another study conducted by **Basile *et al.*** [(3)] they found that the creation of an AVF exerted the cardiac function. Furthermore it causes long-term volume overload characterized by increased SV, LVM and LVMI. The resulting LVH is predominantly eccentric. In another study reported by **Elbaz *et al.*** [(14)] they found that the high flow fistula increased SV, LVM, and LVMI with normal RWT (eccentric hypertrophy). **MacRae**[(15)] stated that patients with high flow AVFs most likely have a greater risk of developing high-output cardiac failure and are also likely to have greater increases in left ventricular end diastolic volume (LVEDV).

Martinez *et al.* [(16)] found that whether AVF or AVG creation leads to new onset heart failure is currently uncertain. One series looked at 562 patients who had preemptive AVF placement and were yet to start dialysis. A multivariate logistic regression analysis found that the most important determinant for developing heart failure was AVF creation (OR: 9.5; $p < 0.0001$). **Iwashima *et al.***[(17)] found that patients with a Qa > 2000 ml/min had a higher tendency toward an increase LVEDV with increased levels of atrial natriuretic peptide.

The main factors increasing the pulmonary blood flow are anemia, fluid overload, and elevated CI due to AV fistula [(18)]. **Hiremath *et al.*** [(19)] **and Wijnen *et al.*** [(20)] showed that creation of arteriovenous fistulas lead to increase CO and significant increases in both left ventricular wall mass and diameter in the long-term**.** Closure of the AV fistula after renal transplantation results in a decrease in left ventricular mass, due to a reduction in left ventricular diameter. The change in LV mass is significantly related to the LV mass and LVEDD before fistula closing [(21)], In addition **Chemla *et al.*** [(22)], monitored the effect of surgical access flow reduction on cardiac output in a group of high access flow patients. Only accesses with flow volume exceeding 1600 ml/min were included. Cardiac output decreased significantly after the surgery together with the access flow, Another study done by **Movilli_*et al.*** [(23)]**,** on post transplantation period after AV fistula closure showed an increase in left ventricular ejection fraction, decrease in left ventricular mass, and mass index, and more favorable shift of cardiac geometry toward normal. Also **Unger and Wissing** [(24)]**,** showed regression of LVH following AVF closure in renal transplant patients.

In our study we found a positive correlation as increase fistula flow rate caused increase in SPAP. These findings are in agreement with **Yigla *et al.*** [25] who showed that the incidence rate of pulmonary hypertension (PH) was significantly higher after initiation of HD with four out of six patients eventually developing PH. As opposed to this, pulmonary artery pressure (PAP) dropped in four out of five HD patients with PH after kidney transplantation following AVF closure. It was noted that mean PAP also dropped with AVF compression (from 52 to 41 mm Hg) along with a drop in CO. In contrast to our findings **Gursel *et al.*** [26] who found no relationship between AV access flow and development of pulmonary hypertension (PH). This discrepancy could possibly be due to small study population and the technique used for measuring PAP and AV fistula flow volume, which is noninvasive and sensitive to physiologic variables such as heart rate, preload, and respiration.

Paneni *et al.* [27] compared echocardiography-derived peak systolic pulmonary artery pressure (PAP) between patients undergoing peritoneal dialysis (PD), and those receiving hemodialysis with radial and brachial AVFs. Systolic PAP was 29.7 ± 6.7, 37.9 ± 6.7 and 40.8 ± 6.6 mm Hg, respectively ($p < 0.001$). **Yigla *et al.*** [25]**, Unal *et al.*** [28]**, and Fabbian *et al.*** [29] found a much less prevalence of pulmonary hypertension (PH) in patients receiving PD compared to matched cohorts of patients undergoing hemodialysis via AVF. Our study found a positive correlation as increased fistula flow rate caused increase in Kt/V, URR and PRR *in group A*

Our study also found a positive correlation as increased fistula flow rate caused increase in Kt/V, and URR, and PRR *in group B.* **Ward *et al.*** [30] found also ***that*** the efficiency and adequacy of HD is largely dependent on arterial blood flow rate from a well-preserved and functioning VA**.** Our study showed that there was statistically significant increase in LVEDD, LVESD, LVEDV, LVESV, BSA, SV, LVM, LVMI, CO, and LA volume in group B in comparison to group A.

CONCLUSION

Increasing of blood and fistula flow rates are effective in increasing dialysis adequacy and phosphate reduction ration and it is more evident on using high-flux hemodialysis. Increasing of fistula flow rate within limit may increase the risk of high output cardiac failure, pulmonary hypertension and may be associated with significant dilatation of left cardiac chambers (LA and LV).

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