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Effect of High Volume Hemodiafiltration on Secondary Hyperparathyroidism among Hemodialysis Patients

Nephrology

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Abstract

Background: Despite increasing knowledge of the uraemic syndrome,both morbidity and mortality remain unacceptably high in patients with chronic kidney disease.

Study investigates the differences between conventional hemodialysis and hemodiafiltration in the context of chronic kidney disease metabolic bone disease findings, serum calcium (sCa), phosphate (sPO4) and intact parathyroid hormone (PTHint) concentrations.

Patients and methods: This prospective cross over study was approved by Almaadi hospital committee and included 95patients with CKD5 on regular hemodialysis for at least 6months.Patients were divided into two groups:Group A:60patients scheduled 6months conventional high flux(hf-HD)(Period1) followed by 6months of post-dilutional –HDF (Period2).

Group B:(controls)included 35patients were kept on conventional hf-HD for12months.(Period3)for 1st 6months and(Period4) for 2nd 6months.The main variables evaluated at the start as well as at the end of each period were sCa, sPO4 and PTH int.

Results: There was highly significant statistical decrease in Phosphorus level in period2 compared to other groups after 2nd to 6th month and average of overall ($p<0.001$).A significant statistical decrease was found in Parathormone level and CRP in period2 compared to other groups after 1month to 6th month and average of overall ($p<0.05$).There was significant statistical decrease in Albumin level in period2 compared to other groups after 2nd to 6th month and average of overall ($p<0.05$).There was a significant statistical increase in kt/v in period2 compared to other groups after 1st to 6th month and average of overall ($p<0.05$).

Conclusion: The switch over from conventional Hf-HD to Ol-HDF results in a significant reduction of both PO4 and PTH concentrations, no significant changes in Ca concentrations.

Keywords: high volume hemodiafiltration**,** secondary hyperparathyroidism, Hemodialysis.

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Authorship: *All authors have a substantial contributions to the article*.

INTRODUCTION

Despite increasing knowledge of the uraemic syndrome, both morbidity and mortality remain unacceptably high in patients with chronic kidney disease. (CKD) [1]

Secondary hyperparathyroidism which characterized by increased secretion of parathermone (PTH), is one of the major serious complications in patients with CKD on long-term hemodialysis (HD). Strict control of serum calcium and phosphate concentrations is very important to prevent secondary hyperparathyroidism in those patients.[2]

Efficient removal of middle-molecular-weight (MMW) uremic toxins is expected to improve patient outcomes in dialysis.[3] Convective transport is the main driver for an enhanced clearance of such toxins. Consequently, hemodiafiltration (HDF), a dialysis procedure effectively combining diffusive and convective transport, has now become the standard dialysis technique in many countries.[4]

MMW substances are not readily cleared by diffusion, which is the main elimination mechanism in low-flux HD.[5]

European Dialysis Working Group (EUDIAL) defined hemodiafiltration as a blood purification therapy combining diffusive and convective solute transport such that the latter is achieved by an effective convection volume of at least 20% of the total blood volume processed. Convection volume is the sum of the substitution fluid volume and the volume of fluid removed during a session (i.e., the difference between the postdialysis and predialysis weights) [1]

In modern HDF, fluid balance is maintained by the infusion of 'online' prepared substitution fluid, which can be administered before the dialyser (pre-dilution), midway (mid-dilution) or after the dialyzer. (post-dilution) [6]

Since the vast majority of publications on HDF and clinical outcome concern online post-dilution HDF, this study will focus on this type of treatment. This prospective switchover study investigated the differences between conventional hemodialysis and hemodiafiltration in the context of chronic kidney disease metabolic bone disease (CKDMBD) findings [serum calcium(sCa), serum phosphate (sPO4) and intact parathyroid hormone (PTHint) concentrations.

PATIENTS AND METHODS

This cross over study investigated the differences between conventional hemodialysis and hemodiafiltration in the context of CKDMBD findings stems from the fact that the same patients were examined by two different therapeutic modalities.

This study was approved by Almaadi hospital committee and included 95 patients with CKD5 on regular hemodialysis (HD) in Almaadi Nephrology Unit for at least 6 months prior starting. Study started October, 2018 and patient followed up till October 2019. They were selected after informing consent, full history examination reviewing their medical records and fulfillment the study inclusion and exclusion criteria. They were divided into two groups: Group A included 60 patients scheduled 6 months conventional high flux hemodialysis (hf-HD) (Period 1)) immediately followed by 6 months of post-dilutional -HDF (Period 2). Group B (controls) included 35 patients. They were kept on conventional hf-HD for 12 months. (Period 3) for 1st 6 months and (Period 4) for 2nd 6 months. The main variables evaluated at the start as well as at the end of each period were s Ca, sPO4 and PTH int.

Variables in this study were evaluated both at the start and at the end of each period of observation. They included serum calcium (sCa; mg/dL), serum phosphorus (sPO4; mg/dL), serum intact parathyroid hormone (PTHint; ng/mL), total serum protein (sProt; g/dL), serum albumin (sAlb; g/dL), plasma sodium (Na; mmol/L), plasma potassium (K; mmol/L), magnesium (Mg; mg/dL), CBC, high sensitive CRP, equilibrated Kt/V (eKt/V), body weight (BW; kg), liver function tests, ECG, pre-dialysis systolic blood pressure (SBP; mmHg) and diastolic blood pressure (DBP; mmHg). All biochemical parameters were drawn before midweek dialysis session to be assayed by their standard methods. Along the study, all patients (95 patients) used ultrapure dialysate as well as the same high flux dialyzer (High flux dialyzer, polysulfone F80 Fresenius Medical Care).Treatment of mineral bone derangement weas performed according to the American Kidney Disease Outcome Quality Initiative clinical practice guidelines for bone metabolism and disease in chronic renal failure recommendations. In group A, prescription and dosage changes of the phosphate binders done before the beginning of period 1 and were kept constant during Period 2. While in group B, changes in the dosage and prescription of phosphate binders' supplementation were allowed according to guidelines. The study included patients above 18 years old on regular HD for at least 6 months and with urinary output below150 mL/interdialytic. While Patient swith active malignancy, chronic infections, decompensated liver cirrhosis, unstable within 3 months before study (myocardial infarction, congestive heart failure, stroke, recent surgery, or severe sepsis), patients who developed hyperphosphatemia were excluded, Vascular access dysfunction (blood flow rate < 300 mL/min) and urinary output more than150 mL/ interdialytic were excluded from the study.

Nephrology

Dialysis prescription

Postdilution HDF was performed using the 5008 CorDiax HDF machine (Fresenius Medical Care, Bad Homburg, Germany).The dialysate solution is bicarbonate for all patients with sodium Na^+ 140mEq/L, K^+ 2mEq/L, Ca^{++} 1.75mEq/L, Mg 0.5mEq/L, Cl^- 109.5mEq/L, HCO3 35mEq/L, CHcooH 3mEq/L & the blood pump was kept between 300-400mL/min with dialysate flow 500 mL/min, and heparin sodium as anticoagulant were given 2500 IU as a bolus on initiation of dialysis followed by 500-1000 IU/Hr. All procedures follow Al-Azhar University Ethical committee regulations, and patient consent was taken from all patients.

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 (χ^2) test of significance was used in order to compare proportions between qualitative parameters. A one-way analysis of variance (ANOVA) when comparing between more than two means. Post Hoc test: Least Significant Difference (LSD) was used for multiple comparisons between different variables. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, 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. (Figure 1-5) (Table 1, 2)

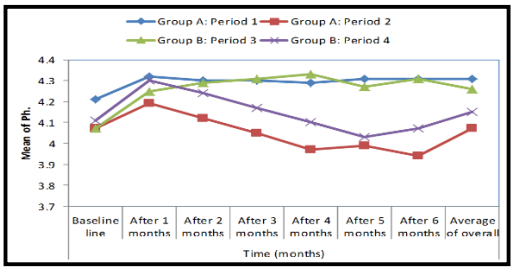

Fig. 1: Comparison between groups according to Ph. This figure shows statistically significant difference between groups according to Phosphorus (Ph) from after 1months to Average of overall.

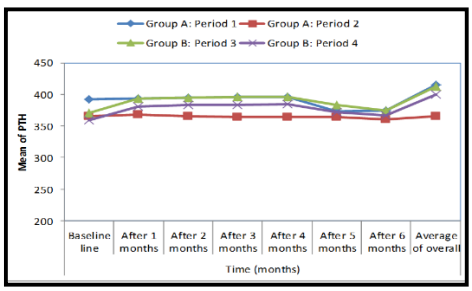

Fig. 2: Comparison between groups according to PTH.

As shown in table (1) and figure (3), there was a statistically significant difference between groups according to Parathormone (PTH) from after 1months to Average of overall. There is no significant statistical difference between the four groups as regard Parathormone level in the basal (p>0.05), While there is significant

statistical derease in Parathormone level in period 2 compared to other groups after 1month to 6th month and average of overall (p<0.05).

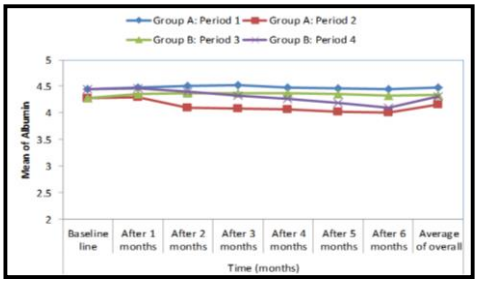

Fig. 3: Comparison between groups according to Albumin.

This figure shows statistically significant difference between period 2 and overall of the periods according to albumin from after 2months to Average of overallThere is no significant statistical difference between the four groups as regard Albumin level in the basal and after 1st month (p>0.05), While there is significant statistical derease in Albumin level in period 2 compared to other groups after 2nd to 6th month and average of overall (p<0.05).

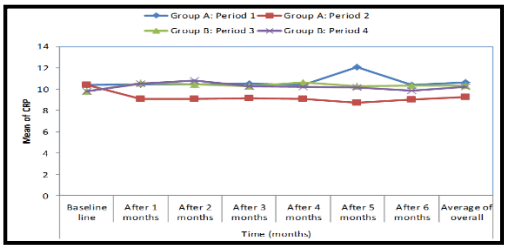

Fig. 4: Comparison between groups according to CRP.

Figure 4 shows statistically significant difference between period 2 and overall of the periods according to CRP from after 1months to Average of overall.

There is no significant statistical difference between the four groups as regard CRP in the basal (p>0.05)), While there is significant statistical decrease in CRP in period 2 compared to other groups after 1st to 6th month and average of overall (p<0.05).

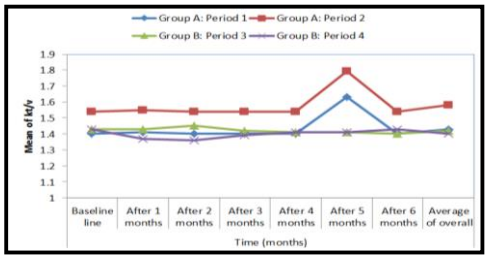

Fig. 5: Comparison between groups according to kt/v.

This figure shows statistically significant difference between groups according to kt/v from after 1months to Average of overall.

There is no significant statistical difference between the four groups as regard kt/v in the basal (p>0.05)), While there is significant statistical inrease in kt/v in period 2 compared to other groups after 1st to 6th month and average of overall (p<0.05).

PTH	Group A		Group B		ANOVA	
	Period 1 (n=60)	Period 2 (n=60)	Period 3 (n=35)	Period 4 (n=35)	F	p-value
Baseline line	392.65±176.69	365.77±164.6	370.04±166.52	358.94±161.52	0.109	0.954
After 1 months	392.83±176.78	367.43±165.34a	392.83±176.78b	381.05±171.47b	3.143	0.013*
After 2 months	394.83±177.68	365.57±164.51a	394.83±177.68b	382.99±172.34b	3.426	0.012*
After 3 months	395.52±177.98	364.00±163.8a	395.52±177.98b	383.65±172.64b	3.734	0.010*
After 4 months	396.58±178.46	364.71±164.12a	396.58±178.46b	384.69±173.11b	3.585	0.009*
After 5 months	372.83±253.28	364.71±164.12a	382.83±253.28ab	371.95±145.68b	2.814	0.024*
After 6 months	374.32±168.44	360.15±131.3a	374.32±168.44b	367.09±163.39b	3.304	0.012*
Average of overall	415.65±187.04	365.42±164.44a	412.42±185.59b	400.05±180.02b	3.172	0.014*

Table 1: Comparison between groups according to Parathormone.

CRP	Group A		Group B		ANOVA	
	Period 1 (n=60)	Period 2 (n=60)	Period 3 (n=35)	Period 4 (n=35)	F	p-value
Baseline line	10.4±4.37	10.4±4.37	9.8±4.12	9.8±4.12	0.188	0.905
After 1 months	10.47±4.4	9.11±3.83a	10.6±4.45b	10.51±4.42b	2.801	0.042*
After 2 months	10.43±4.38	9.07±3.81a	10.43±4.38b	10.8±4.54b	2.320	0.044*
After 3 months	10.52±4.42	9.15±3.85a	10.29±4.32b	10.29±4.32b	4.242	0.008*
After 4 months	10.41±4.37	9.06±3.80a	10.66±4.48b	10.23±4.3b	3.711	0.033*
After 5 months	10.45±5.06	8.74±4.40a	10.26±4.31b	10.14±4.26b	2.779	0.014*
After 6 months	10.4±4.37	9.05±3.80a	10.34±4.34b	9.86±4.14b	2.629	0.037*
Average of overall	10.66±4.48	9.27±3.90a	10.34±4.34b	10.23±4.3b	3.025	0.036*

Table 2: Comparison between groups according to C reactive Protei

DISCUSSION

Hemodiafiltration (HDF) is a newer technique of dialysis that achieves clearance of middle and large molecular weight solutes unlike conventional hemodialysis (HD). HD is based on the diffusive transport of solutes across a semipermeable membrane and is effective in removing small solutes only, whereas HDF also involves the infusion of sterile, pyrogen-free fluid either pre- or post-filter and thereby allows clearance by convection as well as diffusion.[7]

Our study was conducted on 95 chronic hemodialysis patients on regular hemodialysis (HD). They were divided into four groups: Group A included 60 patients scheduled 6 months conventional high flux (hf-HD) (Period 1) immediately followed by 6 months of post-dilutional -HDF (Period 2). Group B (controls) included 35 patients. They were kept on conventional hf-HD for 12 months. (Period 3) for 1st 6 months and (Period 4) for 2nd 6 months.

In group A: 30 of them were females (50%), 30 of them were males (50%).

Anemia is a major comorbidity of patients with end-stage renal disease and poses an enormous economic burden to health-care systems. High dose erythropoiesis-stimulating agents (ESAs) have been associated with unfavorable clinical outcomes.[8]

In our study There is no significant statistical difference between the four groups as regard Hemoglobin level in the basal (p>0.05), While there is significant statistical increase in Hemoglobin level in period 2 compared to other groups after the 1st, 2nd, 3rd, 4th, 5th month and average of overall (p<0.05) and highly significant statistical increase in Hemoglobin level in period 2 compared to other groups after the 6th month (p<0.001), which agree with the study done by [9] and [10] ; but this result disagree with the study done by [11] and [12] which showed no change in Hemoglobin level.

Phosphorus is found in plasma in a variety of compounds, such as pyrophosphates, decametaphosphates or phosphates bound to proteins. These forms of phosphorus have higher molecular weights and lower diffusion rates, so that their removal can be only improved by adding convective clearance.[13]

There is no significant statistical difference between the four groups as regard Phosphorus level in the basal (p>0.05)), While there is significant statistical derease in Phosphorus level in period 2 compared to other groups after the 1st month (p<0.05) and highly significant statistical decrease in Phosphorus level in period 2 compared to other groups after 2nd, 3rd, 4th, 5th,6th month and average of overall (p<0.001); which agree with the study done by [11].but this result disagree with the study done by [14] in which Phosphate levels were higher in patients who were on HDF compared with high-flux HD. High serum PTH levels in ESKD have been related to a poor clinical outcome.[15]

There is no significant statistical difference between the four groups as regard Parathormone level in the basal (p>0.05)), While there is significant statistical derease in Parathormone level in period 2 compared to other groups after 1month to 6th month and average of overall (p<0.05); which agree with the study done by [11]; but this result disagree with the study done by [12] in which there are any changes in serum levels of PTH. Albumin loss during online HDF treatment is dependent both on the filtration volume and the type of membrane was recently confirmed in a controlled study, which however only assessed albumin loss during the first hour of treatment.[16]

The clinical relevance of some extra albumin loss during post dilution online HDF, however, is uncertain [17] did not observe a relation between albumin lossand nutritional parameters.

There is no significant statistical difference between the four groups as regard Albumin level in the basal and after 1st month (p>0.05)), While there is significant statistical derease in Albumin level in period 2 compared to other groups after 2nd to 6th month and average of overall (p<0.05); which agree with the study done by [12],but this result disagree with the study done by [18] in which Mean serum albumin was not significantly different between patients who were treated predominantly with HDFor high-flux HD.

Systemic inflammation is commonly observed in patients with chronic kidney disease and has been shown to have a role in the development and progression of cardiovascular disease (CVD) and to predict mortality in end-stage kidney disease [18].

Online hemodiafiltration (ol HDF) may decrease inflammatory activity through enhanced clearance of middle molecules by convection; on the other hand, the infusion of large amounts of substitution fluid may induce inflammatory activity when water is contaminated. However, the potential risk of contamination is very low as we and others previously showed by analyzing a large amount of samples of dialysis fluids.[19]

There is no significant statistical difference between the four groups as regard CRP in the basal (p>0.05), While there is significant statistical derease in CRP in period 2 compared to other groups after 1st to 6th month and average of overall (p<0.05). This result agrees with the study done by [20] *and* [9] and this result disagrees with the study done *by* [21] and [22], in which there was no difference in the C-reactive protein ratios comparing HD vs. 0l-HDF treatments.

There is no significant statistical difference between the four groups as regard kt/v in the basal (p>0.05)), While there is significant statistical inrease in kt/v in period 2 compared to other groups after 1st to 6th month and average of overall (p<0.05). This result agrees with the study done by [23] and this result disagrees with the study done *by* [11] and [14], in which there are similar kt/v in both groups Online Hemodiafiltration and High-Flux Hemodialysis.

CONCLUSION

In conclusion, in this study, the switch over from conventional Hf-HD to Ol-HDF results in a significant reduction of both PO4 and PTH concentrations, no significant changes in Ca concentrations. This supports the idea that Ol-HDF could be of help in controlling the uraemic mineral metabolism derangement in dialysis patients. Online hemodiafiltration (HDF) may decrease inflammatory activity. Hemoglobin level and kt/v were higher in patients who were treated with Ol-HDF. Loss of albumin was higher in the Ol-HDF group.

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