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Effects of High Flux versus Low Flux on Serum C-Reactive Protein A as an Inflammatory Biomarker in Hemodialysis Patients

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ABSTRACT

Background: Traditional low-flux dialysis cannot improve micro-inflammatory status, while new high-flux dialysis can improve the micro-inflammation and lipid metabolism, it helps to improve the quality of life and survival rate of patients, so how to improve the micro-inflammatory status are a focus for researchers.

Objective: was to observe the effect of high flux hemodialysis (HFHD) with Gambro polyflux 170H dialyser and low flux hemodialysis (LFPD) with polyflux 17L dialyser on high-sensitivity C-reactive protein in patients with maintenance hemodialysis.

Methods: 60 patients with maintenance hemodialysis were randomly divided into HFHD group and LFHD group. Another 20 cases for physical examinations served as normal control group. The maintenance hemodialysis patients were treated with HFHD using 170H dialyser dliahyser and LFHD using 17L dialyser, three times per week, 4 hours once. After 6 months of the treatment, high-sensitive C-reactive protein was determined in patients as well as normal controls before and after treatment.

Results and Conclusion: in two groups, the levels of high-sensitive C-reactive protein before the treatment were higher than normal control ($P < 0.001$). In HFHD group, serum high-sensitive C-reactive protein markedly decreased ($P < 0.01$). In LFHD group, these indices remained unchanged after the dialysis for 6 months. HFHD with 170H polysulfone dialyser is effective in improving micro-inflammation in maintained hemodialysis patients.

Keywords: CRP, ESRD, hemodialysis membrane.

INTRODUCTION

C-reactive protein (CRP) is a large, nondialyzable acute phase reactant with putative roles in modulation of the inflammatory response[1] ..This protein is produced in the liver under the influence of proinflammatory cytokines, and its levels rise rapidly to high concentrations. Furthermore, in patients without kidney this protein has a plasma half-life of 19 hours[2] . This rapid rise to high concentrations and short half-life has made CRP attractive as a marker for acute inflammation. In chronic inflammation, however, C-reactive protein levels may remain elevated indefinitely[3] .

CRP is a more sensitive and accurate reflection of the acute phase response than the ESR (Erythrocyte Sedimentation Rate). ESR may be normal while CRP is elevated. CRP returns to normal more quickly than ESR in response to therapy [4].

Although there are many clinically evident causes of inflammation in patients with chronic kidney disease (CKD), there is an emerging understanding of the importance of subclinical chronic inflammation in this cohort. Potential sources of subclinical inflammation include atherosclerotic disease [5] ,chronic infection (periodontal or arteriovenous graft) [6] , or uremic metabolic alterations including increased oxidative stress[7] and the accumulation of advanced glycation end products [8] .

CRP elevations are thought to be clinically relevant, as associations have been reported between elevated levels and cardiovascular disease and mortality in both the general population, and in patients with chronic kidney disease [9] .

Most of these studies measured a single C-reactive protein value.While a number of therapies and technologies have been reported to increase health-related quality of life in patients with chronic kidney failure, patients report that they remain substantially burdened by limited physical functioning and by dialysis-related symptoms [10].

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The choice of a dialysis membrane should take into account the following: biocompatibility of the material towards leucocytes and complement activation; blood volume priming requirement, which is membrane area related: and permeability, determined in the simplest way by two characteristics of hydraulic permeability and molecular permeability determined at least by molecular weight of the molecule considered [11].

AIM OF THE WORK

The aim of the study is to detect the effect of use high flux dialysis on serum c-reactive protein as an inflammatory marker among regular hemodialysis patients.

PATIENTS AND METHODS

The study was coducted at nephrology unit, internal medicine department, Bab Al Sha`riah Hospital on adult patients (>18 y/o).

Patients were randomly divided into three groups :

- ***Group A*** : 30 patients on high flux hemodialyzer
- ***Group B*** : 30 patients on low flux hemodialyzer .
- ***Group C*** : 20 normal control .

All subjects were subjected to Full history taking, including a detailed medical history consisting of medication.Complete clinical examination including measurement of mean arterial blood pressure and pulse pressure.

Patients were also subjected to the following investigations before and after treatment: CBC, serum creatinine, urea, iron, ferritin, total iron binding capacity (TIBC), calcium, phosphorus, intact parathyroid hormone (iPTH), albumin, alkaline phosphatase (ALP) and C-reactive protein. The C-reactive protein (CRP) levels were assayed with the modification of the laser nephelometric technique (Behring Diagnostics, GmbH, Rarburg,German).

Patients having one of the following conditions were excluded from this study:

Patients have active infections ,Malignancy ,chronic liver disease , a recent myocardial infarction,a recent trauma ,a recent physical stress ,have non-steroidal anti-inflammatory for last three days, corticosteroids intake or statins intakes.

Group A patients treated by high-flux filters three times per week 4 hours per one session for 6 months dialysis prescription parameters (except for ultrafiltration to reach their ideal dry weight as needed). Moreover, the doses of vitamin D analogues or phosphate binders will be kept constant through the study. At the end of the 6 months, the same investigations will be repeated (Post) and compared with those before high-flux dialysis (Pre).

Both high flux and low flux membranes were made of the same material (synthetic polyamide blend membranes: polyflux 170H and polyflux 17L respectively, Gambro Co, USA).

The study was done after approval of ethical board of Al-Azhar universityand an informed written consent was taken from each participant in the study.

RESULTS

This study was conducted on 80 subjects divided into three groups:

- ***Group A***: 30 patients treated by High-flux hemodialyzer , 18 males (60 %) and 12 females (40 %) with ages ranging from 18 to 64 years with mean±SD = 47.70 ± 11.44.
- ***Group B***: 30 patients treated by Low-flux hemodialyzer, 16 males (53.3 %) and 14 females (46.7 %) with ages ranging from 21 to 64 years with mean±SD = 39.15 ± 10.91.
- ***Group C***: Control group 20 normal subjects, 13 males (65 %) and 7 females (35 %) with ages ranging from 20 to 58 years with mean±SD = 39.15 ± 10.91.

Table (1): Comparison between the different groups according to demographic data

		Group A (n= 30)		Group B (n= 30)		Group C (n= 20)		p
		No.	%	No.	%	No.	%	
Sex	Male Female	18 12	60.0 40.0	16 14	53.3 46.7	13 7	65.0 35.0	0.703
Age (years)	Min. – Max. Mean ± SD. Median	18.0 – 64.0 47.70 ± 11.44 50.0		21.0 – 64.0 47.90 ± 11.35 50.0		20.0 – 58.0 39.15 ± 10.91 38.50		0.015*
	Sig. bet. Grps	p_1=0.945,p_2=0.010*,p_3=0.009*						

□□□□□□□□□□□□□□□□□□□□□^{2}, p: □^{2} and p values for Chi square test for comparing between the different groups

F, p: F and p values for ANOVA test, Sig. bet. groups was done using Post Hoc Test (LSD)

p_1: p value for comparing between group A and group B

p_2: p value for comparing between group A and group C

p_3: p value for comparing between group B and group C

*: Statistically significant a

Descriptive and comparative statistics of the demographic data of studied groups are demonstrated in table (1) showing no statistically significant difference between the three groups regarding sex, also there is no significant difference regarding age between group A and group B but between group A and group C and between group B and group C there is statistically significant difference.

Table (2): Comparison between the different groups according to CRP

	Group A (n= 30)		Group B (n= 30)		Group C (n= 20)
	Pre	Post	Pre	Post	
CRP Min. – Max. Mean ± SD. Median	 9.0 – 16.0 13.33 ± 2.02 13.0	 4.0 – 8.0 6.07 ± 1.23 6.0	 8.0 – 16.0 12.60 ± 2.16 13.0	 8.0 – 22.0 13.03 ± 3.36 12.0	 3.0 – 8.0 5.45 ± 1.36 5.0
p	<0.001*	0.102	<0.001*	<0.001*	
Sig. bet. periods	p_1<0.001*,p_2=0.473,p_3=0.180,p_4<0.001*				

p: p value for Student t-test for comparing between group C with each other periods

p_1: p value for **Paired t-test** for comparing between pre and post in group A

p_2: p value for **Paired t-test** for comparing between pre and post in group B

p_3: p value for **Student t-test** for comparing between group A and B for pre

p_4: p value for **Student t-test** for comparing between group A and B for post

*: Statistically significant at $p \le 0.05$

Group A: high flux hemodialyzer, Group B: low flux hemodialyzer, Group C: normal control

Table (2): Shows a significant statistical difference between the studied groups regarding CRP , Mean CRP level showed no significant statistical difference between group A post treatment and the control group due to the significant decrease in CRP level after Highflux HD with Mean±SD = 6.07 ± 1.23 when compared with normal controls with Mean±SD = 5.45 ± 1.36 Statistical significance at ($p \le 0.05$) . also shows statistical difference between pre and post in group A (p1<0.001) , but with Low-flux HD (Group B) no statistical difference between pre and post (p2=0.473), when comparing between group A and B for pre shows no statistical difference (p3=0.180) and when comparing between group A and B for post shows highly statistical difference (p_4<0.001) .

Table (3): Comparison between the two studied groups according to Total Ca , Po4 and iPTH

		Group A (n= 30)	Group B (n= 30)	p
tCa	**Pre**			
	Min. – Max.	6.40 – 10.0	7.30 – 10.0	0.190
	Mean ± SD.	8.23 ± 0.76	8.38 ± 0.60	
	Median	8.15	8.45	
	Post			
	Min. – Max.	8.30 – 9.8	7.30 – 9.6	0.039*
	Mean ± SD.	8.23 ±0.412	8.38 ± 0.43	
	Median	9.1	8.3	
	#**Sig. bet. periods**	<0.001*	0.032*	
Po4	**Pre**			
	Min. – Max.	2.30 – 8.10	2.30 – 7.10	0.219
	Mean ± SD.	5.41 ± 1.55	4.93 ± 1.49	
	Median	5.45	5.25	
	Post			
	Min. – Max.	2.10 – 5.30	2.10 – 5.30	0.021*
	Mean ± SD.	3.78 ± 0.77	3.71 ± 0.70	
	Median	3.90	3.80	
	#**Sig. bet. periods**	<0.001*	<0.04*	
iPTH	**Pre**			
	Min. – Max.	35.0 – 2439.0	14.0 – 1770.0	0.027*
	Mean ± SD.	642.23 ± 621.0	415.96 ± 226.7	
	Median	497.50	165.0	
	Post			
	Min. – Max.	29.0 – 1403.0	23.0 – 2035.0	0.042*
	Mean ± SD.	373.93 ± 356.6	405.75 ± 224.7	
	Median	261.50	216.50	
	@**Sig. bet. periods**	<0.001*	0.190	

t, p: t and p values for **Student t-test** for comparing between the two groups
U, p: U and p values for Mann Whitney test for comparing between the two groups
#Sig. bet. periods was done using **paired t-test** for comparing between pre and post in each group
@Sig. bet. periods was done using **Wilcoxon signed ranks** comparing between pre and post in each group
*: Statistically significant at $p \leq 0.05$

Table (3) shows highly significant increase in tCa values , a highly significant decreases in Po4, and PTH values at the end of the use of **high-flux** filters .

Also a significant decreases in Po4 values , no significant change in iPTH values , significant increase in tCa values at the end of the use **low-flux** filters.

The post treatment values regarding tCa reflected the permeability coefficiency of the dialyzer membrane,when comparing between the effect of **High-flux**(Group A) versus the effect of **Low-flux** (Group B) there was significant difference (p=0.039). Although Po4 was efficiently removed by both filter types, still there was a highly significant decline of iPTH values at the end of the 6 month after the use **high-flux** filter (P <0.001) and no significant decline of iPTH values after the use **low-flux** filter (p < 0.190) .

Table (4): Comparison between the two studied groups according to renal functions

Renal functions		Group A (n= 30)	Group B (n= 30)	p
Creat	**Pre**			
	Min. – Max.	3.30 – 14.14	3.30 – 12.58	
	Mean ± SD.	8.74 ± 2.57	7.52 ± 2.41	0.063
	Median	9.0	7.20	
	Post			
	Min. – Max.	1.90 – 5.90	1.90 – 9.30	
	Mean ± SD.	3.53 ± 1.0	5.42 ± 2.21	<0.001*
	Median	3.35	5.15	
	Sig. bet. periods	<0.001*	<0.001*	
Urea	**Pre**			
	Min. – Max.	120.0 – 301.0	120.0 – 301.0	
	Mean ± SD.	204.50 ± 47.12	208.66 ± 50.73	0.743
	Median	196.0	198.0	
	Post			
	Min. – Max.	50.0 – 139.0	100 – 299	
	Mean ± SD.	104.66 ± 17.81	156.53 ± 46.9	0.04*
	Median	107.5	148.0	
	Sig. bet. periods	<0.001*	0.795	

t, p: t and p values for **Student t-test** for comparing between the two groups
Sig. bet. periods was done using **paired t-test** for comparing between pre and post in each group
*: Statistically significant at $p \leq 0.05$

Table 4 shows a highly significant decline of serum creatinine when comparing between post values of both groups or comparing between pre and post values of each group alone however there was no significant difference between creatinine values at the start of the study, also shows a significant decline of blood urea when comparing between post values of both groups ($p < 0.05$) , a highly significant difference when comparing between pre values and post values in group A ($p < 0.001$) and no significant difference when comparing between pre values and post values in group B ($p > 0.05$) .

Table (5): Comparison between the two studied groups according to Hb

Hb (g/dl)	Group A (n= 30)	Group B (n= 30)	p
Pre			
Min. – Max.	6.60 – 9.80	7.10 – 9.80	
Mean ± SD.	8.66 ± 0.83	8.59 ± 0.85	0.724
Median	8.95	8.90	
Post			
Min. – Max.	10.30 – 14.90	8.0 – 10.5	
Mean ± SD.	12.15 ± 1.41	8.87 ± 0.644	0.790
Median	12.25	8.70	
Sig. bet. periods	<0.001*	<0.051*	

t, p: t and p values for **Student t-test** for comparing between the two groups
Sig. bet. periods was done using **paired t-test** for comparing between pre and post in each group
*: Statistically significant at $p \leq 0.05$

Table 5 shows a high significant difference between pre and post values of each Group according to Hb .but no significant difference when comparing the post treatment values of both groups.

Table (6): Comparison between the two studied groups according to albumin

Albumin	Group A (n= 30)	Group B (n= 30)	p
Pre			
Min. – Max.	1.99 – 5.30	1.99 – 4.50	
Mean ± SD.	3.83 ± 0.60	3.71 ± 0.50	0.64
Median	3.87	3.82	
Post			
Min. – Max.	3.1 – 4.5	3.2 – 4.6	
Mean ± SD.	3.72 ± 0.36	3.65 ± 0.29	0.68
Median	3.65	3.55	
Sig. bet. periods	0.22	0.96	

t, p: t and p values for **Student t-test** for comparing between the two groups
Sig. bet. periods was done using **paired t-test** for comparing between pre and post in each group
*: Statistically significant at $p \leq 0.05$

Table 6 Shows no significant change of serum albumin in Group A when comparing between pre and post values ($p>0.05$), also no significant change of serum albumin in Group B when comparing between pre and post values ($p>0.05$), and no significant difference comparing between the two groups .

Table (7):Comparison between the two studied groups according to ALP

ALP (Iu/dl)	Group A (n= 30)	Group B (n= 30)	MW	p
Pre				
Min. – Max.	150.0 – 720.0	120.0 – 720.0		
Mean ± SD.	374.93 ± 173.98	342.71 ± 160.73	409.0	0.544
Median	348.35	318.20		
Post				
Min. – Max.	75.0 – 401.0	76.0 – 401.0		
Mean ± SD.	210.30 ± 113.63	194.03 ± 105.16	418.50	0.641
Median	175.50	164.0		
Sig. bet. periods	<0.001*	<0.001*		

MW, p: U and p values for Mann Whitney test for comparing between the two groups
Sig. bet. Periods was done using **Wilcoxon signed ranks** for comparing between pre and post in each group
*: Statistically significant at $p \leq 0.05$

Table (7): shows high significant difference between values of ALP when comparing between pre and post values of each group ($p <0.05$) ,but when comparing between post values of Group A and Group B there was no significant difference ($p > 0.05$) .

Table (8): Comparison between the two studied groups according to iron profile

Iron profile		Group A (n= 30)	Group B (n= 30)	p
Iron	**Pre**			
	Min. – Max.	49.0 – 236.0	47.0 – 203.0	
	Mean ± SD.	110.13 ± 51.20	105.03 ± 52.15	0.455
	Median	91.50	81.0	
	Post			
	Min. – Max.	89.0 – 191.0	79.0 – 183.0	
	Mean ± SD.	129.20 ± 32.35	127.67 ± 34.10	0.767
	Median	119.0	120.0	
	@Sig. bet. periods	0.001*	<0.001*	
Ferritin	**Pre**			
	Min. – Max.	120.0 – 3321.0	90.0 – 3576.0	
	Mean ± SD.	1172.47 ± 807.02	1306.27 ± 920.66	0.734
	Median	1128.0	1151.50	
	Post			
	Min. – Max.	152.0 – 1967.0	174.0 – 1967.0	
	Mean ± SD.	602.43 ± 403.49	662.33 ± 425.38	0.574
	Median	593.0	608.50	
	@Sig. bet. periods	<0.001*	<0.001*	
TIBC	**Pre**			
	Min. – Max.	142.0 – 339.0	150.0 – 425.0	
	Mean ± SD.	213.93 ± 40.98	218.93 ± 56.41	0.696
	Median	211.50	208.0	
	Post			
	Min. – Max.	209.0 – 376.0	209.0 – 391.0	
	Mean ± SD.	278.37 ± 41.32	271.43 ± 42.66	0.525
	Median	277.50	271.0	
	#Sig. bet. periods	<0.001*	<0.001*	

t, p: t and p values for **Student t-test** for comparing between the two groups
U, p: U and p values for Mann Whitney test for comparing between the two groups
#Sig. bet. periods was done using **paired t-test** for comparing between pre and post in each group
@Sig. bet. periods was done using **Wilcoxon signed ranks** comparing between pre and post in each group
*: Statistically significant at $p \leq 0.05$

Table (8) Shows a highly significant difference between pre treatment values and post treatment values for the same group as regard mean Serum iron , but no significant difference between pre treatment values and post treatment values when compared for each group (Upre=427.0 Ppre=0.455) (Upost=412.0 Ppost=0.525),also Shows a highly significant difference between pre treatment values and post treatment values for the same group as regard mean Serum ferritin , but no significant difference between pre treatment values and post treatment values when compared for each group (Upre=399.5 Ppre=0.696) (Upost=430.0 Ppost=0.574).and Shows a highly significant difference between pre treatment values and post treatment values for the same group as regard mean TIBC , but no significant difference between pre treatment values and post treatment values when comparing between the two groups (tpre=0.393 Ppre=0.696) (tpost=0.639 Ppost=0.525).
Statistical significance at $p \leq 0.05$.

DISCUSSION

In this study,the level of CRP in patients before the start of the study was higher than that in healthy controls Group (P <0.001) suggesting that the microinflammatory state do exist in maintenance hemodialysis patients, after 6 months of treatment, The level of blood CRP for high-flux dialysis group was significantly lower than that before dialysis (P1 <0.01), Significantly lower than the low-flux dialysis group (P4 <0.01), while the level of blood CRP for low-flux dialysis group before and after treatment showed no significant difference (P2 > 0.05).

The dialysis was performed using a synthetic biocompatible high-flux membranes thus increasing the incidence of inflammation Quality and cytokines clearance, which can reduce the role of complement and leukocyte activation, Fortunately most synthetic membranes adsorb endotoxin which keeps it from entering the blood stream[12] thereby improve the maintenance of blood The microinflammatory state of patients with dialysis.

These results apparently corresponding with ***Fen Ji et al.*** study that showed the significant decrease of CRP levels after 3 months of high-flux heamodialysis treatment, also corresponding with ***Bi Hui et al .*** study however they were using the hsCRP as amarker for thier study after 1 year of treatment use of Germany Fresenius polysulfone membrane F60 or FX80 Blood filter or dialyzer for high-flux dialysis. also corresponding with ***Zhang Z et al .*** study that found CRP was significantly decreased after 3-month of high-flux hemodialysis using the same type of dialyzer.

A study by ***Hadim A et al .*** aimed to evaluate the impact of low-flux , high-flux haemodialysis (HD) and online haemodiafiltration (online-HDF) on inflammation and the lipid profile in HD patients Revealed that The use of Low- and high-flux polysulphone membranes had similar effects on inflammatory markers (including CRP), whereas Online-HDF potently reduced pro-inflammatory cytokines.

In study by ***Hadim A et al .*** 50 HD patients were assigned to two groups for HD with low-flux (n = 25) or high-flux (n = 25) polysulphone dialysers for 6 weeks. Subsequently, all patients were haemodialysed with a low-flux polysulphone dialyser for 6 weeks, then transferred to OL-HDF for another 6 weeks. Blood samples for lipids and inflammatory markers (IL-6, IL-8, TNF-α, hs-CRP) were obtained at baseline and every 6 weeks.

A reduction of inflammatory parameters (CRP) also was noted by ***Merello GJ et al*** who evaluate the 6-month effect of a switch from low- to high-flux dialysers on patients treated in 39 Spanish dialysis centres. Inclusion criteria for the study were the condition of end-stage renal disease (ESRD) on chronic hemodialysis and low-flux dialysis for at least six months before the switch to high-flux dialysis. Of 1,543 patients enrolled in the study between 2000 and 2001, 1,046 patients were considered for the analysis. 497 patients were excluded because they did not complete the follow-up. Outcome measures were the reduction of pre-dialysis beta-2 microglobulin, the improvement of anemia or reduction in rHu-EPO dose required to maintain best correction of anemia, reduction of inflammatory parameters (CRP), improvement in lipid profile.

In our study there was a highly significant decreases in Po4, and PTH values , highly significant increase in tCa values at the end of the use of high-flux filters .

Also a significant decreases in Po4 values , no significant decrease in PTH values , significant increase in tCa values at the end of the use low-flux filters. The post treatment values reflected the permeability coefficient of the dialyzer membrane.

Although Po4 was efficiently removed by both filter types, still there was a highly significant decline of iPTH values at the end of the 6 month after the use high-flux filter (P <0.001) and no significant change of PTH values after the use low-flux filter (p < 0.190) .

Although there was significant differences between levels of iPTH before the start of the study (Group A with higher values) there was significant difference between levels in iPTH post treatment of both groups (p < 0.042) That reflected the higher permeability coefficient of the high-flux dialyzer.

In a study by ***El Arbagy*** there was no statistical significant difference between use of low flux

dialysis and high flux dialysis as regard serum calcium but there was a highly significant reduction in phosphorus level.

Zhang Z et al found significantly increased in serum calcium an hemoglobin levels , but Serum phosphate and CRP were significantly decreased after 3-month of high-flux hemodialysis.

In a study by ***Ayli et al*** there was no statistical significant difference between the high-flux dialyzer group and low-flux group as regard Ca but there was significant reduction in Phosphorus level[13] .

In study of ***Makar et al*** . there was no statistical significant difference between use of low flux dialysis and high flux dialysis as regard Ca but there was statistical significant decrease in serum Phosphorus and ALP after use of high flux dialysis compared to low flux dialysis [14].

In a study by ***El Arbagy*** on 40 adult patients he found that postdialysis highly significant decline of intact PTH after the use of high flux membranes, but not after the use of low flux ones. Also at the end of the one month use of high-flux filters, predialysis intact PTH level showed a significant decline compared to the predialysis level using low-flux filters at the start of the study.

In a study by ***Makar et al***. on 44 pediatric hemodialysis patients switched from low flux dialysis to high flux dialysis for 3 months, postdialysis levels of intact PTH were significantly lower than predialysis levels after use of high flux filter but not after the use of the low flux one.

At end of 3 months of use of high flux filters in study of ***Makar et al***. predialysis intact PTH level showed a highly significant decline compared to the predialysis intact PTH with low flux membranes at the start of the study.

In a study by ***Balducci et al*** .different PTH behavior during hemodialysis with different types of dialysis membranes in 12 adult dialysis patients with secondary hyperparathyroidism. Each HD modality lasted 2 weeks for study period of 6 weeks. The first treatment consisted of standard bicarbonate dialysis with low flux polysulfone, followed by acetate-free biofiltration with high-flux-polysulfone or with polyacrylonitrile-AN69. Intact parathyroid hormone was assayed on the blood and dialysate samples to calculate iPTH adsorption. The results showed that polyacrylonitrile-AN69 and high-flux polysulfone induce a significantly larger drop in PTH serum levels as compared with low-flux-polysulfone, particularly in the first half of the dialysis session.

In the present study, a highly significant decline of serum creatinine when comparing between post values of both groups or comparing between pre and post values of each group alone hower there was no significant difference between creatinine vlues at the start of the study, also shows a significant decline of blood urea when comparing between post values of both groups ($p = 0.04$) , a highly significant difference when comparing between pre values and post values in group A ($p<0.001$) and no significant difference when comparing between pre values and post values in group B ($p > 0.05$).

Although they were not significantly removed by low flux filters for being water soluble and with small molecular weight (eg, urea is 60 Da), still they were more efficiently eliminated by the use of increasingly permeable high-flux dialysis membranes with excellent blood purification. High-flux filters with large pore sizes are efficient in removal of toxins with medium weight, but on the other hand, other smaller substances may be markedly decreased [15]

In our study there was no significant change of serum albumin in Group A when comparing between pre and post values ($p>0.05$), also no significant change of serum albumin in Group B when comparing between pre and post values ($p>0.05$), and no significant difference comparing between the two groups .

In a study by ***El Arbagy et al*** .There was no significant change of serum albumin after the use of high-flux filters.

According to ***Vanholder*** and colleagues, middle-sized molecules were defined as any solute with molecular weights between 500 Da and 40 000 Da [11] .Albumin, with a molecular weight of 65 000 Da, is considered a relatively large molecule to be filtered by both membrane types.

Krieter and Canaud found that highly permeable membranes may increase albumin loss and lead to

harmful consequences; however, they could not estimate accurately the extent of albumin loss through highly permeable dialysis membranes [15].

Lindsay and Spanner noted that switching from low- flux to high-flux dialysis membranes did not increase the protein catabolic rate as previously found through using some high-flux membranes as the AN69 dialyzer [16] instead; a significant increase in predialysis serum albumin levels was observed [17].

It was further postulated that this may be the result of improved dietary intake and potential explanation involving the removal of plasma substances that inhibit appetite, such as the putative factor in uremic plasma, leptin (16kD), and other peptides [18] .

However, in the study of ***Makar et al*** . there was no significant change of serum albumin after use of high flux filters. Also, in a study by ***Ayli et al***. there was no statistical significant difference between low and high flux groups as regard albumin level[13] .

In our study there was a highly significant difference between pretreatment values and post treatment values for the same group as regard mean Serum iron , but no significant difference between pretreatment values and post treatment values when compared for each group (Upre=427.0 Ppre=0.455) (Upost=412.0 Ppost=0.525),also there was a highly significant difference between pretreatment values and post treatment values for the same group as regard mean Serum ferritin , but no significant difference between pretreatment values and post treatment values when compared for each group (Upre=399.5 Ppre=0.696) (Upost=430.0 Ppost=0.574) and there was a highly significant difference between pretreatment values and post treatment values for the same group as regard mean TIBC , but no significant difference between pretreatment values and post treatment values when comparing between the two groups (tpre=0.393 Ppre=0.696) (tpost=0.639 Ppost=0.525). However, in a study by (Locatelli et al., 2000), on 84 adult HD patients, they found that the hemoglobin levels increased non significantly from 9.5 ± 0.8 to 9.8 ± 1.3g/dl in the population as a whole, with no significant difference between the low and high flux groups (P = 0.485).

Zhang Z et al. found that High-flux HD is superior in treating anemia and improving nutrition. And High-flux HD can better correct calcium and phosphorous metabolic disorder and improve micro-inflammatory state.

Also a study by Schneider et al, after 52 weeks, the low-flux and the high-flux groups did not differ with respect to hemoglobin (P = 0.62) [19] .

Khodayar Oshvandi found significant difference as regard dialysis adequacy after using high-flux dialysis [20].

Movilli et al. evaluated 68 cases, and stated that the increase in the Kt / V urea rate significantly reduced EPO use, this effect being more evident in cases in which Kt / V urea value was (1.4) ***Katzarski et al***. compared 59 patients under prolonged (8 hr) HD treatment at the Tassin Center in France, with 53 patients on HD treatment in Sweden, whose sessions were relatively shorter (3-5 hr), and demonstrated that EPO requirement was much lower in the group on prolonged HD treatment. It is possible that this positive effect can be mediated by the improvement in the clearance of moderate and high molecular weight toxins by prolonged HD.

The increase in Hb level in our study may be attributed to potential benefits of high flux membranes in reduction of erythropoietin resistance [21].

This might be related to reduction in the level of PTH among these patients as hyperparathyroidism is usually listed as one of possible reasons for impaired response to recombinant human erythropoietin (rHuEPO) in patients with renal disease [22] .

CONCLUSION

The use of high-flux dialysis membrane result in:

1- High-flux HD can better decrease CRP and improve micro-inflammatory state.
2- More efficient removal of intact PTH (one of the middle-sized uremic toxins) than low-flux membranes.
3- Reduction of serum phosphorus level.
4- Better dialysis adequacy.

RECOMMENDATION

We suggest the use of high-flux dialysis membrane for better quality of life.

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