The Egyptian Journal of Hospital Medicine (October 2020) Vol. 81 (1), Page 1285-1291

Effect of High Flux Hemodialysis versus Hemodiafiltration on Metabolic Status in Hemodialysis Patients

Sara Tito Ibrahem [1], Adela Mahmoud Gad Salama [2], Hanaa Mohammed Eid Elsayed [2], Mahmoud Ahmed Ali [3]

[1] Kobry El Kobba Military Nephrology Hospital,[2] Internal Medicine Department, Faculty of Medicine for Girls, Al Azhar University,[3] Armed Forces College of Medicine

Corresponding author: Hanaa Mohammed Eid Elsayed, **email:** Hana_sozy@yahoo.com, **Mobile:** 01006566308

ABSTRACT

Background: Hemodiafiltration (HDF) is a newly developed renal replacement therapy blood purification technology with more advantageous effects on hemodynamic stability and better removal of B2 microglobulin and phosphorous

Objective: The aim of this study is to compare effect of high flux (HF), low flux (LF) dialysis membranes and hemodiafiltration (HDF) on the metabolic status in hemodialysis patients and quality of life of those patients.

Patients and Methods: This study included 60 patients more than18 years old, clinically stable with end stage renal disease on regular HD for at least three years (3 yrs), selected from HD unit in (Kobry El Kobba Military Nephrology Hospital) in the period from March 2018 to September 2018. The patients were divided into three groups equally. **Group I:** 20 patients on low flux dialyzer, **Group II**: 20 patients on high flux dialyzer, **Group III:** 20 patients on hemodiafiltration.

Results: There was a highly significant decrease in iPTH, B2 microglobulin and Phosphorous in patients received HDF (363.80±149.04, 8.79±7.22 and 4.31±0.74 respectively in comparison with patients received HF hemodialysis (540.10±242.55, 20.47±3.97and 4.58±1.07 respectively) and patients received LF hemodialysis (725.95±270.01, 36.60±7.22 and 5.73±1.34 respectively).Also, there were a highly significant increase in urea reduction ratio in HDF group compared to HF and LF groups (80.43±7.46, 76.03±9.55 and 65.81±7.42 respectively.

Conclusion: Hemodiafiltration is the most effective dialysis technique than high flux and low flux dialysis membrane in removal of medium sized molecule and improvement of quality of life.

Key Words: Online hemodiafiltration, high flux hemodialysis, B2 microglobulin, quality of life.

INTRODUCTION

Chronic kidney disease (CKD) originates from several heterogeneous disease mechanisms that irreversibly alter the function and structure of the kidneys over months or years. The diagnosis of CKD relies on a chronic decrease in kidney function and structural damage of the kidney [(1)].

End-stage renal disease (ESRD) is a dangerous disorder. The universal prevalence is proven to be 260 million people annually. Renal diseases lead to morbidity and mortality as a major part, and have become global issue requiring early identification, assessment and preventive management [(2)].

Chronic kidney disease (CKD) is associated with many forms of metabolic changes induced by the kidney failure and often due dialysis treatment. The metabolic waste products, normally eliminated with the urine, accumulate and the body is overexposed to these uremic toxins and waste products such as increased urea and other electrolytes causing hyperkalaemia and hyponatremia [(3)]. ß2 microglobulin is the most commonly uremic toxins as a guide for preservation and removal of medium sized molecules by hemodialysis. Serum levels of β2-microglobulin (ß2M) are substantially higher in patients with end stage renal disease undergoing hemodialysis (HD) and its aggregation accelerates dialysis related amyloidosis (DRA) [(4)]. The theory of hemodialysis is by the removal of solutes across a semi-permeable membrane by diffusion and ultrafiltration processes. The membranes used are divided into two main groups: low-flux membrane, which is based on using dialyzers with low permeability for water, and high-flux membrane with increased permeability, which is capable of removing medium-sized molecules including many of the inflammatory proteins, ß2-microglobulin and lipoproteins [(5)].

Hemodiafiltration (HDF) is a recently evolved renal replacement treatment, blood purification technique, for scavenging medium and large molecules with more beneficial effects on hemodynamic stability [(6)].

The study goal was to compare the impact of low flux, high flux dialysis membranes and hemodiafiltration on the metabolic status with the intention of improving the quality of life with hemodialysis.

PATIENTS AND METHODS

This was a comparative study that was conducted at the Hemodialysis Unit in (Kobry El Kobba Military

Received:18 /6 /2020
Accepted:17 /8 /2020

Nephrology Hospital) from March 2018 to September 2018. Sixty participants (31 males represented 51.7%) and (29 females represented 48.3%), aged >18 years old and on regular hemodialysis more than three years were included in this study and were divided into three equal groups: **Group I** that included 20 patients on low flux dialyzer, **Group II** which included 20 patients on High flux dialyzers and **Group III** which included 20 patients on hemodiafiltration. Patients with any chronic inflammatory diseases, patients with history of rejected kidney transplantation, diabetic patients, patients with active infection and stroke and patients with any history suggestive of malignancy as (Lymphoma, Leukemia, Multiple Myeloma) were excluded from this study.

Ethical consideration

Before the start of the study, permission was obtained from the hospital and ethical committee of Al Azhar University. Also informed oral and written consent from patients participated in the study was obtained.

The selected participants were subjected to full history taking (Personal history, past history of medical problems, past history of any drugs, present history of any recent infection or inflammation). Clinical examination was done to all participants to reveal any medical problems.

Laboratory investigations were done for all participants in the study before and after treatment:

Complete blood count (CBC), blood urea, serum creatinine, serum (Na, K, uric acid, calcium, phosphorus and serum albumin), Intact parathyroid hormone, lipid profile (total cholesterol, Low density lipoprotein (LDL), high density lipoprotein (HDL**)** and triglycerides (TGs) and erythrocyte sedimentation rate (ESR), serum β2-microglobulin (as a marker of **medium sized** molecules) were done, commercial reagent kits provided by the Roche kits of United States was used to measure the β2-microglobulin (β2-MG).

The QoL assessment was done through the generic 36-item short-form health questionnaire **(SF-36)** before the start of the study and after six months.

Sampling: Samples were collected from arteriovenous fistula into tubes at room temperature and centrifuged within 1 h. The serum was stored at -70°C before analysis.

Procedure:

At first all sixty patients were subjected to all investigations (Baseline investigations) then all sixty participants were on low flux dialyzers for 3 months and investigations were repeated for them (3 months investigations) after that we divided them into three groups: 20 patients continued on low flux dialyzers, 20 patients were switched to high flux dialyzers and 20 patients were switched to hemodiafiltration.

Evaluation and results: The collected data were tabulated and statistically analyzed and discussed.

Statistical analysis

All data were subjected to revision and validation then description and analysis on IBM-compatible PC by using SPSS (Statistical Package for the Social Science) program version 22.0.0, Microsoft Office Excel 2007, and Graph Pad Prism 6. Descriptive statistics were performed for all studied parameters in the three studied groups and were presented in the form of mean, median, standard deviation (SD), minimum, maximum, range, and percentages. The comparison between groups regarding qualitative data was done by using Chi-square test, while the comparison between more than two groups with quantitative data and parametric distribution were done by using One Way ANOVA- Test.

The confidence interval was set up to 95% and the margin of error accepted was set to 5%. So, the p-value was significant as the following:

- $P > 0.05$: Non significant (NS).
- $P < 0.05$: Significant (S).
- $P < 0.01$: Highly significant (HS).

RESULTS

This study included sixty **(60)** adult patients on regular hemodialysis, **31** males and **29** females, with age ranged from **(26 to 58)** years and the mean of age was **(43.33 ± 8.67)** years.

Mean of dialysis duration was 14.95 years with the range from 11.2 to 19.4 years. According to the etiology, 33.3% of patients were hypertensive, 21.7% had chronic glomerulonephritis, 20% were of unknown cause, 13.3% were with obstructive uropathy and 11.7% had polycystic kidney disease. According to the anthropometric measurement, BMI was **26.20± 3.94** kg/m^2 with range from **17.76 to 37.04** kg/m^2.

Table 1 showed statistically significant increase in hemoglobin level, platelets number and serum albumin level and highly significant increase in HDL (High density lipoprotein) in hemodiafiltration group when compared to high flux and low flux dialysis groups. Also, this table showed that there was statistically highly significant decrease in creatinine after dialysis, urea after dialysis, potassium (k), parathyroid hormone (PTH), (phosphorus) PO_4, triglycerides and β2-microglobulin levels in

hemodiafiltration (HDF) group in comparison to low flux and high flux dialysis groups.

Table (1): Comparison between three groups (low flux, high flux and hemodiafiltration) as regard laboratory results after 6 months from the start of the study

	Low flux			High flux			Hemodiafiltration			One way ANOVA	
	Mean	±	SD	Mean	±	SD	Mean	±	SD	F	p value
Hemoglobin /gm	10.08	±	1.04	10.5	±	1.04	11.00	±	1.03	3.9478	0.024 (s)
Total leucocytic count / thousand/H.P.F	7.76	±	2.16	7.8	±	1.16	8.23	±	2.53	0.259	0.773 (NS)
Platelets	200.70	±	9.10	200.70	±	9.10	261.90	±	5.40	4.918	0.011 (s)
Creatinine before dialysis mg/dl	9.64	±	2.84	10.30	±	2.15	10.92	±	2.31	1.365	0.264 (NS)
Creatinine after dialysis mg/dl	6.19	±	1.84	3.92	±	0.43	2.51	±	1.01	45.170	0.001 (HS)
Urea before dialysis mg/dl	135.55	±	6.57	127.00	±	4.11	142.45	±	33.85	1.015	0.369 (NS)
Urea after dialysis mg/dl	45.82	±	12.05	33.25	±	2.26	22.71	±	4.69	25.280	0.001 (HS)
Urea reduction ratio (URR)	65.81	±	7.42	76.03	±	9.55	80.43	±	7.46	16.730	0.001 (HS)
Na MEq/L	139.54	±	4.37	137.09	±	2.00	138.78	±	2.91	3.002	0.058 (NS)
K Meq/L	5.53	±	0.70	4.53	±	0.95	3.85	±	0.068	23.201	0.001 (HS)
Uric acid mg/dl	8.16	±	2.42	8.16	±	2.42	7.04	±	2.35	1.460	0.241 (NS)
Albumin gm/dl	3.40	±	0.31	3.45	±	0.30	3.65	±	0.30	3.578	0.034 (S)
Parathyroid hormone (PTH) / ng	725.95	±	70.01	540.10	±	42.55	363.80	±	49.04	12.782	0.001 (HS)
Cholesterol mg/dl	167.58	±	23.83	168.51	±	20.52	169.58	±	23.83	0.039	0.962 (NS)
Triglyceride mg/dl	206.20	±	29.22	159.52	±	11.10	155.32	±	11.10	43.495	0.001 (HS)
Low density lipoprotein (LDL)	105.47	±	14.56	100.47	±	14.56	96.09	±	16.20	1.925	0.155 (NS)
High density lipoprotein (HDL)	32.73	±	6.78	44.23	±	5.19	45.33	±	5.16	29.360	0.001 (HS)
Ca	8.50	±	0.73	8.50	±	0.73	8.30	±	0.56	0.547	0.582 (NS)
PO_4	5.73	±	1.34	4.58	±	1.07	4.31	±	0.74	9.756	0.001 (HS)
β2-microglobulin (mg/l)	36.60	±	7.22	20.47	±	3.97	8.79	±	2.02	162.483	0.001 (HS)

Table (2): Post Hoc curve of the three groups (Low flux, High flux, Hemodiafiltration):

	Post hoc analysis		
	P1	P2	P3
Hemoglobin /gm	0.209	0.007	0.135
Platelets	1.000	0.010	0.010
Creatinine after dialysis mg/dl	0.001	0.001	0.127
Urea after dialysis mg/dl	0.002	0.001	0.000
Urea reduction ratio (URR)	0.001	0.001	0.112
K Meq/L	0.001	0.001	0.002
Albumin gm/dl	0.607	0.013	0.041
Parathyroid hormone (PTH) / ng	0.028	0.001	0.008
Triglyceride mg/dl	0.001	0.001	0.238
High density lipoprotein (HDL)	0.001	0.001	0.506
PO_4	0.004	0.002	0.359
β2-microglobulin (mg/l)	0.001	0.001	0.001

P1: Low flux VS High flux
P2: Low flux VS Hemodiafiltration
P3: High flux VS Hemodiafiltration

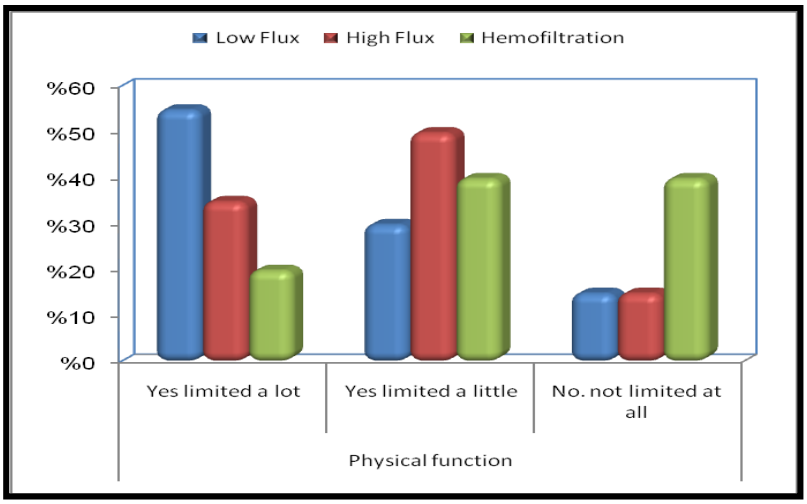

Figure (1): Comparison between physical function in low flux, high flux and hemodiafiltration as there was an increase in physical function in hemodiafiltration group than high flux and low flux dialysis groups.

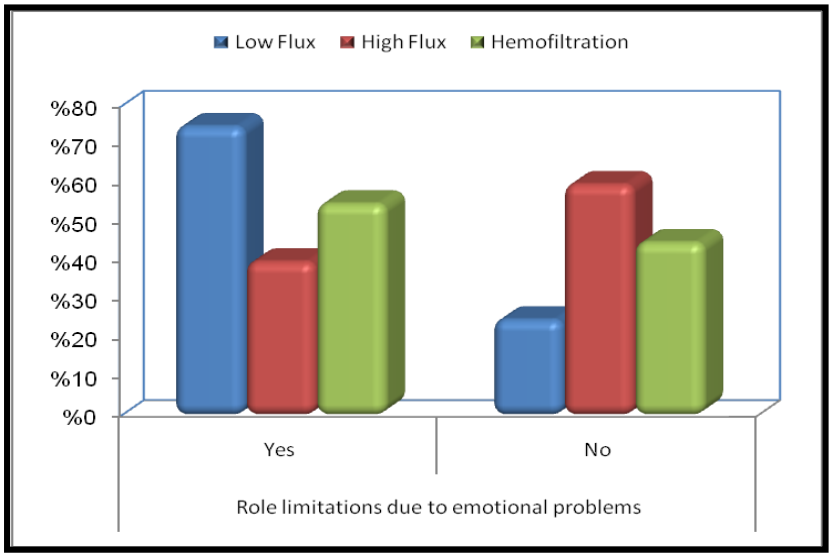

Figure (2): Comparison between limitations due to emotional problems in low flux high flux and hemodiafiltration as there was a decrease in role of limitation due to emotional problems in hemodiafiltration group than high flux and low flux dialysis groups.

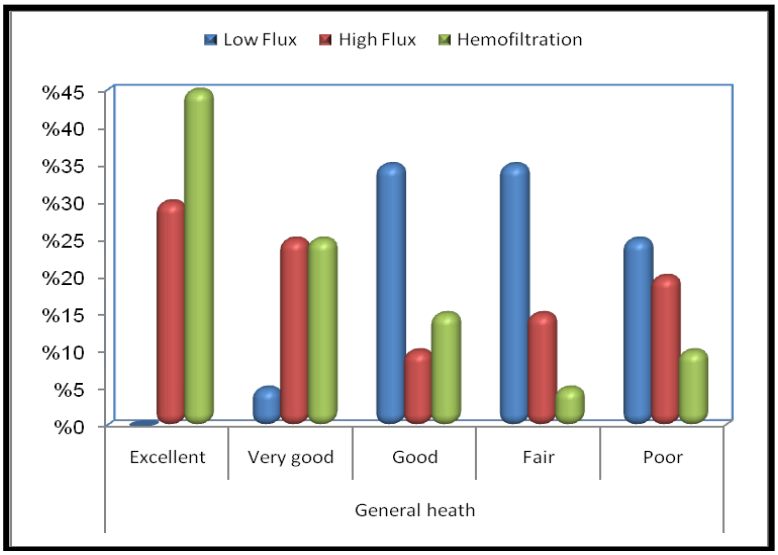

Figure (3): Comparison between general health in low flux, high flux and hemodiafiltration as there was an increase in general health in hemodiafiltration group than high flux and low flux dialysis groups.

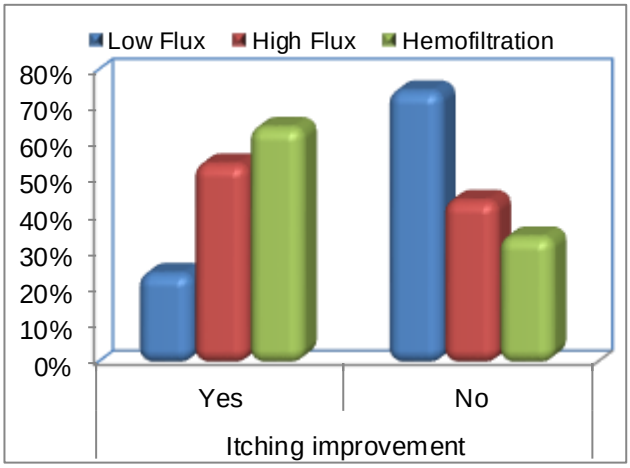

Figure (4): Comparison between low flux, high flux, and hemodiafiltration groups as regard itching, there was a decrease in itching in hemodiafiltration group than high flux and low flux dialysis groups.

DISCUSSION

Chronic kidney disease (CKD) originates from several heterogeneous disease mechanisms that irreversibly alter the function and structure of the kidneys over months or years. The diagnosis of CKD relies on a chronic decrease in kidney function and structural damage of the kidney **.** Hemodialysis is an extracorporeal blood cleaning procedure that used to eliminate metabolic waste product that accumulate in patients with end-stage renal disease (ESRD)**.** Hemodiafiltration is used to achieve large amounts of replacement fluids, which in turn allows optimum clearance of uremic toxins and strong hemodynamic tolerance, thus reducing the complications associated with the conventional therapy [(7)]**.**

A total of 60 patients **met the inclusion criteria**; **29** of them were females **(48.3%)** and **31** were males **(51.7%).** There was no difference in baseline characteristics between patients in the three treatment groups.

The mean age of all patients in the study was **43.33** years which range from **(26 to 58)** years. About **33.3%** were hypertensive (HTN), **21.7%** had chronic glomerulonephritis, **20%** were of unknown cause, **13.3%** had obstructive uropathy and **11.7%** had polycystic kidney disease and no history of diabetes. The mean duration of dialysis was **14.95** years with the range from **11.2** to **19.4** years.

Traditional hemodialysis is able to clear blood small molecules including blood urea nitrogen (BUN) and creatinine, but cannot scavenge other large and medium sized substances such as PTH and beta 2 microglobulin (β2-MG[(8)]**.** Hemodiafiltration (HDF) and hemodialysis with high flux membrane are established to scavenge large and small molecules [(9)]**.**

Beta 2 microglobulin (β2-MG) is the most commonly used uremic toxins as a marker for preservation and removal of medium sized molecules by hemodialysis. Serum levels of β2-microglobulin (ß2M) are substantially higher in patients with end stage renal disease undergoing hemodialysis (HD) and its aggregation accelerates dialysis related amyloidosis (DRA) .

In the current study, post dialysis serum β2 microglobulin in patients using HDF was lower than serum β2 microglobulin in patients using high flux and low flux dialysis membranes with more significant reduction in post dialysis serum β2 microglobulin in HDF sessions than in HF sessions.

Roumelioti et al. [(10)]found that HDF had higher rates of β2-microglobulin levels compared to high flux hemodialysis as it was a systematic analysis concluded that convective dialysis had higher ratios of reduction of β2-microglobulin ratios by 14.3 percentage compared to high flux dialysis.

Fen et al. [(11)]**,** found that hemodiafiltration and high flux dialyzer can significantly improve levels of β2-microglobulin with high flux hemodiafiltration which matches our study.

Another study has also reported a significant decline in ß2-microglobulin levels following switching patients from conventional HD to HDF [(12)]**.**

On the other hand, the **Turkish** online hemodiafiltration (OL-HDF) analysis, which could not observe a lowering of plasma beta 2 microglobulin levels with OL-HDF compared with high-flux HD. Plasma levels of β2 microglobulin did not decrease in both of the groups, and there was no discrepancy between patients received dialysis with high-flux membrane and OL-HDF with higher or lower volumes during the follow-up [(13)]**.**

In our results, as regards urea reduction ratio, there was significantly increase in urea reduction ratio in HDF over high flux. In his research, ***Saadi et al.*** [(14)] found that pre dialysis to post dialysis reduction in the serum urea concentration (URR percent) was substantially higher with HDF compared with hemodialysis (75.6 vs. 66.9 percent) that confirms our urea reduction ratio findings.

Phosphate is a type of small molecule, because complex exchanges and sequestrations in other compartments affect its removal from the blood stream. Hyperphosphatemia is associated with increased risk of mortality from all-causes including the cardiovascular risk [15].

In our study, as regard as phosphate, there was no significantly difference in phosphate level in HDF and in high flux but there was significantly difference in phosphate level in HDF and in low flux .

This is what the research did with a quantification of uremic toxin removal. No difference between hemodiafiltration and high flux hemodialysis was found in phosphate removal, with time being the only important factor making a difference [16].

Dekker et al. [17], recorded higher phosphate removal during hemodiafiltration as compared to conventional hemodialysis. Other researchers [18, 19] have also reported decreased levels of phosphate during HDF and traditional HD and aligned our analysis with those.

Anemia is a common complication of ESRD which affect the majority of patients on dialysis. Convective treatments can easily eliminate the middle molecular weight inhibitors of erythropoiesis [20].

In our study, as regard as hemoglobin levels, there was significant increase in hemoglobin levels when comparing HDF and high flux and highly significant increase in hemoglobin levels when comparing HDF and low flux

After switching from standard low flux hemodialysis to hemodiafiltration by using highly permeable and biocompatible membranes in several small and unregulated studies, an increase in anemia control was observed [20].

Pedrini et al. [21], reported better control of anemia in a large observational study confirmed during hemodiafiltration which also supports our research.

The study by the Italian Cooperative Dialysis showed the comparison between the biocompatible and traditional dialyzers, also as convective and diffuse treatment modalities. A secondary analysis showed significantly increase in hemoglobin levels in patients on high flux hemodialysis and HDF when compared with those on low flux hemodialysis [22].

In our research, as for PTH, there was substantial decrease in PTH levels in HDF than in high flux and highly significant decrease in PTH levels in hemodiafiltration group compared to low flux group.

In a research by ***El Arbagy et al.*** [23], after using high-flux membranes post dialysis there was highly significant decline in intact PTH but not after the use of low-flux ones. This is unlike ***Guillaume et al.*** [24], study which didn't find any changes in serum levels of PTH after moving from conventional HD to HDF (this may be due to the size of the studied cohort was small). A decrease in PTH values was not seen in the contrast analysis after moving from low-flux hemodialysis to hemodiafiltration [25].

As regard as triglyceride, there was dramatically decrease in level of triglyceride in HDF than high flux.

These findings showed that high flux hemodialysis can enhance blood lipid metabolism in dialysis patients, which may reduce cardiovascular problems and extend the life of patients. ***Fen et al.*** [11], supports our outcome in enhancing of lipid profile using HDF and high flux.

In our study, as regard as albumin, there was significant increase in albumin level in HDF than high flux. The study by ***Fen et al.*** [11], supports our result in improving of albumin level in using HDF and high flux.

Contrary to the current findings, there was no substantial improvement in serum albumin after use of high-flux filters in the study by ***Makar et al.*** [26]. However, in a report by ***Emad et al.*** [27], there was no statistically difference between the low-flux and high-flux groups with respect to albumin level.

Cuvelier et al. [28], found that highly permeable membranes could increase albumin loss and have harmful consequences; however, they could not reliably estimate the magnitude of albumin loss through highly permeable dialysis membranes. This could result from improved dietary intake and possible reasons due to the removal of plasma substances that inhibit appetite.

In our research, as regard quality of life, there was substantial improvement of quality of life in HDF group than high flux group and improvement of high flux group than low flux group in physical function, general health, itching and role of limitation due to emotional effect and this study agree with the study of ***Fen et al.*** [11].

Kantartzi et al. [29], identified a prospective cross over study of 24 patients participated in the study. The Short-Form Health Survey assessed quality of life with 36 questions (SF-36), and assessed subscale rating. There were substantial statistical differences in QOL for the total SF-36, bodily pain score, and role limitations due to emotional functioning in favor of online HDF over low-flux HD and both of the previous studies matches our study.

CONCLUSION

Hemodiafiltration is the most effective dialysis technique than high flux and low flux dialysis membrane in removal of medium sized molecule and improvement of quality of life.

REFERENCES

1. **Webster AC, Nagler EV, Morton RL *et al.* (2017):** Chronic Kidney Disease. The Lancet, 389(10075): 1238–1252.

2. **Bagalad BS, Mohankumar KP, Donoghune M *et al.* (2017):** Diagnostic accuracy of salivary creatinine, urea, and potassium levels to assess dialysis need in renal failure patients. Dent Res J., 14: 13-8.
3. **Kain R and Pagitz M (2017):** Chronic kidney failure affects humans and other mammalians. In: Jensen-Jarolim E. (eds) Comparative Medicine. Springer, Cham., pp 27-46.
4. **Michelis R, Sela S, Lanzmann A *et al.* (2017):** Level and oxidation of beta 2 microglobulin in hemodialysis patients treated with intravenous iron during dialysis with high flux compared to low flux dialyzers. Harefuah., 156(5): 289-293.
5. **Zickler D, Schindler R, Willy K *et al.* (2017):** Cellulose, modisfied cellulose and synthetic membranes in the haemodialysis of patients with end-stage renal disease, PLoS One, 12: e0169024.
6. **Ronco C, Neri M, Lorenzin A *et al.* (2017):** Multidimensional classification of dialysis membranes. Contrib. Nephrol., 191: 115–126.
7. **Canaud B, Vienken J, Ash S *et al.* (2018):** Kidney Health Initiative HDF Workgroup. Hemodiafiltration to Address Unmet Medical Needs ESKD Patients. Clin J Am Soc Nephrol., 13(9): 1435–1443.
8. **Brahmbhatt A and Misra S (2016):** The biology of hemodialysis vascular access failure. Semin Intervent Radiol., 33: 15-20.
9. **Brettschneider F, Tölle M, von der Giet M *et al.* (2013):** Removal of protein- bound, hydrophobic uremic toxins by a combined fractionated plasma separation and adsorption technique. Artificial Organs, 37(4): 409-416.
10. **Roumelioti ME, Trietley G, Nolin T *et al. (*2017):** Beta-2 microglobulin clearance in high-flux dialysis and convective dialysis modalities: A meta-analysis of published studies. Nephrology Dialysis Transplantation, 10(33): 311-393.
11. **Fen J, Zhi-Wei C, Wen-Juan W *et al.* (2017):** Comparison of high flux hemodialysis with hemodialysis filtration on pro-inflammatory and oxidative stress related cytokines in uraemic peripheral blood mononuclear cells. Int J Clin Exp Pathol., 10(1): 661-670.
12. **Movilli E, Camerini C, Gaggia P *et al.* (2011):** Effect of post-dilutional on-line haemodiafiltration on serum calcium, phosphate and parathyroid hormone concentrations in uraemic patients. Nephrol Dial Transplant., 26(12): 4032–4037.
13. **Ok E, Asci G, Toz H *et al.* (2013) :** Mortality and cardiovascular events in online haemodiafiltration (OL-HDF) compared with high-flux dialysis: results from the Turkish OL-HDF Study. Nephrol Dial Transplant., 28(1): 192–202.
14. **Saadi MG, Zayed B, Momtaz M *et al.* (2016):** Effect of a single session of haemodiafiltration on nerve conduction, interleukin-6 and β2-microglobulin. J Egypt Soc Nephrol Transplant., 16: 79-88.
15. **Francisco M, Raquel O, Lida R *et al.* (2015):** On-line haemodiafiltration with auto-substitution: assessment of blood flow changes on convective volume and efficiency, 35(1): 1-124
16. **Cornelis T, Van der Sande FM, Eloot S *et al.* (2014):** Acute hemodynamic response and uremic toxin removal in conventional and extended hemodialysis and hemodiafiltration: a randomized crossover study. Am J Kidney Dis., 64: 247-256.
17. **Dekker M, Pasch A, van der Sande F *et al.* (2016):** High-Flux hemodialysis and high-volume hemodiafiltration improve serum calcification propensity. PLoS One, 11(4): e0151508.
18. **Francisco RC, Aloha M, Ramon P *et al.* (2013):** Effects of high-efficiency postdilution online hemodiafiltration and high-flux hemodialysis on serum phosphorus and cardiac structure and function in patients with end-stage renal disease. Int Urol Nephrol., 45(5): 1373–1378.
19. **Oates T, Pinney J, Davenport A *et al.* (2011):** Haemodiafiltration versus high-flux haemodialysis: effects on phosphate control and erythropoietin response. Am J Nephrol., 33(1): 70–75.
20. **Li Y, Wang Y, Lv J *et al.* (2013):** Clinical outcomes for maintenance hemodialysis patients using a high-flux (FX60) dialyzer. Renal Failure, 35: 1240–1245.
21. **Pedrini L, Zawada A, Winter A *et al.* (2019):** Effects of high-volume online mixed-hemodiafiltration on anemia management in dialysis patients. PLoS One, 14(2): e0212795.
22. **Grooteman M, van den Dorpel M, Bots M *et al.* (2012):** Effect of online hemodiafiltration on all-cause mortality and cardiovascular outcomes. J Am Soc Nephrol., 23: 1087–1096.
23. **El Arbagy A, Koura M, El Barbary H *et al.* (2019):** Comparative study of the effect of high-flux versus low flux dialysis membranes on metabolic abnormalities in chronic hemodialysis patients. Menoufia Med J., 27: 677-682.
24. **Guillaume J, Jean-Marc H, Patrik D *et al.* (2015):** Online-haemodiafiltration vs. conventional haemodialysis: a cross-over study. BMC Nephrol., 16: 70.
25. **Jean G and Hurot J (2015):** Online-haemodiafiltration vs. conventional haemodialysis: a cross-over study. BMC Nephrology, 16(1).
26. **Makar S, Sawires H, Farid T *et al.* (2010):** Effect of high-flux versus low-flux dialysis membranes on parathyroid hormone. Iran J Kidney Dis., 4: 327-332.
27. **Emad A, Magdy E, Haytham S *et al.* (2017):** Effects of high flux versus low flux on serum C-reactive protein as an inflammatory biomarker in hemodialysis patients. The Egyptian Journal of Hospital Medicine, 67(2): 645-655.
28. **Cuvelier C, Tintillier M, Migali G, *et al.* (2019):** Albumin losses during hemodiafiltration: all dialyzers are not created equal - a case report. BMC Nephrol., 20(1): 392.
29. **Kantartzi K, Panagoutsos S, Mourvati E *et al.* (2013):** Can dialysis modality influence quality of life in chronichemodialysis patients? Low-flux hemodialysis versus high-flux hemodiafiltration: across-over study. Ren Fail., 35(2): 216–221.