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Emad Allam Mohamed
Department of Internal Medicine and Nephrology, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt.

Ahmed Farag Abdelkader
Department of Internal Medicine and Nephrology, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt.

Amr Ahmed Rizk
Department of Clinical pathology, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt.

Ahmed Qayed Ibrahim Galhom
Department of Internal Medicine and Nephrology, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt., ahmedqay600@gmail.com

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ORIGINAL ARTICLE

The Effect of Hemodiafiltration Versus Hemodialysis on Anemia in Patients on Regular Hemodialysis

Emad Allam Mohamed [a], Ahmed Farag Abdelkader [a], Amr Ahmed Rizk [b], Ahmed Qayed Ibrahim Galhom [a,*]

[a] Department of Internal Medicine and Nephrology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt
[b] Department of Clinical Pathology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

Abstract

Background: **Convective dialysis consists of hemodiafiltration, hemofiltration, and biofiltration devoid of acetate. Hemodialysis (HD) eliminates solutes and water through diffusion over a semipermeable membrane. Hemofiltration (HF) increases transmembrane pressure to increase solvent drag, whereas hemodiafiltration (HDF) combines HF and HD. More than 90% of CKD studied cases with eGFRs below thirty mL/min developed renal anemia. Due to restricted red blood cell transfusions, hemoglobin levels of approximately seven g/dL were clinically acceptable for cure of renal anemia. In practice, there is substantial inter-patient variability, & subset of dialysis studied cases may need greater ESA dose.**

Aim: **To evaluate and compare between the role of Hemodiafiltration and Hemodialysis on Anemia in Patients on regular hemodialysis.**

Subject and methods: **This prospective observational study, include 80 patients was selected from attendee of nephrology dialysis units of National Institute of Nephrology and Urology and Al-Azhar hospitals.**

Results: **There was no statistically significant variation among groups in terms of dialysis characteristics. No statistically significant variation was found among groups in terms of cure doses.**

Conclusion: **Long-term HDF therapy for twelve months was linked to significant improvements in anaemia & nutritional status.**

Keywords: Anemia, Hemodiafiltration, Hemodialysis

1. Introduction

Dialysis or kidney transplant are used to eliminate toxins & fluid from people who have significant renal function loss. Dialysis eliminates waste materials and fluid from the body by filtering them over membrane in dialysis machine (for hemodialysis) (for peritoneal dialysis).[1] Toxins that accumulate in body when kidneys fail come in a variety of sizes, and bigger molecules are eliminated less effectively by regular hemodialysis.[2]

Newer dialysis types 'push' water through dialysis membrane, allowing undesired molecules to be removed more efficiently.[3] Greater molecules are removed more effectively, & dialysis fluid has less contaminants, suggesting that convective dialysis has the potential to enhance how studied cases feel & survive on dialysis.[4] Hemodiafiltration, hemofiltration, & acetate free biofiltration are three kinds of convective dialysis treatment.[5]

Diffusion, removal of solutes & water throughout semipermeable membrane down concentration gradient, is used in standard hemodialysis. Hemofiltration, convection modality, uses enhanced transmembrane pressure to improve clearance across solvent drag, while hemodiafiltration combines HD & HF.[6]

Erythropoiesis is controlled by erythropoietin, which is generated in stromal cells near kidney's proximal renal tubule. Renal anaemia is most common complication in chronic kidney disease studied cases & is caused by relative lack of endogenous

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* Corresponding author.
E-mail addresses: ahmedqay600@gmail.com, drahmedfarag5@gmail.com (A.Q.I. Galhom).

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erythropoietin secretion 1.[7] Renal anaemia is defined as estimated glomerular filtration rate is less than sixty mL/min; it has been confirmed that more than 90% of CKD studied cases with eGFRs less than thirty mL/min have renal anaemia.[8]

Because of limited supply of red blood cells for transfusions, low haemoglobin levels of around seven g/dL were deemed clinically acceptable for treatment of renal anaemia to some extent.[9]

Exogenous administration of erythropoiesis stimulating agents is usually effective in treating anaemia in dialysis studied cases, however there is significant inter-studied case variability in clinical practise, & subset of dialysis studied cases may require greater than usual ESA dose to maintain recommended haemoglobin values among eleven & twelve g/dL. Numerous causes have been on turn advocated to explain this condition: Iron deficiency, vitamin B12 & folic acid deficiency, severe secondary hyperparathyroidism, hemodialysis-related chronic inflammation & oxidative stress, or insufficient dialysis.[10]

Goal of this research was to evaluate and compare between roles of Hemodiafiltration & Hemodialysis on Anemia in studied cases on regular hemodialysis.

2. Patients and methods

This was prospective observational research, include 80 patients selected from attendee of nephrology dialysis units of National Institute of Nephrology and Urology and Al-Azhar hospitals, Samples were collected by the systematic random method. All Males and females aging 30–50 years and had Dialysis for at least three months were contained within the research. Exclusion criteria was chronic infection, malignancy, acute illness, malnutrition, & chronic blood disease. Research protocol was approved by Local Ethics Committee & written informed consents were obtained.

All included studied cases were separated into two groups: **Group (A):** 40 HDF studied cases with anemia Hb < 10 g%. **Group (B):** 40 HD patients with anemia Hb < 10 g%. Both groups were on matched dose of ESA and I.V Iron. Both groups on regular HD for 3 months. All studied cases were subjected to: Complete history taking, Complete physical test: General test: **Vital signs** (Blood pressure, Temperature, Heart rate, Respiratory rate) & Signs of (Pallor, Cyanosis, Jaundice, & Lymph node enlargement). Lab investigations including (CBC, LFT, KFT). Values for Urea Reduction Ratio, creatinine, phosphorus, calcium, blood urea nitrogen, parathyroid hormone, hemoglobin, ferritin, transferrin saturation, serum iron, TIBC and erythropoietin dose were assessed.

SPSS software was used for data entry & analysis (SPSS 23.0 Version). The mean, proportion, & percentage were computed. The χ^2 test was used to establish association.

3. Results

Table 1.

No statistically significant variation was found among groups regarding years old, sex, primary renal pathology, duration of dialysis, and associated comorbidities Table 2.

No statistically significant variation was found among groups regarding characteristics of dialysis Table 3.

No statistically significant variation was showed among groups in terms of treatment doses. No statistically significant variation was showed among groups regarding baseline anemia parameters. High statistically significant variation was showed among groups regarding anemia parameters after 12 months Table 4.

No statistically significant variation was found among groups in terms of baseline laboratory measurements. After 12 months, the HDF group was related to significantly higher levels of albumin, calcium, phosphorus, & intact PTH.

4. Discussion

Global prevalence & incidence of maintenance dialysis are growing.[11,12] According to World Bank & World Health Organization data, 2.16 million Asians will require renal replacement therapy by 2030, 223% rise.[13]

Table 1. Patient characteristics (N = 80).

	HDF (N = 40)	HD (N = 40)	P value
Age (years)			0.446[a]
Mean ± SD	39.5 ± 6.5	38.5 ± 6.1	
Range	30–50	30–49	
Sex			0.496[b]
Female	15 (37.5%)	18 (45%)	
Male	25 (62.5%)	22 (55%)	
Primary Renal Pathology			0.900[b]
Diabetic Nephropathy	19 (47.5%)	18 (45%)	
Hypertensive Nephropathy	11 (27.5%)	11 (27.5%)	
Glomerulonephritis	8 (20%)	10 (25%)	
ADPKD	2 (5%)	1 (2.5%)	
Duration of Dialysis (months)			0.206[a]
Mean ± SD	5.9 ± 1.8	6.5 ± 1.9	
Range	3–9	3–9	
Associated Comorbidities			
Diabetes Mellitus	19 (47.5%)	18 (45%)	0.823[b]
Cardiac Disease	7 (17.5%)	9 (22.5%)	0.576[b]
Cerebrovascular Disease	6 (15%)	7 (17.5%)	0.762[b]

[a] Independent sample *t*-test.
[b] χ^2 test.

Table 2. Dialysis characteristics (N = 80).

	HDF (N = 40)	HD (N = 40)	P value[a]
Session Length (hours)			0.978
Mean ± SD	3.7 ± 0.4	3.7 ± 0.3	
Range	3–4.5	2.9–4.6	
Urea Reduction Ratio			0.994
Mean ± SD	72.5 ± 4.7	72.6 ± 4.6	
Range	65–80	65–80	
Kt/V			0.969
Mean ± SD	1.5 ± 0.3	1.4 ± 0.2	
Range	1–1.9	0.9–2.0	
Blood Flow Rate (ml/min)			0.776
Mean ± SD	266 ± 9.6	267 ± 10.7	
Range	250–280	246–284	
Predilution	5 (12.5)		
Convection Volume (L)			
Mean ± SD	20.3 ± 6.2		
Range	10–30		

[a] Independent sample *t*-test.

Between modalities of RRT, maintenance hemodialysis has been major technique worldwide for studied cases with end-stage renal disease.[12,14] According to US Renal Data System report, in 2016, 87.3% of incident ESRD studied case in US used HD for RRT.[15]

Hemodiafiltration is newer dialysis method that, unlike conventional hemodialysis, achieves clearance of middle & large molecular weight solutes. HD is based on diffusive transport of solutes along semipermeable membrane & is only effective in removing small solutes, whilst HDF involves pre- or post-filter infusion of sterile, pyrogen-free fluid, allowing clearance by convection in addition to diffusion.[16]

The main goal of this research was to evaluate and compare between roles of Hemodiafiltration & Hemodialysis on Anemia in studied cases on regular hemodialysis.

This prospective observational study was conducted in nephrology dialysis units of National Institute of Nephrology and Urology and Al-Azhar hospitals. This research was conducted on 80 ESRD studied cases in Hemodialysis. All studied cases were separated into two groups: group A: 40 HDF studied cases with anemia Hb < 10 g% and group B: 40 HD patients with anemia Hb < 10 g%.

Regarding demographic data of tested groups, we showed that there was no statistically significant variation among HD & HDF groups regarding years old, sex, primary renal pathology, duration of dialysis, and associated comorbidities.

As regard Primary Renal Pathology, we found that in HDF group, 19 (47.5%) patients had diabetic nephropathy, 11 (27.5%) had hypertensive nephropathy, 8 (20%) had GN, and two (5%) had ADPKD. In HD group, 18 (45%) patients had diabetic nephropathy, 11 (27.5%) had hypertensive nephropathy, 10 (25%) had GN, and one (2.5%) had ADPKD. No statistically significant variation was shown among groups regarding primary renal pathology (χ^2 test, $P = 0.900$).

Also, as regard Associated Comorbidities, we found that in HDF group, 19 (47.5%) patients were diabetic, 7 (17.5%) had cardiac disease, and 6 (15%) had cerebrovascular disease. In HD group, 18 (45%) patients were diabetic, 9 (22.5%) had cardiac disease, and 7 (17.5%) had cerebrovascular disease. No statistically significant variation was shown among groups regarding primary renal pathology (χ^2 test, $P > 0.05$).

In line with the present study **Kashgary *et al.*,**[17] who enrolled 164 studied cases in HD group & 77 studied cases in HDF group, this study reported that there were no statistically significant variations

Table 3. Management of anemia (N = 80).

	HDF (N = 40)		HD (N = 40)		P value[a]
	Mean	SD	Mean	SD	
ESA Dose (IU/kg/week)	187	75.4	186	75.4	0.994
IV Iron Dose (mg/day)	5.4	2.3	5.3	2.5	0.982
Hemoglobin (g/dl)					
Baseline	8.4	0.7	8.2	1.0	0.550
After 12 months	11.1	0.6	10.4	0.2	0.000
Ferritin (ng/ml)					
Baseline	9.6	3.3	9.5	3.2	0.925
After 12 months	37.8	8.1	29.7	8.1	0.000
TSAT (%)					
Baseline	11.2	4.4	11.0	4.4	0.994
After 12 months	32.3	7.1	23.6	7.2	0.000

[a] Independent sample *t*-test.

Table 4. Laboratory measurements (N = 80).

	HDF (N = 40)		HD (N = 40)		P value[a]
	Mean	SD	Mean	SD	
Albumin (g/dl)					
Baseline	3.6	0.2	3.5	0.4	0.438
After 12 months	4.0	0.3	3.4	0.2	0.000
Calcium (mg/dl)					
Baseline	8.1	0.4	8.2	0.4	0.429
After 12 months	8.3	0.4	7.9	0.5	0.002
Phosphorus (mg/dl)					
Baseline	4.9	0.3	5.1	0.4	0.137
After 12 months	6.2	0.4	5.9	0.4	0.009
Intact PTH (pg/ml)					
Baseline	309	130	308	130	0.987
After 12 months	442	154	350	183	0.018

[a] Independent sample *t*-test.

among HD & HDF groups regarding age, gender, primary renal pathology, duration of dialysis, and associated comorbidities. The most common comorbidities were hypertension followed by diabetes.

As well, **Ibrahem *et al.*,**[18] compared twenty studied cases on low flux dialyzer, twenty studied cases on high flux dialyzer, and 20 patients on hemodiafiltration. The study reported that the studied groups were similar as regard demographic data and baseline characteristics. 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.

As regard the characteristics of the dialysis process between groups. The mean session length was 3.7 ± 0.4 h in HDF group and 3.7 ± 0.3 h in HD group. Mean URR was 72.5 ± 4.7 in HDF group & 72.6 ± 4.6 in HD group. Mean Kt/V was 1.5 ± 0.3 in HDF group & 1.4 ± 0.2 in HD group. Mean blood flow rate was 266 ± 9.6 ml/min in HDF group & 267 ± 10.7 ml/min in HD group. No statistically significant variation was shown among groups regarding characteristics of dialysis (Independent sample *t*-test, $P > 0.05$). In the HDF group, predilution was performed in five (12.5%) patients. The mean convection volume was 20.3 ± 6.2 L, ranging between 10 and 30 L.

In agreement with our study **Kashgary *et al.*,**[17] discovered that there was statistically significant variation among tested groups as regard characteristics of dialysis (including Session Length, Urea Reduction Ratio, Kt/V and Dialysis Access).

Furthermore, **Smith *et al.*,**[19] enrolled 50 studied cases in HD group & 50 studied cases in HDF group, study described that there was statistically significant variation between the tested groups as regard characteristics of dialysis (including Session Length, Urea Reduction Ratio, Kt/V and Blood Flow Rate. In the HDF group, predilution was performed in 4 (9.1%) patients. mean convection volume was 20.6 ± 4.6 L.

Regarding the anemia treatment doses in both groups and anemia lab parameters, we found that the mean ESA dose was 187 ± 75.4 IU/kg/week in HDF group, and 186 ± 75.4 IU/kg/week in HD group. mean IV iron dose was 5.4 ± 2.4 mg/day in the HDF and 5.3 ± 2.5 mg/day in the HD groups. No statistically significant variation was shown among groups in terms of treatment doses (Independent sample *t*-test, $P > 0.05$).

In agreement with the current study **Lee *et al.*,**[15] revealed that there was no statistically significant variation among groups in terms of anemia treatment doses.

In current research, in HDF group, the baseline values were 8.4 ± 0.7 g/dl, 9.6 ± 3.3 ng/ml and 11.2 ± 4.4% for hemoglobin, ferritin and TSAT, respectively. In the HD group, the baseline values were 8.2 ± 1.0 g/dl, 9.5 ± 3.2 ng/ml, and 11.0 ± 4.4% for hemoglobin, ferritin, and TSAT, respectively. No statistically significant variation was shown among groups regarding baseline anemia parameters (Independent sample *t*-test, $P > 0.05$).

After 12 months, the anemia parameters were significantly different between groups in favor for HDF (Independent sample *t*-test, $P < 0.05$). The mean Hgb was 11.1 ± 0.6 g/dl in HDF group, & 10.4 ± 0.2 g/dl in HD group. Mean ferritin has been 37.8 ± 8.1 ng/ml in HDF group, & 29.7 ± 8.1 ng/ml in HD group. Mean TSAT was 32.3 ± 7.1% in HDF group, & 23.6 ± 7.2% in the HD group.

Furthermore, **Ibrahem *et al.*,**[18] revealed that 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, **Georgatzakou *et al.*,**[20] described that mean Hb was non significantly increased after therapy in HD group, however it was significantly increased in HDF group after treatment.

As well, **Hamzagić *et al.*,**[21] revealed that HDF have significantly higher positive impact on anemia parameters when compared to HD treatment.

However, **Kashgary *et al.*,**[17] described that there was no significant variation in post treatment anemia parameters, the same results were reported by **Smith *et al.*,**[19] in adults and **Galal & Hesham,**[22] in pediatrics. This was in disagreement with our results may be due to the differences in sample size and inclusion criteria as well as the differences in study settings.

In the current study, at baseline, the albumin was 3.6 ± 0.2 and 3.5 ± 0.4 g/dl in HDF & HD groups. Mean baseline serum calcium was 8.1 ± 0.4 & 8.2 ± 0.4 mg/dl in HDF & HD groups. Mean baseline serum phosphorus was 4.9 ± 0.3 and 5.1 ± 0.4 mg/dl in HDF & HD groups, respectively. Mean baseline intact PTH was 309 ± 130 and 308 ± 130 pg/ml in HDF & HD groups, respectively. No statistically significant variation was found among groups in terms of baseline laboratory measurements (Independent sample *t*-test, $P > 0.05$).

After 12 months post-treatment, the HDF group was related to significantly greater levels of albumin, calcium, phosphorus, & intact PTH (Independent sample *t*-test, $P < 0.05$). The mean albumin level increased to 4 ± 0.3 and 3.4 ± 0.2 mg/dl in HDF & HD groups, respectively. Mean calcium level increased to 8.3 ± 0.4 & 7.9 ± 0.5 mg/dl in HDF &

HD groups, respectively. Mean phosphorus level increased to 6.2 ± 0.4 and 5.9 ± 0.4 mg/dl in HDF & HD groups, respectively. Mean intact PTH increased to 442 ± 154 and 350 ± 183 pg/ml in HDF & HD groups, respectively.

Similarly, current study **Ibrahem *et al.*,**[18] reported that the HDF group was related to significantly greater levels of albumin, calcium, phosphorus, & intact PTH (Independent sample *t*-test, $P < 0.05$).

Also, **Smith *et al.*,**[19] reported that Serum albumin levels (3.2 vs. 3.3 g/dl for HDF & HD, respectively; $P = 0.001$) & chloride levels (101 vs 100 mEq/L for HDF & HD, respectively; $P = 0.02$) differed by small but statistically significant amount.

However, **Pedrini *et al.*,**[23] revealed that there were no clear variations in clinical parameters' albumin, calcium, phosphate & parathyroid hormone were observed in HD and HDF groups over time. Also, **Galal & Hesham,**[22] revealed that showed no significant difference in albumin levels in HDF studied cases compared to HD patients 3.519 ± 0.3391 versus 3.350 ± 0.48±0.219 ($P = 0.219$). This was in disagreement with our results may be due to the differences in sample size and inclusion criteria as well as the differences in study settings.

The current study discovered that albumin level was nonsignificantly increased in HDF group however decreased in HD group, however, Albumin level reduction with HDF was reported by several authors (**Stefánsson *et al.*,**[24]; **Tomo *et al.*,**[25]), however without having clear clinical impact. **Combarnous *et al.*,**[26] tested albumin removal with pre-dilutional HDF, most likely due to interaction with polymer surface of the dialysis membrane. Albumin loss during HDF seemed to have no acute effect on plasma albumin.

4.1. Conclusion

Current HDF methods & equipment can effectively deliver high-volume convective treatment to most studied cases & assure clinical performance related to better results. High-volume HDF can be easily & safely implemented in variety of settings, resulting in increased uremic solute clearance. Numerous studies have shown advancements in intermediate, studied case-reported, & clinical results when compared to standard HD. Long-term HDF therapy for twelve months was related to significant improvements in anaemia & nutritional status.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Conflicts of interest

There are no conflicts of interest.

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