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THE EFFECT OF HEMODIAFILTRATION ON BIOCHEMICAL PARAMETERS IN END STAGE KIDNEY DISEASE PATIENTS AT THE IRAQI CENTER OF HEMODIALYSIS

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Abstract

Background

Chronic kidney disease is a chronic ailment that profoundly impacts overall health and quality of life. As kidney function deteriorates, the buildup of toxins and electrolyte imbalances necessitates the use of renal replacement therapy to maintain physiological homeostasis in patients. The predominant options for substitute renal function include hemodialysis and hemodiafiltration, which have become the primary methods for managing end-stage renal disease. The primary objective of hemodialysis is to enhance patient survival, elevate quality of life, and mitigate problems associated with the procedure. To achieve this objective, dialysis prescriptions were formulated, augmenting the biocompatibility of dialysis filters and boosting the efficacy of medium-sized molecule toxin elimination via improved diffusion and convection. Hemodiafiltration with a large convective volume significantly reduces morbidity and mortality in patients undergoing hemodialysis.

Aims of the study:

The Aim of our study is to assess the benefits and effect of hemodiafiltration on biochemical parameters in chronic hemodialysis patients after six months of transferring to hemodiafiltration.

Patients and methods

Our study was conducted retrospectively over a period of six months from March 2024 to August 2024 for patients with ESRD who transfer from HD to HDF in Hemodialysis Unit at Baghdad teaching Hospital and Iraqi Center Of HD. All the patients with ESRD treated with HD and transfer to HDF consisted of 76 patients are included in this study. We exclude the patients do not continue HDF during 6 months for variable causes. SO, the last number of patients who included are 58 one. of them thirty-five patients were male, and twenty-three patients were female The mean age of the included patients was 51.63 years. All patients were hemodialysed with an arteriovenous fistula with blood flow 250 - 300 mL/min. All patients were treated with high flux filter, the session length hemodiafiltration was 4 hours three times a week. Data were collected every month from Medical Report Template and compared the data at the initiation of HDF and after six months of HDF. We analyze the biochemical investigations including blood urea level pre- and post- dialysis, serum creatinine, K, Na, PO4, Ca, ALP, Ferritin, iron albumin, hemoglobin, platlate, and PTH.

Results

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Compared to hemodialysis, hemodiafiltration had significantly lower values with respect to pre-dialysis urea, post-dialysis urea, serum sodium, serum potassium, serum phosphate, serum alkaline phosphatase, and hemoglobin level. Serum calcium was significantly higher in hemodiafiltration. Other parameters were not significantly different between hemodialysis and hemodiafiltration

Conclusion

This study indicates that patients undergoing hemodiafiltration exhibited a more solute clearance, enhanced removal and lower basal levels of uraemic solutes (serum creatinine and blood urea), improved serum albumin level and CKD MBD parameters (serum phosphate , calcium , PTH).
In addition, our study shows that more potassium is cleared through HDF than with hemodialysis .and also showing inconclusive effect of HDF on anemia (low hemoglobin, increase serum iron and ferritin) .

Introduction

Chronic kidney disease (CKD) is an increasingly prevalent comorbid condition that significantly impacts worldwide health systems [1]. In the last 30 years, the prevalence of chronic kidney disease (CKD) has risen significantly by around 30% [2]. Chronic kidney disease is a chronic disorder that profoundly impacts overall health and quality of life. As kidney function deteriorates, the buildup of toxins and electrolyte imbalances necessitates the use of renal replacement treatments (RRT) to maintain physiological homeostasis in patients [3]. The predominant options for renal replacement therapy (RRT) are hemodialysis and hemodiafiltration, which have become the primary modalities for managing end-stage renal disease (ESRD) [4].

The primary objective of hemodialysis is to enhance patient survival, elevate quality of life, and mitigate problems arising from the procedure [5]. To achieve this objective, dialysis prescriptions have been formulated, augmenting the biocompatibility of dialysis filters and boosting the efficacy of medium-sized molecular toxin elimination via improved diffusion and convection [6].

HDF is a kind of renal replacement treatment that integrates the concepts of hemodialysis (HD) with hemofiltration (HF). In traditional hemodialysis, solute removal is mostly accomplished by diffusion, the process by which molecules traverse a concentration gradient between the blood and dialysate, favoring smaller molecules. Conversely, solute removal in HF relies on convective transport, contingent upon the ultrafiltration rate, which remains consistent across varying molecule sizes, provided they can traverse the membrane pores, hence indicating its sieving capability. In HDF, the integration of diffusive and convective processes leads to the efficient elimination of tiny molecules, as well as a significant removal of bigger molecules [7,8].

HDF eliminates substantial plasma water volumes during ultrafiltration, necessitating isovolumetric replacement with a substitution fluid. The replacement fluid is administered into the patient's bloodstream and must be sterile and non-pyrogenic. Multiple modalities of replacement therapy exist, including post-dilution, pre-dilution, mixed-dilution, and mid-dilution HDF [7].

Post-dilution HDF is the predominant method of online HDF. The replacement fluid is administered downstream of the dialyzer into the venous aspect of the extracorporeal circuit. Post-dilution HDF provides elevated convective clearances and efficient elimination rates of soluble uremic toxins at standard or increased blood flow rates. The elevated ultrafiltration rate leads to

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increased serum protein concentrations owing to significant water loss, resulting in heightened blood viscosity and oncotic pressure, which may subsequently cause membrane fouling [7].
Membrane fouling results in an elevation of transmembrane pressure (TMP), which may be monitored by the apparatus. The apparatus may autonomously adjust the ultrafiltration rate to optimize clearance, preventing excessive fouling. The likelihood of fouling rises when blood circulation is disrupted [9]. A dependable vascular access is essential for HDF. For intermittent treatments, it is advised that extracorporeal blood flow rates be a minimum of 350 mL/min for adults and between 5 to 8 mL/min/kg of body weight or 150 to 240 mL/min/m² of body surface area for children [10].
Pre-dilution HDF: The replacement fluid is administered upstream of the dialyzer into the arterial segment of the extracorporeal circuit. In the pre-dilution phase, the levels of solutes in the blood diminish, leading to decreased diffusive and convective clearance rates relative to the post-dilution mode [7]. Pre-dilution HDF lowers hematocrit and oncotic pressure while maintaining the transmembrane pressure gradient across the capillaries, hence mitigating the likelihood of thrombus formation and shear stress inside the capillaries [8].
It promotes convective clearances in certain clinical scenarios linked to reduced blood flow, such as in pediatric patients, limited access flow, and central venous catheters, or in adverse hemorheological states characterized by elevated protein content and high hematocrit. A higher replacement volume, specifically double the size, is necessary to get equal solute clearances as seen in post-dilution HDF, due to the dilution of solutes entering the hemodialyzer [11–16].
Mixed-dilution HDF In mixed-dilution, the replacement fluid is administered into the tube both downstream and upstream of the dialyzer. This integrates the impacts of both postdilution and predilution to enhance the clearance rate. The device may adjust the rates of downstream infusions, upstream, and ultrafiltration based on pressure readings at different locations to optimize clearance while preventing clotting or excessive pore obstruction [17].
Moderate Dilution HDF Specialized dialyzers are utilized in mid-dilution hemodialysis filtration (HDF). Replacement fluid is introduced into the bloodstream via an auxiliary port located midway down the dialyzer's blood channel. This approach has been developed to amalgamate the advantages of both pre- and post-dilution [18]. In online HDF, the replacement fluid is not supplied as pre-packaged, sterile fluid but is generated in real-time from the dialysate fluid during treatment [7].
The replacement fluid undergoes cold sterilization using a two-stage ultrafiltration process utilizing sterilizing ultrafilters [7]. The utilization of specially engineered HDF equipment and corresponding quality oversight of the disinfection process, together with stringent hygiene regulations, is obligatory [7].
Table 1. Acceptable concentrations of germs and endotoxin in normal and ultrapure dialysis fluid [19].

	Standard dialysis fluid	Ultrapure dialysis fluid
Bacterial count	Higher than 100 CFU/mL	Higher than 0.1 CFU/mL

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Endotoxin	Higher than 0.5 EU/mL	Higher than 0.03 EU/mL*

CFU: colony-forming unit; EU: endotoxin unit.
* Less than 0.001 EU/mL in Japan [20].

The filters utilized by HDF require certain criteria that distinguish them from a conventional HD dialyzer, including a precise sieving coefficient curve, increased permeability, and optimal fiber geometry [21].

Initially, a pronounced sieving coefficient curve is required to facilitate the convective evacuation of solutes, especially for medium-sized molecules like B2-microglobulin (~11.8 kDa); hence, the membrane's permeability for these solutes, as shown by the corresponding sieving coefficient, must be adequately elevated.

Membrane permeability is constrained by the requirement to preserve vital proteins like albumin, since the depletion of albumin may result in malnutrition. Consequently, the optimal HDF membrane ought to exhibit a pronounced decline in the sieving coefficient, characterized by coefficients of 1 for medium-sized molecules and coefficients approaching 0 for albumin (~66 kDa) [22].

The second prerequisite for good high-volume hemodiafiltration (HDF) performance was a high permeability of the dialyzer for plasma water, facilitating the substantial convective volumes needed, particularly throughout high-volume HDF remedies [23–26].

Finally, the elevated ultrafiltration rates during HDF, in contrast to HD treatments, need consideration of their possible effects on rheology; the rise in blood viscosity is significant throughout HDF treatments, increasing the possibility of fiber clogging [21,27]. To mitigate these consequences, it is beneficial for the hemodiafilter to provide inadequate blood flow resistance. This is often accomplished by using hollow fiber membranes with an increased inner diameter (for example., >200 m). Furthermore, it was shown that enhanced flow dynamics in dialyzers with bigger inner lumens during HDF treatments result in the benefit of augmented convective volume [28].

The Online HDF Machine

In addition to the significance of high-flux hemodiafilters for attaining elevated replacement fluid amounts, the dialysis machine plays a crucial role in HDF remedies. Elevated transmembrane pressure resulting from substantial infusion volume leads to unstable treatment circumstances, frequent therapy interruptions, and losses of cross-membrane proteins. The pursuit of optimal balance has resulted in several advancements in regulating infusion rates throughout hemodiafiltration [29].

A novel generation of dialysis machines equipped with autosubstitution systems has enhanced the software to augment the total convective volume, consequently maximizing infusion flows (Qi) in accordance with intradialysis variations, resulting in a 13 percent rise in convective volume and a 3.5 percent rise in the proportion of convective volume to total processed blood. The auto-substitution is executed by monitor software that employs dynamic monitoring of the pressure

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pulse signals produced during blood filtration; an internal algorithm enables the machine to optimize the Qi to the maximum feasible volume at any given instant [30].

Clinical Advantages of HDF

HDF has shown a range of therapeutic advantages that significantly influence cardiovascular health and general wellness. HDF lowers cardiovascular risk and improves survival rates in people. It offers enhanced regulation of essential health variables: it efficiently addresses hyperphosphatemia [31], ameliorates inflammatory conditions [32], and optimizes erythropoietin response for improved anemia treatment [33,34]. Furthermore, HDF guarantees improved hemodynamic stability [35,36] and better management of arterial endothelial function [37], left ventricular hypertrophy [38], and excess fluid [39], thus diminishing the likelihood of serum calcification [40]. The incidence of neurological complaints, including restless legs syndrome, polyneuropathy, and pruritus, frequently resulting from the buildup of medium to large-sized molecules, has been substantially decreased [41].

HDF also alleviates pain in the joints and dialysis-related amyloidosis, consequently improving the general standard of life and patient satisfaction [42]. Moreover, the therapy substantially lowers DNA damage levels [43]. and enhances antioxidant levels, highlighting its many beneficial effects on individual health and well-being [44].

It is believed that all patients get advantages from HDF in comparison to standard HD. Individuals deemed likely to get major advantages from HDF are younger, free from diabetes mellitus and cardiovascular illness, and have elevated blood levels of albumin and creatinine [25,45].

Intermittent HDF typically necessitates vascular access capable of consistently attaining blood flow rates of no less than 350 mL/min in adults [14], Despite the generally decreased blood flow rate in central venous catheters in comparison to fistulae [46–48], central venous catheters were utilized successfully for HDF [49].

Postdilution HDF is preferred but may be impractical for patients at high risk of bleeding or for those with elevated blood viscosity: Because postdilution HDF requires anticoagulation, often at higher doses than required for hemodialysis, a high risk of bleeding may preclude the procedure. In contrast to postdilution HDF, hemodialysis (or predilution HDF) may be performed without or with minimal anticoagulation.

Aims of the study

The current investigation aim is to assess the benefits and impact of HDF on biochemical parameters in chronic HD patients after six months of transferring to HD.

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Patients and method

The research was done retrospectively over six months, from March 2024 to August 2024, including patients with end-stage renal disease (ESRD) transitioning from hemodialysis (HD) to hemodiafiltration (HDF) at the Hemodialysis Unit of Baghdad Teaching Hospital and the Iraqi Center for HD.

Inclusion patient

This research includes all 76 individuals with end-stage renal disease (ESRD) who were treated with hemodialysis (HD) and then transferred to hemodiafiltration (HDF).

Exclusion

We exclude the patients not continue HDF during 6 month for variable causes ex; Two patients die, 0ne patients kidney transplant , Seven patients intolerance due to cardiac disease , Eight patients change to HD as their request

SO,the last number of patients who included are 58 one . of them thirty-five patients were male and twenty-three patients were female The mean age of the included patients was 51.63 years

Every individual underwent hemodialysis with an arteriovenous fistula, facilitating bipuncture and a blood flow rate of 250 to 300 mL/min. All patients had treatment with a high flux filter, with OL-HDF sessions lasting four hours, conducted three times weekly.

Data were collected every month from Medical Report Template and compared the data at the initiation of HDF and after six months of HDF.

We analyze the biochemical investigations including blood urea level pre- and post- dialysis, serum creatinine, K, Na, PO4, Ca, ALP, Ferritin, iron albumin, hemoglobin, platlate, and PTH.

Statistical Analysis

Data were administered utilizing Microsoft Excel 2010 and IBM SPSS Statistics version 26. The normality of the data distribution has been determined utilizing the Shapiro–Wilk test. Quantitative variables have been presented as means accompanied by ranges. The variables of hemodialysis and hemodiafiltration were compared utilizing a paired T test. The significance level was established using a p-magnitude threshold of less than 0.05.

Results

Fifty-eight individuals with dialysis-dependent failure of the kidneys have been chosen for the research. The average age of the examined individuals had been 51.63 years, including thirty-five males and twenty-three females. The distribution of gender and age in the research's individuals is shown in Figure 1 and 2, respectively.

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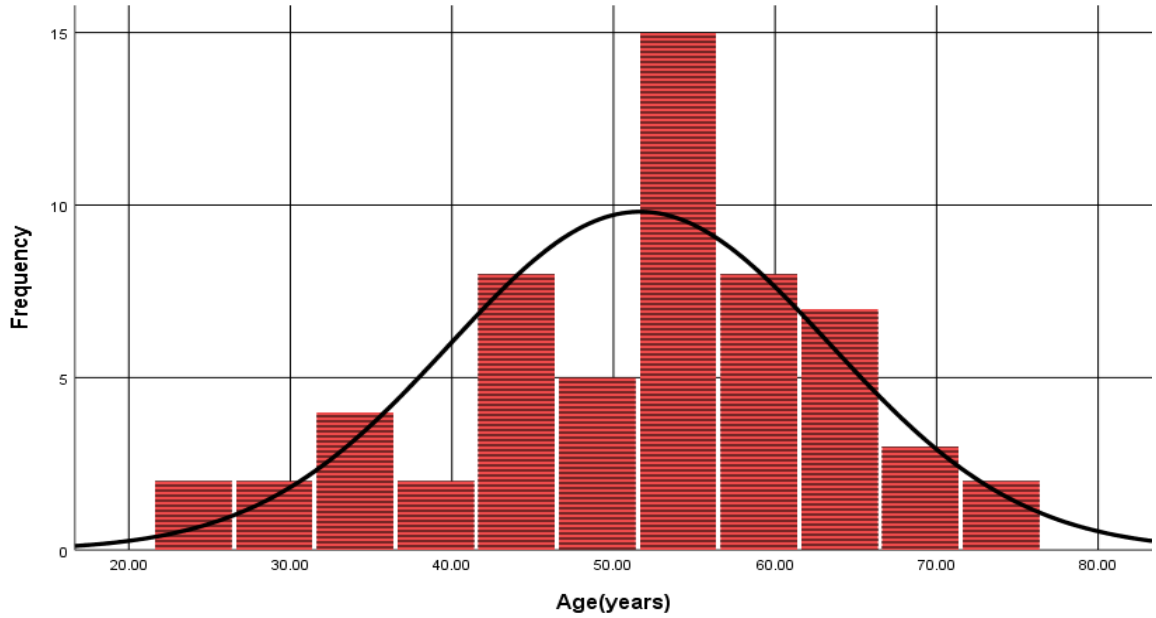

Figure 1. Histogram showing frequencies of various age groups in the study population.

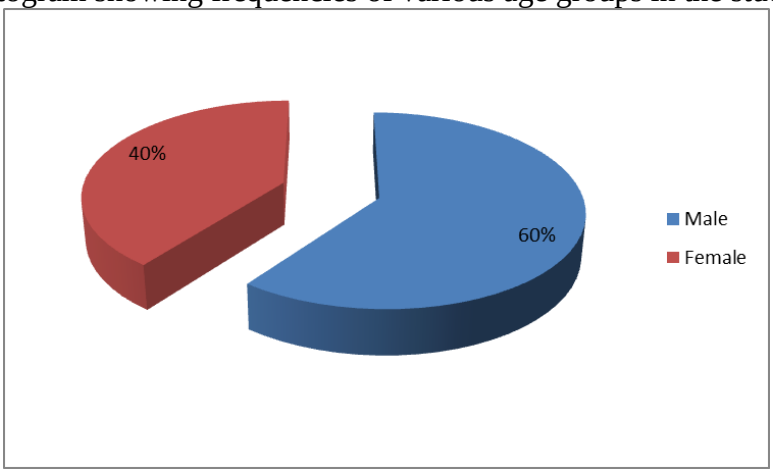

Figure 2: Pie chart showing proportions of male and female patients in the study population.

Compared to hemodialysis, hemodiafiltration had significantly lower values with respect to pre-dialysis urea, post-dialysis urea, serum sodium, serum potassium, serum phosphate, serum alkaline phosphatase, and hemoglobin level. Serum calcium was significantly higher in hemodiafiltration. Other parameters were not significantly different between hemodialysis and hemodiafiltration and as shown in the table 1.

Table 2. Comparison of biochemical and hematological parameters between hemodialysis and hemodiafiltration.

Parameters	**Hemodialysis**	**Hemodiafiltration**	***P-value***
Creatinine (mg/dL) Mean (Range)	9.27(1.2-16.8)	9.142	0.38
Pre-dialysis urea (mg/dL) Mean (Range)	162.81(64-291)	129.24	< 0.0001
Post-dialysis urea (mg/dL) Mean (Range)	60.03(28-167)	46.09	< 0.0001

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Urea reduction ratio Mean (Range)	62.42(29.68-83.02)	63.65	0.42
Serum sodium(mEq/L) Mean (Range)	140.01(130-149)	137.22	< 0.0001
Serum potassium(mEq/L) Mean (Range)	5.70(3.3-10.6)	5.30	0.01
Serum calcium(mg/dL) Mean (Range)	8.20(3.7-11.9)	8.981	0.001
Serum phosphate(mg/dl) Mean (Range)	5.82(2.2-15.6)	5.179	0.02
Serum alkaline phosphatase (IU/L) Mean (Range)	141.70(12.9- 629)	178.51	0.001
Hemoglobin(g/dL) Mean (Range)	10.42 (6.3-13.6)	9.91	0.02
Platelet count (per 10^6) Mean (Range)	164.13(27-282)	151.32	0.11
Serum iron(mcg/dL) Mean (Range)	27.13(3.7-127)	33.47	0.54
Serum ferritin(ng/mL) Mean (Range)	643.81(140-2000)	682.98	0.47
Serum albumin (g/dL) Mean (Range)	3.95(2.3-5.5)	4.01	0.42
Serum parathormone (pg/mL) Mean (Range)	286.31(17-9830)	299.88	0.48
Serum vitamin D_3 (ng/mL) Mean (Range)	22.17(3-51)	19.13	0.19

**P-value* less than 0.05 was considered significant.

Discussion

Numerous investigations have shown that HDF facilitates superior clearance of medium molecules in comparison to HD [50–53]. Significantly enhanced elimination of uremic toxins, including ß2-microglobulin, phosphate, and inflammatory cytokines, was seen in patients receiving HDF [54–59]. These compounds are linked to an elevated risk of cardiovascular disease and mortality [60,61]. This study indicates a slight decrease in serum creatinine levels throughout HDF remediation. in comparison with HD (9.14 vs 9.29 mg/dL, respectively; P = 0.38). Additionally, there is a substantial decrease in pre-dialysis urea (P less than 0.0001), post-dialysis urea (P less than 0.0001), and an increase in the urea reduction ratio (P = 0.42). The HDF experiment demonstrated a substantial decrease in serum urea levels both pre- and post-dialysis. Improvements in urea reducing rate (URR) and KTV, among other metrics, were also seen using online HDF [62]. In the prospective, randomized crossover trial conducted by Pedrini et al., the impacts of long-term online hemodiafiltration (HDF) were compared to hemodialysis (HD). Online HDF demonstrated superior efficiency in the clearance of tiny solutes, with an eKt/V urea of 1.6±0.31 against 1.44±0.26 for HD (p less than 0.0001) [63].

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Potassium abnormalities are prevalent in end-stage renal disease (ESRD) and may induce arrhythmias in patients receiving hemodialysis [64]. Potassium is mostly eliminated by hemodialysis, with up to 30% excreted via stools [65]. This study observed a drop in serum potassium after 6 months of HDF, decreasing from 5.70 to 5.30 (P less than 0.01), a finding congruent with research reported in the Turkish Journal of Nephrology [66]. The potassium removal by HDF exceeded that of HD, attributed to the greater volume of replacement fluid utilized, which has lower potassium levels than those seen in the blood [64].

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Phosphatemia

The impact of HDF on calcium-phosphate metabolism remains ambiguous. Some research reported no changes in phosphate levels between the HD and HDF groups, but other investigations demonstrated phosphate removal during HDF [67]. In this investigation, phosphate levels decreased during the transition from HD to HDF (5.82 to 5.179, $P < 0.02$), however the reduction was not statistically significant. Research indicates that high-volume hemodiafiltration (HDF) demonstrates superior phosphorus clearance relative to hemodialysis (HD) [68]. Nonetheless, this may have a little influence on predialysis serum phosphate, with an anticipated reduction of less than 15%, when patients transition to HDF [68]. Another research conducted by Morena et al. shown an improvement in the regulation of calcium-phosphate metabolism [63]. A multicenter, randomized controlled study including HD patients revealed no significant changes in blood calcium, phosphate, or PTH levels between groups allocated to maintain HD or transition to HDF treatment [24].

The lack of statistical significance in the reduction of phosphate levels may be attributed to an increase in hunger and subsequent consumption of more proteins and phosphorus [24,67–69]. Furthermore, phosphorus quickly attains a plateau phase, after which phosphatemia levels do not decrease further [70,71]. A plasma rebound is seen after the conclusion of the dialysis session [72].

ALBUMIN

The impact of HDF on nutritional status remains contentious [73]. The loss of amino acids and albumin is likely more significant with increased transmembrane pressure than with hemodialysis [74]. It has been reported that there is a modest loss of albumin when using a large convective volume. Minor reductions in albumin levels are strongly correlated with decreased longevity in hemodialysis patients [75]. Consequently, monitoring serum albumin is crucial, particularly in cases with pre-existing low albumin levels. This research observed no significant increase in serum albumin in HDF compared to HD. The research conducted by Fen et al. [76] demonstrates comparable results in the enhancement of serum albumin levels in individuals undergoing HDF treatment. A recent prospective controlled research, which randomly assigned patients to HDF or HD, found no significant reduction in blood albumin levels in the HDF group [34]. Orasan et al. [77] demonstrate that serum albumin levels were considerably lower in patients undergoing HDF compared to those receiving HD after 6 and 12 months of follow-up, concluding that HDF did not improve nutritional status as assessed by serum albumin. Jean et al. [78] shown that blood albumin levels were reduced in patients undergoing HDF when monitored over a period of 3 to 6 months. The findings may be attributed to an enhanced hunger and increased nutritional intake seen in our patients, either from the elimination of plasma chemicals that suppress appetite or owing to more effective

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clearance of leptin and other medium-sized molecules. This may also be attributed to an inflated dry weight prior to the commencement of OL-HDF.

Numerous observational and crossover investigations have shown that patients undergoing HDF have a favorable response to erythropoiesis-stimulating agents (ESAs), perhaps because to the substantial elimination of medium-sized molecules, such as hepcidin, which also promotes iron mobilization [79]. Several other investigations indicated no changes in anemia management among individuals using HDF [80]. Insufficient dialysis dosage and short session duration may have contributed to the issue.

This research observed a rise in serum iron and ferritin levels, accompanied by a non-significant drop in hemoglobin levels. This outcome might be attributed to the patient's noncompliance with ESAs owing to hypertension and occasional unavailability of ESAs at our facility. Systemic, sub-clinical inflammation associated with HD is likely the cause of increased serum ferritin in hemodialysis patients. Testing of haemodialysis devices for bacterial proliferation and endotoxins is not frequently conducted at our institution. The ESHOL trial indicated no significant variations in hemoglobin or ferritin levels, and the dosages of ESA were comparable across individuals undergoing HDF and HD [24]. The CONTRAST trial demonstrated a reduction in the use of ESA, albeit it did not achieve statistical significance [81]. The Turkish OL-HDF research demonstrated a markedly reduced weekly ESA dosage in patients undergoing HDF [67].

Conclusions

This research concludes that patients receiving hemodiafiltration had superior solute clearance, increased elimination, and reduced baseline levels of uremic solutes (blood urea and serum creatinine), as well as better serum albumin levels and chronic kidney disease mineral and bone disorder markers (PTH, calcium, serum phosphate).

The current research demonstrates that a greater quantity of potassium is eliminated using HDF compared to hemodialysis and moreover demonstrating an ambiguous impact of HDF on anemia (reduced hemoglobin, elevated serum iron, and ferritin)

Recommendation.

High-volume HDF has reported encouraging outcomes in patients, perhaps due in part to the elimination of uremic toxins.

So It is essential to continue collecting data of patients on HDF about their quality of life, cardiac status, nutritional status, frequency of complication of dialysis for a period longer than six months

Ensure monthly microbiology investigation which comprises of total bacterial count and endotoxin level from post - RO, first treatment point, last treatment point and from RO water storage tank.

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