Clinical Trial

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Evaluating of Hemodialysis Adequacy using Middle Molecular Indicator (Interleukin-1, Myoglobin Markers). A prospective, crossover study

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Abstract

Background. Uremic toxins accumulate in the body due to kidney dysfunction and are classified by molecular weight into small, middle, and large solutes. Middle-sized molecules, such as myoglobin and interleukin-1 (IL-1), are implicated in chronic inflammation, cardiovascular complications, and dialysis-related issues. Conventional hemodialysis (HD) effectively removes small solutes but is less efficient at clearing middle molecules.

Objective. To assess the removal efficiency of myoglobin and IL-1 using two different high-flux dialyzers (FX80 and Platinum H4, surface area 1.8 m²) in both high-flux hemodialysis (HF-HD) and hemodiafiltration (HDF) modalities.

Patients and Methods. A crossover study was conducted on 30 prevalent ESRD patients undergoing thrice-weekly HD at Ain Shams University Specialized Hospital. Patients received both HD and HDF treatments using FX80 and Platinum H4 dialyzers, with a two-week washout period between modalities. Each session was conducted with blood flow ≥300 mL/min and bicarbonate dialysate. Serum IL-1 and myoglobin were measured before and after sessions, and reduction ratios were calculated.

Results. The mean age of patients was 51.8 ± 12.9 years, and 80% were male. Baseline pre-dialysis IL-1 and myoglobin levels showed no significant differences across groups. Post-dialysis, the highest reduction ratios were observed with HDF-Platinum H4 for both IL-1 (81.6 ± 12.6%) and myoglobin (83.8 ± 10.6%), followed by HDF-FX80, HD-Platinum H4, and HD-FX80 ($p < 0.001$). Urea reduction ratio was also significantly higher with HDF compared to HD (75.2 ± 5.6% vs. 67.1 ± 8.3%, $p < 0.001$). No significant correlations were observed between transmembrane pressure and reduction ratios.

Conclusion. IL-1 and myoglobin are reliable markers for dialysis adequacy. HDF demonstrates superior removal of these middle molecules compared to HF-HD. Among dialyzers, Platinum H4 outperformed FX80, showing greater clearance efficiency in both modalities. ***Clin Ter 2026; 177 (1):55-64 doi: 10.7417/CT.2026.1975***

Keywords: *Hemodialysis Adequacy, Middle Molecular Indicator, Interleukin-1, Myoglobin, HDF, High-Flux Dialysis.*

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Introduction

Uremic toxins are substances that accumulate in body fluids due to impaired kidney function and exert harmful biological effects. According to the European Uremic Toxin Work Group (EUTox), they are classified into three groups: (1) small water-soluble molecules (<500 Da), (2) protein-bound uremic toxins (PBUTs), and (3) middle molecules (>500 Da, up to ~60 kDa) **(1).** Middle molecules such as β2-microglobulin (11.8 kDa), interleukin-1 (IL-1, 17.5 kDa), and myoglobin (17.8 kDa) have been implicated in dialysis-related complications, inflammation, and cardiovascular morbidity.

Conventional low-flux hemodialysis (HD) achieves adequate clearance of small solutes but is limited in removing middle molecules because of membrane permeability restrictions. Even high-flux HD provides only partial clearance, leading to continued toxin retention and complications (2). For example, α1-microglobulin (A1M, ~26 kDa), a representative middle molecule, accumulates in dialysis patients and reflects insufficient clearance (3).

Hemodiafiltration (HDF) offers superior removal of a broad spectrum of solutes by combining diffusive and convective mechanisms (4). However, its widespread use is limited by technical demands, including high volumes of ultrapure substitution fluid and the need for trained staff (5). More recently, medium cut-off (MCO) membranes have been developed, allowing enhanced clearance of middle-to-large molecules while minimizing albumin loss (6).

Among these toxins, IL-1 is a pro-inflammatory cytokine with a central role in immune activation, inflammation, and progression of kidney injury (7, 8). Myoglobin, a muscle oxygen-binding protein, normally cleared within hours, accumulates in renal failure and contributes to oxidative stress and tubular damage (9, 10). Their serum levels are therefore valuable markers of dialysis adequacy beyond standard urea kinetics.

Based on these considerations, the present study aimed to evaluate IL-1 and myoglobin clearance in patients undergoing high-flux HD versus post-dilution HDF, using two high-flux dialyzers with identical surface area (1.8 m²): FX80 and Platinum H4. This approach highlights the influence of dialysis modality and membrane characteristics on the removal of clinically relevant middle molecules.

Patients and methods

Study population

This was a single-center, prospective, crossover study conducted at the Ain Shams University Specialized Hospital dialysis center in a study period from January 2023 till March 2025. Thirty prevalent ESRD patients on maintenance hemodialysis were enrolled. All patients received thrice-weekly dialysis sessions of 4 hours' duration, with blood flow (Qb) ≥300 mL/min and bicarbonate-based dialysate. Patients with temporary dialysis catheters or unstable comorbidities were excluded.

Each patient underwent both high-flux HD and post-dilution HDF using two different dialyzers (FX80 and Platinum H4, each with 1.8 m² surface area). A two-week washout period was applied between modalities. The order of modality application was randomized to minimize sequence bias.

Dialysis Protocol

Each patient received four HD sessions; all patients were subjected to assessment the reduction ratio of both interleukin-1 and myoglobin by 2 different HD modalities using two different dialyzers (FX80 and platinum H4) using a computer-generated random sequence, with wash out period 2 weeks in between them using filter dialyzers fx with surface area less than 1.8 or platinum with low surface area.

Modality A (HD): High-flux hemodialysis using FX80 and Platinum H4.

Modality B (HDF): Post-dilution HDF (substitution volume ≥20 L, Qb ≥300 mL/min) using FX80 and Platinum H4.

All sessions used a dialysate flow (Qd) of 500 mL/min, dialysate temperature of 36°C, and unfractionated heparin for anticoagulation.

Dialyzers' characteristics

The Platinum H4 dialyzer is composed of micro-undulated polysulfone fibers with an ultrafiltration coefficient of 57 mL/h/mmHg, while the FX80 dialyzer uses a helixone membrane with an ultrafiltration coefficient of 64 mL/h/mmHg. Both have effective surface areas of 1.8 m² and were steam sterilized.

Clinical and laboratory data

Blood samples were collected from the arterial line immediately before and after dialysis sessions.

• *Routine labs:* Hemoglobin, complete blood count, serum creatinine, blood urea nitrogen, electrolytes, calcium, phosphorus (mg/dL), parathyroid hormone, serum albumin, iron profile, and ferritin (ng/mL).

• *IL-1 and Myoglobin:*

- IL-1 levels were determined using a quantitative ELISA kit (DLDevelop Biological Technology Co., Ltd, Cat. No. DL-IL1-Hu).
- Myoglobin was measured using a double antibody sandwich ELISA (DLDevelop Biological Technology Co., Ltd, Cat. No. DL-MYO-Hu).

Assays were performed in duplicate by laboratory personnel blinded to dialysis modality.

Blinding

Laboratory analyses were performed by investigators blinded to the dialysis modality and dialyzer type. Clinical staff could not be blinded due to the nature of the interventions but were not involved in data analysis.

Table 1. In Vitro Performance Characteristics of the Platinum H4 Dialyzer

			Platinum H Series
Clearance in vitro (ml/min) QD = 500 ml/min QF0 ml/min T= 37°C Maximum TMP 500 mmHg	QB 200 ml/min	Urea	194
		Creatinine	187
		Phosphate	183
		Vitamin B12	145
		Inulin	109
	QB300 ml/min	Urea	270
		Creatinine	245
		Phosphate	236
		Vitamin B12	170
		Inulin	121
Surface Area (m^3)		1.8	
UF Coefficient (ml/hr*mmHg)		57	
Blood Priming Volume (ml)		105	
Sieving coefficient	Vitamin B12	1.0	
	Inulin	1.0	
	B2 microglobulin	0.85	
	Albumin	<0.001	
Internal Diameter		200 µm	
Wall Thickness		40 µm	
Membrane Material		Micro-Undulated Polysulfone	
Housing Material		Polycarbonate	
Potting Material		Polyurethane	
Sterilization		Steam	

• Performance data were measured in vitro according to standard EN 1283 and 150 8637
• UF measurement: using bovine/human blood (Hct 32%; protein 60 g/l)
• Typical values obtained with an individual batch of fibers, clinical use may illustrate a difference in results in relation to different measuring techniques and possible variation between batches of fibers.

Table 2. In Vitro Performance Characteristics of the FX80 Dialyzer

FX CorDiax High-Flux Dialysers	**FX CorDiaz 80**
Clearance (Q = 300 mL/min)	
Cytochrome c	111
Inulin	127
Vitamin B12	190
Phosphate	248
Creatinine	261
Urea	280
Clearance (Q = 400 mL/min)	
Cytochrome c	117
Inulin	135
Vitamin B12	209
Phosphate	285
Creatinine	303
Urea	336
*Clearance (Q = 200 mL/min)	
Ultrafiltration coeff. (mL/h x mmHg)	64
In vitro performance: Q = 500mL/min, Q=0mL/min, T = 37°C (EN 1283). Sieving coefficients: human plasma, Qmax, Q = 0.2 x Qmax (EN1283). Ultrafiltration coefficients: human blood (Hct 32%, protein content 6%).	
Effective surface (m^2)	1.8
KA Urea	1,429
Priming volume (mL)	95
Article number	F00001591

Calculations

1. Interleukin-1 RR was calculated using the equation (11):

$$RR = \frac{Cpre - Cpost}{Cpre} \times 100\%$$

RR: reduction ratio, $C_{pre,}$ and c_{post} are serum Interleukin-1 *concentrations, pre-, and post-treatment, respectively.*

2. Calculating interleukin-1 post-dialysis concentration corrected for net ultrafiltration, with the following equation (11):

$$Cpost.c = \frac{Cpost}{\left(1 + \frac{\Delta BW}{0.2 \times BWpost}\right)}$$

Cpost.c: serum il-1 level post session after correction of net UF, C_{post} is serum il-1 level post-session, BW_{post} is the body weight after ultrafiltration.

3. Myoglobin RR was calculated using the equation (11)**.**

$$RR = \frac{Cpre - Cpost}{Cpre} \times 100\%$$

RR: reduction ratio, $C_{pre,}$ and c_{post} are serum Myoglobin concentrations, pre-, and post-treatment, respectively.

4. Calculating Myoglobin post-dialysis concentration corrected for net ultrafiltration, with the following equation (11):

$$Cpost.c = \frac{Cpost}{\left(1 + \frac{\Delta BW}{0.2 \times BWpost}\right)}$$

Cpost.c: serum Myoglobin level post session after correction of net UF, Cpost is serum Myoglobin level postsession, BW post is the body weight after ultrafiltration.

Qd: dialysate flow, QUF: ultrafiltration rate, Sub. Volume: substitution volume (in case of HDF only).

5. Calculating urea reduction ratio with the following equation:

$$URR = \frac{U_{pre} - U_{post}}{U_{pre}} \; x\; 100$$

Compliance and Monitoring

Patients' attendance and session completeness were monitored through dialysis unit records. All participants completed assigned sessions without deviation from protocol.

Sample Size Justification

This study included 30 prevalent ESRD patients in a prospective crossover design. The crossover methodology increases statistical efficiency because each patient serves as their own control, thereby minimizing inter-individual variability.

Based on prior studies evaluating middle-molecule clearance with HDF versus high-flux HD, reported differences in reduction ratios for β2-microglobulin and other middle molecules ranged between 15–25% with a standard deviation of 15–20% (11,19). Using these estimates, a sample of 30 patients provides >80% statistical power to detect a ≥15% difference in reduction ratio (two-tailed $\alpha = 0.05$) between modalities.

Statistical methods

Quantitative data were first tested for normality using the Shapiro-Wilk test. All continuous variables were found to be normally distributed ($p > 0.05$), justifying the use of parametric tests including paired t-tests for two-group comparisons, RM-ANOVA for repeated measures across modalities, and Pearson correlation for linear association analysis.

Results

Table 3. Demographic characteristics of the studied groups

Characteristics		Mean±SD
Age (years)		51.8±12.9
Weight (kg)		82.1±17.3
Height (m)		1.7±0.1
BMI (kg/m²)		28.7±4.7
		N(%)
Gender	Male	24(80.0%)
	Female	6(20.0%)

Total=30. BMI: Body Mass Index.

Table 3 showed demographic characteristics of the studied cases. Mean±SD of age (years) was 51.8±12.9. Majority of cases (80.0%) was males.

Table 4. Pre dialysis laboratory findings of the studied groups

Lab	Mean±SD	Range
Hemoglobin (gm/dL)	10.8±1.3	7.7–13.3
Total Leucocytic Count (x10³/mL)	6.8±1.9	3.9–10.2
Platelets (x10³/mL)	221.9±60.8	112.0–381.0
Serum iron (µg/dL)	59.0±20.2	34.0–124.0
Serum ferrtitin (ng/dL)	757.5±592.6	67.5–2163.0
Total Iron Binding Capacity (µg/dL)	217.6±38.1	108.0–302.0
Serum albumin (gm/dL)	3.7±0.4	2.8–4.4
Serum Parathormone (PTH) (pg/mL)	531.6±436.7	60.0–1912.0
Serum Calcium (mg/dL)	8.7±0.7	6.3–9.9
Serum Phosphorus (md/dL)	5.7±7.9	2.9–7.4
Serum Sodium (mEq/L)	135.9±3.5	127.0–142.0

Total=30.

Table 4 showed pre dialysis laboratory findings of the studied cases.

Table (5) showed dialysis parameters of the studied cases.

Table 5. Dialysis parameters of the studied groups

Parameters	Mean±SD	Range
Blood flow (ml/minute)	330.0±33.3	250.0–360.0
Dialysate flow (ml/minute)	500.0±0.0	500.0–500.0
Ultra filtration (ΔBody weight)	2.9±0.9	1.0–4.5
Body weight post dialysis (kg)	82.0±17.3	50.0–123.0
Subistitutional Volume (L)	21.6±0.8	20.0–23.0
Convection volume (L)	24.5±1.2	22.0–26.5
Convection rate (mL/min)	101.1±4.9	91.6–108.0
Filtration fraction (%)	28.8±1.4	26.0–31.0

Total=30.

Table 6. Serum IL-1 (pg/mL) between the studied groups

Time	Group	Mean±SD	p-value
Pre dialysis	HDF-FX80	53.5±22.8	0.627
	HDF-platinum H4	51.4±25.6	
	HD-FX80	54.0±23.4	
	HD- platinum H4	53.3±23.1	
Post dialysis	HDF-FX80	20.7±11.7a	**<0.001***
	HDF- platinum H4	10.9±10.1b	
	HD-FX80	40.7±18.5c	
	HD- platinum H4	31.5±15.7d	
C-post dialysis	HDF-FX80	17.6±9.9a	**<0.001***
	HDF- platinum H4	9.2±8.3b	
	HD-FX80	34.5±15.5c	
	HD- platinum H4	26.8±13.8d	
Reduction ratio	HDF-FX80	65.3±12.9a	**<0.001***
	HDF- platinum H4	81.6±12.6b	
	HD-FX80	35.9±8.4c	
	HD- platinum H4	49.8±13.6d	

*Total=30. ^RMANOVA. *Significant. Homogenous groups had the same symbol based on post hoc Bonferroni test.*

Table 6 showed that: No significant differences between study groups regarding pre dialysis serum IL-1.

Pre-dialysis IL-1 levels were comparable across groups ($p = 0.627$). Post-dialysis reduction ratios differed significantly between modalities (RM-ANOVA, $p < 0.001$, $\eta^2 = 0.42$).

- HDF-Platinum H4: 81.6% (95% CI 77.2–86.0)
- HDF-FX80: 65.3% (95% CI 61.1–69.5)
- HD-Platinum H4: 49.8% (95% CI 44.5–55.1)
- HD-FX80: 35.9% (95% CI 32.0–39.8)

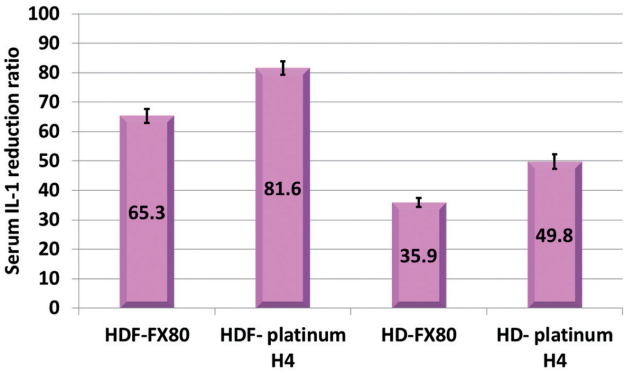

Figure 1. Serum IL-1 reduction ratio across modalities

Table 7. Serum myoglobin (mcg/L) between the studied groups

Time	Group	Mean±SD	p-value
Pre dialysis	HDF-FX80	25.5±14.2	0.623
	HDF- platinum H4	25.5±15.1	
	HD-FX80	26.1±16.4	
	HD- platinum H4	26.2±15.7	
Post dialysis	HDF-FX80	10.6±6.3a	**<0.001***
	HDF- platinum H4	4.1±2.7b	
	HD-FX80	18.6±13.1c	
	HD- platinum H4	15.1±10.9d	
C-post dialysis	HDF-FX80	9.0±5.5a	**<0.001***
	HDF- platinum H4	3.6±2.4b	
	HD-FX80	15.8±11.2c	
	HD- platinum H4	12.9±9.3d	
Reduction ratio	HDF-FX80	63.5±10.5a	**<0.001***
	HDF- platinum H4	83.8±10.6b	
	HD-FX80	40.1±10.1c	
	HD- platinum H4	52.8±11.7d	

*Total=30. RR: Reduction ratio. ^RMANOVA. *Significant. Homogenous groups had the same symbol based on post hoc Bonferroni test.*

Table 7 showed that: No significant differences between study groups regarding baseline pre dialysis myoglobin.

Post-dialysis reduction ratios showed a strong modality effect (RM-ANOVA, $p < 0.001$, $\eta^2 = 0.45$).

- HDF-Platinum H4: 83.8% (95% CI 79.4–88.2)
- HDF-FX80: 63.5% (95% CI 59.2–67.8)
- HD-Platinum H4: 52.8% (95% CI 48.1–57.5)
- HD-FX80: 40.1% (95% CI 36.0–44.2)

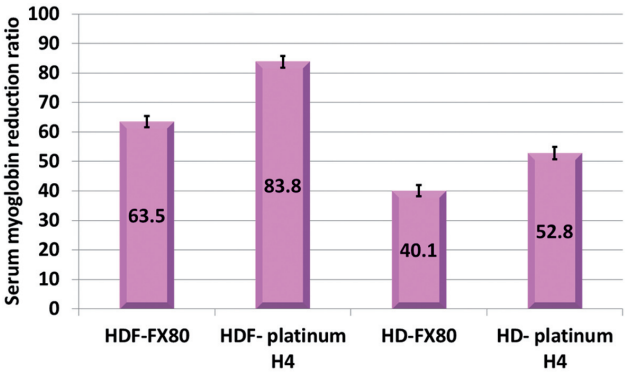

Figure 2. Serum myoglobin reduction ratio across modalities

Table 8. Serum urea (mg/dL) between the studied groups

Time	Group	Mean±SD	p-value
Pre dialysis	HDF	69.6±15.1	0.376
	HD	67.3±17.7	
Post dialysis	HDF	20.3±6.3	**<0.001***
	HD	26.0±9.2	
C-post dialysis	HDF	17.3±5.5	**<0.001***
	HD	22.1±7.8	
Rduction ratio	HDF	75.2±5.6	**<0.001***
	HD	67.1±8.3	

*Total=30. RR: Reduction ratio. ^Paired t-test. *Significant.*

Table 8 showed that: No significant differences between study groups regarding pre dialysis Urea.

Pre-dialysis urea levels were similar between groups (p = 0.376). The mean URR was significantly higher in HDF compared with HD (paired t-test, p < 0.001, Cohen's d = 0.92).

- HDF: 75.2% (95% CI 73.1–77.3)
- HD: 67.1% (95% CI 64.3–69.9)

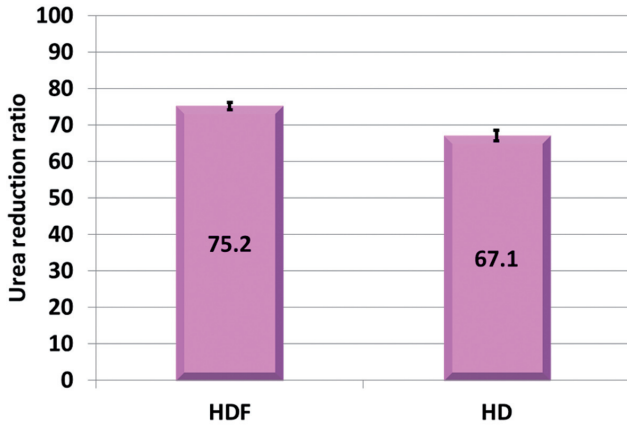

Figure 3. Urea reduction ratio (URR) across modalities

Table 9. TMP (mmHg) between the studied groups

Time	Group	Mean±SD	p-value
TMP-1	HDF	150.5±23.8	**<0.001***
	HD	67.8±17.1	
TMP-2	HDF	159.2±25.9	**<0.001***
	HD	72.9±13.5	
TMP-3	HDF	165.3±36.1	**<0.001***
	HD	77.0±10.2	
TMP-4	HDF	172.2±33.7	**<0.001***
	HD	79.7±8.2	

*Total=30. Total=30. ^Paired t-test. *Significant.*

Table 9 showed that: TMP-1, 2, 3 and 4 were significantly higher in HDF**.** TMP values were consistently higher in HDF compared to HD across all measurement points (paired *t*-tests, $p < 0.001$).

- TMP-1: HDF 150.5 mmHg vs HD 67.8 mmHg
- TMP-2: HDF 159.2 mmHg vs HD 72.9 mmHg
- TMP-3: HDF 165.3 mmHg vs HD 77.0 mmHg
- TMP-4: HDF 172.2 mmHg vs HD 79.7 mmHg

Correlation analysis showed no significant associations between TMP and reduction ratios (all $p > 0.05$).

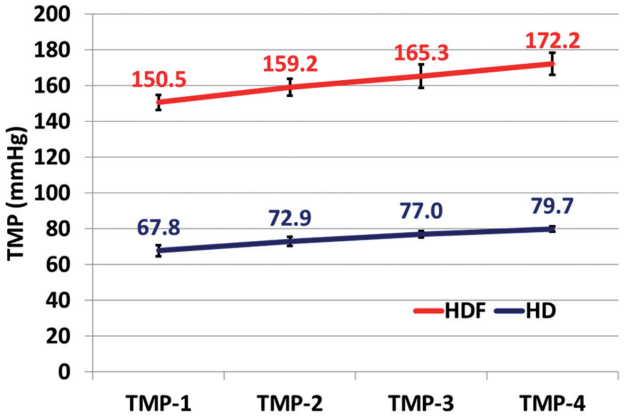

Figure 4. Transmembrane pressure (TMP) across modalities

Table 10. Correlations between TMP-4 and reduction ratios

Reduction ratios	HDF		HD	
	r	p-value	r	p-value
IL-1 (FX80)	0.012	0.952	-0.231	0.220
IL-1 (platinum H4)	-0.023	0.906	-0.336	0.070
Myoglobin (FX80)	0.248	0.187	-0.008	0.968
Myoglobin (platinum H4)	-0.028	0.882	-0.111	0.558
Urea	-0.181	0.337	-0.170	0.370

Pearson correlation.

Table 10 showed that: No significant correlations between TMP-4 and reduction ratios.

Discussion

Despite major advances in dialysis technology, the removal of middle-molecular-weight uremic toxins remains suboptimal with conventional high-flux HD. Molecules such as interleukin-1 (IL-1) and myoglobin are implicated in inflammation, oxidative stress, and cardiovascular morbidity in patients with end-stage renal disease (ESRD). While HDF has been shown to enhance middle-molecule clearance compared with HD, existing evidence is inconsistent, and the impact of dialyzer membrane characteristics has not been fully explored. This represents an important gap in the literature, as most comparative studies have focused primarily on β2-microglobulin and free light chains, with limited attention to IL-1 and myoglobin as alternative markers of dialysis adequacy (11).

The rationale for this study stems from the clinical need to better understand how different dialysis modalities and dialyzer designs influence the removal of inflammatory and oxidative stress–related toxins. Identifying reliable biochemical markers beyond urea kinetics is essential for improving dialysis adequacy assessment and guiding therapy. Unlike many previous studies, our work specifically focused on IL-1 and myoglobin, providing novel insight into their clearance with both HD and HDF (11,12).

This study was conducted at Ain Shams University Specialized Hospital, a large tertiary care center providing maintenance dialysis to a diverse ESRD population. The crossover design, with each patient exposed to both modalities and dialyzers, minimized inter-patient variability and allowed for a robust comparison of solute clearance.

Accordingly, the aim of this study was to evaluate the efficiency of two high-flux dialyzers (FX80 and Platinum H4) in the removal of IL-1 and myoglobin during high-flux HD compared with post-dilution HDF. By doing so, we sought to determine not only the effect of dialysis modality but also the role of membrane characteristics in optimizing middle-molecule clearance.

Several studies have investigated the long-term survival benefits of HDF compared to high-flux HD, with conflicting results (12,13). Recent evidence indicates that high-dose HDF, defined as delivering a convection volume >23 L, improves overall survival by reducing all-cause mortality. Earlier debates regarding this survival advantage suggested that the findings may have been influenced by confounding factors such as treatment indication bias. However, these concerns were addressed by the CONVINCE trial conducted by Blankestijn et al. (14), which was randomized and included only patients eligible for HDF throughout the study.

It is noteworthy that definitions of high-dose HDF vary across studies. Some trials define it as achieving a convection volume ≥23 L, whereas others refer to high-volume HDF as ≥21 L of replacement fluid per 1.73 m² body surface area (15). The survival superiority of HDF is generally attributed to its enhanced capacity for removing large middle molecules. By combining convection with diffusion, HDF achieves greater clearance of middle-molecular-weight toxins than HD alone.

Interleukin-1 (IL-1) is a middle molecule with a molecular weight of approximately 17.5 kDa. It plays a central role in immune regulation, contributing to the activation and differentiation of immune cells, as well as their proliferation, maturation, migration, and adhesion (16). IL-1 has both pro-inflammatory and anti-inflammatory properties, and in recent years its biological and pathological roles have been extensively studied in a wide range of diseases. Inflammation underlies the pathogenesis of many acute and chronic kidney disorders, and IL-1 has been identified as a key mediator in inflammatory kidney diseases and autoimmune conditions such as lupus nephritis (17).

Myoglobin is another middle molecule (17.9 kDa) that functions as an oxygen-binding protein in muscle. It is considered a uremic toxin and has been implicated in rhabdomyolysis and myocardial infarction. Myoglobin toxicity begins with myocyte injury or altered energy metabolism, leading to renal damage. One of the earliest proposed mechanisms of nephrotoxicity is tubular obstruction (18).

The adequacy of dialysis can be assessed by the reduction ratio (RR) of middle molecules such as IL-1 and myoglobin. In this study, we evaluated the elimination of IL-1 and myoglobin using two high-flux dialyzers (FX80 and Platinum H4) during conventional high-flux HD compared with post-dilution HDF. The study was conducted in 30 ESRD patients at the Ain Shams University Hospital hemodialysis units.

The mean age of the patients was 51.8 ± 12.9 years, with a mean body weight of 82.1 ± 17.3 kg and a mean BMI of 28.0 ± 4.7 kg/m². The mean ultrafiltration volume was 2.7 ± 0.83 L. During HDF sessions, the mean convection volume reached 24.3 ± 1.1 L, with an average post-dilution substitution volume of 21.6 ± 0.8 L. The mean blood flow rate across all sessions was 347 ± 8 mL/min.

Our results are broadly consistent with those of Morena et al. (11), who compared four dialyzers (Leoceed-21 HX, 2.1 m²; Polypure22S+, 2.2 m²; Rexsys-27 H, 2.7 m²; and VIE-21A, 2.1 m²). They demonstrated the superiority of HDF over HD for the removal of middle- and large-sized molecules, with reduction ratios exceeding 70% across modalities. Among the tested membranes, the Rexsys-27 H achieved the highest reduction ratio (76% with HDF), which was greater than values previously observed with the Elisio™-210H dialyzer.

El-Sayed et al. (19) also reported improved clearance of free light chains (FLCs) with HDF compared to high-flux HD, supporting our observation that convective modalities enhance the removal of larger solutes, although their markers differed from ours (FLCs vs. IL-1 and myoglobin). In their crossover study, all patients were dialyzed using the BIOPURE (Biorema) 260 HF machine (Allmed Medical Industries, GmbH, Germany) equipped with high-flux dialyzers of up to 2.0 m² surface area. Each patient underwent a single session of conventional HD and online post-dilution HDF, separated by a two-week washout period, under identical dialysis conditions. The reduction ratios achieved with HDF were significantly higher for kappa FLC (45.16 ± 6.53% vs. 29.52 ± 6.38%) and lambda FLC (28.68 ± 4.36% vs. 19.48 ± 1.96%) compared with high-flux HD.

Similarly, Kleeberg et al. (20) evaluated the Polymide HCO 1100 hemofilter (surface area 1.1 m², cutoff 60–80 kDa) and

reported median free light chain reduction ratios of 40.8% (range 13.9–66.4) with HDF and 23.7% (–32.9–55.8) with HD. These reductions were lower than those observed in our study, which may reflect differences in the molecular weights of the target markers (IL-1, 17 kDa; myoglobin, 17.9 kDa; albumin, 66.5 kDa) and the surface areas of the dialyzers used.

In contrast, Donadio et al. (21) performed a randomized crossover study in elderly patients to compare the efficiency and tolerability of high-flux HD, low-flux HD, and online HDF. They reported that clearance of small solutes was similar between high- and low-flux HD, while β2-microglobulin was only removed with high-flux HD. Importantly, high-flux HD demonstrated an efficiency and tolerability profile comparable to online HDF. Proteomic analyses further showed that high-flux membranes uniquely removed and adsorbed small proteins. These findings suggest that, under certain conditions, high-flux HD may serve as an effective alternative to online HDF.

In contrast, Donadio et al. (21) reported comparable efficiency between high-flux HD and HDF, particularly for smaller solutes, suggesting that the benefit of HDF may vary depending on the molecular weight and nature of the target solute. In our study removal of small molecules better by HDF than HD. Our present study resulted in no significant differences between study groups regarding pre dialysis serum IL-1. Serum il-1 reduction ratio was highest in HDF-Platinum H4 (81.6±12.6b) followed by HDF-FX80 (65.3±12.6a), then HD-Platinum H4 (49.8±13.6d) and lowest in HD-FX80 (35.9±8.4c) the differences were significant between all groups with p value <0.001*.

Also as regard serum myoglobin, no significant differences between study groups regarding pre dialysis myoglobin. Serum myoglobin reduction ratio was highest in HDF-Platinum H4 (83.8±10.6b), followed by HDF-FX80 (63.5±10.5a), then HD-Platinum H4 (52.8±11.7d) and lowest in HD-FX80 (40.1±10.1c) the differences were significant between all groups p value <0.001*

Our findings are broadly consistent with Francisco (22), who also observed greater clearance with HDF compared to HD, although differences in dialyzer type and patient characteristics limit direct comparison. Using polysulfone 1.8 m2. In the study Weidhase et al. (23) against our present study which showed Myoglobin clearance using continuous veno-venous hemodialysis with high cutof dialyzer and is better than that with continuous hemodiafltration.

Reque et al. 24 reported contrasting findings to our study. In their trial, the myoglobin reduction ratio was 35% with online HDF compared to 60% with expanded hemodialysis (HDx) using the high-retention onset Theranova 500 dialyzer ($p < 0.001$). They concluded that HDx is not inferior to online HDF for the clearance of small and middle molecules and may even be superior in removing larger middle molecules. Patients in that study underwent online HDF with a PF 210H dialyzer (group 1) or HDx with the Theranova 500 dialyzer (group 2).

Similarly, Belmouaz et al. (25) found that the use of the MCO (Theranova) dialyzer in conventional HD achieved removal of urea, creatinine, β2-microglobulin, and myoglobin comparable to that obtained with online HDF. These findings suggest that the introduction of MCO membranes could represent an alternative strategy to improve middle-molecule clearance, even outside of HDF settings.

Strengths

The crossover design allowed each patient to act as their own control, minimizing inter-patient variability and strengthening internal validity. The study also directly compared two widely used high-flux membranes (FX80 and Platinum H4), thereby generating practical evidence for clinical decision-making in dialysis units. Moreover, the use of objective biochemical markers and blinded laboratory analyses reduced bias in outcome measurement.

Limitations

Despite these strengths, several limitations must be acknowledged. The sample size was relatively small (n = 30), limiting external validity. The evaluation was restricted to a single dialysis session per modality, without longitudinal follow-up, preventing assessment of sustained toxin clearance or clinical outcomes. Clinical endpoints such as hospitalization, cardiovascular events, or mortality were not examined. Finally, although a two-week washout period was implemented, cross-contamination between modalities in the crossover design cannot be fully excluded.

Conclusions

Our findings support the use of IL-1 and myoglobin as reliable biomarkers of dialysis adequacy. HDF demonstrated superior clearance of middle molecules compared with high-flux HD, with the Platinum H4 dialyzer achieving the best removal efficiency. While these biochemical results favor HDF and advanced dialyzer membranes, larger and longer-term studies are needed to determine their impact on patient-centered outcomes.

Routine adoption of middle-molecule markers like IL-1 and myoglobin in dialysis adequacy assessment should be explored. Additionally, greater emphasis should be placed on dialyzer selection in clinical protocols, as membrane composition and design clearly influence solute clearance. Expanding the use of HDF where resources permit may offer patients superior removal of harmful uremic toxins.

List of Abbreviations

A1M – Alpha 1-microglobulin
BMI – Body Mass Index
CI – Confidence Interval
Da – Dalton
ELISA – Enzyme-Linked Immunosorbent Assay
ESRD – End-Stage Renal Disease
EUTox – European Uremic Toxin Work Group
HD – Hemodialysis
HDF – Hemodiafiltration
IL-1 – Interleukin-1

kDa – Kilodalton
MCO – Medium Cut-Off (membrane)
MWCO – Molecular Weight Cut-Off
PBUTs – Protein-Bound Uremic Toxins
PTH – Parathyroid Hormone
Qb – Blood Flow Rate
Qd – Dialysate Flow Rate
RR – Reduction Ratio
RM-ANOVA – Repeated Measures Analysis of Variance
SA – Surface Area
SD – Standard Deviation
TMP – Transmembrane Pressure
UF – Ultrafiltration
URR – Urea Reduction Ratio

Ethical considerations. This study was conducted in accordance with the principles of the Declaration of Helsinki (2013) and adhered to Good Clinical Practice guidelines. The study protocol was reviewed and approved by the Institutional Review Board (IRB) of Ain Shams University, Faculty of Medicine (approval number: FMASU MD 196/2020). Written informed consent was obtained from all participating patients prior to enrollment, after they were provided with detailed information about the study objectives, procedures, potential risks, and benefits. Patient confidentiality was strictly maintained throughout the study; personal identifiers were removed from all data, and results were analyzed anonymously. Participation was voluntary, and patients were assured of their right to withdraw from the study at any time without affecting their standard medical care.

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