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Effect of central dialysis fluid delivery system using high flux dialyzer versus regular water treatment stations on endotoxemia and inflammatory markers among prevalent patients on regular hemodialysis

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ABSTRACT

Purpose: In this study, we compared the effects of a single patient dialysis fluid delivery system (SPDDS) against a central dialysis fluid delivery system (CDDS) on inflammatory markers and endotoxemia in a population of patients receiving routine hemodialysis (HD).

Materials & methods: 80 prevalent HD patients, aged from 18 to 60 years old, who were clinically stable and receiving thrice weekly dialysis treatments via an arteriovenous fistula were the subjects of a cross-sectional research. group I underwent HD using a CDDS water purification system that was implemented at El Demerdash Hospital two years prior, and group II underwent HD using an SPDDS water purification system at Ain Shams Specialized Hospital.

Results: Pre-dialysis endotoxin levels were significantly lower in the CDDS group (0.07±0.05) compared to the SPDDS group (0.20±0.07), p-value<0.001, post-dialysis serum endotoxin levels were significantly lower in CDDS group (0.04±0.02) compared to SDDPS (0.15±0.03), p-value<0.001.

Conclusions: CDDS group's circulating endotoxins had significantly decreased.

Keywords: central dialysis fluid delivery system, flux dialyzer, endotoxemia, inflammatory markers, hemodialysis

INTRODUCTION

Chronic kidney disease (CKD) is a significant independent risk factor for morbidity and mortality [1]. Inflammation is the main cause of morbidity because it promotes the development of insulin resistance, oxidative stress, endothelial dysfunction, atherosclerosis, arterial calcification, and osteodystrophy in CKD [2]. Inflammation can be assessed by S-albumin, C-reactive protein (CRP), and white blood cell count [3], as well as Endotoxin levels, pentraxin-3, fibrinogen, IL-6, and CD14 [4].

The management of the patient's cardiometabolic syndrome and renal function depends on the gut flora. The relationship between the kidneys and gut microbiota, or the gut-kidney axis, becomes increasingly significant when CKD symptoms are present [5].

HD-induced systemic circulatory stress and persistent localized ischemia may lead to increased endotoxin translocation from the stomach. The resulting endotoxemia is also associated with increased mortality, cardiac damage, malnourishment, and systemic inflammation [6].

The dialysis fluid delivery systems that are now available are the single patient dialysis fluid delivery system (SPDDS), sometimes referred to as the individual dialysis fluid delivery system, central concentrates delivery systems, and central dialysis fluid delivery system (CDDS) [7].

CDDS simplifies the necessary upkeep and supervision by allowing the cooperative management of dialysis fluid for several people, the creation of cleaning and antiseptic solutions, and the distribution of these to each patient monitor. One advantage of CDDS is that it is frequently less expensive.

The fact that several patients may be impacted simultaneously by a central proportioning unit malfunction means that dialysis must be stopped at the patient station. This is one disadvantage, though. Furthermore, central systems do not allow for the customization of the composition of the dialysis fluid to meet the unique needs of each patient.

In addition, there is always a risk of contamination while utilizing the long dialysis pipes, and all patients are vulnerable to equipment failure [7, 8].

To ensure a steady supply of ultrapure dialysis fluid, endotoxin retentive filters (ETRFs) are usually installed in the dialysis bedside console of CDDSs immediately before the dialyzer. This is following the 2011 Japanese society for dialysis therapy "standard on microbiological management of fluids for hemodialysis and related therapies." The viable bacterial count in dialysis water should be less than 100 colony forming units/ml. Likewise, the live bacterial count of an endotoxin must be less than 0.050 EU/ml. This study compared the effects of a SPDDS against a CDDS on inflammatory markers and endotoxemia in a large population of patients receiving routine hemodialysis (HD) at Ain Shams University.

MATERIALS & METHODS

Patients

Eighty common HD patients, aged 18 to 60, were included in this cross-sectional study, which was carried out at Ain Shams University hospitals, which include Al Demerdash Hospital and Ain Shams University Specialized Hospital. The research excluded patients with acute infections, patients with central lines (permanent or temporary), and patients with cancer, as well as patients with end-stage liver disease. Patients were divided into two groups based on random selection using a randomization table created by a computer software program between March 2021 and June 2022. Group I consisted of 40 patients who were on maintenance HD and used the CDDS water purification system, which was implemented at Al Demerdash Hospital in Cairo, Egypt, two years prior.

40 patients (group II): Ain Shams University Specialized Hospital, Cairo, Egypt; maintenance HD utilizing SPDDS. Age (years), sex, dry weight (kg), height (cm), body mass index (BMI; kg/m^2), duration of HD (years), etiology of ESRD, and co-morbidities were among clinical data that were documented.

Study Design

Every patient was receiving prevalent HD; each four-hour session used a high flux dialyzer (HFD) (platinum H, 1.8 m^2, steam sterilization [ALLMED]) with a blood flow rate of 300 ml/min and a dialysate flow rate of 500 ml/min, an ultrafiltration coefficient of 58 ml/h×mmHg, urea clearance of 270 ml/min, and high sieving coefficient values (SC of B2-M=0.9, SC of myoglobin=0.45). Based on optimal dry weight and clinical data, each patient's net fluid removal and anticoagulant dosage were determined individually.

At the time of the trial, all patients had arterio-venous fistulas installed for dialyzation and were in a stable clinical state. The endotoxin levels before and after dialysis, as well as post-dialysis IL6, were evaluated. In both groups, the delta change in endotoxin was computed as (pre-dialysis endotoxin)–(post-dialysis endotoxin).

Biochemical Analyses

Blood urea nitrogen (BUN), complete blood count, serum albumin, high sensitivity C-reactive protein (Hs-CRP), serum potassium, serum phosphorus, serum sodium, and serum calcium were among the laboratory data gathered. Blood endotoxin levels, serum IL6, and BUN after dialysis. After clotting for 10-20 minutes at room temperature, all samples were centrifuged for 20 minutes at 2,000-3,000 RPM. Before and after HD, we examined and analyzed changes in electrolytes and inflammatory markers.

Serum samples were taken before and after dialysis to assess the endotoxin levels in each. An ELISA kit (Bioassay Technology Laboratory; China, Cat.NO E1801Hu) with a detection range of (0.02 EU/ml-0.8 EU/ml) and a standard curve range of one EU/ml-300 EU/ml was used to quantify the serum endotoxin level (EU/ml).

Endotoxin delta changes were computed, as follows: Endotoxin delta change=(pre-dialysis endotoxin)-(post-dialysis endotoxin).

Serum samples taken after dialysis were used to calculate the amount of IL6. An ELISA kit (Bioassay Technology Laboratory; China, Cat.NO E0090Hu) with a detection range of less than seven ng/l and a standard curve range of two ng/l-600 ng/l was used to quantify the serum IL6 level (ng/l). High sensitivity C-reactive protein (Hs-CRP) level was measured using post-dialysis blood samples and the monocent, Inc.CRP Ultra-sensitive ELISA (EL1-1049), which has a detection range of 0.2 to 10 mg/l.

Sample Size Calculation

Using PASS program, setting alpha error at 5.0% and power at 80.0%. Check previous studies, the needed sample was 80 Cases.

Statistical Analysis

The collected data were revised, coded, and then loaded into IBM SPSS, version 23, a statistical program for social research. The quantitative data was presented as mean with inter-quartile range (IQR) when the distribution was determined to be non-parametric, and as mean, standard deviations, and ranges when the distribution was found to be parametric. Furthermore, statistics and percentages were employed to depict the qualitative attributes. The qualitative data was compared between the groups using the Chi-square test. Quantitative data with a parametric distribution were compared between two independent groups using the independent t-test. The analysis of the data that did not fit into a normal distribution was done using the Mann-Whitney test.

A parametric distribution and quantitative data were utilized to compare two matched groups using the paired t-test.

The symbols NS, S, and HS denote non-significant, significant, and highly significant (p-value<0.010), respectively.

RESULTS

Demographic, Clinical, & Laboratory Characteristics of Patients

This cross-sectional study was conducted in Ain Shams University hospitals. 80 prevalent HD patients were randomly selected to participate in this study with average three sessions per week, including 46 (57.5%) males and 34 (42.5%) females. The mean age in CDDS group was 47.98±12.19 years. The mean age in SPDDS group was 50.00±10.09 years. There were statistically significant differences between the two studied groups regarding weight of the patients; mean weight was 65.45±14.29 kg in CDDS group and 78.78±13.03 kg in SPDDS group with p-value 0.000 and BMI; mean 24.50±4.47 in CDDS

Table 1. Comparison between CDDS group & SPDDS group regarding demographic data & laboratory data

Variable		CDDS n=40	SPDDS n=40	Test value	p-value	Sig.
Sex	Female	25 (62.5%)	9 (22.5%)	13.095*	0.000	HS
	Male	15 (37.5%)	31 (77.5%)			
Age (years)	Mean±SD	47.98±12.19	50.0±10.09	-0.809•	0.421	NS
	Range	19-59	23-59			
Years of dialysis	Median (IQR)	5.0 (2.5-8.0)	5.5 (3.0-10.0)	-0.310≠	0.757	NS
	Range	2-15	0.25-20.00			
Weight (kg)	Mean±SD	65.45±14.29	78.78±13.03	-4.358•	0.000	HS
	Range	37-102	52-120			
BMI (kg/m^2)	Mean±SD	24.50±4.47	27.59±4.17	-3.201•	0.002	HS
	Range	16.42-36.14	19.57-41.52			
Etiology of ESRD	Hypertension	14 (35.0%)	15 (37.5%)			
	Obstructive uropathy	2 (5.0%)	3 (7.5%)			
	ADPKD	3 (7.5%)	2 (5.0%)			
	Diabetes mellitus	13 (32.5%)	11 (27.5%)			
	Pyelonephritis	2 (5.0%)	1 (2.5%)			
	SLE	1 (2.5%)	0 (0.0%)			
	Drug Induced	0 (0.0%)	2 (5.0%)			
	Chronic GN	2 (5.0%)	3 (7.5%)			
	Unknown	3 (7.5%)	3 (7.5%)			
Albumin (g/dl)	Mean±SD	3.61±0.35	3.38±0.51	2.321•	0.023	S
	Range	2.5-4.3	2.3-4.5			
HGB (g/dl)	Mean±SD	9.89±1.87	10.05±1.36	-0.438•	0.663	NS
	Range	3.4-13.6	7.3-13.5			
WBCS	Mean±SD	4.93±2.36	6.06±2.39	-2.118•	0.037	S
	Range	1.9-13.4	2.9-12.6			
Platelets	Median (IQR)	199.0 (163.0-251.0)	202.5 (154.0-248.0)	-0.115≠	0.908	NS
	Range	60.0-1,647.3	69.0-429.0			
Urea pre-dialysis (mg/dl)	Mean±SD	51.08±9.54	51.58±18.26	-0.153•	0.878	NS
	Range	29-74	28-146			
Urea post-dialysis (mg/dl)	Mean±SD	20.78±7.85	19.98±6.18	0.506•	0.614	NS
	Range	8-37	8-38			
Urea reduction ratio	Mean±SD	30.30±12.07	31.60±17.43	-0.388	0.699	NS
Phosphorus (mg/dl)	Mean±SD	4.91±1.53	5.94±1.63	-2.907•	0.005	HS
	Range	2.8-9.0	1.6-9.7			
Potassium (mmol/L)	Mean±SD	4.47±0.70	5.19±0.51	-5.199•	0.000	HS
	Range	3.4-6.0	3.7-6.0			
Calcium (mg/dl)	Mean±SD	8.87±0.66	8.66±0.61	1.441•	0.154	NS
	Range	7.6-10.5	7.6-10.0			
Sodium (mmol/l)	Mean±SD	134.48±4.08	135.00±3.76	-0.599•	0.551	NS
	Range	128-145	128 -143			
Creatinine (mg/dl)	Mean±SD	7.32±1.64	8.71±1.91	-3.516•	0.001	HS
	Range	4.0-10.4	4.8-15.1			
Ferritin (ng/ml)	Median (IQR)	564.0 (295.5-894.5)	897.0 (463.5-1450.5)	-2.589≠	0.010	S
	Range	28-2,013	115-8,487			
IL6 (ng/l)	Median (IQR)	117.5 (80.0-142.5)	120.0 (100.0-140.0)	-0.540≠	0.589	NS
	Range	40-480	45-640			
Hs-CRP (mg/l)	Mean±SD	6.28±2.29	6.64±1.53	-0.844•	0.402	NS
	Range	2.0-10.0	4.0- 9.5			

Note. p-value>0.05: Non-significant (NS); p-value<0.05: Significant (S); p-value<0.01: Highly significant (HS); *Chi-square test; •Independent t-test; ≠Mann-Whitney test; Hs-CRP: High-sensitive C-reactive protein; IL6: Interleukin 6; ADPKD: Autosomal dominant polycystic kidney disease; SLE: Systemic lupus erythematosus; BMI; Body mass index; chronic; & GN: Chronic glomerulonephritis

group and 27.59±4.17 in SPDDS group with p-value 0.002 (**Table 1**).

Serum albumin level was 3.61±0.35 g/dl in CDDS group and 3.38±0.51 g/dl in SPDDS group with a statistically significant difference with p-value=0.023. Also, phosphorus level was lower in CDDS group versus SPDDS group; 4.91±1.53 mg/dl, 5.94±1.63 mg/dl, respectively with p-value=0.005. CDDS group shows lower potassium level and ferritin level; 4.47±0.70 mmol/l, 564 (295.5-894.5) ng/ml, respectively while SPDDS group shows potassium level 5.19±0.51 mmol/l, ferritin level 897 (463.5-1450.5) ng/ml with a statistically significant difference with p-value=0.000, 0.010, respectively.

IL6 level was lower in CDDS group in comparison to SPDDS group 117.5 (80.0-142.5) ng/l and 120 (100.0-140.0) ng/l, respectively. Hs-CRP level was lower in CDDS 6.28±2.29 mg/l; however, no statistically significant difference was found between CDDS group and regular HD group regarding IL6 and CRP levels with p-value=0.589 and 0.402.

Table 2 shows comparison between CDDS group and SPDDS group regarding levels of endotoxin before and after dialysis.

Table 2 showed highly significant lower levels of pre-dialysis endotoxin in CDDS group (0.07±0.05) in comparison to

Table 2. Comparison between CDDS group & SPDDS group regarding levels of endotoxin before & after dialysis

Variable		CDDS n=40	SPDDS n=40	Test value	p-value	Sig.
Endotoxin before dialysis (EU/ml)	Median (IQR)	0.070 (0.055-0.080)	0.200 (0.148-0.260)	-7.298	0.000	HS
	Range	0.025-0.320	0.120-0.320			
Endotoxin after dialysis (EU/ml)	Median (IQR)	0.04 (0.03-0.05)	0.15 (0.14-0.175)	-7.633	0.000	HS
	Range	0.020-0.135	0.100-0.200			
Wilcoxon rank test		-4.900	-2.802			
p-value		0.000 (HS)	0.005 (HS)			
Endotoxin change	Median (IQR)	0.025 (0.005-0.048)	0.015 (-0.003-0.093)	-0.911	0.363	NS
	Range	-0.010-0.185	-0.070-0.2050			

Note. p-value>0.05: Non-significant (NS); p-value<0.05: Significant (S); & p-value<0.01: Highly significant (HS)

Table 3. Different endotoxin delta changes in both groups

Delta changes in endotoxemia	CDDS	SPDDS
No changes	12.5%	7.5%
Increased	7.5%	22.5%
Reduced	80.0%	70.0%
Median delta changes	-0.02	-0.01

Table 4. Correlation of endotoxin before with other studied parameters in all cases, CDDS group, & SPDDS group

	End toxin before (EU/mL)					
	All cases		CDDS		SPDDS	
	r	p	r	p	r	p
Age (years)	-0.008	0.941	-0.168	0.300	-0.146	0.369
Years of dialysis	-0.041	0.720	-0.067	0.681	-0.110	0.499
Weight (kg)	**0.384****	**0.000**	0.037	0.822	0.035	0.832
Height (kg)	**0.409****	**0.000**	0.110	0.500	0.061	0.710
BMI	**0.249***	**0.026**	-0.035	0.829	-0.047	0.775
IL6 (ng/l)	-0.107	0.346	**-0.326***	**0.040**	-0.166	0.305
CRP (mg/l)	0.035	0.758	0.036	0.823	-0.245	0.127
Albumin (g/dl)	**-0.280***	**0.012**	-0.105	0.518	-0.239	0.138
HGB (g/dl)	-0.082	0.471	-0.203	0.208	-0.089	0.584
WBCS	**0.272***	**0.015**	0.202	0.211	-0.012	0.942
Platelets	0.119	0.293	0.157	0.334	0.197	0.224
Phosphorus (mg/dl)	**0.353****	**0.001**	0.133	0.412	0.103	0.529
Potassium (mmol/l)	**0.434****	**0.000**	-0.022	0.891	0.049	0.762
Calcium (mg/dl)	-0.175	0.120	-0.237	0.142	0.243	0.130
Sodium (mmol/l)	-0.011	0.920	0.056	0.729	-0.302	0.058
Creatinine (mg/dl)	**0.286***	**0.010**	-0.026	0.871	-0.002	0.988
Pre-dialysis urea (mg/dl)	-0.198	0.079	**-0.408****	**0.009**	-0.009	0.957
Post-dialysis urea (mg/dl)	-0.089	0.431	-0.061	0.709	-0.090	0.581
URR	-0.006	0.959	-0.225	0.162	0.061	0.708
Ferritin (ng/ml)	**0.340****	**0.002**	**0.374***	**0.018**	0.068	0.678

Note. p-value>0.05: Non-significant (NS); p-value<0.05: Significant (S); & p-value<0.01: Highly significant (HS)

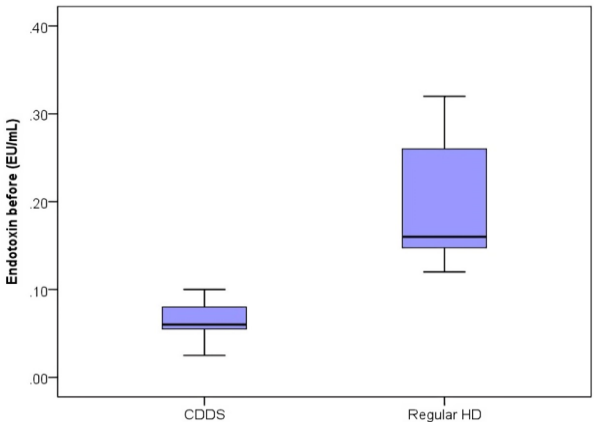

Figure 1. Comparison between CDDS group & SPDDS group regarding endotoxin levels before hemodialysis session (Source: Authors' own elaboration)

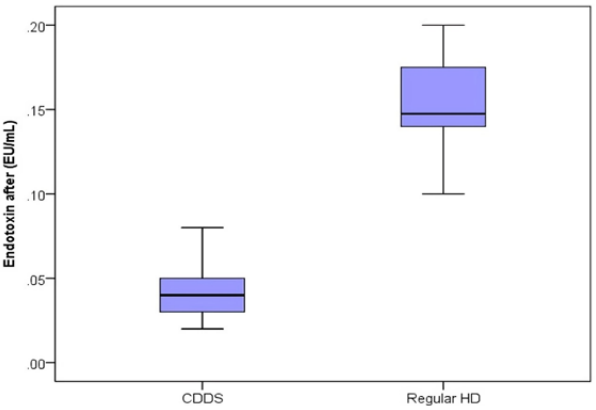

Figure 2. Comparison between CDDS group & SPDDS group regarding endotoxin levels after hemodialysis session (Source: Authors' own elaboration)

SPDDS group (0.20±0.07) (p-value<0.001). Moreover, it showed highly significant lower post-dialysis serum endotoxin levels in CDDS group (0.04±0.02) in comparison to SDDPS (0.15±0.03) (p-value<0.001). There was no statistically significant difference as regard endotoxin delta change (reduction between before and after endotoxin levels) between the two studied groups with p-value=0.363.

Table 3 shows different endotoxin delta changes in both groups.

Table 3 showed different endotoxin delta changes in both groups, in CDDS endotoxemia reduced in 80.0% of patients, increased in 7.5% of patients and no changes in 12.5% of patients. In the other hand, in SPDDS group, it was reduced in 70.0% of patients, increased in 22.5% of patients and no changes in 7.5% of patients.

Table 4 shows correlation of endotoxin before with the other studied parameters in all cases, CDDS group and SPDDS group. **Table 4** shows that the endotoxin level showed statistically significant positive correlation with weight, height, BMI, WBCs, phosphorus, potassium, C-reatinine, and ferritin level and negative correlation with albumin level in all cases. Also, **Table 4** shows that there was statistically significant positive correlation found between endotoxin level and ferritin level and negative correlation with IL6 and pre-dialysis urea in CDDS group while in SPDDS group the end toxin level did not show any correlation with the other studied parameters.

Figure 1 and **Figure 2** depict comparison between CDDS group and SPDDS group regarding endotoxin levels before hemodialysis session.

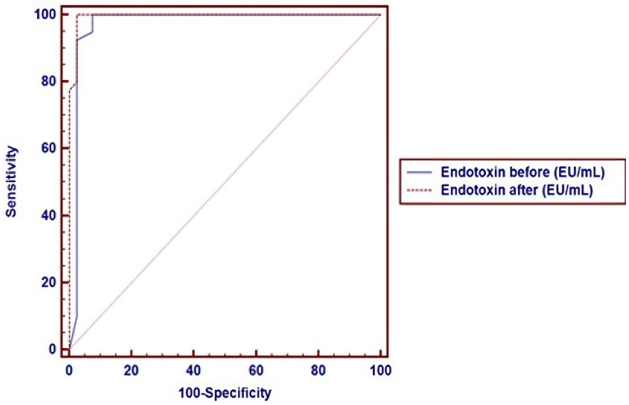

Figure 3. ROC of endotoxin before & after to differentiate between both groups (Source: Authors' own elaboration)

Table 5. ROC of endotoxin before & after to differentiate between both groups

Parameter	AUC	Cut-off	Sensitivity	Specificity	PPV	NPV
Endotoxin before	0.973	>0.10	100.0	92.5	93.0	100.0
Endotoxin after	0.995	>0.08	100.0	97.5	97.6	100.0

Figure 3 and **Table 5** show receiver operating characteristic curve (ROC) of end toxin before and after to differentiate between both groups. ROC curve shows that the best cut off point to differentiate between CDDS group from SPDDS group before was found >0.10 with sensitivity of 100%, specificity of 92.5% and area under curve (AUC) of 97.3% while after the best cut off point was found >0.08 with sensitivity of 100%, specificity of 97.5% and AUC of 99.5%.

DISCUSSION

CDDS water treatment system consists of bedside consoles, a central dialysate proportioning unit, a powder dialysate mixing unit, and a fluid distribution pipe system that links them together. An established system, CDDS is affordable, safe, effective, and labor-saving. Microbiological concerns have been alleviated by a well-planned system architecture, a robust RO membrane, many ETRFs, and regular system disinfections. It was developed as a unique dialysis tool in Japan and has since become well-known [9].

The exterior cell wall of gram-negative bacteria contains a combination of proteins and lipopolysaccharide molecules known as endotoxins, which are either released upon cell lysis or shed during growth [5]. Serum endotoxin levels were about six times greater in CKD patients undergoing dialysis than in those not, as HD was related with a risk of dialysate bacterial contamination with endotoxin and bacterial DNA fragment release. Moreover, the endotoxin permeabilities of various synthetic dialyzer membrane types may vary. Concern should be expressed over endotoxin transfer across the dialysis membrane by convective transfer (back filtration) or down a concentration gradient (back diffusion) [10].

A retrospective cross sectional study was carried out using information from the Japan renal data registry, a nationwide annual survey, where CDDS is extensively used. Thirty-seven thousand patients who had been getting thrice-weekly in-center HD for over six months had been recruited by 2,746 institutions in Japan by the end of 2006. Based on the facility endotoxin level, the patient groups <0.001, 0.001 to <0.010, 0.010 to <0.050, 0.050 to <0.100, and ≥0.100 EU/ml were formed. 91.2% of the 130,781 HD patients had facility endotoxin levels that were less than the 0.05 EU/ml Japanese limit for dialysis fluid [11].

The current cross-sectional study compared differences in many laboratory indicators and endotoxemia between the two dialysis models, CDDS and SPDDS. The study included 46 (57.5%) males and 34 (42.5%) females as participants. In SPDDS, the average age was 50.00±10.09 years, whereas in CDDS, it was 47.98±12.19 years. Among the most common causes of end-stage renal disease were hypertension and diabetes.

CDDS group showed considerably lower levels of pre-dialysis endotoxin (0.07±0.05), with a p-value<0.001, than SPDDS group (0.20±0.07). Furthermore, it demonstrated that, with a p-value<0.001, CDDS group's post-dialysis serum endotoxin levels were substantially lower (0.04±0.02) than those of SDDPS group (0.15±0.03). There was no statistically significant difference between the two groups under examination in terms of endotoxin delta change (reduction between pre- and post-endotoxin levels; p-value=0.363). It is possible that the higher endotoxin clearance in both groups was caused by the use of HFD membranes by all of the patients in the current study.

This is in variance with the findings of Ibrahim et al.'s study, which showed an abrupt rise in the mean post-HD endotoxin levels (0.367±0.110) EU/ml. Using ELISA for 40 patients on regular HD, he was evaluating the potential relationship between circulating endotoxin levels and CVDs in prevalent HD patients using SPDDS [12].

Furthermore, in opposition to our research, it was shown noticeably higher endotoxin levels in dialysis patients [0.64 EU/ml in HD and 0.56 EU/ml in peritoneal dialysis (PD)] [13]. Using SPDDS, they examined endotoxemia in 120 patients with typical HD and 25 patients with PD, spanning the range of CKD [13].

The majority of studies revealed a rise in post-dialysis endotoxin levels; however, our findings support the hypothesis that, when it was measured endotoxemia in 25 common HD patients who switched from HD using conventional water treated with reverse osmosis to ultrapure dialysate for four weeks (by implementing ultrafilters within the dialysis machine's fluid pathway) [14]. The serum endotoxin level decreased from 0.302±0.083 to 0.209±0.044 EU/ml and then remained static. This illustrates the function of the purification and treatment of water as well as how it contributes to the inflammatory cascades later on.

It was concured with our findings and assert that HFD is preferable to low flux dialyzer (LFD) because it allows for the removal of intermediate molecules and does not pose a risk of endotoxin transfer against LFD that might be associated with the dialyzer membrane's retention capacity [15]. In order to prevent the late complication of middle molecule retention when using LFD, they promote the usage of HFD among the HD population in our nation [15].

Furthermore, after adjusting for baseline variables, Hoedt et al. found a statistically significant difference in the rate of change of inflammatory markers, including CRP, between high and low flux dialysis patients [16]. They also documented a higher anti-inflammatory effect of HFD than LFD.

In this study, CDDS group had lower levels of IL6, ferritin, and CRP than SPDDS group, indicating a more favorable

impact on systemic inflammation. While SPDDS group had a median IL6 level of 120.00 (100.00-140.00), CDDS group had a median CRP level of 6.28±2.29 and SPDDS group had a mean level of 6.64±1.53. However, with p-values of 0.589 and 0.402, respectively, no significant differences were discovered between CDDS and SPDDS with regard to IL6 and CRP levels.

Serum albumin levels were 3.61±0.35 g/dl in CDDS group and 3.38±0.51 g/dl in SPDDS group, respectively, with a statistically significant difference (p-value=0.023) according to the current study. Additionally, the levels of ferritin, potassium, and phosphorus were lower in CDDS group compared to SPDDS group (p-values=0.010, 0.000, and 0.005, respectively). Similar to this, a case control study in [17] on 100 HD patients with end-stage renal illness revealed that CDDS appears to have a greater impact on systemic inflammation (IL6 and hsCRP) than SPDDS. Ultrapure dialysate was found to significantly reduce mean CRP levels of 3.19 mg/l (95% confidence interval (CI): -4.62, -1.75; p<0.001), significantly decrease mean IL6 levels of 5.43 pg/mL (95% CI: -8.38, -2.48; p<0.001), and significantly increase serum albumin levels of 0.11 g/dl (95% CI: 0.02, 0.19; p=0.011) in a meta-analysis of 23 study arms (n=2,221) [18].

A retrospective analysis was conducted in [19] to determine the effect of modernizing water systems on clinical parameters associated with inflammation. The distribution loop was expanded to include pyrogen filters (0.05-micron hollow fiber polysulfide filter, Fibercor, Minntech Corp, MI, USA), and every machine was outfitted with a Diasafe® (Fresenius Medical Care, Lexington, USA) filter, which produced the dialysate prior to being run through the dialyzer. The results indicated a significant increase in albumin (p=0.0001), TSat, ferritin, and hemoglobin (all p<0.0001), as well as a decrease in CRP [20], as the water quality increased.

There are several restrictions on this study. There was a little sample size. The study's methodology did not include a crossover design; neither the endotoxin level in dialysis fluid nor its variability over time were measured. Despite these drawbacks, we tried to use the same HFD (Platinum H, 1.8 m^2), steam sterilization (ALLMED), blood flow rate, dialysate flow rate, and dialysis time in each group to arrange the dialysis treatment parameters as uniformly as feasible.

CONCLUSIONS

According to our findings, CDDS group's circulating endotoxin level was much lower than SPDDS group's, however there were no statistically significant differences between CDDS group and the regular SPDDS group's levels of IL 6 and Hs CRP. Since finding relevant articles for debate is one of our challenges, we suggest conducting further research on CDDS in relation to endotoxemia clearance.

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