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ORIGINAL ARTICLE

Comparison of serum beta-2 microglobulin level between dialysis patients on high flux hemodialysis *versus* hemodiafiltration

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ABSTRACT

BACKGROUND: End-stage renal disease (ESRD) is a serious health issue that may have life-threatening consequences for those who have it. The buildup of medium molecular weight solutes, most notably beta-2 microglobulin (B2M), is one of the main consequences of end-stage renal disease (ESRD). Serum beta-2 microglobulin levels in high flux hemodialysis and hemodiafiltration patients will be compared in this research.

METHODS: Samples came from Basrah Teaching Hospital. All research patients gave written informed consent. This research comprised 200 end-stage renal disease patients aged 20-70. Disposable syringes were used to draw 5 mL of venous blood from each patient in plain tubes without anticoagulant and identify them with their name and date. The samples were processed promptly. Urea, creatinine, blood gases, complete blood count, calcium, phosphate, parathyroid hormone, Serum beta-2 microglobulin, potassium, sodium, and bicarbonate were measured in blood serum after centrifugation at 10,000 rpm for 5 min at 4°C.

RESULTS: Patients under hemodiafiltration (HDF) showed a notable decrease in B2M compared to those under hemodialysis (HD) and a longer dialysis period. Both HD and HDF patient groups exhibited a significant positive correlation between B2M and potassium, with no significant correlation between B2M and other factors like age or ferritin. Notably, HD was more linked with hypertension, while HDF was more associated with diabetes mellitus (DM).

CONCLUSIONS: The data that were obtained in this study supported the benefits of HDF in B2M clearance, with patient conditions influencing dialysis choice. The strong B2M-potassium link in both modalities underscored the importance of diligent monitoring.

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KEY WORDS: Beta 2-microglobulin; Dialysis; Hemodiafiltration.

End-stage renal disease (ESRD) is a critical health concern that has severe implications for affected individuals. One of the major complications of ESRD is the accumulation of middle molecular weight solutes, notably beta-2 microglobulin (B2M). This protein has been frequently linked with detrimental effects on numerous body tissues and is especially associated with adverse cardiovascular and infectious outcomes in ESRD patients.[1] Beta-2 microglobulin, a low molecular weight protein, usually eliminated from the body through the kidneys, starts to build up in patients with reduced kidney function. Its toxic accumulation has been studied for its potential role in dialysis-related amyloidosis, a disorder where B2M precipitates to form fibrillary structures and amyloid deposits. These deposits primarily localize in bones, periarticular tissues,[2] vessel walls, and several internal organs, with the heart being a primary concern.[3] Over time, these

amyloid deposits can cause significant morbidity by compromising the normal function of affected organs. Although the clinical manifestations of dialysis-related amyloidosis may not be immediately evident, there is increasing evidence suggesting that the accumulation and dysfunctional processing of B2M commence early during chronic kidney disease (CKD). This raise concerns not only about the progression of CKD itself but also about the potential causal link with cardiovascular disease (CVD) – a condition that presents with a high prevalence among ESRD patients.[4] Adequate clearance of B2M is essential in the management of ESRD, and this has brought attention to the efficiency of different dialysis techniques. Conventional dialysis, which is the cornerstone of renal replacement therapy for many ESRD patients, uses dialyzers that can be categorized into low-flux (LF) and high-flux types based on their permeability. High-flux dialyzers, compared to their low-flux counterparts, have shown better efficiency in removing B2M. Several meta-analyses of randomized controlled trials (RCTs) have found an association between the use of high-flux dialyzers and improved cardiovascular outcomes.[5] These points towards the potential advantages of using high-flux dialyzers in routine care for ESRD patients. Furthermore, advancements in renal replacement therapy have led to the introduction of convective therapies like hemodiafiltration (HDF) and hemofiltration. These modalities provide even superior middle molecule clearances compared to high-flux dialysis, potentially offering an enhanced solution to the chronic retention of B2M observed with thrice-weekly high-flux dialysis.[6] This study aims to determine difference between level of serum beta-2 microglobulin in dialysis patients on high flux hemodialysis *versus* hemodiafiltration.

Materials and methods

The samples were collected from the Basrah Teaching Hospital. Written informed consent was obtained from all the patients who participated in the study. This study included 200 patients within the age range of 20-70 years with a diagnosis of end stage kidney disease. In particular, 5 mL of the venous blood sample was drawn from each patient by using disposable syringes in plain tubes without any anticoagulant and labeled with the patient's name and date of collection. Collected samples were processed immediately. Blood serum was separated by centrifuge at 10,000 rpm for 5 min at 4°C for urea, creatinine, blood gases analysis, complete blood count, calcium, phosphate, parathyroid hormone, potassium, sodium, and bicarbonate. Serum β2M was measured by an immunoturbidimetric assay (Roche Cobas c702; Roche Diagnostics, Lewes, UK).

Regarding dialysis:

- hemodialysis was performed using Dialog plus B Braun machine (B Braun, Melsungen, Germany) with high flux hemodialyzer with target Kt/v reached target more than 1.2;
- hemodiafiltration was performed using Dialog plus B Braun machine with postdilution HDF and substitution volume of 23 L/session.

Statistical analysis

Statistical analysis was processed using SPSS 22 (SPSS Inc., Chicago, IL, USA). Pearson's correlation displayed the correlation between continuous data, while chi-square is used to evaluate associations between categorical variables. The *t*-test is used to assess variations between the mean and median of continuous data. A P value of 0.05 or less was regarded as significant.

Results

As shown in Table I, there was a significant decrease in B2M in patients under HDF rather than in patients under hemodialysis (HD). Also, Table I showed significant increase in period of dialysis in group patients under HDF compared to patients in group HD. Furthermore, there was no significant difference in mean of age, ferritin, Ca, parathyroid hormone [PTH], bicarbonate, hemoglobin, K^+ between HDF and HD group of patients. As shown in Table II, 70.9% of patients under HD was significantly associated with hypertension, while 75% of patients under HDF was significantly associated with diabetes mellitus (DM). As shown in Table III, there was a strong significant positive correlation between B2M and potassium, while there was no significant correlation between B2M and (age, ferritin,

TABLE I.—*Differences in mean of variables in current study for both study groups.*

Variables	Type	N.	Mean	SD	P value
Age	HD	103	49.43	15.9	0.9
	HDF	100	49.66	15.1	
B2M	HD	102	935.64	521.6	0.002*
	HDF	100	730.26	417.3	
Ferritin	HD	103	240.48	282.1	0.2
	HDF	100	197.97	232.1	
Ca	HD	103	9.25	6.6	0.3
	HDF	100	8.58	1.3	
PTH	HD	103	258.62	272.1	0.5
	HDF	100	283.87	288.3	
Bicarbonate	HD	103	43.09	31.6	0.4
	HDF	100	40.39	8.5	
Dialysis period	HD	103	28.31	28.9	0.0001*
	HDF	100	54.18	35.7	
Hemoglobin	HD	103	8.89	1.6	0.8
	HDF	100	8.96	1.6	
K^+	HD	103	4.94	2.9	0.8
	HDF	100	5.01	1.0	

HDF: hemodiafiltration; HD: hemodialysis; PTH: parathyroid hormone.
*Statistically significant (P value ≤0.05).

TABLE II.—*Distribution of patients in both groups if they have hypertension or DM.*

Variables	Session type		
	HD	HDF	P value
Hypertension			
No	30	77	
	29.1%	77.0%	
Yes	73	23	0.0001
	70.9%	23.0%	
Total	103	100	
	100.0%	100.0%	
Diabetes			
No	66	25	
	64.1%	25.0%	
Yes	37	75	0.0001
Mellitus	35.9%	75.0%	
Total	103	100	
	100.0%	100.0%	

HDF: hemodiafiltration; HD: hemodialysis.
*Statistically significant (P value© ≤0.05).

Ca, PTH, HCO_3, dialysis period, Hb) in HD patients' group. As shown in Table IV, there was a significant positive correlation between B2M and potassium and no significant correlation between B2M and (age, ferritin, Ca, PTH, HCO_3, dialysis period, Hb) HDF patients' group.

Discussion

The management and outcomes of patients undergoing dialysis are of paramount importance in nephrology. The presented results shed light on the differential impact of hemodiafiltration (HDF) and hemodialysis (HD) on various clinical parameters, most notably on beta-2 microglobulin (B2M) levels, a critical marker associated with dialysis-related amyloidosis. A striking observation from the provided data is the significant reduction in B2M levels in patients undergoing HDF compared to those on HD. This is consistent with previous studies that have indicated HDF's superior clearance of middle molecular weight solutes, including B2M.[7] HDF, with its mixture of diffusive and convective solute elimination, tends to complete good permission for greater molecules like B2M, which may not be as professionally detached by HD alone.[8] This enhanced clearance can be an essential factor in preventing the long-term problems associated to B2M accretion. Another notable finding is the lengthy dialysis period in the HDF group compared to the HD group. Longer sessions or increased occurrence can enhance solute removal, emphasizing the efficacy of HDF in solute clear-

TABLE III.—*Correlation between parameters in HD patients group.*

		Age	Ferritin	Ca	PTH	HCO_3	Dialysis Period	Hb	K
B2M	R	-0.14	0.006	-0.04	0.001	-0.004	0.11	0.02	0.34*
	P	0.15	0.95	0.65	0.98	0.97	0.26	0.81	0.0001*

HD: hemodialysis; PTH: parathyroid hormone.
*Statistically significant (P value ≤0.05).

TABLE IV.—*Correlation between parameters in HDF patients group.*

		Age	Ferritin	Ca	PTH	HCO_3	Dialysis period	Hb	K
B2M	R	0.20	-0.09	-0.04	0.07	-0.03	0.10	0.09	0.21*
	P	0.04	0.37	0.69	0.45	0.71	0.31	0.35	0.03*

HDF: hemodiafiltration; PTH: parathyroid hormone.
*Statistically significant (P value ≤0.05).

ance.[9] Though, it is necessary to weigh these aids against potential disadvantages, such as increased reserve use and potential challenges for patient compliance with prolonged or more frequent sessions. Despite the differences in B2M levels and dialysis periods, there was no significant difference in age, ferritin, Ca, PTH, bicarbonate, hemoglobin, and K+ between patient groups. These findings highlight that while the dialysis modality can influence specific outcomes, other biochemical parameters might be more resilient to change based solely on the dialysis type. It is crucial to recognize that multiple factors, including nutritional status, bone metabolism, and erythropoiesis-stimulating agent use, among others, can influence these markers and may not necessarily be impacted by the chosen dialysis modality.[10] The data also underscored significant associations of hypertension with HD and DM with HDF. While the direct relationship between the dialysis modality and these comorbidities warrants further investigation, it is known that patients with DM may benefit from HDF due to enhanced removal of advanced glycation end products, which might be particularly toxic in diabetic patients.[11] Correlation analyses further unveiled a strong positive association between B2M and potassium in both HD and HDF groups. Therefore, this relationship is intriguing. In fact, elevated B2M levels, indicative of reduced clearance, might also imply reduced clearance of potassium, a known complication of inadequate dialysis. Maintaining potassium within a narrow range is essential in dialysis patients due to its significant cardiovascular implications.[12]

Conclusions

The observed data aligns with existing literature suggesting the benefits of HDF, especially concerning B2M clearance. However, patient-centric factors like the presence of hypertension or DM and other biochemical parameters might play a role in the choice of dialysis modality. The robust association between B2M and potassium across both modalities emphasizes the need for vigilant monitoring and efficient dialysis practices.

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Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions

Mohammed Y. Al Atbee and Hala S. Tuama have given substantial contributions to the study conception and design, and to the data collection, analysis and interpretation; all authors equally contributed to the statistical analysis, and to the manuscript draft and critical revision for important intellectual content. All authors read and approved the final version of the manuscript.

History

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