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Effect of Different Dialysis Membranes on Protein Loss During Hemodialysis

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ABSTRACT

Objective: To compare the loss of proteins with high and low flux hemodialysis membranes.
Study Design: Cross-sectional analytical study.
***Place and Duration of Study*:** Department of Nephrology, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Nov 2019 to Feb 2020.
Methodology: This study was conducted on patients with end-stage renal disease on maintenance haemodialysis. We excluded patients on haemodialysis for less than one month, those with poor compliance to hemodialysis, those undergoing hemodialysis for less than four hours per session and unwilling patients. Patients were divided into two groups: one was dialyzed with high flux membranes, whereas low flux membranes were used for the other group. Dialysate samples were collected during the first hour and then during the last hour of each haemodialysis session to estimate protein losses in each group.
Results: Data were recorded during 133 hemodialysis sessions, the patients underwent. There were 22 patients, including 12 (54.55%) males, having a mean age of 46.45±13.99 years. Most patients (17, 77.27%) were on twice-a-week dialysis, whereas the rest were dialyzed thrice weekly. Protein loss was 0.45± 0.23g/L with low flux membranes and 1.20±0.60g/L with high flux membranes. This difference was statistically significant (p= <0.001).
Conclusion: High flux dialysis membranes are associated with greater protein loss during hemodialysis.

Keywords: Flux, Haemodialysis, Protein loss.

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INTRODUCTION

The annual incidence of new end-stage renal disease (ESRD) cases in Pakistan is estimated at >100 per million population.[1] Haemodialysis remains the most prevalent modality for renal replacement therapy, with only a small percentage getting a renal transplant and just a handful of patients treated with peritoneal dialysis. Hemodialysis techniques have continued to evolve. Dialyzer membranes, originally made of cellulose, are now totally synthetic. With the currently available dialyzers, urea removal is affected minimally by choice of the dialyzer, specifically the chemical composition.[2] Dialysis adequacy depends more on blood and dialysate flow rates, duration and frequency of treatment and well-functioning vascular access.[3] While we specifically address the delivery of adequate dialysis doses to our patients, we tend to neglect another important aspect, i.e., protein loss during haemodialysis. This is more important in our patients because of already low protein and caloric intake. Malnutrition is fairly common in patients with ESRD. It is strongly associated with mortality in HD patients.[4] Malnutrition in patients with chronic kidney disease has various causes, including reduced appetite and nutrient intake, metabolic abnormalities, inflammation, increased catabolism and dialysis-related problems.[5] It is unknown whether the choice of hemodialysis membrane regarding its flux affects protein loss in the Pakistani population. However, it has been delineated that high-flux dialyzers lead to a better quality of life than low-flux membranes.[6] Conversely, no mortality benefit was shown in patients who underwent hemodialysis using high flux dialyzers compared to those dialyzed with low flux dialyzers.[7] We planned this study to compare two dialyzer membranes commonly used in our setup. The aim was to determine if the degree of protein loss during haemodialysis could affect our choice of using a specific dialyzer membrane.

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METHODOLOGY

The cross-sectional analytical study was conducted at the Department of Nephrology, Pak Emirates Military Hospital, Rawalpindi Pakistan, from November 2019 to February 2020. Approval from the Ethics Review Committee of the Hospital was obtained (A/28/EC/44/19 dated 20 Nov 2019). Sample size calculation was based on results of a previously

published study, estimating losses of 8± 2.8 g per dialysis session with high flux membranes and 6± 1.5g per dialysis session with low flux membranes.[8] Assuming an equal enrollment ratio in both groups, a minimum overall sample of 62 dialysis sessions (31 in each group) was calculated.

Inclusion Criteria: Patients undergoing haemodialysis for end-stage renal disease for over a month were included in the study.

Exclusion Criteria: Patients undergoing haemodialysis for less than four hours in each session (irrespective of the reason), patients on haemodialysis for less than one month, those with poor compliance to haemodialysis were excluded from the study.

After obtaining informed written consent, we enrolled patients from the haemodialysis unit using consecutive sampling. First, their demographic data were recorded. Then, using computer-generated random number tables, we randomized patients to either of the two groups: one was dialysed using high flux membrane (Gambro Polyflux 170 H, membrane composition Polyamix, surface area 1.7m2, KUF 70 ml/h/mmHg, Vitamin B12 sieving coefficient 1.0) and the other with low flux membrane (Gambro Polyflux 17L, membrane composition Polyamix, surface area 1.7m2, KUF 12.5 ml/h/mmHg). Standard haemodialysis was performed in all the patients for 3.5 hours during each session, with a blood flow of 300 ml/min and dialysate flow of 500 ml/min. Dialysers were not reused in any patient. Dialysate samples were collected in two 20ml aliquots from the dialysate sampling port towards the end of the first hour of dialysis and during the last ten minutes of the haemodialysis session. Both were mixed. The total protein level was measured in this dialysate sample.

Data were analysed using Statistical Package for the Social Sciences (SPSS) version 20:00. Results were expressed as mean± standard deviation. In addition, protein levels in dialysate samples were compared between the high and low flux groups using an independent samples t-test. The *p*-value of ≤0.05 was considered significant.

RESULTS

The total number of patients included in this study was 22. The baseline characteristics of patients are shown in Table-I. Most (17,77.27%) were on twice-a-week dialysis, whereas the rest (5,22.73%) were dialysed thrice weekly. Data were recorded during 133 hemodialysis sessions these patients underwent. Protein loss was almost three times greater with high flux membranes. However, the difference in ultrafiltration volume amongst patients on high and low-flux membranes was statistically insignificant (Table-II).

Table-I: Baseline Characteristics (n=22)

Characteristics	Values
Age (years)	46.45±13.99
Gender	
Male	12(54.55%)
Female	10(45.45%)
Haemodialysis vintage (months)	16.48±7.00
Cause of end stage renal disease	
Diabetic nephropathy	10(45.45%)
Hypertension	6(27.27%)
Chronic glomerulonephritis	5(22.73%)
Adult polycystic kidney disease	1(4.55%)
Vascular access	
Arteriovenous fistula	20(90.91%)
Tunneled catheter	2(9.09%)

Table-II : Comparison of Protein Loss and Ultrafiltration Volumes based on Membrane Flux (n=22)

	Low Flux Membrane (Mean±SD)	High Flux Membrane (Mean±SD)	*p*-Value
Protein loss (g/L)	0.45±0.23	1.20±0.60	<0.001
Ultrafiltration volume (L)	2.44±0.94	2.50±1.16	0.757

DISCUSSION

Haemodialysis is an essential procedure for removing harmful substances from the blood of patients with reduced renal function. However, the procedure of haemodialysis also removes small-sized nutrients. Protein loss during haemodialysis is a universal phenomenon. About 16 g of protein is lost during each dialysis session, including amino acids removed in dialysate as well as the catabolic effect of the procedure itself.[9] This amount of amino acids lost in a single session of haemodialysis equals about 20 % of plasma total amino acids. This is equal to the number of proteins provided by a full meal.[10] Some of the morbidity and mortality associated with end-stage renal disease have been attributed to the retention of middle molecules with low flux membranes during haemodialysis. It was shown by El-Wakil *et al.* that high-flux membranes are more efficient in removing middle molecules like beta-two microglobulin as compared to low-flux membranes.[11] Another study showed that variations in materials and the general structure of the dialyzer could affect protein loss. However, differences in the pore size of the dialyzer do not have a large effect.[12] Oshvandi *et al.*also demonstrated that high flux dialyzers improved the

quality of life of patients as compared to low flux dialyzers.[13]

Our study associated high-flux membranes with greater protein loss than low-flux membranes. Our results are in contrast to observations made previously. In a Korean study, Gil *et al* reported no difference in total amino acid loss into dialysate using high-flux or low-flux membranes.[14] Similarly, a study done in Iran by Makar *et al.* proved no increase in protein losses with high flux membranes.[15] A study done 25 years ago demonstrated a significant loss of amino acids into the dialysate with high flux membranes compared to low flux membranes. However, the results lost significance after adjustments to surface area and blood flow.[8] It is generally believed that with a molecular weight of 65000 Da, albumin is too large to be filtered by both low and high-flux membranes.[16]

We limited biochemical testing to dialysate samples only. Changes in serum markers during dialysis sessions were not evaluated because the loss of amino acids into dialysate leads to the mobilization of amino acids from skeletal muscles.[14] This phenomenon is, fortunately, less common with the latest, more biocompatible synthetic membranes.

The major strength of this study is its design. We collected data during multiple haemodialysis sessions with a limited number of study participants. This helped us minimize individual differences between patients during a greater number of haemodialysis sessions, which would have otherwise been a confounding variable. Many centres with limited resources reuse dialysers to minimize the financial impact. Repeated bleach processing increases the permeability of dialysers and, thus, the protein loss.[17,18] Dialysers were not reused during this study, per our centre's general policy. Different dialyser membranes are associated with variable degrees of amino acid loss and adsorb proteins to a different extents. Our study design was powerful since both the low and high-flux membranes were made of the same material. This eliminated the potential bias of membrane characteristics affecting protein loss. Another important hallmark is the uniqueness of this study. Despite an extensive literature search, we could not identify a similar study from Pakistan published during the last ten years.

LIMITATIONS OF STUDY

This study has a few limitations. The handling of albumin during dialysis depends on the dialysis membrane's chemical composition. Protein loss also occurs by adsorption to the membranes, an effect that the estimation of dialysate protein levels cannot quantify. Access recirculation affects the loss of amino acids in the dialysate. We did not assess recirculation in our patients due to resource limitations. However, since most of our patients had well-functioning AV fistulas, access recirculation could be considered to be minimal

CONCLUSION

High-flux dialysis membranes are associated with greater protein loss during hemodialysis.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

AWM & KMR: Study design, data interpretation, critical review, approval of the final version to be published.

MNA & ARA: Conception, drafting the manuscript, approval of the final version to be published.

TT & S: Data acquisition, data analysis, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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