Comparison of Adequacy of Dialysis between Single-use and Reused Hemodialyzers in Patients on Maintenance Hemodialysis

Amna Hamid, Murtaza F. Dhrolia, Salman Imtiaz, Ruqayya Qureshi and Aasim Ahmad

ABSTRACT

Objective: To compare adequacy of dialysis between single-use and reused dialyzer in order to ascertain whether reuse of dialyzers provides adequate dialysis and thereby enable provision of effective yet affordable renal replacement therapy in resource-limited countries.

Study Design: Observational cross-sectional study.

Place and Duration of Study: Department of Nephrology, The Kidney Centre, Postgraduate Training Institute (TKC-PGTI), Karachi, from December 2017 to February 2018.

Methodology: Equal number of patients on thrice weekly hemodialysis with either single-use (group A; n=33) or reuse (group B; n=33) dialyzer for at least six months were reviewed. Both groups were compared for dialysis adequacy measured as urea reduction ratio (URR); as well as adequacy of patient care in terms of anemia, bone-mineral control and nutritional status. Serum hemoglobin and erythropoietin stimulating agent (ESA) dose were taken as markers for anemia management, serum calcium, phosphate and intact parathyroid hormone (iPTH) for bone-mineral control and serum albumin as index for nutritional status.

Results: The mean age of patients in Group A was 51.36 ±13.9 years and in Group B was 54.78 ±15.4 years. Female to male ratio was 1.75:1. The mean number of dialyzer reused in group B was 47.5 ±27.8. There was no significant difference between the study groups in terms of URR (p=0.362), hemoglobin (p=0.347), ESA dose (p-=0.556), serum calcium, phosphorus and iPTH (p=0.868, p=0.138 and p=0.323, respectively), and serum albumin (p=0.777). All the parameters were in accordance with KDOQI guidelines.

Conclusion: Reuse of dialyzer does not affect dialysis efficiency. Adequate dialysis therapy can be provided economically through reprocessed dialyzers in at least resource-poor countries.

Key Words: *Hemodialysis, Hemodialyzer, Reuse, Single-use, Dialysis adequacy.*

INTRODUCTION

Chronic kidney disease is a global health concern. An alarming increase in annual mortality rate from chronic kidney disease was observed worldwide between the years 1990 and 2010.[1] Furthermore, progression to end stage renal disease (ESRD) has profound effect on morbidity and mortality as well as huge economic and social implications.[2]

Less than 10% of the patients with renal failure receive renal replacement therapy worldwide; only 20% of these belong to developing countries.[3] Although accurate estimation of population on ESRD is difficult in the absence of renal registries in our region, an Indian population-based study reported approximately 220000-275000 new cases require hemodialysis each year in South Asia; and dialysis population is growing at an annual rate of 10-20%.[4] In Pakistan, an estimated incidence of ESRD is 100 patients/million population.[5] Majority of these patients either do not receive treatment or drop out in the first three months due to enormous cost of therapy.[3]

Low income countries constantly strive to provide renal replacement to the disproportionately growing burden of renal failure.[1,2] In order to make dialysis affordable, dialyzer reuse is common practice in low income countries which has shown to reduce cost by 32 to 34.6% in various studies.[6] Dialyzer reuse is being practised in TKC-PGTI for more than two decades and there is a reported 23.66% cost reduction per session of hemodialysis merely by reuse of dialyzer.[6] The practice of reusing dialyzers has been disputed for several years. Its advantages like cost-effectiveness, reduced waste disposal, lower frequency of first use syndrome and better biocompatibility have been contested with disadvantages such as risk of infections, biochemical and immunologic reactions, improper sterilisation, altered membrane permeability and loss of performance. However, there is no consensus on superiority of single-use or reused dialyzer.[7]

The aim of this study was to compare dialysis adequacy, anemia and bone-mineral control and nutritional status among patients on maintenance hemodialysis with reuse dialyzer and single-use in order to highlight that adequate dialysis and patient-care can be provided through reuse dialyzers in developing countries, if recommended protocols are followed.

Department of Nephrology, The Kidney Centre, Postgraduate Training Institute, Karachi, Pakistan

Correspondence: Dr. Amna Hamid, Department of Nephrology, The Kidney Centre, Postgraduate Training Institute, Karachi, Pakistan
E-mail: amnahamid.88@gmail.com

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METHODOLOGY

This observational cross-sectional study was conducted at The Kidney Centre, Postgraduate Training Institute (TKC-PGTI) after approval from Ethical Review Committee. A total of 66 patients on regular hemodialysis were selected for the two study groups, *i.e.* those undergoing hemodialysis with single-use (group A) or reuse hemodialyzers (group B). An equal number of participants (n=33) were present in both the groups. Patients were from both genders and between ages 16-75 years. Patients tested negative for HBsAg, Anti HCV and HIV were included. For group B, a minimum of ten times reuse of dialyzer was considered for inclusion in the study. Those who had any hospitalisation, sepsis or vascular access problem were excluded. Patients who were on single-use dialyzer due to medical conditions like thrombocytopenia, hematological disorder or surgical procedure were also excluded.

All participants underwent four hours session of thrice per week hemodialysis for 6 months or more. The blood flow ranged between 250-300ml/min and dialysate flow was fixed at 500ml/min. Polysulfone dialyzers were used by group A and cellulose triacetate (CTA) dialyzers were used by group B as CTA membranes are translucent and suitable for gross assessment of membrane integrity. The dialyzers were reprocessed following Advancement of Medical Instrumentation (AAMI) protocols using Renatron Automated Dialyzer Reprocessing System with Renalin cold sterilant.

Background information including age, gender, cause of renal failure and years on hemodialysis were obtained from medical records at the study centre. Urea reduction ratio (URR) was taken as the index of hemodialysis adequacy. Bone mineral metabolism (serum phosphate, calcium, iPTH), anemia management (serum hemoglobin and ESA dose), and nutrition (serum albumin) were also assessed. C-reactive protein was taken as marker of inflammation; and seroconversion to hepatitis B or C was also checked in medical records. All the parameters were compared between the two groups and ascertained whether they met KDOQI recommendations.

Data analyses were performed by using software IBM SPSS license version 21. Cleaning and coding of the data were done prior to analysis. All continuous variables were described in mean ± standard deviation or median with IQR (interquartile range). Categorical variables were presented in the form of frequencies and percentages. To see the difference between two dialysis groups, student t-test was applied in case of normally distributed variables; while for skewed data, Mann-Whitney U test was used. Normality was checked by Shapiro-Wilk test. P-value less than 0.05 was considered as significant.

RESULTS

A total of 66 patients were randomly recruited for both groups of the study, *i.e.* those on hemodialysis with single-use dialyzer (Group A) and reused dialyzer (Group B). An equal number of patients (n=33) were present in each study group. All the participants had been on thrice weekly maintenance hemodialysis for at least 6 months. The mean number of dialyzer reuse in group B was 47.5 ±27.8 times. Mean weight of the participants was 66.1 ±14.9 Kg and 66.8 ±11.7 Kg in Group A and Group B, respectively.

The mean age of patients in Group A was 51.36 ±13.9 years and in Group B was 54.78 ±15.4 years. There was female dominance in study population with female to male ratio of 1.75:1. Twenty females were present in Group A and 22 in Group B. The predominant cause of ESRD in study was unknown etiology followed by diabetes as the second most common cause in both the groups. Table I compares the demographic data of Group A and Group B.

Table II demonstrates the indexes related to dialysis and compares it between Group A and Group B. Adequate dose of dialysis in terms of urea reduction ratio was delivered to all the participants of the study and there was no significant difference among the two groups (72.8 ±6.3 in Group A and 71.4 ±6.3 in Group B. The

Table I: Demographic data.

	Single-use dialyzer Group A	Re-use dialyzer Group B
No. of patients	33	33
Age (in years)	51.36 ±13.9	54.78 ±15.4
Gender		
Male n (%)	13 (39.4)	11 (33.3)
Female n (%)	20 (60.6)	22 (66.7)
Weight (in Kg)	66.1 ±14.9	66.8 ±11.7
Cause of ESRD n (%)		
Unknown	15 (45.4)	14 (42.4)
Diabetes	11 (33.3)	9 (27.3)
Hypertension	0	4 (12.1)
Glomerulonephritis	1 (3)	3 (9)
ADPKD	1 (3)	2 (6)
Other	5 (15.2)	1 (3)
Number of time of dialyzer reuse	-	47.5 ±27.8

ESRD = End stage renal disease, ADPKD= Autosomal dominant polycystic kidney disease; HD = Hemodialysis.

Table II: Comparison of indexes of hemodialysis therapy.

Indexes related to hemodialysis	Single-use dialyzer Group A (Mean ± std/ Median, IQR)	Re-use dialyzer Group B (Mean ± std/ Median, IQR)	p-value
URR* (%)	72.8 ±6.3	71.4 ±6.3	0.362
Heparin dose (units)	2500, 2500	12500, 5000	<0.001
Anemia			
Hemoglobin g/dL	10.8 ±1.3	11.1 ±1.2	0.347
ESA dose IU/week)	7500, 6000	5000, 8000	0.556
ESA dose (IU/Kg)	109.8, 75.7	86.9, 122.2	0.617
Bone mineral metabolism			
Phosphate (mg/dL)	4.5 ±1.65	5.1 ±1.7	0.138
Calcium (mg/dL)	9.1 ±0.73	9.2 ±0.64	0.868
iPTH (pg/ml)	198.4, 235.6	281.4, 258.3	0.323
Nutrition albumin (g/dL)	3.6 ±0.59	3.6 ±0.37	0.777

IQR = Interquartile range; URR = Urea reduction ratio; ESA = Erythropoietin stimulating agents; iPTH = Intact parathormone.

$* \; URR = \frac{(upre - upost)}{upre} \times 100$

Where, upre and upost are predialysis and postdialysis urea level respectively.

mean hemoglobin was maintained 10.8 ±1.3 g/dL in Group A and 11.1 ±1.2 g/dL in Group B with no significant difference in dose on erythropoietin stimulating agent to maintain this level (5000, IQR 8000 units and 7500, IQR 6000 units respectively). Serum calcium, phosphorus and iPTH levels also had no significant difference between the two groups. Mean serum albumin was 3.6 ±0.59 g/dL in Group A and 3.6 ±0.37 g/dL in group B. C-reactive protein (CRP) was raised in only one participant in each group demonstrating no significant inflammatory changes in either group. All these indices met KDOQI recommendations signifying comparable outcomes of dialysis therapy with reuse dialyzers to that from single-use dialyzer.

DISCUSSION

Hemodialysis is a common renal replacement therapy for ESRD, but it presents considerable financial burden. Hemodialyzer reuse was introduced more than 50 years ago for economic reasons and was globally practised.[8] According to USRDS, more than 80% of the centres reprocessed dialyzers until 1997,[7] nevertheless it remained controversial. Narrative reviews have documented it as cost-effective and better biocompatible, conversely also highlighted the risks of adverse reactions, infections, improper techniques and changes in membrane permeability and efficiency of clearance.[7] Trend of reusing dialyzers declined over the years and only 40% centres followed it in US by 2005.[7] Reuse is less common in Europe, Canada; and forbidden in Japan.[9] However, developing countries continue to reprocess dialyzers due to economic reasons and have reported efficient dialysis.[10,11]

Dialyzer can be reused safely and provide effective dialyses if standard protocols, devised by Association for the Advancement of Medical Instrumentation (AAMI),[12] are followed. Hemodialyzer reprocessing and reuse has been followed at TKC-PGTI for more than two decades. It has reported total direct cost-effectiveness of this practice including cost of chronic kidney disease (CKD), management and hospitalisation.[6] Present study compared dialysis dose adequacy as well as anemia control, ESA requirement, bone mineral status among patients on hemodialysis with single-use and reuse dialyzers and found similar results. The results were in accordance with KDOQI recommendations.[13-16]

Dialyzer reprocessing has frequently been deterred on the basis of reduced efficiency; and hence, inadequate dialysis delivery. Inadequate hemodialysis is independently associated with increased morbidity and mortality of the patients.[17] Dialysis outcomes and practice patterns study (DOPPS) and KDOQI recommend a minimal dialysis dose of single pool KT/V 1.2 and urea reduction ratio (URR) of 65%.[14,18] Sherman *et al*. reported reduced dialysis dose delivery (difference of 0.05 KT/V) when dialyzers were reused upto 13.8 times.[19] Murthy and colleagues observed reduced urea and creatinine clearance (5-10%) with 10th reuse of dialyzer.[19] Similar trend of solute clearance was shown by Leypoldt *et al*. and HEMO study.[19] However, these results were noted in dialyzers reprocessed with formaldehyde and bleach. Statistically, insignificant differences in small molecule clearance were noted in Renalin reprocessed dialyzers in a number of studies.[7,8,19] The average number of Renalin reprocessed dialyzer reuse in this study was 47.5 ±27.8 and URR achieved was 71.4 ±6.3, which was similar to that seen in single-use group. Similar results have been observed by Ni Made *et al.* with 7 times reuse of dialyzer and Mandhar *et al*. when dialyzer were reprocessed nine times.[10,20] In view of these observations, the authors believe that dialyzer efficiency and dialysis dose delivery are centre specific and raise concern towards monitoring the reprocessing protocols.

Quality of life and survival of patients on hemodialysis with ESRD is dependent on adequate patient care as much as on adequate dialysis dose.[13] Adequate patient care involves appropriate management of factors such as anemia, mineral bone metabolism and nutritional status in order to reduce morbidity and mortality. KDOQI recommends maintaining hemoglobin levels 10-11.5 g/dL in all hemodialysis patients and use of erythropoietin stimulating agents to achieve this level in iron efficient population.[15] Inverse association of hemoglobin and poor survival has been reported.[21] Participants of this study maintained hemoglobin levels of 11.1 ±1.2 g/dL in reuse group and 10.8 ±1.3 g/dL in single-use group with weekly ESA requirement of 5000, IQR 8000 units and 7500, IQR 6000 units, respectively. There was no significant difference in ESA requirement among both the groups to attain KDOQI recommended hemoglobin levels. These findings were similar to results observed by Petar Kes and colleagues.[22]

Alteration in bone mineral regulation as commonly seen in ESRD can cause soft tissue and vascular calcification as well as increase morbidity and mortality.[23] KDOQI guidelines recommend maintaining corrected serum calcium levels 8.5-9.5 mg/dL, serum phosphorus 3.5-5.5 mg/dL and intact parathormone level 2 to 9 times normal.[16] In present study, serum calcium, phosphorus and intact parathormone were within recommended range among both groups.

Furthermore, inadequate hemodialysis can result in anorexia and malnourishment. Increased mortality is associated with hypoalbuminemia reported in a number of studies.[17,24] Participants in both groups of the study had mean albumin level of 3.6 mg/dL, indicating satisfactory nutritional status of these patients. This finding suggests that dialysis with reprocessed dialyzers can be adequate and helps sustain good nutritive state.

In this study, significantly higher heparin dose was used in reuse group compared to single-use (12500 IQR 5000 *vs.* 2500 IQR 2500). However, no bleeding episodes were noted. Same observation was made by Ahmed *et al*.[11] Increased heparin is generally required in reprocessed dialyzers in order to avoid clotting of blood and, therefore, deterioration of dialyzer membrane.[25] None of the patients in this study seroconverted to hepatitis B or C, which signifies that with proper reprocessing and handling by dialysis unit staff, transmission of infections can be avoided.

In view of the above discussion, the authors believe that reprocessed dialyzers do not lose efficiency and adequate dialysis can be provided through reuse of dialyzer, if reprocessing is performed in compliance with standard protocols devised by AAMI. Breach in protocols and lack of quality control could compromise the safety and efficacy of reused dialyzers.

The study has few limitations. Firstly, the sample size is small; thus larger, prospective, randomized and multi-center studies are required to confirm the findings of this study. Secondly, intradialytic symptoms, frequency of infections, and hospitalisations were not evaluated; and hence, these suspected risks of dialyzer reuse cannot be excluded.

CONCLUSION

Effective and adequate dialysis comparable to that achieved from single-use dialyzers can be provided through dialyzers reuse. Therefore, appropriate reuse of dialyzers should be encouraged in low income countries like Pakistan, in order to prevent treatment dropouts due to expense of management. Dialysis units should ensure quality assurance and compliance with standard reprocessing protocols so that high quality dialysis is provided to patients in developing countries without jeopardising their safety and treatment efficacy.

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