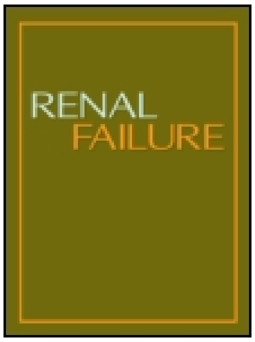

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CLINICAL STUDY

Influence of Dialysis Modality and Membrane Flux on Quality of Life in Hemodialysis Patients

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Abstract

Background: The quality of life in patients undergoing hemodialysis is significantly disturbed. There are data that hemodiafiltration (HDF) may be more effective than conventional hemodialysis in the removal of uremic toxins and may reduce frequency and severity of intradialytic and postdialysis adverse symptoms in patients. Also, some researchers suggest advantages of using high-flux membranes compared with low-flux. *Objective*: The aim of this study was to examine whether hemodialysis modality and membrane flux, independent of membrane biocompatibility, make differences in quality of life in patients. *Methods*: In our cross-sectional study, we evaluated 124 patients who were divided, based on therapy, into three groups: online HDF, high-flux hemodialysis, and low-flux hemodialysis. Data were collected using the Short Form-36 questionnaire combined with special questionnaire, which included demographic and clinically related questions. *Results*: Health-related quality of life was better in patients on HDF compared with patients on hemodialysis, especially compared with low-flux hemodialysis patients in most of the scales and in both dimensions: physical component scale and mental component scale. There were no statistically significant differences in Short Form-36 domains between high-flux hemodialysis and low-flux hemodialysis. *Conclusion*: Our data suggest the potential advantages of HDF with regard to influence on quality of life, which is sufficient to justify further research in prospective and longitudinal study design.

Keywords: hemodialysis, hemodiafiltration, quality of life, high-flux membrane, low-flux membrane

INTRODUCTION

It is a fact that patients with chronic kidney disease and various renal replacement therapies have a worse quality of life compared with a general population.[1–3] Poorer health-related quality of life (HRQOL) is associated with increase in morbidity and mortality among patients.[4,5] Previous studies reported that HRQOL depends on treatment modality.[6,7] Thus, the transplant recipients scored better quality of life in comparison with hemodialysis (HD) and peritoneal dialysis patients.[8,9] Hemodialysis patients have lower score in most of the scale than peritoneal dialysis patients, especially for mental functions.[6,7,10,11] There are a limited number of studies, which evaluate the impact of various HD treatments themselves on HRQOL. Results are inconsistent too.[12,13]

In addition to the correction of fluid and electrolyte imbalance, it is the fact that patients' outcomes depend on the dialysis adequacy based on the amount of low-molecular weight substances removed from the patient's blood. The role of middle- and large-size molecules in uremic toxicity is identified, especially after a prolonged treatment. The accumulation of polymerized β_2-microglobulin during the years of dialysis therapy leads to severe bone and soft tissue damage.[14,15]

Two different dialysis modalities for solute transport across artificial kidney membranes are possible: diffusion and convection. Diffusive-based HD modality provides good removal of small molecules, but removal of middle- and large-size uremic toxins is limited even when high-flux membranes are used.[15,16] Hemodiafiltration (HDF) is a system that includes both convection and diffusion in

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the removal of solutes. Clearance of small molecules during HDF is similar to that during high-flux HD, but clearance of middle- and large-size molecules is significantly greater during HDF.[16,17]

The results of previous studies that evaluated the possible clinical advantages of HDF in comparison with HD are not consistent, and it is not possible to make any precise conclusion out of them.[17–21] Compared with low-flux dialysis, high-flux HD might have a beneficial effect on mortality and clinical outcomes in the patients[22–27] or not.[28] The use of synthetic high-flux membranes should be considered to delay the long-term complication of HD therapy: amyloidosis, hyperphosphatemia, cardiovascular risk, and anemia.[29,30] However, it cannot be concluded whether possible clinical differences are based on differences in membrane flux or on membrane biocompatibility, because most of the studies did not randomize patients by membrane biocompatibility.

Effect of dialysis modality and membrane permeability on quality of life measures is under-determined.[12,13,19,20] In certain studies, patients on HDF had better quality of life,[20] but in other, there were no significant difference.[17] With regard to membrane flux, no statistically significant differences in HRQOL was found.[12,13]

The objective of this study is to examine whether HD modality and membrane flux, independent of membrane biocompatibility, bring differences in the quality of life in patients. For this purpose, we compared HRQOL among patients on HDF (high-flux membrane), high-flux HD, and low-flux HD. All patients were on biocompatible polysulfone membranes.

SUBJECTS AND METHODS

Subjects

Our observational cross-sectional study was conducted between July 2011 and September 2011 at the Clinic of Nephrology, Clinical Centre Nis. The study was approved by the local Ethics Committee. We evaluated 124 patients who were undergoing HD. Based on the therapy, patients were divided into three groups: online polysulfone bicarbonate HDF (online HDF), high-flux polysulfone bicarbonate HD (Hf-HD), and-low flux polysulfone bicarbonate HD (Lf-HD). All patients who were receiving dialysis therapy during the mentioned period and met study inclusion criteria participated in the research. The criteria for including patients in the study were terminal renal disease with negligible residual renal function, being on dialysis for more than 3 months, age >18 years, no communication barrier, and provided informed consent. All patients were treated three times per week and were undergoing adequate dialysis (Kt/V > 1.2). The effective weekly treatment time was 12 hours in each group. All patients were in day shifts (morning, noon, or afternoon).

HDF was performed as post-dilution online HDF with polysulfone dialyzer F80 S (Fresenius Medical Care, Bad Homburg, Germany) and with effective blood flow of minimum 250 mL/min and dialysate flow of 500 mL/min. The amount of post-dilution infusate was approximately 41–57 L/week. High-flux HD were performed with F60 and F70 polysulfone dialyzer (Fresenius Medical Care), effective blood flow of minimum 250 mL/min, and dialysate flow of 500 mL/min. Low-flux HD was performed with F8 HPS polysulfone dialyzer (Fresenius Medical Care), effective blood flow of minimum 250 mL/min, and dialysate flow of 500 mL/min. In all of these three mentioned groups we used dialysate with identical composition. The final dialysate usually contained 137 mmol/L of sodium, 2.5 mmol/L of potassium, 1.5 mmol/L of calcium, 0.75 mmol/L of magnesium, 27–30 mmol/L of bicarbonate, and 100 mg/dL of glucose.

METHODS

We used the Short Form-36 questionnaire (SF-36) to assess the quality of life in patients. The SF-36 contains 36 questions of which 35 are used in the formation of 8 quality of life scales: physical function, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. These scales were summarized into two dimensions of quality of life: physical component scale (the first five scales) and mental component scale (the last five scales). Score in each scale ranged from 0 to 100. Higher score represented better quality of life.

Other data were collected by using a special questionnaire that included questions about age, gender, marital status, educational status, employment status, economic status, duration of therapy, vascular access, dialysis adequacy, and comorbidity disease. Both questionnaires were completed in a form of interview. The patients were interviewed separately.

Statistical Methods

Data were expressed as mean ± standard deviation and frequency (%). The Kolmogorov–Smirnov test was used for testing the variable's normality. Because of non-normal distribution of data, the statistical significance among the study groups was assessed by using the non-parametric Kruskal–Wallis test. Post hoc tests with Bonferroni corrections were used to estimate between which groups there was statistically significant difference. Chi-square test was applied to compare percentage. Multiple stepwise regression analysis was used to determine factors affecting physical component scale/mental component scale. Analyses were performed using SPSS, version 13.0 (SPSS Inc., Chicago, IL, USA). p-Value $\leq$ 0.05 was considered statistically significant.

RESULTS

We evaluated 124 patients, who were divided into three groups: online HDF ($n = 45$), Hf-HD ($n = 39$) and Lf-HD ($n = 40$). Sociodemographic and clinical characteristics of patients included in the study are presented in Table 1. As shown in the table, there were no statistically significant differences in age, gender, marital status, educational status, employment status, economical status, duration of dialysis, vascular access, and dialysis adequacy (Kt/V) among groups. The mean age of patients was 56.0 ± 11.9 (online HDF), 53.7 ± 9.8 (Hf-HD) and 58.0 ± 16.8 (Lf-HD). There was no statistically significant difference among groups ($p = 0.079$). Also, we found no statistically significant differences among groups with regard to some clinical characteristics (ischemic heart disease, diabetes, hypertension, hemoglobin, and albumin).

Table 2 shows the scores of the domains of SF-36 among groups. Significant difference was found in all domains except general health domain. Additional tests showed that patients on HDF had better score in most of the domains compared with patients on HD, especially compared with low-flux HD patients. There were no statistically significant differences in SF-36 domains between high-flux HD and low-flux HD.

A Multiple stepwise regression analysis showed that age, economic status, dialysis modality, and present ischemic heart disease were significantly and independently associated with physical component score (Table 3). Age, sex, economic status, dialysis modality, and vascular access are significantly and independently associated with mental component score (Table 4).

DISCUSSION

We compared socioeconomic and other conditions among the groups in order to reduce differences of these factors among the groups that can have influence on the quality of life. We found no statistically significant difference among the groups with regard to socioeconomic conditions. It was expected due to the way of forming the sample (we included all patients who were receiving dialysis therapy and met study inclusion criteria).

The mean duration of time on therapy was 56.7 ± 46.1 (online HDF), 55.6 ± 54.3 (Hf-HD), and 64.5 ± 70.9 (Lf-HD) months. There was no statistically significant difference in the duration of the therapy among the groups ($p = 0.063$). We highlight the following: when we formed groups, we included in each group only those patients who were receiving appropriate HD therapy constantly for at least the last 3 months. The mean value of dialysis adequacy was slightly higher in high-flux and HDF patients groups compared with low-flux dialysis group, but not statistically significant.

Table 1. Demographic and clinical characteristics of patients.

Demographic and clinical variables	Online HDF ($n = 45$)	Hf-HD ($n = 39$)	Lf-HD ($n = 40$)	p-Value
Age (mean ± SD)	56.0 ± 11.9	53.7 ± 9.8	58.0 ± 16.8	0.079
Men [% (n)]	73.3% (33)	64.1% (25)	55.0% (22)	0.211
Married	80% (36)	71.8% (28)	77.5 (31)	0.667
Educational status				0.059
Elementary school	13.3% (6)	28.2% (11)	30.0% (12)	
High school	75.6% (34)	69.2% (27)	52.5% (21)	
University education	11.1% (5)	2.6% (1)	17.5% (7)	
Employment status				0.159
Employed	8.9% (4)	10.3% (4)	0% (0)	
Unemployed	8.9% (4)	15.4% (6)	22.5% (9)	
Retired	82.2% (37)	74.4% (29)	77.5% (31)	
Economic status*				0.417
<11,000 RSD	24.4% (11)	35.9% (14)	40.0% (16)	
11,000–30,000 RSD	57.8% (26)	56.4% (22)	50.0% (20)	
>30,000 RSD	17.8% (8)	7.7% (3)	10.0% (4)	
Duration of dialysis (months)	56.7 ± 46.1	55.6 ± 54.3	64.5 ± 70.9	0.630
Vascular access				0.051
Arteriovenous fistula	97.8% (44)	82.1% (32)	85% (34)	
Catheter	2.2% (1)	17.9% (7)	15% (6)	
Kt/V	1.5 ± 0.2	1.7 ± 0.4	1.4 ± 0.2	0.192
Comorbidity				
Ischemic heart disease	24.4% (11)	20.5% (8)	40% (16)	0.188
Hypertension	48.9% (22)	43.6% (17)	52.6% (21)	0.727
Diabetes	13.3 (6)	12.8 (5)	12.5% (5)	0.998
Hemoglobin	114.6 ± 13.0	111.8 ± 14.9	112.3 ± 16.7	0.307
Albumin	34.7 ± 2.7	34.9 ± 2.8	33.1 ± 3.6	0.564

Note: *Monthly income per member of patient's family.

Table 2. SF-36 results.

SF-36	Online HDF ($n = 45$)	Hf-HD ($n = 39$)	Hf-HD ($n = 40$)	p-Value	Multiple comparison*
Physical function					
Mean ± SD	76.2 ± 19.8	49.6 ± 31.6	48.5 ± 28.2	<0.001	HDF/Hf-HD HDF/Lf-HD
Median	85	45	45		
Role physical					
Mean ± SD	55.0 ± 39.4	39.1 ± 33.8	26.9 ± 28.5	0.003	HDF/Lf-HD
Median	50	50	25		
Bodily pain					
Mean ± SD	80.6 ± 29.2	62.2 ± 39.8	56.8 ± 27.7	0.002	HDF/Lf-HD
Median	100	74	51		
General health					
Mean ± SD	44.7 ± 17.7	37.1 ± 16.2	45.6 ± 19.6	0.116	
Median	45	37	40		
Vitality					
Mean ± SD	64.4 ± 23.3	43.1 ± 26.3	42.4 ± 21.8	<0.001	HDF/Hf-HD HDF/Lf-HD
Median	70	40	35		
Social functioning					
Mean ± SD	77.2 ± 24.8	52.2 ± 30.6	47.8 ± 26.5	<0.001	HDF/Hf-HD HDF/Lf-HD
Median	87	50	50		
Role emotional					
Mean ± SD	75.6 ± 38.5	56.4 ± 38.4	36.7 ± 38.3	<0.001	HDF/Lf-HD
Median	100	66.7	33		
Mental health					
Mean ± SD	80.8 ± 16.5	58.9 ± 21.4	56.0 ± 19.7	<0.001	HDF/Hf-HD HDF/Lf-HD
Median	84	48	52		
Physical component score					
Mean ± SD	64.2 ± 19.4	45.3 ± 23.7	43.5 ± 16.8	<0.001	HDF/Hf-HD HDF/Lf-HD
Median	67	45	41.3		
Mental component score					
Mean ± SD	68.5 ± 17.1	48.9 ± 21.3	45.7 ± 15.6	<0.001	HDF/Hf-HD HDF/Lf-HD
Median	70.1	51.6	45.1		
Total SF-36 score					
Mean ± SD	69.3 ± 18.0	49.8 ± 23.9	45.1 ± 14.9	<0.001	HDF/Hf-HD HDF/Lf-HD
Median	71.7	48	45.5		

Note: *Groups between which there was statistically significant difference.

Table 3. Relation between physical component score (PCS) and independent determinants.

Predictive variables	Unstandardized B coefficients	Standard error	Standardized B coefficients	t	p-Value
Age	−0.628	0.185	−0.369	−3.395	**0.001**
Sex	−2.655	4.465	−0.057	−0.595	0.554
Education status	5.203	4.018	0.131	1.295	0.199
Marital status	−1.247	5.005	−0.025	−0.249	0.804
Employment status	5.044	3.705	0.143	1.361	0.177
Economic status	9.869	3.801	0.269	2.597	**0.011**
Dialysis modality	−7.717	2.481	−0.296	−3.111	**0.003**
Time of dialysis (months)	−0.033	0.047	−0.073	−0.709	0.480
Vascular access	13.314	7.512	0.195	1.772	0.080
Hemoglobin	−0.124	0.161	−0.084	−0.771	0.443
Diabetes	−6.625	6.276	−0.105	−1.056	0.295
Ischemic heart disease	−10.347	4.749	−0.215	−2.179	**0.032**
Phosphate	−7.444	4.930	−0.145	−1.510	0.135

Notes: Dependent variable: physical component scale, $R^2 = 0.45$. Bold p-values are statistically significant, $p < 0.05$.

Also, we did not find significant difference in hemoglobin level among groups. Anemic patients in our study were treated with recombinant human erythropoietin (Epo). Well-randomized prospective studies did not prove significant differences in hematological parameters, no matter if the patients were treated by low-

Table 4. Relation between mental component score (MCS) and independent determinants.

Predictive variables	Unstandardized B coefficients	Standard error	Standardized B coefficients	t	p-Value
Age	−0.408	0.168	−0.248	−2.423	**0.018**
Sex	−9.974	4.064	−0.222	−2.454	**0.016**
Education status	4.654	3.658	0.121	1.272	0.207
Marital status	−7.526	4.556	−0.156	−1.652	0.103
Employment status	2.052	3.372	0.060	0.608	0.545
Economic status	9.413	3.460	0.266	2.721	**0.008**
Dialysis modality	−10.062	2.258	−0.399	−4.456	**0.000**
Time of dialysis (months)	−0.003	0.042	−0.006	−0.062	0.951
Vascular access	18.395	6.838	0.278	2.690	**0.009**
Hemoglobin	−0.100	0.147	−0.070	−0.684	0.496
Diabetes	−7.805	5.713	−0.128	−1.366	0.176
Ischemic heart disease	−6.130	4.323	−0.132	−1.418	0.160
Phosphate	−7.608	4.488	−0.153	−1.695	0.094

Notes: Dependent variable: mental component scale, $R^2 = 0.51$. Bold p-values are statistically significant, $p < 0.05$.

flux bicarbonate dialysis or by HDF technique, in the absence of any Epo therapy.[31,32] Other studies, which included patients with Epo therapy, showed that in the high-flux dialysis group Epo doses were significantly lower and Hb levels showed a significant increase compared with the low-flux dialysis group, where Hb levels showed no significant increase, despite the steady increase in Epo doses.[33]

When the SF-36 domains were analyzed, the lowest values were observed in role physical, physical function, and general health domains in all groups, which is in accordance with results of previous studies in HD patients.[34–38] Mental health and bodily pain were the least impaired.

Our study shows that patients on HDF have better HRQOL score compared with patients on HD, especially compared with low-flux HD patients.

Data about influence of dialysis modality on quality of life were available from a small number of studies. The study of Ward[17] found no significant difference in the quality of life between patients on high-flux HD and post-dilution HDF, using Kidney Disease Questionnaire. But, this study included a small number of patients (about twenty per group). Lin (2001) showed that patients on HDF (online post dilution) had significantly higher physical well-being score compared with high-flux HD. In this study, patients scored their physical conditions such as subjective well-being, work tolerance, and mental alertness weekly. All patients are dialyzed on biocompatible polysulfone membrane.[20] Also, Schiffl[21] found that HDF was associated with partial improvement of quality of life.

Additional tests also showed that there were no statistically significant differences in SF-36 domains between high-flux HD and low-flux HD in our sample. These data match the reports of previous studies.[12,13] It is interesting that high-flux HD patients have slightly higher score in most of the domains compared with low-flux HD patients in our study.

A 6-year prospective study carried out in HD patients in the Serbian population showed improved HRQOL (in several domains) and clinical outcomes during the years.[38] It is known that the treatment of HD patients has been improving during the study period, including increase in number of patients on high-flux HD and HDF.

Can better quality of life in HDF patients in our study be attributed only to dialysis modality and membrane flux? We tried to find additional causes. We presumed that patients' awareness of being on the dialysis treatment, which is better and costs more than standard HD, made them feel more optimistic, which could had an influence on their answers in SF-36. Also, about half of the patients included in the HDF study group (53.3%) were dialyzed in a new dialysis unit in hospital, where they felt more comfortable and friendly to hospital staff, which affected their mood.

In our study, we found a connection between physical component score and age, economic status, dialysis modality, and ischemic heart disease. Also, we observed a relation between mental component score and age, sex, economic status, dialysis modality, and vascular access. Gender was an independent determinant of mental component score in our study. We supposed that this was caused by the fact that some mental diseases (depression in the first place) were more frequent among females, generally.[39] Relation between vascular access and mental component score can be explained by the fact that catheter in our patients was used as primary access for dialysis when they were referred to clinic late, usually in very bad health condition.

Potential limitations of the study may include small sample and cross-sectional study design. It is necessary, for a future research, to use prospective and longitudinal study design for a more precise examination of interactions of dialysis process-related factors and clinical outcomes with HRQOL in HD patients. Despite these limitations, by using validation tool, this study clearly noted the potential advantages of HDF, with regard to influence on quality of life.

CONCLUSION

Our data suggest the potential influence of dialysis modality on quality of life in HD patients, which is sufficient to justify further research in prospective and longitudinal study design.

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