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ORIGINAL ARTICLE

Comparison of Different Hemodialysis Frequencies per Week on Adequacy Parameters Including Electrolytes in Patients on Chronic Hemodialysis

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Abstract

Introduction: Due to the limitations in finding the right donor, the majority of patients with renal failure (chronic kidney disease stage 5) are treated with hemodialysis. In literature, we have extensive evidence of different hemodialysis prescriptions based on different frequencies per week and duration of each session. We tried to assess the impact of different hemodialysis frequencies on the adequacy of dialysis based on nutritional parameters, electrolyte imbalances and quality of life (QoL) parameters. **Material and Methods:** It was a single center, prospective, observational study conducted over three consecutive months on patients on hemodialysis and their biochemical, and QoL parameters were recorded. We could enroll 29 patients for this study. The objective was to assess the effect of different hemodialysis frequencies per week on hemodialysis adequacy parameters and QoL indices. **Results:** The baseline characteristics were uniform with respect to age (p=0.761) and commonly associated co-morbidities like obesity (BMI p=0.971), hypertension (p=0.927), diabetes mellitus (p=0.822). The serum albumin was observed to be similar in patients receiving either thrice weekly or twice weekly hemodialysis (p=0.736). The URR and kt/v were marginally higher in patients receiving thrice weekly dialysis but with no statistical significance (p=0.938 for URR & p=0.615 for kt/v). **Discussion and Conclusions:** The biochemical indices of nutrition along with electrolyte imbalance and quality of life parameters observed with different frequencies of hemodialysis per week were identical over three consecutive months.

Keywords: Dialysis adequacy, dialysis frequency, dialysis nutrition

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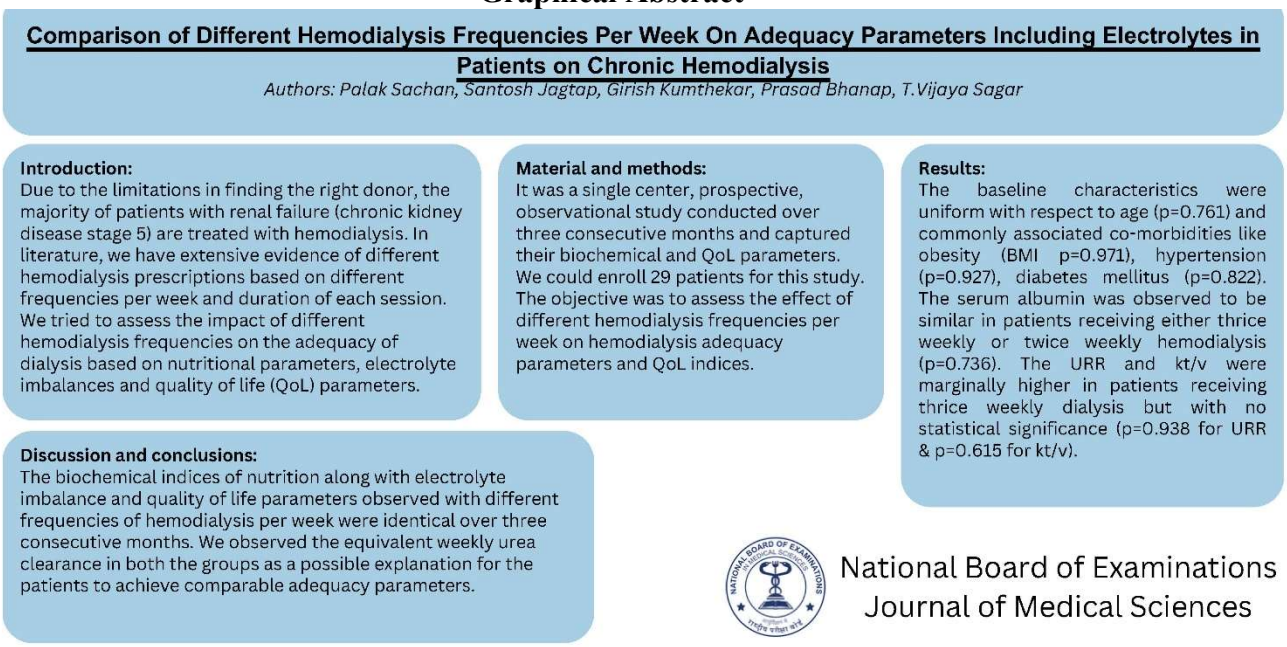
Graphical Abstract



Abbreviations

CKD - Chronic Kidney Disease
ESRD- End Stage Renal Disease
URR- Urea Reduction Ratio
Kt/V- (Daughards formula) where k is dialyzer clearance, t is time and V is distribution volume of urea
RKF- Residual kidney function
QoL- Quality of Life
HD- Hemodialysis
MHD- Maintenance Hemodialysis
NKF-KDOQI - National kidney foundation-kidney disease outcomes quality initiative
MH-Mental Health
PS- Psychological Health
PH- Physical Health
KID- Kidney Induced Diseases

Introduction

Kidneys are responsible for maintaining electrolyte and fluid balance in the body and removal of toxic waste products. Injury to kidneys results in derangements in electrolytes and fluids due to accumulation of uremic toxins. Uremic Syndrome is a result of accumulation of fluid and substances normally excreted by the kidney.

Patients suffering from renal failure Chronic kidney disease (CKD 5) are treated with hemodialysis, peritoneal dialysis or kidney transplantation. Due to the limitations of finding the right donor most of the patients are receiving chronic hemodialysis [1]. Since the beginning, hemodialysis therapy has two essential goals: to control the signs and symptoms of uremia and rehabilitation. de Palma et al. defined hemodialysis as adequate when it allows a satisfactory nutritional intake, be fully rehabilitated, maintains normal blood pressure and hemoglobin levels and prevents neuropathy.

Hemodialysis is a procedure to remove waste products and water from the blood with the help of a dialysis machine and

a dialyzer. The therapy is given to patients with a glomerular filtration rate of less than 15 ml/min which is also known as CKD stage 5 or end stage renal disease (ESRD). Hemodialysis is an approach to provide patients with a stable life to ensure total physical, social, and mental well-being. In literature, we have extensive evidence of different hemodialysis prescriptions of different frequencies i.e. once/twice /thrice a week or daily and durations i.e. 3/4/5 hours. It is a therapy to support the metabolic needs of the patient's body. Hemodialysis adequacy is paramount in achieving desired goals. The adequacy parameters commonly used are hemoglobin concentration, urea concentration, URR (Urea Reduction Ratio), and Kt/V.

Three hemodialysis sessions are usually the most common method adopted at most dialysis centers. It is presumed that more frequent dialysis per week leads to better adequacy parameters and higher quality of life indices in these patients. Various studies in the United States and Germany have drawn an association between shorter dialysis periods and poorer results [2-4]. Urea Reduction Ratio (URR), is the measure of proportionate reduction in the level of blood urea nitrogen over the process of hemodialysis.

The National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) 2015 guidelines recommended a target single pool Kt/V (spKt/V) of 1.4 per hemodialysis session for patients treated thrice weekly (minimum delivered spKt/V of 1.2). For hemodialysis schedules other than thrice weekly, NKF-KDOQI suggested a target standard Kt/V of 2.3 volumes per week (minimum delivered dose of 2.1). These calculations must be based on the contributions of ultrafiltration and residual kidney function for individual patients. NKF-KDOQI suggested in-center short frequent hemodialysis as an alternative to conventional in-center thrice weekly hemodialysis based on patient preferences, quality of life (QoL) indices and clinical benefits, and the risks involved [12].

The objective of this study is to assess hemodialysis therapy adequacy based on the adequacy parameters rather than adopting empirical dialysis prescription for all patients. The study also aims to identify the problems affecting the treatment and thereby affect the adequacy parameters and the frequency and duration of therapy.

Material and Methods

The present study was a single center, prospective, observational study carried out over a period of 3 consecutive months. The study involved patients receiving hemodialysis treatment at the dialysis unit of Symbiosis University Hospital and Research Centre in Pune, Maharashtra, India for more than three months. We selected the target population based on those fulfilling the inclusion criteria of the study. We analyzed records for three consecutive months i.e. June, July, and August of 2022. We followed the patients for 3 consecutive months and captured the biochemical and QoL parameters. We could enroll 29 patients for this study.

Primary objective:

To evaluate the effect of hemodialysis frequency per week on hemodialysis adequacy parameters and QoL indices.

Secondary objectives:

1. To assess the well-being of hemodialysis-dependent patients with differing dialysis frequencies.
2. To assess electrolyte imbalances (sodium, potassium, chloride, calcium, phosphorus) in patients receiving different duration and frequencies of hemodialysis.

Inclusion criteria:

1. hemodialysis-dependent patients above the age of 18 years and undergoing hemodialysis for more than 3 months.

Exclusion criteria

1. Patients below the age of 18 years
2. Patients not consenting to participate and uncooperative patients.

Data was collected via Google sheets. We used Quality of life (KDQOL ™ - 36) questionnaire for assessing the quality of life score (QoL). Continuous variables were represented as mean and standard deviation where data follows the normal distribution, or median with range. Categorical variables are represented as mean, frequency and percentage. The statistical significance of the difference in the outcome variables between the groups was Fisher exact test, chi-square test, t-test, and ANOVA. We analyzed data using the SPSS program.

Approval from the Independent Ethics Committee (IEC) of Symbiosis International University (SIU) was taken before starting the study (Reference Number: SIU/IEC/425). Informed consent was taken from the patients participating in the study at time of filling the questionnaire for assessing their quality of life (QoL) and calculating QoL score. Out of the 5 possible ways of doing chronic maintenance dialysis, we included twice a week 4 hours HD and thrice a week 4 hours HD for the present study. Standard eKt/V was calculated using the Daugirdas formula. Out of the total 29 patients, those receiving twice a week (2/7) dialysis were 12 and thrice a week (3/7) dialysis were 17 (Table 1).

Results

Table 1. Baseline features of patients on chronic hemodialysis (CKD stage 5D).

Dialysis Frequency	**2/7(4 hours)**		**3/7(4 hours)**		**P value**
AGE (Mean ± SD)	51.00±16.398		52.76±15.073		0.761
GENDER Male(M) Female(F)	M(8)	F(4)	M(14)	F(3)	0.403
BMI (Mean ± SD)	24.483 ±4.2065		24.431±3.3775		0.971

DIABETES MELITUS	8	12	0.822
HYPERTENSION	9	13	0.927
Dialysis Vintage (Mean ± SD)	38.636 ± 7.991	40 ± 18.303	0.285
Residual Kidney Function (Mean ± SD) ml/min	15.217 ± 11.633	6.909 ± 6.59	0.0185

M: Male
F: Female
SD: Standard deviation
BMI: body mass index

We could categorize patients based on dialysis frequency and session length. Patients were receiving either twice weekly or thrice weekly dialysis with 4 hours as a uniform dialysis session length. The baseline characteristics were uniform with respect to age (p=0.761) and commonly associated co-morbidities like obesity (BMI p=0.971), hypertension (p=0.927), diabetes mellitus (p=0.822).

The vintage dialysis was identified as time spent on chronic maintenance hemodialysis in months. We found that patients with thrice weekly hemodialysis (40 months) had similar dialysis vintage compared to those having twice weekly hemodialysis (38.6 months).

Residual kidney function (RKF) in patients with end-stage renal disease (ESRD) undergoing hemodialysis (HD) therapy is the ability of the native kidneys to excrete water and uremic toxins. We observed lower RKF in patients requiring thrice weekly dialysis (6.90 ml/min) and higher RKF in patients on twice weekly hemodialysis (15.21 ml/min). These observations were registered in those patients with a native kidney output of 100 ml/day or more. We observed these observations being statistically significant (p=0.01) (Table 2).

Table 2. Nutritional adequacy parameters

Dialysis Frequency		2/7(4 hours)	3/7(4 hours)	P value
Hemoglobin (Mean ± SD)	1 ST MONTH	8.675±1.9864	9.700±2.2564	0.217
	2ND MONTH	8.767±2.1296	10.275±2.0773	0.071
	3RD MONTH	8.950±1.807	10.013±2.68	0.168
Albumin (Mean ± SD)	1 ST MONTH	3.133±0.916	3.200±0.589	0.736
	2ND MONTH	3.267±0.379	3.194±0.493	0.673
	3RD MONTH	3.225±0.4413	3.131±0.5986	0.652

SD: Standard deviation

We observed higher hemoglobin in patients receiving thrice-weekly hemodialysis compared to those receiving twice-weekly hemodialysis. This was seen in all the three months follow up (p=0.071). The serum albumin was observed to be similar in patients receiving either thrice weekly or twice weekly hemodialysis (p=0.736) (Table 3).

Table 3. Urea clearance in different categories of patients on maintenance hemodialysis

Dialysis Frequency		2/7(4 hours)	3/7(4 hours)	P value
URR (Mean ± SD)	1 ST MONTH	0.6950±0.8555	0.712±0.06865	0.553
	2ND MONTH	0.6900±0.11394	0.7035±0.05809	0.678
	3RD MONTH	0.7017±0.10008	0.7047±0.10308	0.938
Kt/V (Mean ± SD)	1 ST MONTH	1.7808±0.34447	1.9519±0.39482	0.242
	2ND MONTH	1.9033±0.49778	1.9694±0.36439	0.688
	3RD MONTH	1.8500±0.39655	1.9318±0.44579	0.615

SD: standard deviation; URR: Urea reduction ratio; Standard Kt/V: K – standard, t – time spent on dialysis, V – Volume removed on dialysis (measure of ultrafiltration)

Urea kinetic modeling is a commonly used tool to assess the dialysis adequacy to clear small molecular uremic toxins. Standard Kt/V was calculated using various parameters. Urea clearance is also postulated to be higher in patients receiving more frequent dialysis translating into higher urea reduction ratio (URR) and higher kt/v. We observed near equivalent urea clearance with twice and thrice weekly MHD. The URR and kt/v were marginally higher in patients receiving thrice weekly dialysis but with no statistical significance (p=0.938 for URR & p=0.615 for kt/v) (Table 4).

Table 4. Patient generated quality parameters in different categories of patients on maintenance hemodialysis

Dialysis Frequency	2/7(4 hours)	3/7(4 hours)	P value
QoL (MEAN±SD) PH	63.2738±14.92340	62.9174±16.64324	0.951
QoL (MEAN±SD) MH	53.6111±11.63958	57.5327±12.03530	0.194
QoL (MEAN±SD) KID	73.1720±4.58490	70.7116±5.84387	0.117
QoL (MEAN±SD) PS	66.2868±8.10503	66.4430±10.85596	0.483
QoL (MEAN±SD) Total	64.0859±8.64886	64.4012±8.01651	0.920

MH-Mental Health
PS- Psychological Health
PH- Physical Health
KID- Kidney Induced Diseases
QoL- Quality of Life
SD: Standard deviation

We assessed scores of patient generated quality of life indices (QoL) using the Kidney Disease and Quality of life (KDQOL ™ - 36) questionnaire and compared the QoL score among patients receiving twice and thrice weekly dialysis. We found identical scores in all the four domains of the QoL questionnaire (p=0.920). In the domain of mental health (MH), patients receiving thrice weekly dialysis had higher scores (57.53) but it was found not to be statistically significant (p=0.194) (Table 5).

Table 5. Electrolyte disturbances in different categories of patients on maintenance hemodialysis

Dialysis Frequency		2/7(4 hours)	3/7(4 hours)	P value
CALCIUM (Ca) mEq/L	1 ST MONTH	7.913±1.1243	8.500±1.10480	0.240
	2ND MONTH	7.860±1.1472	8.200±0.6772	0.360
	3RD MONTH	8.300±1.16858	8.369±0.6829	0.884
POTASSIUM (K) mEq/L	1 ST MONTH	5.222±1.1077	5.231±0.6824	0.982
	2ND MONTH	5.509±0.8215	5.347±0.8733	0.635
	3RD MONTH	5.575±1.1913	5.219±0.6921	0.361
CHLORIDE (Cl) mEq/L	1 ST MONTH	106.11±2.713	103.31±3.816	0.073
	2ND MONTH	104.73±3.409	102.13±3.461	0.070
	3RD MONTH	105.00±3.891	102.25±3.357	0.086
SODIUM (Na) mEq/L	1 ST MONTH	137.78±3.153	135.54±3.072	0.112
	2ND MONTH	135.82±2.960	134±3.359	0.165
	3RD MONTH	135.25±3.359	134.38±2.986	0.517
PHOSPHORUS (P) mEq/L	1 ST MONTH	4.837±1.6422	4.823±1.5589	0.984
	2ND MONTH	4.520±1.5526	4.781±1.6857	0.696
	3RD MONTH	4.545±1.2832	4.856±1.6717	0.608

Electrolyte imbalance is a commonly encountered situation in patients undergoing dialysis. We tried to assess the extent of abnormalities in commonly measured electrolytes like sodium, potassium, chloride, phosphorus and calcium. The calcium levels were higher in patients belonging to thrice weekly dialysis compared to patients belonging to twice weekly dialysis. This association was not statistically significant (p=0.884). Potassium levels were near identical on all the three occasions among patients belonging to either group (p=0.361). Chloride levels were lower in patients receiving thrice weekly dialysis compared to patients receiving twice weekly dialysis. We observed higher phosphorus levels in patients belonging to thrice weekly dialysis than patients on twice weekly dialysis on all the three occasions. Nonetheless, this association was not observed to be statistically significant (p=0.608).

Discussion

Chronic kidney disease (CKD) and end-stage renal disease (ESRD) are important global health issues with prevalence of 11–13% and 0.1% respectively [7]. The definition of CKD is based on the presence of kidney damage (i.e. Albuminuria) or decreased kidney function (i.e. Glomerular filtration rate <60 mL/min/ 1.73 m2) for 3 months or more. The term “end- stage renal disease” (ESRD) generally refers to CKD stage 5 treated with either dialysis or transplantation. Standard hemodialysis (HD) consists of three sessions a week with a duration of about four hours per session. Patients receiving chronic hemodialysis treatment have high hospitalization rates associated with higher mortality and morbidity. The age-adjusted incidence rate of ESRD in India has been estimated to be 229/million population [8]. The survival rates have not improved in this group of patients due to multiple issues which includes inadequacy and unavailability of renal replacement therapies [9,10].

Quality of Life

Likewise, the patient QoL indices could not follow the expectations set by the massive burden of resources required for managing CKD patients on dialysis. Previous studies showed a poorer QoL in patients with ESRD than those with other chronic diseases including cancer [13].

Hemoglobin and serum albumin are commonly used nutritional parameters to assess dialysis adequacy. It has been proven that an adequate dialysis improves appetite, reduces systemic inflammation, mitigates bone marrow suppression and erythropoietin resistance. An adequate dialysis improves anemia due to preventing GI blood loss and sequestration of iron under the influence of hepcidin [14].

Patients with higher frequency HD per week would have an improved QoL due to better nutritional intake [11]. The shorter intradialytic period and longer dialysis duration observed during HD could be expected to alleviate the complications of malnutrition to a certain extent, thus making the patient more functional, which contributes to an objectively improved QoL.

This study compared two categories of patients receiving maintenance hemodialysis. It included patients with twice weekly dialysis and thrice weekly dialysis.

We expected that the patients receiving more frequent dialysis (thrice weekly) would have better clearance of phosphate, urea and potassium. This was as per the prevailing logic of more dialysis translating into higher clearance rates. Consequently, higher clearances of small molecules like urea and electrolytes would translate into better quality of life (QoL) indicators. If we would put everything together, more frequent dialysis would also generate better nutritional parameters in these patients. But, this traditional thinking was not supported in our study.

Electrolytes

We observed equivalent serum levels for phosphorus (p=0,69), potassium (p=0.982) and calcium (p=0.884) in patients who received twice weekly and thrice weekly hemodialysis. The small molecule urea was used to measure dialysis adequacy. The dialysis adequacy was identical for both groups with the urea reduction ratio (p=0.678) and Kt/V (p=0.688) not being statistically different. The mean URR calculated for twice weekly dialysis (0.69) and for thrice weekly dialysis (0.70) were found to be nearly identical. Similar observations were made for Kt/V in twice weekly (Kt/V 1.8) and thrice weekly (Kt/V 1.9) dialysis.

Urea Clearance

As the weekly urea clearance and electrolyte levels were similar, the nutritional parameters were also near similar in these two groups. We found a slightly elevated hemoglobin in patients who received thrice weekly dialysis in the second month of follow up (p=0.071) but it was not statistically significant. In the first (p=0.21) and third month (p=1.68) the hemoglobin levels were nearly the same in patients who received either frequency of dialysis. We also measured serum albumin as a nutritional parameter in both the groups. The mean serum albumin in patients who received twice weekly dialysis was 3.13 gm% and 3.20 gm% in those on thrice weekly dialysis (p=0.67).

It is a well-known fact that better nutrition and small molecular clearances reflect in better quality of life (QoL) for patients on chronic hemodialysis. We tried to capture the QoL indicators in three consecutive months of the study. We could use a well validated scale using physical health, mental health and personal health included into the questionnaire. It indicated a nearly equivalent QoL in both the groups.

Thus, the two different frequencies of dialysis per week had no effect on the nutritional status, Quality of Life indices (QoL) and clearance parameters. The age groups, gender distribution and BMI were identical (p=0.76, p=0.40, p=0.97 respectively) to nullify a selection bias**.** This could be a thought provoking exercise for larger trials comparing the thrice and twice weekly dialysis schedules head-on. Although we had a smaller sample size, we presumed the equivalent weekly urea clearance in both the groups rendered the patients achieve comparable adequacy parameters.

Residual Kidney Function

Residual kidney function (RKF) is less frequently used for haemodialysis (HD) patients in routine clinical care. Residual

kidney function (RKF) in dialysis patients is defined by the ability of the native kidneys to excrete water and uremic solutes [15]. We observed that the patients with higher residual kidney function had lesser frequency of dialysis per week but equivalent QoL parameters, nutritional and electrolyte parameters. This prompted us to presume frequency of hemodialysis per week be based on the RKF provided the standard Kt/V remains at par with patients receiving higher frequency dialysis per week. We could not analyze interdialytic weight gain due to extensive intra- and interpersonal variations. The vintage dialysis was found to be almost identical in two groups and hence was not a statistically significant variable (p=0.28).

Conclusion

The biochemical indices of nutrition along with electrolyte imbalance and quality of life indices (QoL) in patients receiving different frequencies of hemodialysis per week were identical over three consecutive months. It indicated that nutritional indices and QoL indices were comparable irrespective of the frequency of hemodialysis per week. Different dialysis frequencies per week with near identical small molecular clearance (kt/v & URR) correlated with identical nutritional and QoL indices. Patients with higher residual kidney function had the similar benefits of thrice-weekly dialysis possibly due to similar small molecular clearances (std Kt/V).

Limitations

Small sample size could be a limitation for the present study though it could prove useful as a pilot study.

Future Research Recommendations

We recommend having a higher sample size to look into interactions between residual kidney function and urea kinetic modeling. This might shed some light on prescribing dialysis based on residual kidney function as a standard of care. It could be interesting to assess the effect of middle molecular weight uremic toxins clearance by the native kidneys contributing to lesser requirement of hemodialysis for individuals with higher RKF.

Conflicts of interest

The authors declares that they do not have conflict of interest.

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