

RESEARCH ARTICLE

Effect of Hemodialysis Duration on Urea Reduction Ratio and KT/V Target among End-Stage Renal Failure Patients

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Abstract

Background: The study aimed to determine the association of dialysis treatment duration with the adequacy of hemodialysis among patients as indicated by Urea Reduction Ratio, URR and Kt/V.

Methods: The study employed a quasi-experimental clinical research study design of purposive sampling technique from 60 samples of hemodialysis patients in a private hospital in Kota Kinabalu. The two groups were categorised as shorter 3 hours and conventional 4 hours dialysis duration. Blood urea levels of pre and post-dialysis treatment were used as biomarkers to identify the adequacy of dialysis treatment.

Results: The study paired t-test findings indicate that participants of 3 hours HD duration had a mean blood urea level pre-dialysis of 24.34 (SD =4.99), which was significantly higher than the 43 participants of 4 hours HD duration mean blood urea level of 20.11, $t(42) = 2.59$, $p < 0.13$. Similarly, for participants of shorter HD duration, the mean blood urea level post dialysis of 9.31 (SD =3.41) was also significantly higher than the 4 hours HD duration participants with mean blood urea level of 6.59, $t(29) = 2.81$, $p < 0.009$. The major finding of the study using a two-way analysis of variance yielded a main effect for the Kt/V, $F(1,58) = 6.36$, $p < 0.14$, such that the average Kt/V was significantly higher in 4 hours HD durations ($M=1.38$, $SD=0.29$) than the 3 hours HD durations ($M=1.17$, $SD=0.30$). It is also similarly significant for the Urea Reduction Ratio, $F(1,59) = 4.425$, $p < 0.04$, in which 4 hours HD durations ($M=67.78$, $SD=8.63$) compared to 3 hours HD durations ($M=62.45$, $SD=.44$).

Conclusion: Achieving the advised treatment durations regime a bare minimum of 4 hours per session are recommended for patients with significant weight gain, high ultrafiltration rates, difficulty achieving dry weight, or inadequate metabolic control (such as hyperphosphatemia, metabolic acidosis, and hyperkalaemia) may require additional hemodialysis sessions or longer hemodialysis treatment times.

Keywords: Dialysis Adequacy, Urea Reduction Ratio, KT/V, Dialysis Duration.

1. Introduction

End-stage renal disease (ESRD) patients cannot sustain life without dialysis support. With advanced

technology, reducing dialysis time from long dialysis durations of more than 4 hours to shorter 3 hours became possible. However, shortening dialysis

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without scrutinising the clinical condition and solute elimination may have harmful consequences. (Held et al., 1991). The relationship between dialysis treatment duration and dialysis adequacy has become a topic of interest for the nephrology society; few studies have been done in response to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) guidelines 2015 updates (Rocco et al., 2015). This study emphasised dialysis adequacy by using simple laboratory parameters measurement. The study aims to compare dialysis treatment duration on dialysis adequacy by Urea Reduction Ratio (URR) and Kt/V among haemodialysis patients in a private hospital.

The adequacy of hemodialysis refers to how well toxins and waste products are removed from the patient's blood and has a major impact on the patient's well-being. The success of therapeutic dialysis is primarily due to removing small, water-soluble (dialysable) toxins. Although admittedly one of the least toxic, urea is the most abundant and commonly studied representative of these small solutes. Dialysis delivery should be adequate to improve quality of life and prolong survival.

Although the absolute number of publications in nephrology is increasing, the number and quality of randomised clinical trials (RCTs) in nephrology cannot match the needs of the rising disease burden. In the local setting of this study, very limited research has been done to compare dialysis treatment duration on dialysis adequacy by Urea Reduction Ratio (URR) and Kt/V among haemodialysis patients in a private hospital. In Malaysia, a population-based study has been conducted to determine the prevalence of CKD to obtain accurate information for health care planning (Hooi et al., 2013). The number of new patients has continued to increase over the last ten years. The number of prevalent dialysis patients also increased to 44,136 in 2018 (from 19,430 in 2008), with 39,593 prevalent HD patients. The total number of prevalent Renal Replacement Therapy, RRT patients in 2018 was 45,937 (National Renal Registry, 2018). The study's relevance is determining the recommended dialysis treatment durations for dialysis patients to achieve standard dialysis adequacy per clinical practice guidelines. The minimal time taken for urea removal during dialysis treatment is unclear. Thus, the purpose of this study is to provide baseline information on the recommended dialysis duration of each dialysis session should be done. Practice modifications, biocompatible membranes, dialysate based on bicarbonate, high-flux-high efficiency dialysers,

In the dialysis population, this group of people are vulnerable and at high risk for the effects of dialysis inadequacy. The consequences of inadequate dialysis are related to their quality of life, malnutrition, and anaemia, leading to morbidity and mortality risk. Thus, the significant problem for this study is identifying the minimal dialysis treatment duration required to achieve the targeted Urea Reduction Ratio using the simplest measurement method (Liang et al., 2019).

The study aimed to compare (1) blood urea level pre-post dialysis treatment, (2) Urea Reduction Ratio (URR), (3) the Kt/V target achieved, and (4) dialysis adequacy among shorter-time and conventional hemodialysis patients. The study outcomes would be valuable to hemodialysis patients in achieving dialysis adequacy.

The urea reduction rate can measure the adequacy of dialysis and the percentage of urea clearance. The importance of dialysis adequacy is to prevent inadequate dialysis treatment complications. Thus, inappropriate additional dialysis treatment can be avoided if the patient achieves targeted urea clearance. This study is also important in renal nursing to evaluate the efficiency of health education regarding the importance of completing dialysis treatment as prescribed. Specific health education on the effect of inadequate dialysis can reinforce the patients. Additionally, achieving the targeted URR for the nephrology services is important to reduce or minimise additional dialysis treatment costs. The cost of dialysis treatment itself is considered expensive, taking in all the associated costs of dialysis equipment, consumables, consultation, and workforce per session. By managing the resources efficiently, the cost saved can be used for other treatments, such as providing more nutritious meals or channelling the saved money to fund the transportation costs of dialysis patients or, particularly in the anaemia treatment of this group.

2. Methodology

2.1 Research Design

A quasi-experimental design was used in this study. Selected samples from the population were divided into two categories of: shorter and conventional dialysis duration.

2.2 Participants

The researcher obtained determined sample size based on Krejcie and Morgan formula and table for determining sample size (Krejcie et al., 1996). More

than 100 patients were registered in the hemodialysis unit receiving hemodialysis treatment from January 2023 to February 2023. In this study, 80 patients were taken as the sample from the population of 100 hemodialysis patients in the private hospital. The population for this study were patients coming for hemodialysis treatment at the dialysis unit. A non-probability purposive sampling technique was used. The criteria for sample recruitment were 4 hours of dialysis treatment duration and 3 hours of dialysis treatment.

2.3 Data Collection

This study used a pre-validated questionnaire to collect the data from the sample. The checklist consisted of 3 parts. Section A had set questions on socio-demographic characteristics consisting of 7 questions. Section B had a checklists on laboratory data and calculation URR and Kt/V. For the laboratory data, values were retrieved from the laboratory report and then calculated for URR and Kt/V. In section C, three questions were used to evaluate dialysis adequacy.

The researcher identified samples for the experimental and control groups based on the calculated sample number. The experimental group are collected from 3 hours of dialysis treatment, and the control group are the 4 hours of dialysis treatment duration. Blood samples were collected and sent to the laboratory before the first dialysis session to measure blood urea levels. It should be mentioned that blood samples were obtained from the arterial line after the initiation of dialysis treatment for sample preparation before dialysis. The blood sample is free from heparin and sodium chloride solution. Evaluation of the characteristics of the dialysis machine during the dialysis performed observationally. At the end of the dialysis, to avoid re-circulation of blood samples, 2 mL of blood samples were obtained using a low flow speed method to evaluate blood urea levels after dialysis. The samples were taken from the arterial line since the differences between arterial-venous urea concentrations are at the lowest. Blood samples were then sent to the laboratory. After receiving the test results, the urea reduction ratio formula was used to calculate the reduction of blood urea, and the logarithmic Daugirdas 2 formula was used to evaluate dialysis adequacy. In this calculation, the patient's weight also contributed to the value. The Kt/V level was calculated based on the logarithmic Daugirdas 2 formula:

$$Kt/V = \ln(R-0.008t) + (4-3/5R) + UF/W$$

In which \ln is the negative natural logarithm, R is BUN after dialysis divided by BUN before dialysis, T is dialysis time in hours, UF is weight loss in kilograms during dialysis, and W is weight in kilograms after dialysis. In addition, the urea reduction ratio (URR) is obtained through the following equation.

$$URR = 100 \times 1 - (\text{pre-dialysis urea}/\text{post-dialysis urea}).$$

Finally, the study coordinator will be asked to complete the checklist for the laboratory finding results. At this point, the researcher will complete the adequacy.

Data Analysis

In this study, the pre-dialysis urea level collected from the laboratory results was categorised into abnormal and normal levels based on the urea limit range, similar to all participants' post-dialysis urea blood levels. The urea reduction ratio was then calculated by using the standard formula. The total URR achieved more than 65% and less than 65% were then calculated into mean, median, standard deviation, and frequency percentage statistics.

Based on the URR, the further derived calculation determined the Kt/V to measure the dialysis adequacy target of more than 1.2 or less than 1.2. The kt/v achieved more than 1.2 was calculated into mean, median, standard deviation, and frequency percentage statistics.

3. Results

3.1 Demographic Profile of the Respondents

Chronic Kidney Disease patients on regular hemodialysis treatment became the participants in this study. All the patients are taken from men and women groups ranging from 21 to 85 years old. The patients are multiracial of local Sabahan ethics, representing the local data of Kota Kinabalu citizens. Primary causes of chronic kidney disease leading to hemodialysis treatment are also considered. Other than that, the dialysis vascular access of the hemodialysis patients was also taken.

Of the 80 eligible patients, 60 were enrolled. Twenty patients were not approached because of acute illness and the inability to complete the dialysis treatment minimally in 3 hours. Twelve patients did not wish to participate because they were non-long-term dialysis patients and did not plan to become long-term dialysis patients during the survey. There was a higher proportion of males in the patient group than females. The patient's age group are between 21-89 years old. The highest number of elderly with CKD is between

51 to 70 years old. Chinese were the highest in this study population with 22 participants, followed by local natives, Bajau of n=17. The largest ethnicities of Sabah were Kadazan and Dusun at the third rank of n=6. Hypertension is the major primary diagnosis

known as the cause of chronic kidney disease among the population at 61.7%, followed by Diabetes Mellitus at 35%. As for vascular access commonly used, the population are native arteriovenous fistula at 95%, while the remaining use HD catheters.

Table 1. Gender, Age, Race, Primary Cause of CKD and HD access distribution

		Frequency (N=60)	Percentage, %
Gender	Male	37	61.7
	Female	23	38.3
Age	21-30	1	1.7
	31-40	6	10.0
	41-50	9	15.0
	51-60	14	23.3
	61-70	15	25.0
	71-80	11	18.3
	81-90	4	6.7
Race	Chinese	22	36.7
	Bajau	17	28.3
	Dusun	6	10.0
	Kadazan	6	10.0
	Brunei	4	6.7
	Filipino	2	3.3
	Others	3	5.0
Primary Cause of CKD	Diabetes Mellitus	21	35.0
	Hypertension	37	61.7
	Polycystic Kidney Disease	1	1.7
	Glomerulonephritis	1	1.7
HD Access	AVF	57	95.0
	HD Catheter	3	5.0

Table 2. Blood Urea Level Pre and Post Dialysis among shorter time and conventional hemodialysis patients.

	HD Duration	Mean	Median	Std. Deviation	F	t	df	Sig.
Pre-Urea Level	3 hours	24.3353	23.7000	4.99924		2.218	58	.030
	4 hours	20.1140	20.0000	7.17043	1.874	2.585	42.021	.013
Post-Urea Level	3 hours	9.3118	9.0000	3.41319		2.828	58	.006
	4 hours	6.5884	5.8000	3.34082	.358	2.802	28.840	.009

The 17 study participants of 3 hours HD duration had a mean blood urea level pre-dialysis of 24.34 (SD =4.99), significantly higher than the 43 participants of 4 hours HD duration mean blood urea level of 20.11, $t(42) = 2.59, p < 0.13$. The 17 participants with 3 hours

HD duration mean blood urea level post dialysis had a mean of 9.31 (SD =3.41), also significantly higher than the 4 hours HD duration participants with mean blood urea level of 6.59, $t(29) = 2.81, p < 0.009$.

Table 3. Urea Reduction Ratio, URR percentage among shorter time and conventional hemodialysis patients.

	HD Duration	Mean	Median	Std. Deviation	F	t	df	Sig.
Urea Reduction Rate, %	3 hours	62.4471	62.6000	9.44432	.210	-2.103	58	0.040
	4 hours	67.7884	70.7000	8.63173		-2.022	27.183	0.053

The 43 participants in the 4 hours HD duration group URR achieved are ($M=67.79$, $SD=8.63$). The 17 participants in the 3 hours HD duration group achieved ($M=62.45$, $SD=9.44$), demonstrated a significance

different in performance ($t(27) = -2.02$, $p=0.05$; as expected the longer duration of dialysis treatment will achieve better clearance of urea target at 65%.

Table 4. Kt/V among shorter time and conventional haemodialysis patients.

	Variables	Mean	Median	Std. Deviation	F	t	df	Sig.
Kt/V	3 hours	1.1694	1.0800	0.29556	0.033	-2.522	58	0.014
	4 hours	1.3788	1.4400	0.28766		-2.492	28.695	0.019

3.1.1 KDOQI 2015 Guidelines: Haemodialysis Kt/V Target ≥ 1.2

The 43 participants in the 4 hours HD duration group ($M=1.38$, $SD=0.29$) and the 17 participants in

the 3 hours HD duration group ($M=1.17$, $SD=0.30$) projected a significant difference in Kt/V achievement $t(29) = -2.49$, $p=0.019$; as expected, the longer duration of dialysis treatment will achieve higher Kt/V target at 1.2.

Table 5. Dialysis adequacy based on URR and Kt/V among shorter time and conventional hemodialysis patients.

		Mean	Std. Deviation	df	Mean Square	F	Sig.
Urea Reduction Ratio	Between Groups	62.4471	9.44432	1	347.586	4.425	.040
	Within Groups	67.7884	8.63173	58	78.559		
	Total	66.2750	9.11694	59			
Kt/V	Between Groups	1.1694	.29556	1	.534	6.360	.014
	Within Groups	1.3788	.28766	58	.084		
	Total	1.3195	.30274	59			

An analysis of variance yielded a main effect for the Kt/V, $F(1, 58) = 6.36$, $p < 0.14$, such that the average Kt/V was significantly higher in 4 hours HD durations ($M=1.38$, $SD=0.29$) than the 3 hours HD durations ($M=1.17$, $SD=0.30$). It is also similarly significant for the Urea Reduction Ratio, $F(1, 59) = 4.425$, $p < 0.04$, in which 4 hours HD durations ($M=67.78$, $SD=8.63$) compared to 3 hours HD durations ($M=62.45$, $SD=.44$).

4. Discussion

In this study, 28 % of the participants are dialysed at 3 hours of dialysis treatment duration, and 72 % complete the 4 hours of dialysis treatment. Comparing the worldwide dialysis population based on previous studies, the number of dialysis patients with shorter dialysis treatment times is relatively lower than their international counterparts. All participant’s blood urea samples were taken before and after completion of dialysis treatment according to the prescribed duration of treatment. The baseline blood urea level compared for both groups regarding the normal range of blood urea nitrogen is 2.0-6.8 mmol/L for healthy adults. The study participants of 3 hours HD duration had a mean blood urea level pre-dialysis of 24.34 mmol/L, significantly higher than those of 4 hours HD

duration means a blood urea level of 20.11 mmol/L. As for the participants of 3 hours HD duration, the mean blood urea level post dialysis was 9.31 mmol/L, also significantly higher than the 4 hours HD duration participants with a mean blood urea level of 6.59 mmol/L. Biomarkers in blood urea nitrogen range dialysis patients are normally beyond that value and usually persistently high in uremic patients with Chronic Kidney Disease, CKD. According to KDOQI guidelines, CKD classification depends on consideration for remaining renal function. Patients with a high estimated Glomerular Filtration Rate, eGFR of 30%-40% are asymptomatic chronic kidney patients with remaining kidney function that may not require dialysis treatment soon. Thus, patients with a high percentage of eGFR will have lower blood urea levels (Wang et al., 2018).

In this study, participants in the 4-hour HD duration group proved that the mean URR achieved 67.8%, while participants in the 3-hour HD duration group achieved a mean URR of 62.5%. Longer dialysis treatment duration demonstrated better clearance of urea target of more than 65%. Previous studies have shown that shorter dialysis duration is a higher mortality risk. Observational studies of dialysis session length have produced conflicting results,

perhaps relating to one or more of the factors influencing the Urea Reduction Ratio, surface area size, and volume of fluids removal during dialysis treatment. Changes in practice such as bicarbonate-based dialysate, biocompatible membranes, high-efficiency high-flux dialysers, the introduction of erythropoietin, and routine measurement of dialysis dose occurred simultaneously with the decrease in session length and thus may confound the analyses. Second, based on usual practice, session length is correlated or collinear with several other outcome factors, including sex, body size, nutritional status, and serum phosphorus concentration. Multivariable analyses and large sample sizes are required to distinguish these associations in observational data. Third, several studies did not control for conventional measures of dialysis dose (Kt/V or URR), and none simultaneously controlled for dialysis dose and body size. Because time is a key component of dialysis dose and is also associated with body size, analyses controlling for the dialysis dose without accounting for body size may be confounded (Abedi-Samakoosh et al., 2018) According to the Kt/V criteria, the mean dialysis adequacy index was 1.6 ± 0.22 and 41.7% of the patients had the optimum dialysis adequacy (Kt/V of greater than 1.2.)

The small-solute clearing is considered the most accurate indicator of HD and its sufficiency. The most accurate and thoroughly studied indicator of the dialyser's impact on a patient's life is Kt/V, or fractional urea clearance, the most widely used indicator of the delivered dialysis dose. The agreement was defined as the number of episodes in which URR and Kt/V recorded dialysis adequacy as outlined above ($\geq 65\%$ and ≥ 1.2 , respectively). Extended-hours dialysis offers substantially longer treatment times. In this study, the mean Kt/V of patients who underwent dialysis for 4 hours was higher than those who underwent dialysis for 3 hours. This finding agrees with that study done by using data from more than 71,000 hemodialysis patients by the Japanese Society for Dialysis Therapy who reported a lower risk for complications of the inadequacy of dialysis associated with increased session length up to 5.5 hours after controlling for Kt/V. In the same analyses, the risk of death associated with shorter dialysis sessions decreased with increasing dialysis doses, up to a Kt/V of 1.8 (Shinzato & Nakai, 1999). Observational studies reported that the association between survival and dialyser Kt/V improved after body surface area adjustment. These studies also demonstrated that the conventional prescription of hemodialysis based on

current Kt/V targets leads to shorter dialysis treatment duration delivered to women. Due to body size and surface area, there is a proven result of higher Kt/V in females than males (Vongsanim & Davenport, 2019).

Although there was a disagreement between current measures of dialysis adequacy used, the most striking result of this study is that protracting dialysis time results in a higher total amount of solute removed from the patient's body, whereas Kt/V also projected better performance for longer dialysis duration. The average Kt/V was significantly higher in 4-hour HD durations with a mean of 1.38 than in the 3-hour HD durations of mean Kt/V 1.17. It is also similarly significant for the Urea Reduction Ratio, in which 4-hour HD durations mean 67.8%, compared to 3-hour HD durations of 62.5%.

Although assessing an adult's clinical indicators on dialysis is important, there also needs to be regular assessment of delivered dialysis doses. Due to dialysis patients' higher incidence of intradialytic symptoms such as headaches, nausea, vomiting, muscle cramps and hypotension, which may result in a shortened dialysis session, regularly assessing dialysis adequacy becomes more important (Rees, 2008).

Limitations

The limitation of the study was the limited number of samples for the experimental group undergoing 3 hours of dialysis treatment sessions. To overcome this limitation, the sample numbers for the experimental group are obtained from 1 year of census statistics record with URR value retrieved from medical records. Thus, the sample is evaluated, and equality between the control and experimental groups is maintained. The online clearance is theoretically not applied and is practically limited in this study. Online clearance is used when calculating the dialysis dose by measuring conductivity or ionic clearance across the dialysis membrane. Multiple ions can be tracked simultaneously to minimise error, and the delivered Kt/V can be predicted in real-time before the treatment is over (Basile et al., 1990) the current methods of calculating Kt/V are too complex for routine clinical use and require great care in order to avoid major inaccuracies. As percent reduction in blood urea concentration during dialysis (PRU). Additionally, there is also a tendency to overestimate the time on dialysis. Interruptions for saline administration, dialysis machine alarms, dialyser clotting, and so on all tend to be included as "time on dialysis".

Recommendations

The advised treatment durations by a nephrologist prescribe a bare minimum of 3 hours per session for patients receiving hemodialysis three times per week and have low residual kidney function (less than 2 mL/min). Patients with significant weight gain, high ultrafiltration rates, difficulty achieving dry weight, or inadequate metabolic control (such as hyperphosphatemia, metabolic acidosis, and hyperkalemia) may require additional hemodialysis sessions or longer hemodialysis treatment times. Correlate with the reducing intradialytic complications, advise of dietary sodium restriction and appropriate sodium or water elimination with hemodialysis is critical. Moreover, prescribe an ultrafiltration rate for each hemodialysis session that achieves the ideal balance between euvolemia, sufficient blood pressure management, and solute clearance while minimising hemodynamic instability and intradialytic symptoms is also crucial for patients on dialysis.

5. Conclusion

The study findings highlighted that the control group of patients undergoing 4 hours of dialysis treatment showed a higher Urea Reduction Ratio of more than 65% according to the practice guideline. Meanwhile, the experimental group of patients undergoing 3 hours of dialysis showed a lower Urea Reduction Ratio. The findings were correlated with the Kt/V goal used and dialysis adequacy evaluation. It was proven that the longer duration of dialysis treatment of more than 3 hours achieved better dialysis adequacy. The result findings also show the benefits of achieving adequate dialysis in hemodialysis populations.

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