Original Article

Assessment of hemodialysis adequacy in patients undergoing maintenance maneuver by laboratory tests

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ABSTRACT

Background and Objectives: **Hemodialysis (HD) is one of the therapeutic modalities in ESRD patients. Since inadequate dialysis increases mortality and morbidity of patients, therefore, assessment of dialysis adequacy is clinically important. For this reason, hemodialysis adequacy was determined in patients undergoing maintenance HD at the Mostafa Khomeini Hospital, Tehran, Iran.**

Materials and Methods: **The cross-sectional, descriptive, and analytic strategy of this research study was conducted on 54 patients in 2005. All of the patients were consented and informed of the study purposes. Data were collected using a reliable questionnaire including age, gender, height, weight, and dialysis duration. Prescribed, delivered, and equilibrated kt/v and URR (urea reduction ratio) were calculated using urea kinetic modeling formulas. All data analysis was carried out using t-test, Fisher exactly test, and Pearson correlation analysis (SPSS software).**

Results: **The study population consisted of 54 patients undergoing conventional maintenance HD (36 males and 18 females) aged 18-83 years. The mean value of age was 55.27 ± 17.28 years. The mean values of prescribed kt/v, dkt/v (delivered), ekt/v (equilibrated), and URR were 1.11 ± 0.19, 0.94 ± 0.18, 0.8 ± 0.15, and 55.33 ± 7.05 respectively. Based on DOQI guidelines, the percentage of adequate prescribed kt/v, ekt/v, and URR were 33.3 %, 11.1 %, and 11.1 % respectively. The mean value of age in inadequate ekt/v group was greater than adequate ekt/v group, although t- test analysis did not show a statistically significant correlation ($p = 0.085$). In addition, Fisher exactly test showed a statistically significant correlation between adequate ekt/v and gender ($p = 0.013$) and also between ekt/v and URR ($p<0.001$). On the other hand, Chi-square test did not show a statistically significant correlation between ekt/v and underlying cause of ESRD ($p = 0.685$).**

Conclusion: **It was found out that hemodialysis in this center is inadequate in a great percentage of patients, especially in male ones. Further research study with a larger sample size is suggested to evaluate contributing factors in dialysis adequacy. According to these findings, new treatment strategies may also be necessary.**

Key words: **Hemodialysis, Adequacy of dialysis, chronic renal failure, kt/v**

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Introduction

A central and key issue in the management of patients undergoing maintenance hemodialysis is the assessment of adequacy of dialysis. Simply following up the blood urea nitrogen (BUN) is insufficient because a low BUN can reflect inadequate nutrition rather than sufficient dialytic urea removal. Monitoring the patient symptoms alone is also insufficient. Thus, in addition to symptoms, patient nutrition and survival appear to appropriately reflect dialysis adequacy.

Initially, the national cooperative dialysis study (NCDS) established that the average urea concentration and the protein catabolic rate (PCR) are important determinants of morbidity and mortality in hemodialysis patients (1, 2). Later, Gotch used a mechanistic analysis of these data and showed that the kt/v of urea is an important indicator of its clinical outcome (3). In addition, in the HEMO study, similar outcomes were observed with high and standard dialysis doses as well as dialysis using high and low flux membrane (4, 5). In this respect, a significant increased survival was observed for women receiving a high dialysis dose (6). Urea has been selected as the clearance marker for the kt/v by the NCDS, since it is a reflection of both dietary protein intake and the efficiency of removal of small uremic toxins (7).

Individualizing the hemodialysis prescription to a particular patient using kt/v can be a useful tool in providing a safe and cost-effective dialysis treatment. This can be accomplished with urea kinetic modeling (UKM), which allows for variations in dialysis time, use of high flux dialyzer, and optimization of dietary protein intake. In this regard, UKM is a method for verifying that the amount of dialysis prescribed (the prescribed kt/v) equals the amount of dialysis delivered (the effective kt/v). Kt/v has been defined as the dialyzer clearance of urea (K is obtained from the manufacturer as ml/min) multiplied by duration of dialysis treatment (t, in minutes) divided by the volume of distribution of urea in the body (V, in ml), which is approximately equals to the total body water (7). The following formulas show various kt/v calculations (8, 9):

$$dkt/v = -\ln (R - 0.008 * t) + (4 - 3.5\ R) * UF/W$$

$$ekt/v = dkt/v - 0.6 \times (dkt/v)/t + 0.03 \text{ (for arterial access)}$$

$$URR = 100\ (1 - \frac{post\ BUN}{pre\ BUN})$$

R = 1- URR

UF = volume of fluid removed during dialysis (in liters), W = post dialysis weight

Measuring the kt/v by these equations provides guidance concerning which elements of the prescription require modification to achieve the target dialysis dose. These equations correlate reasonably well with the more rigorous urea kinetic modeling when the kt/v and PCR are in the normal or expected range (8). Using prescribed dialysis, length of dialysis session can be obtained and dkt/v and ekt/v can be used for assessment of dialysis adequacy. Although the URR is useful as an epidemiologic tool, its efficacy in individual patients is more limited.

Therefore, the aim of this study was assessment of HD adequacy in Mostafa Khomeini Hospital in order to design new treatment strategies and enhancement of patient's well being and survival.

Patients and Methods

This cross-sectional, descriptive, and analytic study was conducted in Mostafa Khomeini Hospital (Tehran, Iran) in 2004. The study group composed of 54 patients (36 males and 18 females) undergoing maintenance hemodialysis. All patients were consent and informed of the study purposes. A consent form was signed by each patient. Data were collected using a questionnaire including age, gender, underlying cause of ESRD, dialysis session length, and weight reduction during dialysis treatment.

Then, two blood samples were taken before beginning and after ending of dialysis session

from each patient to measure pre- and post-dialysis BUN. For obtaining the post-dialysis BUN sample, blood was pumped at a flow of 50-100 ml/min for 10-20 seconds, then pump was stopped and a blood sample was drawn from arterial line (7, 10, 11, 12). Using UKM formulas as mentioned previously, prescribed, delivered, and equilibrated kt/v and URR were calculated and compared with NKF-DOQI guideline values of hemodialysis adequacy (prescribed kt/v>1.2, ekt/v>1, URR>65%) (10-13). All data analysis was carried out using t-test, Fisher exactly, and Pearson correlation test (SPSS software).

Results

The study population composed of 54 patients undergoing conventional (low flux) maintenance dialysis, aged 18-83 years. Out of 54 patients, 66.7% were males and 33.3% were females. The mean value of age was 55.3 ± 17.3 years. Diabetes mellitus and hypertensive nephropathy as underlying causes of ESRD were found in 31.5% and 44.4% of cases respectively. Glomerulonephritis, ADPKD, nephrolithiasis, and SLE were the underlying causes of ESRD in the remainder of patients (24.1%). Table 1 shows descriptive analysis of URR, delivered, equilibrated, and prescribed kt/v.

Table 1. Descriptive analysis of dkt/v, ekt/v, pkt/v and URR

Dialysis adequacy	Minimum	Maximum	Mean	Std. Deviation
dkt/v	0.61	1.43	0.9401	0.1835
ekt/v	0.53	1.20	0.8009	0.15051
pkt/v	0.8	1.86	1.1105	0.19563
URR	40.85	71.75	55.3333	7.05638

Adequate dialysis prescription is defined as prescribed kt/v value of 1.2 or higher. In this study, 33.3% of patients had normal values for this parameter. Also, adequate equilibrated dialysis is defined as ekt/v value of 1 or higher. Based upon this, 11.1% of patients had normal values. Meanwhile, ratio of (dkt/v)/(pkt/v) in 31.4% of cases was considered normal based on its normal range of 0.9-1. This ratio was less than 0.9 in 59.3% and above 1 in 9.3 percent of patients. Urea reduction ratio (URR) value of 65% or higher is normal and 11.1 percent of studied patients in this research had normal values. For evaluation of correlation between age and ekt/v, t-test was used. Table 2 shows the results of correlation analysis.

Table 2. Correlation between age and ekt/v

ekt/v	Number of Patients	Mean	Std. Deviation	p value
adequate	6	43.8333	22.56915	0.085
Inadequate	48	56.7083	16.24540	

The mean value of age in patients with inadequate dialysis (56.7 ± 16.24) was higher than ones with adequate dialysis (43.8 ± 22.56). Because of possibly a small sample size for inadequate dialysis group, a statistically significant difference was not found out. Fisher exactly test was used for evaluation of correlation between gender and ekt/v. Table 3 shows the results of this test.

Table 3. Correlation between gender and ekt/v

eKT/V	males		females		Total	
	Frequency	percent	frequency	percent	frequency	percent
adequate	1	2.8%	5	27.8%	6	11.1%
Inadequate	35	97.2%	13	72.2%	48	88.9%
total	36	100%	18	100%	54	100%

The results of Fisher exactly test showed that inadequate ekt/v in males was more frequent than females. This difference was statistically significant (p = 0.013). For evaluation of correlation between underlying disease and ekt/v, χ^2 test was used. Table 4 shows the results of such analysis.

The results of χ^2 test showed that underlying disease had no statistically significant correlation with dialysis adequacy as of a small sample size. Fisher exactly test was used for evaluation of correlation between URR and ekt/v. There was a

Table 4. Correlation between underlying disease and ekt/v

ekt/v		Underling disease			Total
		DM	HTN	miscellaneous	
adequate	frequency	1	3	2	6
	percent	5.9%	12.5%	15.4%	11.1%
Inadequate	frequency	16	21	11	48
	percent	94.1%	87.5%	84.6%	88.9%
Total	frequency	17	24	13	54
	percent	100.0%	100.0%	100.0%	100.0%

Table 5. Correlation between URR and ekt/v

ekt/v		URR		Total
		Inadequate	adequate	
adequate	frequency	0	6	6
	percent	0	100.0%	11.1%
inadequate	frequency	48	0	48
	percent	100.0%	0	88.9%
Total	frequency	48	6	54
	percent	100.0%	100.0%	100.0%

statistically strong correlation between URR and ekt/v ($p<0.001$). Table 5 shows the related result.

Discussion

The results of this research study showed that the mean value of prescribed KT/V was 1.11 that is less than currently recommended minimum value of 1.2. Indeed, in 66.7% of patients, dialysis prescription was inadequate and causes of the inadequacy should be re-investigated. This issue may be attributed to vascular access problems including recirculation, body surface area of patients, treatment duration error including: late arriving of patients, late initiation of dialysis, and/or early termination, methods of obtaining BUN samples, inadequate machine calibration, low blood flow rates, hypotension, and so forth (7, 13).

In the annual report of the year 2003, the mean delivered kt/v of in-center dialysis for adult patients in the United States was 1.52 (14). By comparison, a 2004 survey of dialysis practices in the years 1998 to 2000 in five European countries found that the mean delivered kt/v varied from 1.28 to 1.5 (15). The mean value of ekt/v in this study was 0.8 that was less than currently recommended minimum value of 1. Therefore, 88.9% of patients had inadequate ekt/v. It means that in addition to 66.7% of patients with inadequate dialysis prescription, 22.2% with adequate dialysis prescription also had ekt/v less than standard values. Further research is suggested for assessment of inadequate dialysis in this group.

HEMO study (hemodialysis study) in which 1846 patients were randomly assigned to a standard or high dose of dialysis determined standard dose goal as ekt/v of 1.05, which is equivalent to a URR of 65% or a single pool kt/v (spkt/v) of 1.25 (16). In addition, the mean URR in this study was 55.33%, which was less than currently recommended minimum value of 65%. Based on this finding, as mentioned for ekt/v, 88.9% of patients had inadequate dialysis. An inadequate dose of dialysis is more likely among males, blacks, and those with a larger body surface area. This has been shown in a study on 147 children being dialyzed in 32 centers in the United States (17, 6). A significant survival rate for women receiving a high dialysis dose was observed upon

analysis of the related subgroup (6, 18).

In this study, it was also found out that ekt/v in females was higher than males (ekt/v >1 in 27.8% of cases versus 2.8% respectively). In this regard, no statistically significant correlation between ekt/v and underlying disease was found. This may be attributed to small sample size of the study group. Further studies are required to confirm this finding. In addition, there was a strong correlation between URR and ekt/v. Although the URR is useful as an epidemiologic tool, its efficacy in individual patients is more limited because of a relatively broad range of kt/v that may be seen at a given URR. One study has found that a median URR of 0.62 was associated with a median kt/v of 1.12 (19). However, kt/v values below 1.0 (indicating underdialysis) and above 1.30 (indicating adequate dialysis) were each seen in 10 percent of cases with this URR. Meanwhile, another study evaluated the correlation between various demographic characteristics and a URR of less than 65%. Among all variables analyzed, heavy patients (as defined by body weight in the heaviest quartile) were those most likely to receive inadequate dialysis (odd ratio of 6.1) (20). Despite the higher mean value of age (56.7 years) in patients with inadequate dialysis in comparison with adequate dialysis group, a statistically significant correlation between age and ekt/v was not found out. This may be due to small sample size of this study.

Furthermore, the difference between prescribed dialysis and delivered dialysis was also analyzed in this study. A ratio of (dkt/v) /(pkt/v) in the range of 0.9-1 is considered as normal. In the present research study, only 31.4% of cases had normal values and the remainder (68.6%) had an abnormal ratio. These may be attributed to erroneous estimation of body volume, blood flow rate, dialysis session length, membrane clearance, recirculation, and technical problems regarding needle.

Conclusion

It can be concluded that hemodialysis modality in this center is inadequate in a great number of patients. Further research studies with a larger sample size are suggested. Meanwhile, exploitation of new treatment strategies may be necessary.

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