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How to increase dialysis adequacy; A randomized clinical trial

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ABSTRACT

Introduction: Studies have shown when hemodialysis treatment is sufficiently effective, complications of uremic syndrome, additional treatment costs and hospitalization length are reduced. Several methods have been proposed to improve hemodialysis adequacy.

Objectives: In this study, the effects of the synchronic use of the stepwise profile dialysis fluid flow rate with increased blood flow rate (BFR) were studied on hemodialysis adequacy.

Patients and Methods: This is a cross-over clinical trial study conducted on 34 hemodialysis patients selected from a hemodialysis center of Qazvin University of Medical Sciences, Qazvin, Iran. The patients were randomly allocated into two groups (n= 17 patients in each group) in two sequences. In the first sequence, the subjects received four routine hemodialysis sessions in group one and four hemodialysis sessions with the stepwise profile of the fluid flow rate with increased BFR in group two. In the second sequence, the treatment methods were exchanged. Hemodialysis sessions were performed in both sequences, consecutively. Each session was at least three hours. Hemodialysis adequacy was measured using Kt/V software on the hemodialysis machines after each session.

Results: The mean score of dialysis adequacy was 0.89 in the routine method and 1.26 in the profile with increased BFR. There was a statistically significant difference between the methods ($t= -7.9$, $df = 33$, $P < 0.001$).

Conclusion: The results of the study suggest that the stepwise profile of the dialysis fluid flow rate with increased BFR should be used synchronously to improve hemodialysis adequacy.

Trial Registration: The trial protocol was approved in the Iranian registry of clinical trial (identifier: IRCT20180407039218N1; https://www.irct.ir/trial/31405, ethical code; IR.QUMS.REC.1396.418).

Original Article

Implication for health policy/practice/research/medical education:
Today, efforts are being made to reduce the treatment costs, complications and hospitalization length by improving hemodialysis adequacy. The results of this study showed that the synchronic use of the stepwise profile dialysis fluid flow rate with increased blood flow rate improved hemodialysis adequacy.

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Introduction

Chronic kidney disease is the progressive and irreversible kidney damage leading to the loss of kidney function. End-stage renal disease (ESRD) is the last and most critical stage of chronic kidney disease (1–3). The incidence of ESRD is increasing globally at an annual growth rate of 8% (4). The number of patients with ESRD was 3 1730 000 at the end of 2016. Hemodialysis is the most common renal replacement therapy (5,6). It is a process whereby blood waste such as toxin and metabolites is passed out of the body through a semi-permeable membrane by using a hemodialysis solution (7). According to the Iranian hemodialysis association, the number of patients with ESRD was 57 800 in 2016, of whom 29 200

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people were undergoing hemodialysis (8). Hemodialysis complications are hypertension, muscles cramps, nausea, vomiting, headache and chest pain (9). Intolerance to hemodialysis causes a reduction in blood flow rate (BFR) and hemodialysis time and thus decreases hemodialysis adequacy. Hemodialysis is a successful treatment approach to improving clinical symptoms and delaying death incidence. Studies have shown that hemodialysis patients are more at risk of death than healthy people (10). The concept of hemodialysis quality or hemodialysis adequacy is the implementation of a dialysis that enables the patient to have a normal condition of life, with minimal problems during and between dialysis sessions (11,12). Despite the advancements in medical care and hemodialysis, the mortality rate in such patients is unexpectedly high (13). Hemodialysis adequacy is defined as comparing the condition of patients undergoing hemodialysis with the condition of healthy people in terms of renal function (11). Hemodialysis inadequacy is one of main causes of death in patients with ESRD (14). The results of studies conducted in Iran on dialysis adequacy showed that it was low in half of the patients (15-17). Unlike other countries, the length of hospitalization in Iran increases every year after starting dialysis (18). Through modifying factors influencing hemodialysis adequacy, negative consequences, hospitalization length and treatment costs are greatly reduced, and also the quality of life in patients with hemodialysis will increase (16,19). Factors influencing hemodialysis adequacy are high flux filter, increased BFR, number of hemodialysis sessions, increased fluid flow rate and hemodialysis time (6,20,21). Various studies have shown that in addition to several patient-related factors (e.g., hypotension, weight over 100kg, decreased duration of dialysis due to intolerance and BFR below350 ml/min), the experience of nurses who provide hemodialysis is also one of the barriers to adequate dialysis (22). A marker commonly used for hemodialysis adequacy is the Kt/V ratio. The most important factors affecting Kt/V are blood flow and the fluid flow rate (23). It has been shown that a 30% increase in BFR results in a 23% increase in urea clearance while decreasing BFR can reduce hemodialysis adequacy (24–26). Studies carried out by Borzu et al (27), Ryan et al (28) and Rafik et al (29) have shown that an increase in BFR increases hemodialysis adequacy. Studies have detected that an increase in the dialysate fluid flow rate can increase dialysis adequacy through filtration of more urea from blood during hemodialysis (30–35). However, the study by Ward et al, showed that increasing the hemodialysis flow rate over 600 mL/min had no effect on Kt/V and increased water consumption by 25% (36). The use of the stepwise fluid flow profile of hemodialysis is a paradigm method that supplies a higher concentration of urea with a higher flow of gradients and increases the value of urea clearance. The stepwise dialysis fluid flow profile is designed for hemodialysis fluid flow. This method includes ten columns in advanced hemodialysis devices. Fluid flow is highest in the first column and is set to the lowest in the last column. Therefore, the device automatically reduces the amount of fluid stepwise from the highest to the lowest desired level.

Objectives

Given the 15% increase in the number of hemodialysis patients in Iran (8) and to improve the quality of life and life expectancy in these patients, it is required to carry out studies on the effect of various factors on hemodialysis adequacy. Therefore, this study was conducted to investigate the effect of the stepwise fluid flow profile with increased BFR on hemodialysis adequacy.

Patients and Methods

Study design and participants

This cross-over clinical trial was conducted on 34 patients in a hemodialysis center under the supervision of the Qazvin University of Medical Sciences, Qazvin, Iran, (February to June 2018). The patients were selected using the simple random sampling method based on inclusion criteria. The sample size was calculated using the Cochrane formula and based on the related literature (27,30) with 95% confidence interval.

Inclusion and exclusion criteria

The inclusion criteria were age above 18 years, undergoing hemodialysis three times per week, at least a three-hour hemodialysis session, history of hemodialysis for more than three months, having a fistula, hemodialysis tolerance and willingness to participate in the study, no history of acute cardiac failure, active infection, mental disorder and stress in the past month and no drug addiction. The exclusion criteria were hypotension, hemodialysis complications and hemodialysis time below three hours.

Intervention

A cross-over clinical trial was used in two phases to reduce the influence of confounding variables including body mass index (BMI), weight, gender and vascular access. In this design, each patient serves as their control and also the optimal crossover design is statistically efficient and requires fewer subjects compared to non-crossover designs (37). Thirty-four patients who were referred to the hemodialysis center were selected randomly based on the inclusion criteria. They were allocated randomly into two groups, each with 17 subjects. The patients were undergoing hemodialysis by two methods in each phase. The first method was routine hemodialysis with common conditions (patient's BFR and a 500 mL/min dialysate flow rate). The second method was the stepwise fluid flow rate profile with increased BFR. In the cross-over plan, the hemodialysis methods were exchanged in the phases.

The first phase

It consisted of four sessions of routine hemodialysis followed by four sessions of the stepwise fluid flow rate profile with increased BFR.

The second phase

It consisted of four sessions of the stepwise fluid flow rate profile with increased BFR followed by four sessions of routine hemodialysis.

In the first phase, one group was randomly allocated to the intervention and the other group received routine hemodialysis. In the second phase, the treatment methods were changed between the groups. The results of the two types of treatment in each group and between the groups were compared. There was a six-day period of washout between the methods. After completing the demographic information sheet for each patient, they underwent hemodialysis with both methods and therefore, confounding factors were controlled.

All the patients in the phases received hemodialysis machine. This machine had a Kt/V online calculation software. Before the start of each treatment session, numerical values of height, dry weight, dialysis time, target Kt/V and gender for each patient were entered in the device to calculate Kt/V. In each session of hemodialysis, temperature was set as 37°C along with soluble bicarbonate dialysate (dialysate constant concentration and 138 meq/L sodium concentration). Other parameters were kept constant for each patient, such as hemodialysis shift, ultrafiltration rate, use of drinks containing caffeine before and during hemodialysis, diet and administration of antihypertensive medications before hemodialysis. In the first phase, 17 patients received four sessions of routine hemodialysis with a 500 mL/min hemodialysis solution flow rate since patient's routine BFR was conducted without any change in the other parameters. The other 17 patients received four sessions of hemodialysis through the stepwise fluid flow rate profile. Thus, the hemodialysis solution flow rate was set initially at 800 mL/min, which automatically and step by step decreased to 500 mL/min at the end of hemodialysis. Additionally, BFR increased by 20% in patients with a weight above 65 kg, and by 15% in patients with a weight below 65 kg, which was added to the patient's routine BFR. In the second phase, the treatment methods were changed between the groups. All the patients were evaluated for the complications of hemodialysis before and after each dialysis session. In the cases of hemodynamic impairment and clinical symptoms, the pump was reduced and the patient was excluded from the study. In this study, two patients were excluded due to intolerance. Accordingly, two patients were excluded due to acute infection and lack of completing hemodialysis sessions. The hemodialysis machine showed the progression of Kt/V in the forms of numerical and diagram on the screen from the beginning to the end of hemodialysis. After each hemodialysis session, Kt/V was recorded in the checklist and the results of the two treatment methods were compared. All stages of patient selection, random allocation and implementation of interventions on patients were performed by the researcher (Figure 1).

Ethical issues

The research followed the Tenets of the Declaration of Helsinki. This paper was extracted from the thesis of Afsaneh Dashti, Department of Nursing and Midwifery, the Qazvin University of Medical Sciences. Moreover, the study protocol was registered in the Iranian Registry of Clinical Trials (identifier: IRCT20180407039218N1; https://www.irct.ir/trial/31405). This study was approved by the ethics committee affiliated with the Qazvin University of Medical Sciences (the ethics committee reference number: QUMS.REC.1396.418). All the participants were informed of the process of the study and informed consent forms were signed.

Statistical analysis

Descriptive analysis, frequency, mean and standard deviation (SD) were used to describe the participant demographic variables. The Shapiro-Wilk and Mann-Whitney U tests were used to evaluate the normality of data. Paired t test and independent t tests were applied to compare the methods. The obtained data were analyzed using the SPSS version 24 software. The significance level was set as $P < 0.05$.

Results

Participant characteristics

The demographic characteristics of the patients are summarized in Table 1. The mean age of the subjects was 60.2 years (±16.3). The majority of them (64.7%) were male and the mean duration of hemodialysis in the patients was 46.6 months. Diabetes and hypertension were the most common (38.3%) causes of ESRD.

Dialysis adequacy in each group

The mean score of hemodialysis adequacy was 0.89 in the routine method and 1.26 in the profile with increased BFR in the first group (17 patients). There was a statistically significant difference between the two methods. In the second group (17 patients), a significant difference was reported in terms of hemodialysis adequacy between the

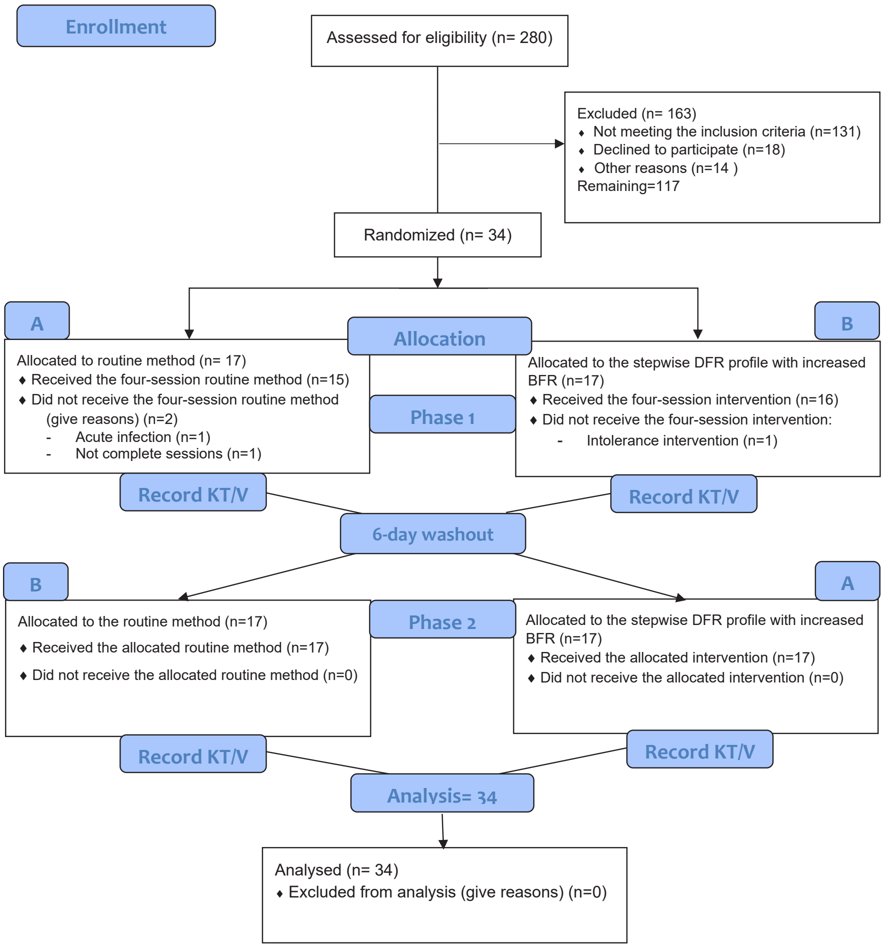

Figure 1. The CONSORT flow diagram.

routine method (0.9) and the stepwise fluid flow rate with increased BFR (1.2). The comparison of the two groups showed that the mean of hemodialysis adequacy increased in the stepwise fluid flow rate profile with increased BFR (Table 2).

Total hemodialysis adequacy

All the patients were arranged in the routine and intervention groups, regardless of priority. The mean of hemodialysis adequacy was 0.94 in the routine method and 1.25 in the stepwise fluid flow rate profile with increased BFR (Table 3). Increasing hemodialysis adequacy in the stepwise fluid flow rate with improved BFR compared with the routine method was confirmed by the independent and paired statistical t-tests. The findings showed that the Kt/V mean was not acceptable in the patients undergoing the routine method. However, the Kt/V mean was above 1.2 in the patients undergoing the stepwise fluid flow rate profile with increased BFR (Figure 2).

Discussion

Inadequate hemodialysis can impair quality of life, shorten life, decrease life satisfaction, and increases mortality rate in patients with ESRD undergoing hemodialysis.

Table 1. The demographic characteristics of the patients

Demographic Characteristics	Age (y)		Gender		Height (cm)		Weight (kg)		ESRD Etiology			Hemodialysis Duration	Sessions
	Mean	SD	Male	Female	Mean	SD	Mean	SD	DM	HTN	DM+HTN	Month	
Group 1	63.05	14.2	70.5%	29.4%	164.4	9.4	66.2	12.6	23.5%	23.5%	41.1%	42.8	136
Group 2	57.2	18.2	64.7%	35.2%	166.5	9.1	61.3	14.04	11.7%	35.2%	35.2%	50.5	136
Total	60.2	16.3	64.7%	35.3 %	165.5	9.1	66.2	13.1	17.06%	29.4%	38.3%	46.65	272

Table 2. The mean Kt/V of the two treatment methods in the two groups

Kt/V Score	Treatment Method			
	Routine Method		Stepwise DFR profile with increased BFR	
	Mean	SD	Mean	SD
Group 1	0.89	0.17	1.26	0.07
Group 2	0.99	0.11	1.25	0.2
Independent *t* test	T= -1.5, *P*= 0.07		T = 0.09, *P* = 0.9	

Abbreviations: DFR, descending fluid rate; BFR, blood flow rate.

Table 3. The total mean Kt/V in the two methods

Tteatment Method	Kt/V Score		Independent *t* test
	Mean	SD	
Routine method	0.94	0.15	
Stepwise DFR profile with increased BFR	1.25	0.17	*t* = -7.78, *df* = 66, *P* < 0.001
Paired t test	t= -7.9, df = 33, P < 0.001	t = 0.09, P = 0.9	

Abbreviations: DFR, descending fluid rate; BFR, blood flow rate.

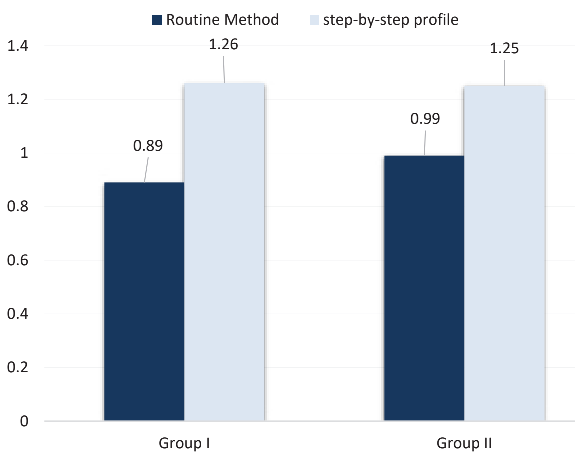

Figure 2. The Kt/V mean of the two methods in the two groups.

Therefore, applying methods that can enhance dialysis adequacy is essential (23). The findings of this study showed that hemodialysis adequacy in this center was less than the international standard, which has been supported by some studies in Iran (15-17). The result of this study also showed that the mean of hemodialysis adequacy was 0.9 in the routine method and 1.2 in the stepwise dialysate flow rate profile. It is essential to design a highly adequate safe hemodialysis method. According to the paired *t* test, the stepwise dialysate flow rate with increased BFR enhanced hemodialysis adequacy. Salehi et al studied the effects of increasing the hemodialysis flow rate as the stepwise hemodialysis flow rate profile on hemodialysis adequacy. They reported that the stepwise hemodialysis flow rate could increase the distribution of urea as well as clearance of waste and poisons in the blood, which improved hemodialysis adequacy (30). In this study, the stepwise dialysate flow rate profile with increased BFR was used. It should be considered that BFR increased by the percentage of patients' weight and the pump rate was different in patients. However, in the study by Salehi et al, only the stepwise hemodialysis flow rate profile with constant BFR (300-350) was used (30). Some studies showed that the increase of the hemodialysis flow rate enhanced adequacy through increasing urea filtration (32–35). As Ward et al used a linear profile for increasing the fluid flow rate in dialysis, water consumption was increased. Therefore, increasing hemodialysis time was a more suitable alternative (36). In our study, the descending stepwise hemodialysis flow rate profile was used and thus less water was consumed. In the study by Azar et al, increasing the hemodialysis flow rate significantly increased Kt/V only in the high flux dialyzer. However, in our study, hemodialysis adequacy increased despite using low flux filters; high flux filters could not be used in all patients as it was not cost-effective. In this study, increased BFR was associated with high hemodialysis adequacy. These results are consistent with those of previous studies (33). The rate of metabolite's diffusion increased by high BFR. As a result, electrolytes and poisons were more quickly removed from the blood flow, which ultimately increased hemodialysis adequacy (36-39). Previous studies showed that increase of both BFR and the hemodialysis flow rate increased hemodialysis adequacy in an effective manner. Therefore, the application of these methods is effective on hemodialysis adequacy. This study evaluated the effect of the synchronic use of the stepwise fluid flow rate with increased BFR on hemodialysis adequacy. The results showed significant differences between the two methods.

Conclusion

The synchronic use of the stepwise profile of the dialysis fluid flow rate with increased BFR improved adequacy of hemodialysis. Therefore, application of this method based on patients' tolerance is suggested.

Strengths and limitations

The patients were selected from a specific hemodialysis center that should be taken into consideration when interpreting the results. The intervention using the cross-over design was the strength of this study.

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Authors' contribution

AD and SH were the main investigators, collected the data and wrote the first draft. MM analyzed the data. SH led the team and designed the study, and also read and corrected the first draft. FG collected the data and helped in writing the draft. NS collected the data and wrote the final draft.

Conflicts of interest

The authors declare that they have no conflicting interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, and double publication) were completely observed by the authors.

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