

## **A comparison of adequacy and complications of hemodialysis: A quasi-experimental study.**

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### **Abstract**

**Background:** Hemodialysis, as one of the most commonly used chronic renal failure treatments, increases the level of blood toxins, complications of illness, hospitalized days, imposed costs, and mortality if it does not have the required quality. One of the factors that can be effective in increasing dialysis adequacy in case of patient tolerance and lack of complications is an increasing blood flow, the stepwise profile of dialysis fluid flow. The present study intends to compare these methods in terms of efficiency in increasing the dialysis adequacy against their complications.

**Materials and methods:** In this semi-experimental single-group study, before and after-intervention trials, 22 patients with hemodialysis under the coverage of Special Patients Center in Zabol, who had the criteria to be included in the study were selected by random sampling method and underwent dialysis for 4 sessions using routine methods, increasing blood flow, stepwise profile of dialysis fluid flow, while maintaining all parameters (such as the type of fluid, type and concentration of dialysis fluid, shifts, etc.). At the beginning and the end of the each dialysis session in two methods, the BUN sample was taken before and after dialysis to study the adequacy of dialysis. During the 12 sessions of dialysis, patients were examined before dialysis in terms of lack of hypertension and some symptoms including nausea, vomiting, muscle cramps and other symptoms and then they were monitored directly every 30 min for hypertension, nausea, vomiting, muscle cramps, headaches, and so on.

**Results:** The mean score of adequacy of dialysis was  $0.834 \pm 0.22$  in the routine session,  $1.19 \pm 0.45$  in the method of increasing blood flow and  $1.07 \pm 0.35$  in the stepwise profile of dialysis fluid flow, and there was a significant difference between the mean score of dialysis adequacy in routine session and each method of increasing blood flow and stepwise profiles of dialysis fluid flow using paired t-test ( $p=0.001$ ). The results from Cochran statistical test showed that there is a significant difference between the routine methods, an increase in blood flow, stepwise profile of dialysis fluid flow profile in terms of the frequency of muscle cramp during hemodialysis ( $p<0.05$ ) and this difference was statistically significant between the routine session and an increase in blood flow based on McNemar test ( $p=0.021$ ). Based on the McNemar statistical test, the difference in headache frequency during hemodialysis was significant between the routine session and the stepwise profile of fluid flow ( $p=0.039$ ).

**Conclusion:** Although the increase in blood flow and dialysis fluid flow in the stepwise method leads to an increase in the adequacy of dialysis, but they are not safe due to their complications and side effects.

**Keywords:** Blood flow increase, Stepwise profile of dialysis fluid flow, Dialysis adequacy, Complications during hemodialysis.

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### **Introduction**

Today chronic kidney disease is a major public health problem in the world. According to available statistics in Iran, the overall prevalence of chronic kidney disease (CKD) in Iran is 15.4% [1]. Hemodialysis is the most common treatment for these patients. The main goal of hemodialysis is the adequacy and safety of dialysis therapy in such a way that the physical

condition of patients is improved and future problems and complications associated with uremia are prevented [2,3]. One of the most important reasons for mortality in hemodialysis patients is dialysis inadequacy. Inadequacy of dialysis can cause complications such as inappropriate nutrition, nausea, vomiting, anorexia, hypoalbuminemia, restless leg syndrome, insomnia, hypertension, pericarditis, electrolyte imbalance, and headache [4]. High adequacy of dialysis can relieve these

complications [5]. KT/V is the most common marker for dialysis adequacy. KT/V can be adjusted by dialysis adequacy, dialysis period, frequent dialysis, blood flow, and dialysis fluid flow. However, increased dialysis period and time is not recommended for patients due to lack of dialysis machines, and High Flux dialyzers are not suggested due to cost-effectiveness and intolerance for patients [6,7]. Therefore, increase of the blood flow and dialysis fluid flow seems to be appropriate.

The boundary layer resistance of filter and inappropriate distribution of dialysis fluid flow are among the important factors limiting the intake of sufficient urea during dialysis. Based on previous studies, including the Leypoldt study, increasing fluid flow from 500 to 800 mL/min increases the urea intake in filter (KoA) [8] and improves the adequacy of dialysis. Salehi [7] states that, among the suitable methods for increasing the fluid flow of dialysis, is stepwise profile of dialysis fluid flow which economically does not lead to a 25% water loss compared to the linear increase in fluid flow of dialysis and, with higher incidence of gradient, provides higher concentration of urea release and increases the amount of urea clearance. The study of Sun in 2016 also indicates that increase of dialysis flow rate to 700 mL/min can significantly increase the adequacy of dialysis. Then it is better to consider it in patients who do not achieve dialysis adequacy with increasing of time and blood flow rates [9]. Studies by Yan, Frank, Ward and Hauk [10-13] also show that increased fluid flow of dialysis can increase dialysis adequacy. However, studies by Azar [14] Ward [15], and Albalate [16] emphasize the low benefits of this method.

There is contradictory evidence regarding the increase in blood flow as one of the effective parameters in the adequacy of dialysis. As some studies suggest one of the factors that can increase dialysis adequacy without increasing time and additional costs is the increase in the rate of blood flow delivered to the hemodialysis apparatus [6]. Hariprasad et al. also found that high blood flow rate is a tool for achieving dialysis adequacy and is associated with improved survival in end stage renal disease (ESRD) patients [17]. Shahdadi et al., Borzue et al. and Kim et al. in their research showed that increased blood flow to 15- 25% of previous blood flow is more effective in achieving dialysis adequacy [6,18,19]. However, increasing blood flow can also result in inability to achieve proper adequacy depending on the type of vascular access and factors such as hypotension and muscle cramps followed by intolerance to continue dialysis [7].

Given the limited and contradictory evidence regarding the effectiveness of methods for increasing blood flow and dialysis fluid flow to improve the adequacy of dialysis, as well as the lack of study on the complications during hemodialysis, each of the methods for increasing blood flow and stepwise increasing of fluid flow of dialysis, the present study intends to compare these two methods (increasing blood flow rate and stepwise profile dialysis fluid flow) in terms of the effect on dialysis adequacy and complications during hemodialysis.

## Methods

The present study is a semi-experimental single-group research before- and after- intervention trials aimed at comparing the adequacy of dialysis and hemodialysis complications between two methods of increasing blood flow and stepwise increase of fluid flow of dialysis in dialysis center of imam Khomine in Zabol city in the year 2016-2017 on 22 hemodialysis patients. It should be noted that the sample size was obtained using the following statistical formulas and a reference study [7].

First, the researcher selected patients based on inclusion criteria included: being in final stage of renal disease, 3 dialysis per week and 4 h per session, after at least 6 months from the onset of hemodialysis, having Fistula, tolerance in dialysis sessions, the ability to participate in the implementation of the plan, the absence of cardiopulmonary disease and acute illness, ultrafiltration less than 3 L, age over 15 y, hemoglobin more than 10 mg/dL. Twenty-two patients were randomly selected and after the introduction and explanation of the purpose, methodology and obtaining written consent, the study was performed in 4-stages during 3 sessions. In the first stage, all samples were dialyzed for 4 sessions with routine method with blood flow characteristics of 250 and low flux filter and dialysis fluid flow with 500 mL/min, and then 4 sessions with increasing blood flow, so that for patients with weight approximately 65 kg, patients underwent dialysis while stabilizing other parameters of the routine method, and in the third stage, all units underwent dialysis while stabilizing other parameters for 4 sessions was dialyzed by stepwise profile dialysis fluid flow method. According to Salehi's study, stepwise fluid profile of dialysis fluid flow is one of the methods for increasing fluid flow of dialysis [20]. In the present study, adjusting stepwise profile of dialysis fluid flow was done manually, so that the fluid flow of dialysis was adjusted to 800 mL/min in the first hour, and then gradually decreased over the next hours, so that it was adjusted to 700 mL/min in the second hour and in 600 mL/min in the third hour and 500 mL/min in the fourth hour.

Also, before all sessions, patients were examined for temporary exclusion criteria, including anti-cramp drugs, nausea, vomiting and blood pressure, 4 hours prior to the study, having blood pressure greater than 140/190 and less than 60/100 mm Hg at the beginning of hemodialysis, smoking one hour before hemodialysis, having nausea, vomiting and muscle cramps before each session and changing the diet during the study and they were removed from the study if they had these criteria. They were studied again at the next session. In all sessions, units of research before the onset of dialysis to the end of it were directly monitored to study complications. It should be noted that in each session, a B. Braun hemodialysis machine with a dialysis solution, bicarbonate dialysis solution, a constant concentration of dialysis solution at a temperature of 37°C, and a concentration of 140 mEq/L were used for all research units. Also, variables such as hemodialysis shifts, ultrafiltration rate, consumption or non-consumption of caffeine beverages before and during hemodialysis, diet, consumption or non-consumption of antihypertensive drugs

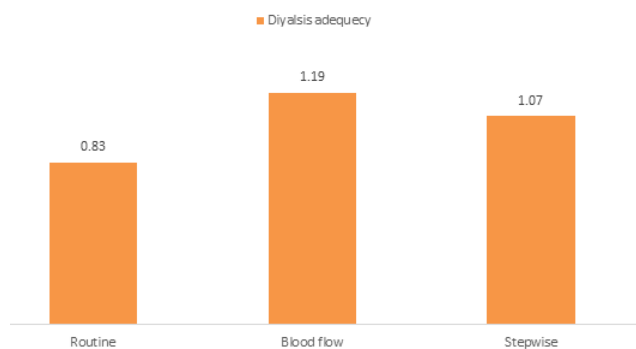
before dialysis were kept for each patient individually. Furthermore, at the beginning and end of last session at each stage, a blood sample for each of the units was taken to determine the adequacy of dialysis. The result of the BUN test was used before and after the fourth session of each step and the weight value before and after dialysis (at the fourth session) was used to determine the adequacy of dialysis using the KT/V criterion with the Daugirdas2 formula.

**Data analysis**

Data analyses were done using the SPSS software Version 22. All categorical variables were summarized using frequencies and proportions. Cochran statistical test was used to determine the associations between routine sessions, blood flow increase, and stepwise profiles of dialysis fluid flow. Other statistical used tests included: paired statistical t-test, paired t-test and Bonferoni correction, and McNemar statistical test. P-value less than 0.05 was considered as significant level.

**Results**

The mean value of adequacy of dialysis in routine condition was  $0.834 \pm 0.22$ , which increased in blood flow method to  $1.19 \pm 0.45$  and in the stepwise profile of fluid flow of dialysis reached to  $1.07 \pm 0.35$  (Figure 1). A paired statistical t-test showed a significant statistical difference between the mean value of dialysis adequacy in routine session with each of the methods for blood flow increase and stepwise profile of fluid flow of dialysis ( $P < 0.005$ ). There was no significant difference between the mean value of dialysis adequacy of the method of blood flow increase and the stepwise profiles of fluid flow of dialysis according to the paired t-test and Bonferoni correction ( $p > 0.005$ ) (Table 1).



**Figure 1.** Compare the dialysis adequacy in three methods.

The frequency percentage of hypotension in the routine session was 9.1%, which increased by 18.2% in the method of blood flow increase. Moreover, Hypotension rate was 18.2% in the stepwise profile of dialysis fluid flow which had an increase compared to routine method, but the results of the Cochran test showed that there is no statistically significant difference between routine sessions, blood flow increase, and stepwise profiles of dialysis fluid flow ( $p > 0.05$ ).

The frequency percentage of headache was 31.8% in the routine method, and in the methods of blood flow increase and

stepwise profiles of dialysis fluid flow increased to 36.4% and 63.4%, respectively. The results of the Cochran statistical test showed that there is a significant difference between the routine methods, blood flow increase, the stepwise profile of dialysis fluid flow profile of dialysis in terms of headache frequency during hemodialysis ( $p < 0.05$ ) which, based on the McNemar statistical test, the frequency difference of the headache during hemodialysis was significant between routine method and stepwise profile of dialysis fluid flow ( $p = 0.039$ ).

The frequency percentage of muscle cramp was 9.18% in the routine method which increased to 45.5% in the method of blood flow increase and increased to 18.2% in the stepwise profile. The results of the Cochran statistical test showed that there is a significant difference between the routine methods, the increase in blood flow, the stepwise profile of dialysis fluid flow profile in terms of the frequency of muscle cramp during hemodialysis ( $p < 0.05$ ). According to McNemar test, this difference was significant between the routine method and the increase in blood flow ( $p = 0.021$ ).

The results showed that the frequency of nausea was 4 (18.2%) patients in routine method, which decreased to 1 person (4.5%) in the methods of increase in blood flow and stepwise profile of dialysis fluid flow. The results of the Cochran test showed that there is no statistically significant difference between the routine methods, increase in blood flow, and stepwise profile of dialysis fluid flow in terms of the frequency of nausea during hemodialysis ( $p > 0.05$ ).

**Table 1.** Comparison of mean value of dialysis adequacy of routine sessions, increasing blood flow rate, stepwise profile of dialysis fluid flow.

Variable	Dialysis adequacy	Mean variations	Significance level
Routine	$0.834 \pm 0.22$	-0.364	<0.001
Increasing blood flow rate	$1.19 \pm 0.45$		
Routine	$0.834 \pm 0.22$	-0.245	<0.001
Descending profile	stepwise $1.07 \pm 0.35$		
Increasing blood flow rate	$1.19 \pm 0.45$	0.119	0.172
Descending profile	stepwise $1.07 \pm 0.35$		

The results showed that the frequency of nausea was routine in 4 (18.2%) patients, which decreased to 1 person (4.5%) in the methods of increasing blood flow and progressive profile of dialysis fluid flow. The results of the Cochran test showed that there is no statistically significant difference between the routine methods, increased blood flow, dialysis fluid flow profiles in terms of the frequency of nausea during hemodialysis ( $p > 0.05$ ).

The results showed that in a total of 4 routine sessions, 1 person (4.5%) had vomiting and none of the patients experienced vomiting in blood flow increase method, stepwise profile of dialysis fluid flow.

## Discussion

The findings of this study showed that the mean score of patients' dialysis adequacy was 250 and 500 ml/min,  $0.83 \pm 0.22$ , in routine session (before intervention) using low flux filter and blood flow and dialysis fluid and all patients in this stage had less than  $\frac{1}{2}$  dialysis adequacy. Studies by Kavyannejad, Shahdadi, Farhadi, Hashemi, Beladi, Mogharab also showed that most dialysis patients of dialysis centers in Iran do not have the least required dialysis adequacy which is consistent with our study [5,21-25]. Also, a study by Baral [3] states that more than half of the hemodialysis patients do not achieve dialysis adequacy with the usual dialysis method that is in agreement with our study.

In the present study, with an increase in blood flow, the mean value of dialysis adequacy reached to  $1.19 \pm 0.45$  which was significantly higher than routine method ( $P < 0.001$ ). The study of Nafar et al. in 21 provinces of Iran also showed that patients with higher dialysis adequacy had high blood flow [26], which is consistent with our study. Our study is also in agreement with the study of Borzuo et al. in terms of effective improvement of dialysis adequacy by interfering with increase in blood flow. Chang et al also found that patients with a blood flow greater than 250 ml/min had higher dialysis adequacy than patients with a blood flow rate of 250 ml/min [27]. A study by Gutzwiller entitled "Increasing blood flow increases  $kt/V$  (urea) and potassium removal" but fails to improve phosphate removal" is also in agreement with our study in terms of significant increase in the adequacy of dialysis with increase in blood flow. A study by Kim et al. also showed that the mean value of dialysis adequacy ratio increased significantly after 15-20% increase in blood flow [28]. In his study, "A study of the extracorporeal rate of blood flow and blood pressure during hemodialysis," Hariprasad states that low rate of blood flow is associated with low dialysis adequacy, and vice versa [17].

Given the fact that the amount of clearance depends on the amount of blood flow of filter, by increasing blood flow rate in a filter with a specific  $K_0A$ , clearance can be increased by producing the highest emission levels in the metabolic substances and accelerate the removal process of electrolytes and waste materials. Therefore, increasing blood flow rate by 15 to 20% of the initial blood flow can increase the adequacy of dialysis.

The mean value of dialysis efficacy was  $1.07 \pm 0.35$  in the stepwise profile of dialysis fluid flow and based on the paired statistical t-test, stepwise profile significantly increased dialysis adequacy. The results of this study were consistent with the findings of a study by Salehi et al. that studied the effect of stepwise profile of dialysis fluid flow as one of the methods increasing fluid rate of dialysis on dialysis adequacy ( $p=0.001$ ) [7]. Studies by Sun, Yan and Behimani also showed an increase in the adequacy of dialysis with increasing fluid rate of dialysis [9,10,29].

The results of this study show that each of the methods of increasing blood flow rate, increasing fluid flow of dialysis

(stepwise profiles) can effectively increase the adequacy of dialysis, while studies by Albalt and Ward showed that increase in fluid flow is not appropriate to increase dialysis adequacy [15,16], and a study by Asef also states that increasing fluid flow in dialysis improves the efficiency of clearance, not increasing blood flow rate [12]. The reason for the difference in these studies is the use of different filters during intervention, however, in our study the same filter was used in routine methods, increase in blood flow and stepwise profile of dialysis fluid flow. Due to the increase in dialysis adequacy with both blood flow rate and stepwise profile of dialysis fluid, the least complicated procedure should be considered in choosing any of these methods to increase the adequacy of dialysis.

Results showed that 9.1% of the patients had hypotension in the routine method, and hypotension increased in the method of increase in blood flow and stepwise profile of dialysis liquid flow, so that 18.2% of the patients had hypotension. Cochran statistical test showed no significant difference between the routine sessions, increase in blood flow, stepwise profile of dialysis fluid flow in terms of hypotension ( $p=0.23$ ). In the studies by Shahdadi and Claudia, after the intervention in increased blood flow, the frequency of hypotension was 20.2% and 28.2%, respectively [7,30]. Despite the fact that the current study used higher blood flow than the above studies, the incidence of hypotension was lower. In this regard, Hariprasad states in his study in 2007 that research findings do not support this logic that by increasing blood flow (blood flow rate), decreased blood pressure rises up, resulting in increased coronary, renal and organs' hematopoiesis, but it is higher than systolic blood pressure and low blood flow (200 mL/min) over high blood flow (400 mL/min) [17]. On the other hand, factors such as the occurrence of multiple diseases, age and sex are factors that can affect the blood pressure that can be the cause of this difference [7]. The findings showed that the only complication of 15-20% increase in blood flow was muscle cramp. The results from studies by Shahdadi and Alice are in agreement with the results of the present study in terms of lack of significant difference in the incidence of hypotension, nausea, vomiting and headache before and after the increased blood flow intervention. However, they are not in agreement with present study in terms of significant increase in muscle cramp with increasing blood flow.

The findings also showed that the frequency of headache in the routine method was 31.8%, and during the intervention, the stepwise profile of dialysis fluid flow was 63.4%. The McNemar statistical test showed that the stepwise profile of dialysis fluid flow has a significant increase in headache compared to the routine method ( $p=0.03$ ), which is consistent with the study of Shahdadi [31]. Shahdadi states that, since from the beginning of dialysis, high fluid flow is used for dialysis during stepwise profile, at this high speed, toxic and accumulated substances appear to be discharged at a higher rate from the body, and this rapid decrease in plasma urea at the beginning of dialysis reduces osmolality of the plasma and presents the probability of syndrome imbalance. Most of the implications are that the imbalance syndrome is related to

increase in brain water content when the plasma solubility level decreases rapidly during dialysis. Clinical manifestations of imbalance syndrome are similar to the symptoms of cerebral edema and increased ICP, which can include nausea and vomiting, dizziness, high blood pressure, headache, and so on [31,32].

## **Conclusion**

In general, the findings of this study showed that the stepwise profiles of dialysis fluid flow and increased blood flow are associated with increased frequency of headaches and muscle cramp, respectively. Therefore, it is recommended that, despite increasing dialysis adequacy with methods of increase in blood flow and stepwise profiles of dialysis due to their complications, other methods such as increasing dialysis time and period, high efficiency filters, ascending stepwise profile of dialysis fluid flow should be used.

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