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**Research Article**

# Effect of Ascending and Descending Stepwise Dialysate Flow Rate Profileson Adequacy and Complications of Hemodialysis

**Hosien Shahdadi[1], Maryam JahantighHaghighi[2],**
**Abdolghani Abdollahimohammad[3]and Mahdieh PoodinehMoghadam[1]**

[1]Lecturer, Department of Nursing, School of Nursing and Midwifery,
Zabol University of Medical Sciences, Zabol, Iran.
.[2]MSc Student, Student Research Committee, Nursing and Midwifery School
Zabol University of Medical Science, Zabol, Iran
[3]PhD in Nursing, Assistant Professor, Faculty of Nursing & Midwifery,
Zabol University of Medical Sciences,Zabol, Iran
Corresponding Author: Maryam JahantighHaghighi, Msc Student, Student Research Committee,
Nursing and Midwifery School, Zabol University of Medical Science, Zabol, Iran.

## ABSTRACT

**Background and Objective:** In Iran, dialysis adequacy is low in more than 60% of hemodialysis patients.Dialysis inadequacyisa main cause of morbidity and mortality in dialysis patients.Resistance of filter boundary layer and poor distribution of dialysate flow are important factors limitingthe adequacy.Ascending and descending stepwise dialysate flowrate profiles are two methods to improve fluid distribution and dialysis adequacy and each maydiffer with the other in terms of patient comfort andcomplications.

**Methodology:** In this quasi-experimental,single group, pre- and post-intervention research,22 hemodialysis patients covered by the SpecialPatients Center of Zabol were dialyzed through the routine method (dialysate flow rate of 500 min/mL) andascending and descending stepwise dialysateflow rate profiles,while keeping constant all parameters(such as filter type, blood flow rate, type and concentration of dialysate, shift, *etc*.).The patients were dialyzed through each method for 2 sessions. To assess the adequacy of dialysis, BUN was measured at the beginning and end of the second session of each method before and after dialysis.During the sixth sessions of dialysis, patients were checked before dialysis in terms ofblood pressure, symptoms such as nausea,vomiting, muscle cramps,headaches, and other symptoms andthen their blood pressure, nausea, vomiting,muscle cramps, and headaches were directly monitored every 30 minutes.

**Findings:** The mean score of dialysis adequacy was 0.834±0.22 in the routine method,1.0032±0.28 in the ascending stepwise dialysate flow rate profile, and1.07±0.35 in the descending stepwise dialysate flow rate profile.According to paired *t*-test,the difference between routine and each of the stepwise profiles was significant ($p$=0.000).But there was no significant difference between routine and stepwise dialysate flow rate profile in terms of complications (headache, muscle cramps, nausea, vomiting, *etc*.)($p$<0.05).There was no significant difference between the mean scores of dialysis adequacy in ascending and descending stepwise dialysate flow rate profiles($p$=0.346), however, according to chi-square test, a significant difference existed between these two profiles in terms of complicationssuch as headache ($p$=0.026).

**Conclusion:**The stepwise dialysate flow rate profileis an efficient method for increasing dialysis adequacy andthe ascending stepwise profileis more appropriate to improve dialysis adequacy than the routine method due to insignificant complications,and thanthe descending stepwise profile due to lower complications.

**Keywords:** dialysate flow rate profile, dialysis adequacy, hemodialysis

## INTRODUCTION

Chronic renal failure (CRF) which is defined as glomerular filtration rateof less than 15 mL/min per 1.73 $m^2$ of body surface arearepresents the end-stage renal disease (ESRD) (1).Kidney transplant or dialysis is needed at this stage (ESRD) to sustain life (2,3).At the end of 2014, the number of ESRD patients was estimated at about 3.346 million people in the world.Given

5-6% annual growth of the disease and 1% growth of the population,ESRD is one of the most important problems of health in all countries of the world (4).Over 90% of ESRD patients who need long-term treatment alternative undergo chronic hemodialysis (5).In hemodialysis, a synthetic semi-permeable membrane is used instead of renal glomeruliand tubules to correct water and electrolyte andblood chemicals disequilibrium(3).Despite the fact that hemodialysis is the most important treatment of chronic renal failure and can save patients from certain death,it is associated with some complications that lead toearly dissociation of patientsfrom machinesand hence to inadequate dialysis (6); which can result in turn in high levels of blood toxins andpoor control of clinical symptoms andan increased death rate.In addition, dialysis inadequacy increases the costs of treatment and the duration of hospital stay (7). Therefore, evaluation of dialysis adequacy is one of the important aspects of hemodialysis patientscare(8).Many factors affect dialysis adequacy, including duration of dialysis, dialysate flow rate,use of high level dialyzers,and blood flow rate (9, 22). However, these methods are not recommendeddue to lack of dialysis machines,unaffordability, and intolerance of high coefficientfilters, and intolerance of complications such as hypotension andmuscle cramps (9,10).Some studies show that the boundary layer anddialysate flow misdistributionare the most important factors limiting the removal of urea by dialysis (dialysis adequacy) (11). Also studies carried out by Salehi (2013),Yan (2012), Ward (2001), Hauk(2000), andLeopold (2001) show that an increase in dialysate flowrate can increase dialysis adequacy by filtration of more urea from the blood into the dialysate (9,12-15),however, some studies such as that of Azar in 2009showed that an increase in dialysate flow rate to 800 mL/min is effective only in high flux dialyzers (16).In addition, Ward (2011) showed that increaseddialysate flow rate has no effect on KT/V while water use is increased (17).Albalate emphasizedthe low benefits of this method and stated that the use of high rates of dialysateflow is associated withmuch water consumptionand no benefitsare achieved (18).

Stepwise dialysate flow rate profile is an appropriate methodfor increasing the flow rate of dialysate and in comparison with linear increase of dialysate flow rate, it is economically not associated with waterloss of 25%.The higher the slope, the higher the concentration of urea diffusion and clearance rate. Stepwise dialysate flow rate profile can be applied in two ways of ascending and descending.In the descending stepwise dialysate flow rate profile, thedialysate flow rate is 800 mL/min at the beginning of dialysis and is reduced stepwise during dialysisto reach 500 mL/min at the end of dialysis (1).In the ascending stepwise dialysate flow rate profile, the dialysate flow rate is 500 mL/min at the beginning of dialysis and is increased stepwise during dialysis to reach 800 mL/min at the end of dialysis.Since in the descending method, the dialysate flow rate is high at the beginning of dialysis,it seems that in this fast rate,the accumulated toxins are eliminated more quickly from the body andthe rapid decline in plasma urea can decrease plasma osmolality,imposing the risk of disequilibrium syndrome (3).Perhaps if the ascending stepwise profile is applied, so that the flow rate begins with 500 mL/min, andgradually increases during dialysis,not only the dialysis adequacy may be improved, but also less risk of complications may be imposed.

Since no comparative studywas found regarding the effect of these two different methodsof increasing dialysis flow rate on adequacy andcomplications of hemodialysis,the present study intendsto compare the ascending and descending stepwise dialysate flow rate profiles in terms of their effect on dialysis adequacy andcomplications in hemodialysis patientscovered by the Special Patients Center of Zabol.

## METHODOLOGY

This is a quasi-experimental, pre- and post-intervention study which was carried out in the Special Patients Center of Zabol.A total of 22 patients were enrolled in this study through the census method. The inclusion criteria were ESRD,three 4-hour sessions of dialysis per week,passing at least 6 months after beginning of treatment with hemodialysis,having a fistula, the ability to participate in the project,no cardiopulmonary and acute diseases,age 15 to 65 years,hemoglobin levels of higher than 10 mg/dL,lack of hepatitis, AIDS,septicemia, and chemotherapy, no history of mental disorder andstressful events in recent months,and no drug addiction. First, the necessary explanations were provided to the subjects and they were assured of confidentiality of personal information. Then a written informed consent was obtained from them and a demographic questionnaire was completed through interviewand medical record.After completion of the sample size,ensuring the accuracy of dialysis machines,evaluation of the subjects in terms of temporary criteria of exclusion in each sessionincluding anti-cramp medications, nausea andvomiting, and high blood pressure 4 hours prior to the study,blood pressure greater than 90/140 mmHg andless than 60/100 mmHg at the start of hemodialysis,smoking one hour prior to initiation of dialysis,suffering from nausea, vomiting, and muscle cramps before each session, and changes in diet during the study,the patients were assessed in three situations of routineand ascending and descending stepwisedialysate flow rate profiles, each situation for two sessions.The patients were dialyzed at first through the routine method for 2 sessions withdialysate flow rate of 500 mL/min and blood flow rate of 250 mL/min using the same type of low flux filters.In the second and third stages, all patients were undergone the ascending and descending stepwise dialysate flow rate profiles, respectively, for 2 sessions, where the flow rates were adjusted manually and other parameters were kept constant.In the descending method, the dialysate flow rate was set on 800 mL/min in the first hourand reduced to 700 mL/min in the second hour,600 mL/min in the third hour, and500 mL/min in the fourth hour.In the ascending method, the dialysate flow rate was gradually increased from 500 mL/min to 800 mL/min (500 mL/min the first hour, 600 mL/min the second hour, 700 mL/min the third hour, and 800 mL/min the fourth hour).In all sessions, the patients were monitored from before starting until after the end of dialysis to directly assess the complications.In each session, a B. Braun hemodialysis machine, 37 °C dialysate,bicarbonate dialysate,constant concentration of dialysate, sodium concentration of 140 mEq/L, andsame filterswere used for all patients.In addition, variables such as hemodialysis shift,ultrafiltration rate, dialyzer type,use or non-use of caffeinated drinksbefore and during hemodialysis,diet, use or non-use of antihypertensivebefore dialysis were kept constant separately for each patient.It should be noted that at the beginning and end of the second session in each stage,a blood sample was collected from patients to determine the adequacy of dialysis.The first sample was taken after attaching the dialysis needles before starting dialysis from the arterial lineand the second sample after the end of hemodialysis before dissociation of patientsfrom the machine; so that the flow rate was declined to 50 mL/minand after 15 to 30 seconds,blood was taken from the sampling site of dialysis line. The samples were immediately sent to the lab. The adequacy of dialysis was determined according to the results of BUN and patients' weight before and after the fourth session of each stage using the criterion of KT/V with Daugirdas2 formula.

## RESULTS

A total of 22 hemodialysis patients participated in this study including 13 women (59.1%) and 9 men (40.9%) with a mean age of 43±3.21 years.

The mean score of dialysis adequacy was 0.834±0.22 in the routine method, 1.0032±0.28 in the ascending stepwise dialysate flow rate profile, and 1.07±0.35 in the descending stepwise dialysate flow rate profile. According to paired *t*-test, the difference between routine and each of the ascending and descending stepwise profiles was significant ($p<0.005$) (Table 1).According to paired *t*-test, there was no significant difference in the mean score of dialysis adequacy between ascending and descending stepwise dialysate flow rate profiles ($p=0.346$) (Table 2).The findings showed that systolic blood pressure of patients was 129.86±13, 133.36±15.98, 134.13±19.4, and 138.86±25.25, before, at start, middle, and end of dialysisin the routine method, respectively; 129.09±11.95, 132.63±14.7, 139.86±20.6, and 144.54±25.8, before, at start, middle, and end of dialysis in the ascending stepwise dialysate flow rate profile, respectively; and 129.54±14.76, 134.36±17.6, 144.63±19.2, and 145.36±23.1, before, at start, middle, and end of dialysis in the descending stepwise dialysate flow rate profile, respectively.Changes in systolic blood pressure during dialysis in the routine method andstepwise profileshad an increasing trend,however they were not statistically significant ($p>0.05$).Also, none of the patients had hypotension.During the two sessions of routine dialysis, 10 cases of headache, 2 cases of muscle cramp, and 2 cases of nausea without vomiting were reported;while in the two sessions of ascending dialysate flow rate profile, there were 15 cases of headache, 4 cases of muscle cramp, 3 cases of nausea without vomiting, andone case of itching. In addition, 20 cases of headaches and 2 cases of muscle cramps were reported in the two sessions of descending dialysate flow rate profile.The results showed that headache was occurred more in the descending stepwise profilethan the routine method and the ascending stepwise profile.No significant difference was observed between the routine method and each of the stepwise profilesin terms of complications ($p=0.750$, $p=0.47$) (Table 3).The chi-square test showed a significant difference between the ascending and descending stepwise profiles in terms of headache incidence ($p=0.026$), but the difference was not significant in terms of other complications($p>0.05$) (Table 4).

**Table 1:** Comparison of the mean of dialysis adequacy between the routine method and the ascending and descending stepwise dialysate flow rate profiles

| Dialysis method | Mean±SD | Significance level (*p*-value) |
|---|---|---|
| Routine (constant flow rate) | 0.0±83.22 | $p<0.05$ |
| Ascending stepwise profile dialysate flow rate | 1.0±003.28 | |
| Descending stepwise profile dialysate flow rate | 1.0±07.35 | |

**Table 2**: Comparison of the mean of dialysis adequacy between the ascending and descending stepwise dialysate flow rate profiles

| Mean KT/V | Ascending stepwise profile | Descending stepwise profile | Paired test statistics | | |
|---|---|---|---|---|---|
| | Mean±SD | Mean±SD | *p* | df | *t* |
| | 1.0±003.28 | 1.0±07.35 | 0.34 | 21 | 0.96 |

**Table 3:** Comparison of the mean of dialysis adequacy between the routine method and the ascending and descending stepwise dialysate flow rate profiles

<table>
<tr><th rowspan="2">Variable</th><th colspan="4">Frequency</th><th rowspan="2">McNemar's test</th></tr>
<tr><th>Routine</th><th colspan="2">Ascending profile</th><th>Descending profile</th></tr>
<tr><td>Nausea</td><td>2</td><td colspan="2">3</td><td>0</td><td></td></tr>
<tr><td>Vomiting</td><td>0</td><td colspan="2">0</td><td>0</td><td></td></tr>
<tr><td>Muscle cramp</td><td>2</td><td colspan="2">4</td><td>2</td><td></td></tr>
<tr><td>Itching</td><td>0</td><td colspan="2">1</td><td>0</td><td></td></tr>
<tr><td>Variable</td><td colspan="4">Frequency</td><td>Statistical test</td></tr>
<tr><td rowspan="2">Headache</td><td>1st session routine</td><td>2nd session routine</td><td>1st session stepwise profile</td><td>2nd session stepwise profil2</td><td rowspan="2">Chi-square=0.101, p-value>0.05</td></tr>
<tr><td>4</td><td>6</td><td>7</td><td>8</td></tr>
</table>

**Table 4:**Comparison of the headache rate between the ascending and descending stepwise dialysate flow rate profiles

| Dialysis method | Headache frequency | Chi-square test, *p*-value |
|---|---|---|
| Ascending stepwise profile dialysate flow rate | 15 | $p=0.026$ |
| Descending stepwise profile dialysate flow rate | 20 | |

## DISCUSSION AND CONCLUSION

The findings showed thatthe mean score of dialysis adequacy was 0.834±0.22 in the routine method, 1.0032±0.28 in the ascending stepwise dialysate flow rate profile, and 1.07±0.35 in the descending stepwise dialysate flow rate profile. According to paired *t*-test, the difference between routine and each of stepwise profiles was significant.According to paired *t*-test,the stepwise profile significantly increased the dialysis adequacy.The results of this study were consistent with those of Salehi*et al.* (2014)who studied the effects of stepwise dialysate flow rate profile,as a dialysate flow rate increasingmethod, on dialysis adequacy.Given that urea is more filtrated in the stepwise dialysate flow rate profile, resulting in an improved dialysis adequacy ($p$=0.001) (10),it should be noted that the stepwise dialysate flow rate profile was manually adjusted in the present study. In addition,both ascending and descending stepwise dialysate flow rate profiles were used in this study, while Salehi used only the descending stepwise dialysate flow rate profile. So that, dialysate flow rate was 800 mL/min at the beginning of dialysis and was automatically reduced during dialysis to reach 500 mL/min at the end of dialysis.In addition, the study of Salehihas only addressed the dialysis adequacy while in the present study,complications during hemodialysis and blood pressure in each methodwere directly examined.There is no study about the effect of stepwise dialysate flow rate profileon dialysis adequacy,but Salehi*et al.* (2016) studied the effect of stepwise sodium and ultrafiltration profileon dialysis adequacyand showed an increase in the adequacy of hemodialysis.Many studies have examined the effect of increasing dialysate flow rate on dialysis adequacyand have shown that increased dialysate flow rate increases the adequacy of hemodialysis. Studies of Yan, Bahimani, Leopold, Ossef and Hauk respectively in 2012, 2010, 2001, and 2000 showed thatincreased dialysate flow rate increasesdialysis adequacy by increasing urea filtration(13-15).While the study of Albalate*et al.*(2015) entitled “Is it useful to increase dialysate flow rate to improve the delivered Kt?” showed that an increase in dialysate flow rate from 400 to 500 mL/min increased Ktby 4%and increasing dialysate flow rate from 500 to 700 mL/minincreased Kt by 3%; theseresults were not statistically significant and it seems that linear increase in dialysate flow rate in new dialyzers haslimited benefits and increasing time is a more suitable alternative with less water consumption (18). However, in the present study the stepwise dialysate flow rate profileis used which is recommended according to previous studies, including Salehi (10),to raise the adequacy of dialysis and avoid wasting water.The study of Azarin 2009 entitled “Increasing dialysate flow rate increases dialyzer urea clearance and dialysis efficiency” showed that increasing dialysate flowrate from 500 to 800 mL/min significantly increasedKT/V only in high flux dialyzers, while despite using low flux filters in the present study,dialysis adequacy increased significantly (16).The reason for not using high level filters in this study was that although the use of filters with high ultrafiltration coefficientcan increase dialysis adequacy,they cannot be used in all sessions and for all patientsbecause they are not cost effective and may not be tolerated by patients (9, 10).Other findings of this study showed thatalthough the ascending and descending stepwise dialysate flow rate profilescan provide higher urea filtration by creating a higher gradient flow,lead to a better clearance of blood soluble toxins by raising the amount of ultrafiltration, and provide a same increase in dialysis adequacy, they differ in terms of complications incidence, so that the amount of headache in the descendingstepwise dialysate flow rate profile was higher than the ascending ($p$<0.05).On the other hand, no significant difference existed in the incidence of headache between the ascending stepwise dialysate flow profile and the routine method ($p$>0.05), which indicates the safety of the ascending stepwise profilein increasing dialysis adequacy.Perhaps, a reason for this is the fact thata high dialysate flow rate is used in the descending stepwise dialysate flow rate profile at the beginning of dialysis and it seems that in this fast rate, the accumulated toxins are eliminated more quickly from the body,andthe rapid decline in plasma urea at the beginning of dialysiscan decrease plasma osmolality andpose the risk of disequilibrium syndrome.Disequilibrium syndromeis mainly related to an increase in brain water contentwhen plasma levels of soluble chemicals lowerrapidly during dialysis. The symptoms of disequilibrium syndrome aresimilar to those of brain cells edema and increased ICP and may include nausea and vomiting, dizziness, hypertension, headaches, *etc.* (3,19).

Other findings of the study showed no significant difference between the routine methods andascending and descending stepwise dialysate flow rate profilesin terms of complications, such as nausea, vomiting,muscle cramps, itching, chills and ... ($p>0.05$).In our study, blood pressure increased during dialysis in the routine method and ascending and descending stepwise profiles,and the increasewas not statistically significant.This finding is consistent with thatof Shahdadi (9).While in the study of KavianNejad, blood pressure decreased gradually during dialysis (21).This may arise from this fact that the filters can clear chemicals and drugs thus they can affect the clearance of antihypertensive. On the other hand, after starting dialysis, a considerable amount of blood enters the dialysis lines and hence exits the body,this in turn declines blood supply to the kidney and activates the renin-angiotensin system resulting in an elevated blood pressure (3).

Overall,the stepwise dialysate flow rate profile can effectively increase dialysis adequacy by filtratingmore urea, but it should be noted that which pattern of these stepwise profiles can safely improve dialysis adequacy with no complications.The results showed that the descending stepwise dialysate flow rate profile which is commenced with a highflow rate (800 mL/min) creates more complications and are intolerable for patients,resulting inearly dissociation of patients from dialysis machine and hencehemodialysis inadequacy, while the ascending stepwise dialysate flow rate profile which is also a stepwise method for gradual increase in dialysate flow rate has no significant difference in the incidence of complications with the routine method and can effectively increase dialysis adequacy.

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