Original Article

The Effect of Different Intermittent Intervals of Flushing Extracorporeal Circuits to Dialysis Adequacy and Vital Signs in Heparin Free Hemodialysis

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Abstract

Background: Hemodialysis without anticoagulation can be applied to patients who have high risk of bleeding or the risk of bleeding is more than the loss of blood with clotting in the dialyzer, especially to acute cases. There are different suggestions about flushing time with 0.9% saline solution in the literature.
Aim of the study: The aim of this study is to compare the effect of intermittent intervals of flushing extracorporeal circuits with %0.9 saline solution in 100 ml/15 min and 150 ml/30 min to vital signs (especially blood pressure) and dialysis adequacy in heparin free hemodialysis in ESRD (End Stage Renal Disease) patients.
Methodology: The research is an experimental study. This study was conducted in Gulhane Military Medical Academy Nephrology Department and in a private dialysis center from 1st April 2015 to 30th May 2015. The sample of the study was included total of 22 heparin free hemodialysis patients who had ESRD, met the research criteria and accepted to participate to the study.
Results: There was no significant difference between Kt/V-URR values (used in determining the adequacy of dialysis) of both intermittent intervals of flushing extracorporeal circuits ($p>0.05$). While there was no significant difference between vital signs of both applications, the difference between mean ultrafiltration amount of both applications was significant ($p=0.001$). There was no significant difference between dialyzer clotting degree of both applications ($p=0.122$).
Conclusion: According to our findings, we suggest that while flushing extracorporeal circuits intermittent during hemodialysis treatment in heparin free hemodialysis patients, 150 ml/30 min application can be used instead of 100 ml/15 min.

Key Words: Heparin free hemodialysis; dialysis adequacy; intermittent flushing extracorporeal circuits; end stage renal failure

Introduction

Hemodialysis procedure can be applied with or without heparin (Bozfakioglu, 2003; Doğan & Kırcali, 2011; Çınar, 1995; Laville, *et al.*, 2014). Hemodialysis without anticoagulation can be applied to patients who have high risk of bleeding or the risk of bleeding is more than the loss of blood with clotting in the dialyzer, especially to acute cases. In this instance, except for patients with cardiovascular disease or hypertension, the blood flow rate should be kept on 280-300 ml/min or above and clotting in the extracorporeal circulation is checked by intermittent intervals of flushing with 0.9% saline solution (Doğan & Kırcali, 2011; Kim, 2003; Suranyi & Chow, 2010). Intermittent intervals of flushing with 0.9% saline solution is suggested by European Best Practice for Hemodialysis and performed in many hemodialysis units (Laville *et al.*, 2014; European Renal Best Practice, 2016). It is the application of checking the clotting in the extracorporeal circulation and dialyzer by clamping artery line (by closing the blood entrance) and flushing 100-300 ml of 0.9% saline solution in every 30 minutes. Number of flashings' can be customized depending on the

requirement. The amount of ultrafiltration is increased to prevent overhydration due to 0.9% saline solution given to patients. (Bozfakioglu, 2003; Doğan & Kırcali, 2011; Kim, 2003; Suranyi & Chow, 2010). The purpose of intermittent intervals of flushing with 0.9% saline solution is to be aware of clotting in "Hollow-fiber" dialyzer, to ensure finishing the treatment in time or to exchange the dialyzer promptly to prevent patients' blood by clotting. Flushing with 0.9% saline solution also can reduce the dialyzer clotting tendency and can inhibit clotting formation itself (1). However there are different suggestions about flushing time with 0.9% saline solution in the literature, 100-300 ml of 0.9% saline solution flushing at 20-60 minute intervals is recommended. (Doğan & Kırcali, 2011; Çınar, 1995; Kim, 2003; Holden, Harman, Wang, Holland & Day, 2008; Roma˜o, Fadil, Sabbaga & Marcondes, 1997; Shen, Mitani, Chang & Winkelmayer, 2013; Suranyi & Chow, 2010; Lavaud, Canivet, Wuillai, Maheut, Randoux, Bonnet & Renaux, 2003; McGill, Blas, Bialkin, Sandromi & Marcus, 2005; Ziai, Benesch, Kodras, Neumann, Dimopoulos & Haas, 2005; Caruana, Raja, Bush, Kramer & Goldstein 1987; Sanders, Taylor & Curtis, 1985; Sahota & Rodby, 2014; Stamatiadis, Helioti, Mansour, Pappas, Brokes & Stathakis, 2004; Guéry *et al*, 2014; Schwab, Onorato, Sharar & Dennis, 1987)

Vital signs of heparin free hemodialysis patients must be monitored strictly. It is essential not to let clotting in extracorporeal circulation and dialyzer. Heparin free hemodialysis is a method that requires intensive follow-up (Çınar, 1995). However there is not any study about the effect of intermittent intervals of flushing extracorporeal circuits to dialysis adequacy, vital signs and clotting degree in heparin free hemodialysis patients in the literature.

The aim of this study is to compare the effect of intermittent intervals of flushing extracorporeal circuits in 100 ml/15 min and 150 ml/30 min to dialysis adequacy and vital signs (especially blood pressure) in heparin free hemodialysis and ESRD (End Stage Renal Disease) patients.

Methods

The aim of this study is to compare the effect of intermittent intervals of flushing extracorporeal circuits with %0.9 saline solution in 100 ml/15 min and 150 ml/30 min to vital signs (especially blood pressure) and dialysis adequacy in heparin free hemodialysis in ESRD patients and it is conducted as an experimental study.

This study was conducted in GMMA (Gulhane Military Medical Academy) Nephrology Department and in a private dialysis center from 1st April 2015 to 30th May 2015. The sample of the study was included total of 22 heparin free hemodialysis patients who had end-stage renal failure, met with the research criteria and accepted to participate to the study. There were Fresenius 4008S and Braun Dialogue Hemodialysis machines in one of the research center and the other had only Fresenius 4008S Hemodialysis machines.

The population of the study consisted of 100 patients admitted to two dialysis units in two months. Twenty five patients, who met the research criteria, underwent heparin free hemodialysis and agreed to participate to study, were included to the study. Three patients who wanted to continue the hemodialysis treatment at another center (due to vacations, etc. conditions) did not participate to second application and they were excluded from the study. Consequently the sample of the study was included total of 22 hemodialysis patients.

Data collection forms used in the study were consisted of ''Data Collection Form Devoted to Socio-demographic and Medical Characteristics of Patients'' and ''Data Collection Form Devoted to Biochemical and Medical Parameters in Dialysis Adequacy Assessment of Patients''. Devoted to Socio-demographic and Medical Characteristics data included questions such as socio-demographic characteristics; patients' age, gender, medical characteristics; primary diagnoses, presence of chronic disease, drugs used, how long underwent dialysis of the patients and these data were collected by researcher's face to face interviews. Data Collection Form Devoted to Biochemical and Medical Parameters in Dialysis Adequacy Assessment of Patients contains results of blood samples drawn from patient during the hemodialysis treatment, pre-dialysis, post-dialysis and dry weights of patient, location of hemodialysis vascular access, duration of dialysis, blood flow rate, type of dialyzer, amount of ultrafiltration, blood pressure changes seen during hemodialysis and how many times dialysis treatment received per week. Results of blood samples drawn from patient before and after each application were recorded to these forms. Kt/V, URR, potassium, sodium,

input-output of urea and creatinine, albumin, calcium, phosphorus, hemoglobin and platelet were the results that recorded. Dialysis adequacy of patients was determined due to results. Daugirdas formula was used in Kt/V calculation.

*KtV Daugirdas = -ln[(BUNPost/BUNPre) - (0.008 x hour)] + {[4 - (3.5 x BUNPost / BUNPre)] x UFVol / weight} (http://www.tsn.org.tr/formul).

Clotting classification is based on the amount of visually estimated clotting ‘‘fiber’’ percentage to standardize clotting on dialyzer. First degree of clotting is less than 10% "fiber" clotting, the second degree of clotting is less than 50% clotting, and the third degree of clotting is more than 50% clotting (Bozfakioglu, 2003). Dialyzer clotting degrees was recorded via observation by the same researcher in all applications.

After necessary explanations about the purpose of study and application were made and written consents were taken, hemodialysis of patients' who met the research criteria was conducted by researchers. All patients included to the study were being received hemodialysis treatment for 4 hours and 3 times a week. Blood flow rate was usually maintained between 250 to 300 ml/min in studies related to heparin free hemodialysis (Caruana, Raja, Bush, Kramer & Goldstein 1987; Sanders, Taylor & Curtis, 1985; Sahota & Rodby, 2014; Stamatiadis, Helioti, Mansour, Pappas, Brokes & Stathakis, 2004; Guéry *et al*, 2014). Blood flow rate should be maintained at least 250 ml/min for an adequate dialysis. Keeping the blood flow rate high could help to prevent clotting of the extracorporeal system during hemodialysis. Hollow fiber dialyzers of 1.9 m^2 were used in dialysis sessions of all patients to ensure standardization, blood flow rate and dialyzate flow rate were set to 300 ml/min and 500 ml/min respectively during dialysis and dialysis was performed with bicarbonate. Artery-vein set and dialyzer were flushed with 1000 ml of %0.9 saline solution including 2500 unit pure heparin before starting dialysis. In the first application, artery-vein set and dialyzer were flushed with 100 ml of %0.9 saline solution in every 15 minutes and the 4-hour heparin free hemodialysis were performed. At least one week after the first application, artery-vein set and dialyzer were flushed with 150 ml of %0.9 saline solution in every 30 minutes and second application were performed. Blood samples were drawn according to recent guidelines (European Renal Best Practice, 2016; 2006 Updates Clinical Practice Guidelines and Recommendations) properly before and after hemodialysis (Pre dialysis blood samples were drawn shortly after fistula needles were inserted and before starting dialysis, post dialysis blood samples were drawn at the end of the 4-hour hemodialysis while blood flow rate of dialysis machine were 50-100 ml/min for 15 seconds. All of blood samples were drawn from arterial line.), results of blood samples and vital signs of patients were recorded to data collection forms.

Data about socio-demographic and disease-specific questions were collected by face to face interviews with patients. The conversations were approximately for 10-15 minutes. Data devoted to biochemical and medical parameters in dialysis adequacy and dialyzer clotting degrees were collected twice, including the first and second application.

Statistical Analysis: MS-Excel, SPSS for Windows version 15.00 (SPSS Inc., Chicago, IL, USA) software package was used to evaluate the data and statistical analysis. Means and standard deviations were used for descriptive statistics of continuous numeric variables, while counts and percentages were used for descriptive statistics of categorical variables. Paired-samples t-test was used for normal distributed variables, nonparametric two-sample paired (Wilcoxon) signed rank test was used for variables not normally distributed while comparing variables in two different times (first application and second application that done at least one week later) in dependent group. Mc Nemar test was used for the comparison of discrete variables. One-way analysis of variance (One-way ANOVA) was used for the comparison of results of more than two groups made in different time. $p \leq 0.05$ was considered statistically significant for all measures.

Ethical Consideration

Required written permission and research approval for study was obtained from GMMA Clinical Research Ethics Committee of March 31, 2015 and in accordance with the decree no 50687469-1491-98-15/SEK.1677. After the necessary explanations, "Volunteer Information Consent (Approval) Forms" were signed and "Data Collection Forms" were implemented to patients who accepted participate to the study to collect data.

Results

The mean age of individuals participated to the study was 56±19.22 and 36.4% of them is in the 65 and over age group. Most of the participants were male (63.6%), 36.4% of them had hypertension, 18.2% of them had diabetes mellitus, 63.6% of them has received hemodialysis treatment for 4-60 months.

Table 1: Comparing Kt/V-URR values (used in determining the adequacy of dialysis) of intermittent intervals of flushing extracorporeal circuits participants of study

Applications	Kt/V*				URR**			
	Insufficient (≤1.19)		Sufficient (>1.20)		Insufficient (≤0.64)		Sufficient (>0.65)	
	n	%	n	%	n	%	n	%
100 ml/15min	4	18.2	18	81.8	5	22.7	17	77.3
150 ml/30min	4	18.2	18	81.8	5	22.7	17	77.3
p***	1.000				1.000			

***** Hemodialysis adequacy, ** Urea reduction ratio, ***Mc Nemar test

Table 2: Comparing ultrafiltration amounts, post-dialysis weights, URR and Kt/V values of both intermittent intervals of flushing extracorporeal circuits and in participants of study

Applications	UF* amount	Post-dialysis weight	URR**	Kt/V**
	mean±sd	mean±sd	mean±sd	mean±sd
100ml/15min	3702.27±962.69	67.32±11.40	0.69±0.05	1.48±0.25
150ml/30min	3070.45±833.33	67.22±11.40	0.70±0.06	1.51±0.28
t-test ***	t=4.014	t=1.386	t= -1.615	t= -1.066
p	**0,001**	0,180	0,121	0,298

*****Ultrafiltration, **Hemodialysis adequacy,*******Paired-samples t-test

In both applications, Kt/V and URR values of more than half of patients (81.8%-77.3%) were within a normal range. There was no significant difference between Kt/V-URR values (used in determining the adequacy of dialysis) of both intermittent intervals of flushing extracorporeal circuits (100 ml/15 min and 150 ml/30 min) in heparin free hemodialysis (p>0.05) (Table 1).

Hourly mean systolic blood pressures of participants in both intermittent intervals of

flushing extracorporeal circuits during hemodialysis were compared. Mean systolic blood pressures of two applications were 122.27±24.81 and 121.81±23.63 for first hour, 115±21.65 and 114.54±24.82 for second hour, 113.63±24.4 and 113.4±27.57 for third hour, 110±26.14 and 112.04±31.72 for fourth hour respectively. There was no significant difference between first, second, third and fourth hour mean systolic blood pressures of both applications (p>0.05).

Hourly mean diastolic blood pressures of participants in both intermittent intervals of flushing extracorporeal circuits during hemodialysis were compared and no statistically significant difference was found (p>0.05). Mean diastolic blood pressures of two applications were 75.23±13.49 and 75.91±11.4 for first hour, 71.59±11.99 and 71.36±11.25 for second hour, 71.82±13.32 and 69.09±13.42 for third hour, 69.77±13.13 and 69.55±15.88 for fourth hour respectively.

Hourly heart rate of participants in both intermittent intervals of flushing extracorporeal circuits during hemodialysis was compared and no statistically significant difference was found (p>0.05).

First degree clotting was observed 59.1%, second degree clotting was observed 31.8% and third degree clotting was observed 9.1% in individuals of dialyzers in 100 ml/15 min application. In 150 ml/30 min application, first degree clotting was observed 40.9%, second degree clotting was observed 18.2% and third degree clotting was observed 40.9% in individuals of dialyzers. However there was no significant difference between both applications according to the dialyzer clotting degree (p=0.122). There was no statistically significant difference between dialyzer clotting degree and initial urea values before hemodialysis (p>0.05).

There was no statistically significant difference between mean values of post-dialysis weights, URR, Kt/V in both intermittent intervals of flushing extracorporeal circuits (p>0.05). However, statistically significant difference was found between mean ultrafiltration amounts in both applications (p=0.001) (Table 2).

Discussion

In our study, the adequacy of dialysis was compared, but there was no significant difference between Kt/V and URR values of intermittent intervals of flushing extracorporeal circuits in heparin free hemodialysis patients (p>0.05). Kt/V and URR values are used as indicators of the dialysis adequacy. Targeted minimum Kt/V ratio is 1.2, minimum URR value is 65% (2006 Updates Clinical Practice Guidelines and Recommendations, Sunanda, Santosh, Jusmita & Prabhakar, 2012; Dunne, Campbell, Fitzpatrick & Callery, 2014; Couchoud *et al.*, 2009; Kara & Acikel 2010; Kim, 2003), below 1.2 ratios for Kt/V and below 65% for URR are considered to be inadequate for hemodialysis. While calculating URR, dialysis duration and ultrafiltration are not taken into account. Therefore URR is not as effective as Kt/V (2006 Updates Clinical Practice Guidelines and Recommendations).

McGill, Blas, Bialkin, Sandromi & Marcus (2005) found that Kt/V value was 1.49±0.30 while flushing extracorporeal circuits with 200 ml of 0.9% saline solution for 30 minutes in 21 heparin free dialysis sessions with arteriovenous fistula in their study. Although flushing time with saline solution was different, hemodialysis adequacy of patients was sufficient according to Kt/V that is a parameter of hemodialysis adequacy in this study. However targeted Kt/V ratio of study was found slightly lower in heparin free dialysis patients, it is not statistically significant (McGill, Blas, Bialkin, Sandromi & Marcus, 2005).

Stamatiadis, Helioti, Mansour, Pappas, Brokes & Stathakis (2004) applied heparin free dialysis to patients with high risk of bleeding in their study. 266 patients were flushed with 50 ml of 0.9% saline solution per hour in 1224 session and the urea reduction ratio was 0.50±0.12 in this study. Flushing with 50 ml of 0.9% saline solution per hour or in other words flushing with less solution in a relatively longer time and other factors that affect URR might be the reasons for the low URR (0.50 ± 0.12), one of the dialysis adequacy parameters.

In our study, URR values were 0.69±0.05 and 0.70±0.06, Kt/V ratios were 1.48±0.25 and 1.51±0.28 in 100 ml/15 min and 150 ml/30 min applications respectively. These results showed that the dialysis of participants was adequate in terms of dialysis adequacy parameters for both applications.

Adequate hemodialysis could also be ensured with flushing with 150 ml/30 min of 0.9% saline

solution without overhydration in heparin free hemodialysis patients according to our results.

We expected hypotension, one of an undesirable side effect of hemodialysis, less common in 150 ml/30 min flushing group than the other group in our study. However, a statistically significant difference was not found between applications and probably the reason was small sample.

In our study, there was no significant difference between dialyzer clotting degrees in both applications (p=0.122). Dialyzer clotting has been reported as the most important complication in heparin free hemodialysis since 1979 (Sanders, Taylor & Curtis, 1985). Sanders, Taylor & Curtis, (1985) showed that dialyzer clotting rate was 5.13% in heparin free hemodialysis patients and 150 ml of blood could not be transfused averagely. The severe dialyzer clotting rate was found 5.1%, partial dialyzer clotting rate was found 5.8% in the same study. In this study, the reason of the high incidence of dialysis clotting degree could be depend on flushing of pre-dialysis arterial-venous sets and dialysers with heparin-poor solution (1000 ml of 0.9% saline with 3000 unit heparin) than other studies.

Clotting rate was 1% in total and clotting was observed in three quarters patients with catheter in the study of Sahota & Rodby,(2014). However this result was not significant. Stamatiadis, Helioti, Mansour, Pappas, Brokes & Stathakis (2004) found the clotting rate 5% in extracorporeal circulation and they stated that this result had fallen short of the mark. Partial dialyzer clotting rate was 26% (11/43), totally dialyzer clotting rate was 58% (25/43) in the study of Guery *et al*. (2014) respectively. In this study, more than half of the participants (56%) underwent dialysis with catheters and this could be the cause of the high incidence of clotting. We found no significant difference between both applications according to the dialyzer clotting degree; 150 ml/30 min application that provided less hydration could be preferred instead of 100 ml/15 min.

In our study, mean ultrafiltration amount was found 3702.27±962.69 in 100 ml/15 min application and 3070.45±833.33 in 150 ml/30 min application in four hours respectively. The amount of ultrafiltration was much more in 100 ml/15min application, it caused to be added 1500 ml flushing solution to ultrafiltration in each patient. 1000 ml flushing solution would be added in 150 ml/30 min application. Therefore the difference between mean ultrafiltration amount of both applications were significant (p=0.001). The mean ultrafiltration amount of McGill et al. (2005) was 2600 ml±1600 ml in four hours. Schwab, Onorato, Sharar & Dennis (1987) found the maximum ultrafiltration rate 1360±3 ml per hour in heparin free hemodialysis.

Conclusions

As a result we recommended that while flushing extracorporeal circuits intermittent, 150 ml/30 min application could be used instead of 100 ml/15 min application during the dialysis treatment in heparin free hemodialysis.

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