

# Brain Hemodynamics in Patients With End-stage Renal Disease Between Hemodialysis Sessions

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**Keywords.** hemodialysis, end-stage renal disease, Doppler ultrasonography, intracranial arterial diseases

**Introduction.** End-stage renal disease has been associated with premature atherosclerosis of the cerebral circulation. The risk of stroke, a frequent complication of uremia as a result of cerebral blood flow reduction, is high in dialysis patients. This study aimed to assess brain hemodynamics between hemodialysis interval periods by transcranial Doppler ultrasonography.

**Materials and Methods.** In a case-control study, to evaluate cerebral circulation hemodynamics, 20 hemodialysis patients and 20 age-gender-matched healthy control subjects underwent transcranial Doppler ultrasonography. Blood parameters were also measured simultaneously. Among hemodialysis patients, these studies were performed 48 hours after a dialysis session.

**Results.** The mean blood flow velocity (MV) values were significantly higher in the middle cerebral artery ( $P = .007$ ), anterior cerebral artery ( $P = .003$ ), posterior cerebral artery-segment 2 ( $P = .03$ ), basilar artery ( $P = .05$ ) in hemodialysis patients compared to the controls. The MV had a negative meaningful correlation with hemoglobin and hematocrit in most intracranial arteries of the patients, but no significant correlation was observed between these variables and MV of the arteries in the control group.

**Conclusions.** The MV of the cerebral arteries significantly increases in hemodialysis patients, which could be due to the decrease in hemoglobin levels in these patients.

IJKD 2012;6:110-3  
www.ijkd.org

## INTRODUCTION

End-stage renal disease (ESRD) has been associated with accelerated vascular disease and premature atherosclerosis of the cerebral circulation due to uremic toxins and augmentation of traditional risk factors of atherosclerosis.<sup>1</sup> The risk of stroke as a frequent complication of uremia, which can result from acute cerebral blood flow reduction, is 5 times higher in dialysis patients than the general population.<sup>2,3</sup>

Decreasing of brain tissue perfusion has deleterious nature in uremic patients, as it increases the incidence of cerebral atrophy, especially in combination with a low hematocrit

and in the presence of accelerated and premature atherosclerosis along with traditional risk factors. Also, anemia of ESRD increases cerebral oxygen extraction fraction in hemodialysis patients, and the increased oxygen extraction fraction suggests that the cerebral vasodilatory capacity might be impaired in these patients.<sup>4</sup> In addition, some findings suggest a lowered metabolic demand of the brain tissue in patients with kidney failure on or before the start of hemodialysis therapy. The cause for depressed brain oxygen metabolism is considered to be either dysregulation of cerebral circulation or lower brain cell activity.<sup>5-7</sup>

Transcranial Doppler ultrasonography (TCD) is

a noninvasive, safe, repeatable, simple procedure that obtains hemodynamic information related to brain circulation and shows continuously cerebral blood flow velocity in the basal and main brain arteries in dialysis patients.<sup>2,7-9</sup> Because published data is only about the effect of hemodialysis on cerebral hemodynamics, we decided to evaluate the cerebral arteries blood flow velocity with TCD ultrasonography in patients on maintenance hemodialysis through a case-control study.

## MATERIALS AND METHODS

To evaluate cerebral circulation hemodynamics in hemodialysis patients, we examined the mean blood flow velocity (MV), resistance index (RI), and pulsatility index (PI) in the middle cerebral artery (MCA), anterior cerebral artery (ACA), intracranial internal carotid artery, posterior cerebral artery (PCA), vertebral artery in both right and left side, and basilar artery in 20 hemodialysis patients. All of the participants underwent TCD ultrasonography 48 hours after a dialysis session to avoid probable effects of hemodialysis on the results. Twenty age- and sex-matched otherwise healthy control individuals with no traditional risk factors of atherosclerosis (hypertension, diabetes mellitus, smoking, and hyperlipidemia) were also recruited and examined by TCD ultrasonography. The complete blood cell count and lipid profile of these volunteers were normal.

Hemodynamic study was performed in the supine position, using a 2-MHz TCD ultrasound probe, 22 mm in diameter, which used a focused beam operating at a depth of 20 mm to 100 mm by the TCD machine (Multi Dop P, DWL, Sopligen, Germany). Mean velocity, RI, and PI were automatically calculated by the TCD equipment according to the following formula:

$$MV = (\text{peak systolic velocity} + 2 \times \text{end-diastolic velocity})/3$$

$$PI = (\text{peak systolic velocity} - \text{end-diastolic velocity})/MV$$

$$RI = (\text{peak systolic velocity} - \text{end-diastolic velocity})/\text{peak systolic velocity}$$

Except for the basilar artery, we used the mean values of the right-side and left-side arteries for analyses. To rule out possible effects on intracranial hemodynamics, patients with internal carotid artery stenosis were excluded. Simultaneously,

blood parameters including serum urea, serum creatinine, hemoglobin, hematocrit, and lipid profile were measured.

The statistical analyses were carried out using the SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc, Chicago, Ill, USA). The Mann-Whitney test was used to determine the mean differences. The degree of correlation between measurements was assessed using the Pearson correlation coefficient and linear regression. A level of  $P < .05$  was considered significant.

## RESULTS

The mean age of dialysis patients was  $39.8 \pm 14.9$  years (9 men and 11 women). They had been on dialysis for  $35.85 \pm 16.69$  months. Causes of kidney failure in the 20 dialysis patients were as following: polycystic kidney disease in 2, glomerulonephritis in 5, nephrolithiasis in 2, postrenal disease in 1, hypertensive nephropathy in 6, and unknown in 4 cases.

The mean hemoglobin in the patients ( $9.51 \pm 0.93$  g/dL) was significantly lower than that in the control group ( $14.55 \pm 1.14$  g/dL;  $P < .001$ ). In addition, the mean serum urea and creatinine levels ( $106.05 \pm 12.29$  mg/dL and  $7.89 \pm 0.98$  mg/dL) in patients were significantly higher than those in the controls ( $22.46 \pm 8.39$  mg/dL and  $0.84 \pm 0.16$  mg/dL, respectively;  $P < .001$ ). The mean serum cholesterol and triglyceride levels, however, were not significantly different ( $141.45 \pm 30.40$  mg/dL and  $153.40 \pm 52.02$  mg/dL, respectively, in the patients).

The cerebral arteries hemodynamic findings are shown in the Table. According the Table, the mean MV values in the patients was significantly higher in the MCA ( $P = .007$ ), ACA ( $P = .003$ ), PCA-segment 2 ( $P = .03$ ), and basilar artery ( $P = .05$ ) compared with those in the control group. There were no significant differences in the PI and RI of all cerebral arteries between the two groups. The MV had a meaningful inverse correlation with hemoglobin and hematocrit in the MCA, PCA-segment 1, basilar artery, and vertebral artery in the patients group, but no significant correlation was found between these variables and MV of the arteries in the control group. Serum cholesterol and high-density lipoprotein cholesterol levels had significant correlations with the MV of the ACA, PCA-segment 1, and VA.

Transcranial Doppler Ultrasonography Indexes in Arteries of Hemodialysis Patients and Controls\*

Artery	RI			PI			MV, cm/s		
	Patient	Control	P	Patient	Control	P	Patient	Control	P
MCA	0.49 ± 6.49	0.50 ± 4.80	> .99	0.73 ± 0.13	0.77 ± 0.15	.37	73.17 ± 19.13	59.25 ± 10.43	.007
ACA	0.51 ± 6.28	0.52 ± 5.04	> .99	0.79 ± 0.15	0.82 ± 0.14	.52	66.22 ± 17.73	51.25 ± 10.30	.003
IICA	0.52 ± 6.50	0.53 ± 4.90	> .99	0.82 ± 0.16	0.86 ± 0.14	.41	38.63 ± 12.44	36.78 ± 6.95	.56
PCA1	0.49 ± 6.06	0.50 ± 4.30	> .99	0.73 ± 0.13	0.77 ± 0.11	.30	48.95 ± 14.48	42.90 ± 7.51	.11
PCA2	0.49 ± 6.69	0.51 ± 3.66	> .99	0.72 ± 0.15	0.79 ± 0.10	.09	51.10 ± 13.02	43.75 ± 6.14	.03
VA	0.47 ± 5.93	0.48 ± 3.50	> .99	0.67 ± 0.11	0.71 ± 0.10	.24	45.10 ± 12.92	40.87 ± 10.34	.26
BA	0.49 ± 6.20	0.49 ± 4.70	> .99	0.72 ± 0.13	0.74 ± 0.12	.62	54.80 ± 17.19	46.25 ± 8.74	.05

\*RI indicates resistance index; PI, pulsatility index; MV, mean blood flow velocity; MCA, middle cerebral artery; ACA, anterior cerebral artery; IICA, intracranial internal carotid artery; PCA1, posterior cerebral artery-segment 1; PCA2, posterior cerebral artery-segment 2; VA, vertebral artery; and BA, basilar artery.

## DISCUSSION

We demonstrated that dialysis patients' blood flow velocities of the ACA, MCA, and PCA were significantly higher than those of age- and sex-matched control individuals, but there were no significant differences between the PI and RI of all cerebral arteries between the two groups. These findings were expectable, because PI and RI are ratios of velocities and global increase of MV can induce no significant changes in PI or RI.

There are many before-after studies on cerebral flow velocity changes during hemodialysis that have shown decreases of the cerebral blood flow velocity by hemodialysis. Factors responsible for the velocity changes of cerebral arteries in dialysis patients are various, and factors such as blood pH, arterial carbon dioxide, hematocrit, urea, mean arterial pressure, stroke volume, and cardiac output may be important.<sup>2,3,8,10-13</sup> However, only one case-control study has been reported on hemolytic uremic syndrome in children that recorded only one child with TCD findings of low PI, and hemodialysis was not performed.<sup>14</sup> Our report is a case-control study that shows cerebral hemodynamic state when the patient is off the dialysis. In our study, there was an inverse meaningful correlation between hemoglobin and hematocrit in the MCA, PCA-segment 1, basilar artery, and vertebral arteries. Increase of blood flow velocity in cerebral arteries of dialysis patients in our investigation can be due to hemoglobin decrease. Anemia can affect cerebral flow velocity and blood flow rate by oxygen metabolism changes.<sup>15</sup> However, the effects of kidney failure on cerebral hemodynamic are not well documented in the literature and needs more study. Since almost all of the examined patients were anemic, we cannot differentiate the effect of

anemia from dialysis in this study.

## CONCLUSIONS

Cerebral blood flow velocity increases in hemodialysis patient between dialysis interval periods that may be due to decreased hemoglobin, but other probable causes should be studied.

## CONFLICT OF INTEREST

None declared.

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Received February 2010  
Revised October 2011  
Accepted November 2011