DOPPLER ULTRASOUND EVALUATION OF CEREBRAL BLOOD FLOW IN ANAEMIA OF CHRONIC RENAL FAILURE

Muhammad Shahid, Muhammad Saeed*, Saima Irum

Combined Military Hospital Lahore Pakistan, *Combined Military Hospital Gilgit Pakistan

ABSTRACT

Objective: To determine mean cerebral blood flow in anemia secondary to chronic renal failure by doppler ultrasound and to compare the results with data gathered from healthy control subjects.
Study Design: Case control study.
Place and Duration of Study: Combined Military Hospital, Lahore, from Jan 2011 to Jun 2011.
Patients and Methods: A total of 60 subjects were included who were divided into two groups. Group I had 30 patients with anemia due to chronic renal failure while group II consisted of 30 healthy control subjects. Doppler for both groups was performed with a 7.5-MHz transducer of color doppler machine ALOKA SSD-5500 in a dimly lit room with a comfortable temperature (22°C–24°C) after an adaptation period of at least 15 minutes rest, in supine position. The internal carotid and vertebral arteries on both sides were examined in both groups and analyzed.
Results: Patients with anemia due to chronic renal failure were found to have increased cerebral blood flow as compared to normal healthy individuals.
Conclusion: Cerebral blood flow increases in patients with anemia due to chronic renal failure.

Keywords: Anemia, Cerebral blood flow, Chronic renal failure.

INTRODUCTION

Chronic renal failure is defined as irreversible deterioration in renal function[1]. The characteristic features are progressive destruction of renal mass with irreversible sclerosis and loss of nephrons[2]. Whatever the cause, the end impact of reduction in nephron mass is an alteration in function of virtually every organ system in the body. Introduction of dialysis and transplantation has changed the outlook in such patients[3].

Anemia is a universal abnormality in chronic renal failure (CRF)[4]. Inappropriate erythropoietin production is the main deficiency accountable for the anemia of chronic renal failure[5]. The decrease in cerebral oxygen supply due to anemia results in brain tissue hypoxia which thus increases cerebral blood flow (CBF)[6,7]. Doppler sonography is a well-established method for evaluating cerebrovascular circulation. It has been used for assessing the effects of various diseases and conditions[8]. The main objective of cerebrovascular doppler sonography is the analysis and characterization of cerebral haemodynamics under physiologic and pathologic circumstances[9]. Presently the quantitative assessment of brain perfusion is made by nuclear medical techniques which expose the patient to radiation, expensive and are not widely available. Doppler ultrasound has advanced the noninvasive diagnosis of cerebrovascular diseases and is precise and reliable in measurement of cerebral blood flow[10,11]. The objectives of this study were to determine mean cerebral blood flow in anemia secondary to chronic renal failure by doppler ultrasound and to compare the results with data gathered from healthy control subjects.

Correspondence: Dr Muhammaad Shahid, Dept of Radiology, CMH Lahore Pakistan *(Email:mshahid1991@gmail.com)*
Received: 23 Aug 2013; revised received: 23 Jul 2014; accepted: 25 Jul 2014

PATIENTS AND METHODS

This case-control study was carried out at the Department of Radiology, Combined Military Hospital Lahore, from Jan 2011 to Jun 2011. Permission from hospital ethical committee was sought. A total of 60 subjects were included, 30 patients with anemia due to chronic renal failure and 30 healthy control subjects. Patients of both genders between 25 to 60 years of age with

hemoglobin level <11g/dL and creatinine levels above 124 µmol/L and controls having Hb level >13g/dL in women and >14g/dL in men and creatinine level less than 100 µmol/L were included in the study from outpatient department of nephrology and medical department of CMH Lahore. Controls with normal hemoglobin (Hb) and renal functions were the volunteers for the study. Patients undergoing dialysis, arterio-venous grafts or fistulas in either arm, history of cerebrovascular disease or cardiac insufficiency, notable hemodynamic disturbances such as hemorrhage or onset of anemia in the previous 3 months, smoking, alcohol or caffeine use in the previous two days, sonographic evidence of vertebral artery occlusion or plaque formation in common carotid arteries and internal carotid arteries were excluded from the study. Written informed consent was obtained. Doppler sonography was performed for both groups with a 7.5-MHz transducer of color doppler machine ALOKA SSD-5500 in a dimly lit room with a comfortable temperature (22°C–24°C) after an adaptation period of at least 15 minutes rest, in supine position. The internal carotid and vertebral arteries on both sides were examined. Flow measurements of the internal carotid arteries (ICA) were performed 1.5 to 2 cm distal to the carotid bifurcation. Measurement of vertebral arteries (VA) was done between the transverse processes of the C4 and C5 vertebrae. The cross-sectional diameter of each vessel was measured with B-mode imaging as the distance between the internal layers of the parallel walls. The mean flow velocity was determined as the integral of the mean flow velocities of all moving particles passing the sample volume over 3 to 5 complete cardiac cycles. The intravascular flow volume was calculated with the equation FV = TAV × cross sectional area of the vessel = TAV × [(diameter/2)2π], where TAV is time averaged flow velocity. The net internal carotid artery and vertebral artery blood flow was detected by calculating the sum of blood flow of the right and left side. Cerebral blood flow was calculated by the summation of net internal carotid artery and net vertebral artery blood flow volume.

Data had been analyzed using statistical package for social sciences, (SPSS) version-10. Mean and standard deviation was calculated for quantitative variables that is age, Hb, serum creatinine and CBF in both groups. Frequency and percentage was presented for qualitative variable i.e. gender. Wilcoxin Signed Ranks test was used for non normal variable to compare increase CBF in both groups and *p*-value of < 0.05 was considered statistically significant.

RESULTS

The mean age of the patients in group-I was 42.71 ± 10.66 years (range 26-60 years). Mean hemoglobin was 7.70 ± 1.25 g/dl and mean creatinine was 327.75 ± 141.50 umol/L. In group-II mean age of the individuals taken as controls was 40.42 ± 11.02 years (range 26-60years). Mean hemoglobin was 14.83 ± 1.54 g/dl. Mean creatinine was 80.3 ± 16.85 umol/L. There was insignificant difference between age of cases and controls (p=0.468) but difference was significant for hemoglobin (p=0.001) and creatinine (p<0.001). The mean cross sectional areas of the right and left VA's were significantly higher in patients than control group (p<0.001). Although cross sectional areas of ICAs were higher in patient group, this difference was not statistically significant (table-I). There was statistically significant difference between anemia and control groups for right VA blood flow and CBF (p<0.05). However no significant difference was found between anemia and control groups for bilateral ICA and left VA. The cerebral blood flow was significantly raised in cases than the control group (table-II).

DISCUSSION

Chronic renal failure is a gradual loss of renal function over a period of months or years and defined as an abnormally low glomerular filtration rate. Blood serum creatinine level measurement also gives some clue but GFR calculation gives the accurate. Whatever the cause may be, the final result of severe reduction

in nephron mass is a change in function of every organ system in the body. The social and economic consequences of chronic renal failure are considerable. With the advent of dialysis and transplantation the outlook in such patients has been transformed[12]. Anemia of chronic renal failure is one of the most characteristic manifestations. The cause of the anemia of chronic renal failure is threefold: reduced production of erythropoietin by damaged kidneys; production of inhibitors to red blood cell (RBC) production in uremic serum and hemolysis of red blood cell[13]. The reduced cerebral oxygen hematocrit level. This is an expected result of hemodynamic changes occurring in chronic anemia that was also detected in this study. Metry et al[17] also noted a cardiac output increase in hemodialytic patients with chronic anemia and showed an increase in regional CBF with positron emission tomo-graphy. This and similar studies regarding the effects of changing cardiac output have focused on either ICA blood flow or CBF. Although it was not measured in this study, cardiac output increase is a recognized issue in chronic anemia. Eicke et al[18] who established extracranial doppler sonography for the measure-

Table-I: Comparison of means of cross sectional areas of explored vessels between anemia and control groups (n=60).

Parameter	Control group (n=30) Mean ± SD	Control group (n=30) Mean ± SD	*p*-value
Right VA mm^2	7.8 ± 3.6	4.9 ± 1.3	0.001
Left VA mm^2	8.4 ± 2.8	5.9 ± 1.9	0.001
Right ICA mm^2	17.2 ± 2.9	14.3 ± 4.5	0.065
Left ICA mm^2	16.9 ± 6.8	15.1 ± 4.7	0.278

Values presented as Mean ± SD. VA= vertebral artery, ICA=Internal Carotid Artery

Table-II: Comparison of blood flow values in all explored vessels between anemia and control groups (n=60).

Parameter	Anemia group (n=30) Mean ± SD	Anemia group (n=30) Mean ± SD	*p*-value
Right VA FV ml/min	130.20 ± 9.70	54.01 ± 3.11	0.001
Left VA FV ml/min	132.10 ± 11.01	108.23 ± 4.30	0.586
Right ICA FV ml/min	379.01 ± 28.14	277.02 ± 11.10	0.086
Left ICA FV ml/min	410.02 ± 31.01	344.12 ± 13.21	0.663
CBF ml/min	1051.33 ± 79.86	783.38 ± 31.72	0.001

Values are presented as Mean ± SD

supply due to anemia causes brain tissue hypoxia, which thus enhances cerebral blood flow.

Measurement of cerebral blood flow (CBF) volume is used for the identification and quantification of focal or generalized perfusion disturbances in the course of cerebrovascular, traumatic, or neurodegenerative disorders[14]. Chronic anemia cause a global increase in cardiac output and enhances CBF[15]. Volstrup[16], in his observation with single-photon emission tomo-graphy for the CBF in long-term hemodialytic patients with CRF, noted a significant negative relation between CBF and ments, found no association between common carotid artery blood flows and cardiac output. But as they did not include VAs in their measurements, it is not possible to make any comment on CBF in their study.

Seidel et al[19] noted non-significant left side dominance for VAs in 50 patients with nonvascular neurological conditions; and Hong et al[20] found left VA dominance in the 35 healthy Korean adults. In our study right VA blood flow was increased in patients with renal failure when compared with the control subjects. These hemodynamic behaviors of the right VA may indicate more flexibility of this vessel

in hemodynamic alterations. Most likely explanation for these findings includes anatomic variations of the circle of Willis, a neuro-physiologic component, and difference in originating sites of the left and right vertebral arteries. A further study considering all the factors in detail may help in better understanding of the significant increase in the right VA in my study.

The pathophysiologic explanation of the different susceptibilities of cervical arteries to the hemodynamic effects of chronic anemia needs to be elaborated by further assessment of doppler measurements with neurophysiologic and functional studies.

Based on our results, It is however, suggested that VA Doppler parameters of chronically anemic patients must not be expected as in healthy individuals, especially for clinical situations such as vertebrobasilar insufficiency.

CONCLUSION

In this study the total cerebral blood flow volume in patients having anaemia due to chronic renal failure was noted to be significantly higher than that of healthy control subjects. The right vertebrtal artery was most prone to increase in blood flow among these arteries. This effect also appeared as increasing net VA blood flow and CBF.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES

1. Zaki MR, Ghazanfar A, Hussain S, Khan FA. Presentations, etiology and outcome of patients with chronic renal failure admitted at urology department, Mayo hospital Lahore. A retrospective analysis of 1257 patients over a period of 10 years. Ann King Edward Med Coll 2003; 9(1): 58-61.
2. Gooneratne IK, Ranaweera AK, Liyanarachchi NP, Gunawardane N, Lanerolle RD. Epidemiology of chronic kidney disease in a Sri Lankan population. Int J Diabetes Dev Ctries 2008; 28(2): 60–64.
3. Disney APS. Demography and survival of patients receiving treatment for chronic renal failure in Australia and New Zealand: report on dialysis and renal transplantation treatment from the Australia and New Zealand dialysis and transplant registry Am. J. Kidney Dis 1995; 25: 165-175.
4. McClellan W, Aronoff SL, Bolton WK, Hood S, Lorber DL, Tang KL, et al. The prevalence of anemia in patients with chronic kidney disease. Curr Med Res Opin 2004; 20(9): 1501–10.
5. Kliger AS, Fishbane S, Finkelstein FO. Erythropoietic stimulating agents and quality of a pt's life: individualizing anemia and its treatment. Clin J Am Soc Nephrol 2012; 7: 354-7.
6. Kuwabara Y, Sasaki M, Hirakata H, Koga H, Nakagawa M, Chen T, et al. Cerebral blood flow and vasodilatory capacity in anemia secondary to chronic renal failure. Kidney International 2002; 61(2): 564-69.
7. Hare GM. Anaemia and the brain. Curr Opin Anesthesiol 2004; 17(5): 363–10.
8. Acar M, Degirmenci B, Yucel A, Albayrak R, Haktanir A, Yaman M. Comparison of vertebral artery velocity and flow volume measurements for diagnosis of vertebrobasilar insufficiency using color duplex sonography. Eur J Radiol 2005; 54(2): 221–4.
9. Csiba L. Carotid intima-media thickness measured by ultrasonography: effect of different pharmacotherapies on atherosclerosis progression. Orv Hetil 2005; 146: 1239-44. 10.
10. Damjanovic T, Djuric S, Schlieper G, Markovic N, Dimkovic S, Radojicic Z, et al. Clinical features of hemodialysis patients with intimal versus medial vascular calcifications. J Nephrol 2009; 22(23): 358-66.
11. Purkayastha S, Sorond F. Transcranial Doppler Ultrasound. Technique and Application. Semin Neurol 2012; 32(4): 411–20.
12. Guddard J, Turner AN, Cumming AD, Stewart LH. Kidney and urinary tract disease. In Boon NA, Colledge NR, Walker BR, Hunter J AA (Edi). Davidson's principles and practice of medicine. Edinburgh: Churchill Livingstone 2006; 455-518.
13. Santoro A, Canova C. Anemia and erythropoietin treatment in chronic kidney diseases. Minerva Urol Nefrol 2005; 57(1): 23-31.
14. Nedelmann M, Stolz E, Gerriets T, Baumgartner RW, Malferrari G, Seidel G, et al. Consensus recommendations for transcranial color-coded duplex sonography for the assessment of intracranial arteries in clinical trials on acute stroke. Stroke 2009; 40(10): 3238-44.
15. Osmani MH, Farooqui S. Cardiac changes in Chronic Renal Failure. J Surg Pakistan 2002; 7:31-3.
16. Vorstrup S, Lass P, Waldemar G, Brandi L, Schmidt JF, Johnsen A. Increased cerebral blood flow in anemic patients on long-term hemodialytic treatment. J Cereb Blood Flow Metab 1992; 12:745–9.
17. Metry G, Wikstrom B, Valind S, Sandhagen Bo, Linde T, Beshara S, et al. Effect of normalization of hematocrit on brain circulation and metabolism in hemodialysis patients. J Am Soc Nephrol 1999; 10: 854–63.
18. Eicke BM, von Schlichting J, Mohr-Ahaly S, , Schlosser A, von Bardeleben RS, Krummenauer F. Lack of association between carotid artery volume blood flow and cardiac output. J Ultrasound Med 2001; 20(12): 1293–8.
19. Seidel E, Eicke BM, Tettenborn B, Krummenauer F. Reference values for vertebral artery flow volume by duplex sonography in young and elderly adults. Stroke 1999; 30(12): 2692–6.
20. Sook HH, Gyu CJ, Jin PS, Hee JJ, Soung PJ, Ho KD, et al. Normal reference values for vertebral artery flow volume by colour doppler sonography in Korean adults. J Korean Soc Med Ultrasound 2003; 22(23): 165-69.
21. Lorenz MW, Karbstein P, Markus HS, Sitzer M. High-sensitivity C-reactive protein is not associated with carotid intima-media progression: The carotid atherosclerosis progression study. Stroke 2007; 38: 1774-9.
22. Ranjit N, Diez-Roux AV, Chambless L, Jacobs Jr DR, Nieto FJ, Szklo M. Socioeconomic Differences in Progression of Carotid Intima-Media Thickness in the Atherosclerosis Risk in Communities Study. Arterioscler Thromb Vasc Biol 2006; 26(2): 411-6.