

The Effect of Frequency of Dialysis Session On Efficiency of Brain Natriuretic Peptide as Cardiac Biomarker Among Patient with End Stage Renal Disease

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ABSTRACT

Background: There is overwhelming evidence about the importance of brain natriuretic peptide as a cardiac biomarker. However, the hemodynamic changes and associated abnormal body fluid homeostasis in patient with impaired renal function will add further complexity to the situation and may make the validity of brain natriuretic peptide as predictor of heart performance questionable. This prospective cross-sectional study tends to appraise the role of brain natriuretic peptide in determining left ventricular performance in patient with end stage renal disease treated by regular haemodialysis and its relation to the frequency of dialysis.

Methods: the present study included ninety patients with end stage renal disease who attend Al-Hussein hospital in Thiqar governorate /Iraq for regular haemodialysis. The patients were further classified into 3 groups depending on the frequency of dialysis session. Ten ml of venous blood were taken from every patient to measure the plasma level of brain natriuretic peptide and creatinine. Glomerular filtration rate was estimated from plasma creatinine values utilizing Cockcroft-Gault equation. Left ventricular ejection fraction was determined by transthoracic two-dimensional echocardiography. Chi-square test used to assess the relationship between different studied variables. The relation considered significant when P value < 0.05.

Results: There was a statistically significant negative relation between the plasma level of brain natriuretic peptide and left ventricular ejection fraction (P<0.001). The mean of plasma level of brain natriuretic peptide was significantly higher (P <0.001) in patients who underwent single dialysis each week when compared with patients who underwent three dialysis session each week. There was a strong negative association (P <0.001) between the renal function represented by the mean of glomerular filtration rate and level of brain natriuretic peptide in the plasma.

Conclusion: Estimation of brain natriuretic peptide values in the plasma seems to be efficient in predicting left ventricular function among patients with end stage renal disease. However, utilizing brain natriuretic peptide measurement together with estimation of left ventricular ejection fraction seems to be necessary in these patients to avoid the bias in brain natriuretic peptide level which may contribute to other factors like volume status or impaired excretion of BNP rather than impaired left ventricular function.

Keywords: Left Ventricular Function, End Stage Renal Disease, Brain Natriuretic Peptide, Dialysis Frequency.

1. INTRODUCTION

Brain natriuretic peptide (BNP) is a counter regulatory peptide related to the family of natriuretic peptide which include also urodilatin, atrial natriuretic peptide (ANP), C-type natriuretic peptide (CNP) and dendroaspis-type natriuretic peptide (DNP) ⁽¹⁾. The

main function of BNP includes vasodilation, diuresis, natriuresis, antagonizing the effects of the renin-angiotensin aldosterone system and damping the activity of sympathetic system ^(2,3,4). Brain natriuretic peptide secretion is stimulated by any condition that increase ventricular wall myocyte stretch ^(5,6). End Stage Renal Disease (ESRD) is one of the main health

care problems that challenge health authorities worldwide, it kills millions of populations each year⁽⁷⁾. Glomerular filtration rate (GFR) is an essential tool of assessing renal function and aid in diagnosis and classification of ESRD⁽⁸⁾. Cardiovascular disease is very common among patients with ESRD and represent the principal cause of complications and death among these patients^(9,10). Precocious determination of left ventricular (LV) function in patients with ESRD seems to be essential strategy of management of these patients. The primary stimulus for secretion of BNP among patients with ESRD is ventricular hypertrophy which is a common finding among these patients⁽¹¹⁾. However, patients with impaired renal function fail to excrete adequate amount of water and electrolyte, which predispose to more increase in body fluid volume with further increase in BNP secretion by ventricular myocytes^(12,13). The aim of this prospective cross-sectional study is to assess the effect of dialysis session frequency on the efficiency of BNP in predicting the performance of LV in patient with ESRD treated by regular haemodialysis (HD).

2. SUBJECTS, MATERIALS AND METHODS

This prospective cross-Sectional study conducted on ninety patients with ESRD treated with HD. These patients were selected randomly from over all patients with ESRD who attend Al-Hussien hospital in Thiqr governorate/Iraq for HD, from March 2017 to April 2018. All patients included in this study had normal LV function as manifested by normal values of cardiac ejection fraction (EF%). Forty-six of them are males and remaining 44 are females with their ages range from 25-65years. Depending on the frequency of dialysis process performed weekly, they were classified into 3 groups, group I (4 patients) underwent one dialysis session every week, group II (34 patients) underwent two dialysis session every week, and group III (52 patients) underwent three dialysis session each week. Dialysis process performed with patients on supine state, the average time of each dialysis session is 3 hours. Concerning the ethical issues, the principle and steps of the study were explained to participant and a written consent was obtained from every patient.

Ten ml of venous blood was obtained from every patient from a suitable vein, for the estimation of plasma level of creatinine and BNP. Depending on plasma creatinine values, creatinine clearance (Ccr) was calculated for every patient by utilizing Cockcroft-Gault equation⁽¹⁴⁾, the values of estimated creatinine clearance was taken as index of glomerular filtration rate (GFR) after correction for age, gender and body surface area:

$$C_{Cr} = \frac{(140 - \text{age /years}) \times \text{body weight/kg}}{\text{mL /min} \times \text{PCr (mg/dL)} \times 72}$$

The LV function was determined by calculating EF% utilizing M-mode echocardiogram⁽¹⁵⁾.

Statistical package of social science version 23 (SPSS) was used to study the association between different studied parameters using Chi-square test, the test considered significant statistically when P value < 0.05.

3. RESULTS

The effect of frequency of dialysis session on plasma level of brain natriuretic peptide

Table (1), Shows the values of the plasma level of BNP in patients with ESRD who underwent different number of dialysis session each week. There was a statistically significant negative association (P< 0.0001) between number of dialysis sessions per week and plasma level of BNP. The plasma level of BNP tends to be higher among patients who had only one session of dialysis per week and exhibit lower values among patients who underwent two or three session of dialysis per week as shown in table (1).

Table (1): The values of the plasma level of brain natriuretic peptide in patients with End Stage Renal Disease who underwent different number of dialysis session each week.

No. of dialysis / week	Brain natriuretic peptide pg/ml				X2 P value
	<125	125 - 450	>450	TOTAL	
Three sessions	6 (11.5%)	41 (79%)	5 (9.5%)	52 (100%)	16.00 3 0.000 1
Two sessions	14 (41%)	14 (41%)	6 (18%)	34 (100%)	
One Session	0 (0%)	1 (25%)	3 (75%)	4 (100%)	
TOTAL	20	56	14	90	

Renal function and plasma level of brain natriuretic peptide among patients with End Stage Renal Disease.

There was a statistically significant negative association between ventricular performance manifested by plasma level of BNP and renal function exhibited by GFR. The values of BNP were significantly higher in patient with GFR values less than 15 ml/min. in comparison with those patients who

had GFR values greater than 15ml/min. (P value =0.001), as shown in table (2).

Table (2): plasma level of brain natriuretic peptide and glomerular filtration rate among patients with End Stage Renal Disease.

GFR ml/min	Brain natriuretic peptide pg/ml			Total	X2 p value
	<125	126-450	>450		
<15	8 (40%)	25 (46.4%)	13 (92.3 %)	46	26.4 14 .001
>15	12 (60%)	31 (53.6%)	1 (7.7 %)	44	
total	20 (100%)	56 (100%)	14 (100%)	90	

Left ventricular performance and plasma level of brain natriuretic peptide

There was a statistically significant negative association (P< 0.0001) between the mean of EF % of LV and plasma level of BNP in patients with ESRD included in this study. The majority of patients with EF% values ranging from 56 to 70% had plasma level of BNP less than 450 pg/ml, while most patients who had EF% values ranging from 40 to 55% had plasma level of BNP more than 450 pg/ml, as shown in table (3).

Table (3): plasma level of BNP and left ventricular EF% in patients with End Stage Renal Disease.

EF %	Brain natriuretic peptide pg/ml			Total	X2 p value
	<125	125-450	>450		
56-70	20 (31.2 %)	44 (68.8%)	0 (0.0%)	64 (100 %)	29.4 41 .000
40-55	0 (0.0 %)	12 (46.2%)	14 (53.8 %)	26 (100 %)	
Total	20	56	14	90	

Renal function and frequency of dialysis sessions per week among patients with End Stage Renal Disease.

There was a statistically significant positive relationship between frequency of dialysis sessions per week and the renal function test represented by GFR values. The patients who had only one dialysis session per week found to had low GFR values. On the other hand, patients who had two or three dialysis session weekly had higher GFR (p< 0.001) as shown in table (4).

Table (4): The values of glomerular filtration rate among patients with End Stage Renal Disease in relation to frequency of dialysis.

No. of dialysis/ week	Glomerular filtration rate ml/min			X2 P value
	>15 ml/min	< 15 ml/min	TOTAL	
Three sessions	32 (61.5 %)	20 (38.5 %)	52 (100%)	14.264 0.0001
Two sessions	11 (32.3%)	23 (67.7%)	34 (100%)	
One Session	1 (25%)	3 (75%)	4 (100%)	
Total	44	46	90	

The relationship between left ventricular EF% and frequency of dialysis sessions among patients with End Stage Renal Disease.

The result of study showed a statistically significant positive relationship (p< 0.005) between values of left ventricular EF% and number of dialysis sessions per week among patients with ESRD. The patients who had only one session of dialysis each week exhibit low cardiac performance manifested by low value of left ventricular EF%. However, patient who underwent two or three session of dialysis per week found to have better cardiac performance manifested by high values of left ventricular EF%, as shown in table (5).

Table (5): The values of left ventricular EF% in relation to the number of dialysis sessions every week among patients with End Stage Renal Disease.

No. of dialysis/ week	Ejection fraction %			X2 P value
	40-55	56-70	TOTAL	
One Session	3 (75%)	1 (25%)	4 (100%)	10.004 0.005
Two sessions	11 (32.3%)	23 (67.7%)	34 (100%)	
Three sessions	12 (23%)	40 (77%)	52 (100%)	
Total	26	64	90	

4. DISCUSSION

The subject of natriuretic peptides attracts great attention in the last decades and a large number of researches in this aspect showed the importance of these peptides and specially BNP in determining LV performance among general population with normal renal function (16,17). However, patients with ESRD represent special pathophysiological entity where a lot of factors tend to exert extra burden on cardiovascular system and may alter the efficiency of BNP as excellent cardiac biomarker among these patients. The finding of this study showed that BNP is efficient marker of LV

performance among patients with ESRD as manifested by a statistically significant negative association ($P < 0.0001$) between plasma levels of BNP and left ventricular EF %.

The data of this paper consolidate the observation reported by many previous researches and confirm the role of BNP as excellent biomarker of left ventricular function in patients with ESRD^(18,19,20,21). Left ventricular hypertrophy is common finding among patients with ESRD, this abnormality is possibly the main stimulus for increase plasma level of BNP among these patients^(20, 21,21). Sommerer C, et al. found that BNP levels were almost invariably elevated in patients with ESRD who maintained on HD or peritoneal dialysis compared with the normal cutoff values⁽²⁵⁾. Cardiovascular involvement among patients with ESRD is a complex puzzle, several mechanisms may contribute to such abnormality like hemodynamic alteration^(26,27), the inflammatory process associated with chronic kidney disease^(28,29,30), dyslipidemia^(31,32), and associated pathological changes in the structure of cardiac myocytes known as uremic cardiomyopathy^(33,34,35).

In fact, the interpretation of elevated plasma level of BNP among patients with ESRD seems to be multifactorial. Expansion of body fluid volume may be an additional cause to elevated plasma level of BNP among these patients^{36,37,38}.

It is well-known that kidneys are the major site of excretion of different substances including BNP⁽³⁹⁾, in fact patients with ESRD exhibit a tremendous decline in renal excretory function^(40,41). This fact explains in part the extra increase in plasma BNP level among patients with ESRD included in this study, it also identifies why patients who underwent frequent dialysis tend to manifest lower plasma level of BNP than those patients who had only one HD each week. This finding again indicate that impaired renal excretion of the peptide may contribute to high BNP among patients with ESRD in addition to cardiovascular disorders and volume expansion.

One of the exciting findings in this study is that patients with ESRD who receive frequent dialysis tend to exhibit a better renal performance in comparison with those who had less frequent dialysis as explained by statistically significant higher values of GFR among patients receiving more dialysis session.

5. DISCUSSION

In conclusion estimation of plasma level of BNP seems to be efficient in predicting LV function in hemodialyzed patients. However, utilizing BNP measurement together with assessment of left ventricular EF% among patients with ESRD appear to be necessary to avoid the bias in BNP level which may contribute to other factors like volume status or

impaired excretion of BNP rather than impaired LV function.

6. CONCLUSION

Estimation of brain natriuretic peptide values in the plasma seems to be efficient in predicting left ventricular function among patients with end stage renal disease. However, utilizing brain natriuretic peptide measurement together with estimation of left ventricular ejection fraction seems to be necessary in these patients to avoid the bias in brain natriuretic peptide level which may contribute to other factors like volume status or impaired excretion of BNP rather than impaired left ventricular function.

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