Risk Factors for Left Ventricular Disorders in Chronic Haemodialysis Patients

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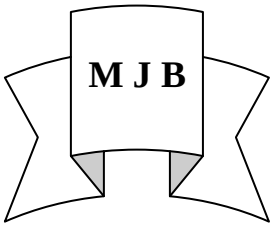

Abstract

Background : Cardiovascular diseases are highly prevalent in patients with chronic kidney disease and represent the major hazard for mortality in this population , anomalies of left ventricular structure and function are very frequent and shows negative impact on cardiovascular prognosis.

Objective : To study left ventricular disorders in patients with chronic renal failure on haemodialysis program including left ventricular dysfunction , hypertrophy and dilatation and their relation with risk factors .

Methods : 62 patients with end stage renal failure on dialysis were studied by echocardiography, patients were divided into 4 groups G1 with normal echo , G2 left ventricular dysfunction , G3 left ventricular hypertrophy , G4 left ventricular dilatation, risk factors including age , sex , duration of dialysis , hypertension, S. calcium S. albumin and hemoglobin were compared between G1 and G2 , G3 , G4 .

Results : Left Ventricular disorders occurred in 67.7% (17% left ventricular dysfunction , 63% left ventricular hypertrophy and 27% left ventricular dilatation) , older age group, longer duration of dialysis , hypertension ,hypocalcaemia , hypoalbuminemia and anemia were found to be significantly associated with left ventricular disorders .

Conclusion : Left ventricular disorders are common in patients with end stage renal failure on haemodialysis and it is important to correct risk factors like hypertension , anemia and hypocalcaemia.

عوامل الخطورة لاعتلال البطين الأيسر لدى مرضى غسل الكلى الدموي

الخلاصة

خلفية الدراسة : أمراض القلب شائعة لدى المرضى المصابين بفشل كلوي مزمن وهي سبب رئيسي للوفاة . اعتلال البطين الأيسر شائع أيضاً وله تأثير سلبي على هؤلاء المرضى .

أهداف الدراسة : لدراسة اعتلال البطين الأيسر لدى مرضى الفشل الكلوي المستمرين على الغسل الدموي ويشمل الاعتلال ضعف تقلص البطين ، تثخن البطين وتوسعه وعلاقة ذلك بعوامل الخطورة .

طرق الدراسة : أجريت الدراسة على (٦٢) مريضاً مصابين بالعجز الكلوي ومستمرين بالغسل الدموي ، اجري لهم فحص الايكو وقسموا إلى أربعة مجاميع ، المجموعة الأولى تشمل المرضى ذوي فحص الايكو الطبيعي ، والمجموعة الثانية تشمل المرضى المصابين بضعف تقلص البطين الأيسر ، وتشمل المجموعة الثالثة المرضى الذين لديهم تثخن في البطين الأيسر ، وتشمل المجموعة الرابعة المرضى الذين لديهم توسع في البطين الأيسر دُرست عوامل الخطورة وتشمل العمر ، الجنس ، مدة الغسل ،ضغط الدم ، نسبة الكالسيوم ، نسبة الالبومين ونسبة الهيموغلوبين وقورنت النتائج بين المجاميع .

نتائج الدراسة : اعتلال البطين الأيسر حدث بنسبة ٦٧,٦% (١٧% ضعف البطين ، ٦٣% تثخن البطين ، ٢٧% توسع البطين) زيادة العمر ، طول فترة الغسل ، ارتفاع ضغط الدم انخفاض نسبة الكالسيوم والالبومين والهيموغلوبين كانت إحصائيا أكثر لدى المرضى الذين لديهم اعتلال عضلة القلب . المرضى المصابين بالسكر كانت لديهم نسبة أكثر لضعف عضلة القلب .

الاستنتاج : اعتلال عضلة القلب شائع لدى مرضى الغسل الدموي وهم بحاجة إلى معالجة عوامل الخطورة .

Introduction

Cardiovascular disease is the leading cause of death 40% in patients with chronic kidney disease regardless of severity. In patients receiving renal replacement therapy the incidence is even higher. The risk of accident event in patients receiving renal replacement therapy is 3.5-50 folds higher than the general population .Annual mortality in patients with renal disease is 20 to 25% with 45% of death due to cardiovascular disease [1].

A large number of pathological changes have been described in the heart of uremic patients such as valvular heart disease (mitral and tricuspid regurgitation), uremic pericardial effusion, uremic endocarditis, arrhythmia and diastolic dysfunction. Left ventricular disorders including left ventricular dysfunction, left ventricular hypertrophy and dilatation have important role and are associated with high risk of heart failure and death [2,3]. Epidemiologic studies have shown that classic cardiovascular risk factors including hypertension, dyslipidemia, diabetes and smoking do not fully explain the high cardiovascular morbidity in this population thus the scientific community is seeking further emerging risk factors such as anemia, metabolic disorders ,calcium and hyper volemia [4] may explain the high morbidity and mortality.

To see the incidence of left ventricular disorders in our patients and their possible relation with risk factors (including age, sex, duration of dialysis, hypertension, hypocalcaemia, hypoalbuminemia, and anemia) this study was done.

Patients and Methods

A total of 62 patients with end stage renal failure on regular haemodialysis in Merjan teaching hospital were included in this study which was done between January 2011 to June 2011

Patients with ischemic heart disease (recognized by history or evidence of angina or myocardial infarction on electrocardiogram, history of previous coronary arteriobypass surgery or coronary angioplasty), pericardial effusion, severe valvular heart disease or regional wall motion abnormality on echocardiography and poor echo image were excluded from the study.

Complete history and physical examination was done for each patient regarding age, sex, duration of dialysis, presence of diabetes mellitus [patient was considered diabetic if he had history of diabetes or had fasting blood sugar at or above 126 mg/dl (7.0 mmol/l) or random blood sugar concentration≥200 mg/dl (11.1 mmol/l) [5], blood pressure was measured for every patient and diastolic blood pressure was recorded in Korotkoff phase 5.

In each patient fasting venous sample was drown, the laboratory parameters studied were serum calcium, albumin and level of hemoglobin, in patients with low S. albumin, total calcium was corrected by adjusting it's level upward by 0.1mmol/l for each 5 gm/l reduction in albumin below 40 gm/l [5].

Echocardiography:

Two dimensional echocardio-graphy was performed for each patient in non invasive cardiology department in Merjan Teaching Hospital using Envisor version c.o.2 with 2-4 MHz probe, patient was examined in left decubitus position.

Ejection fraction was measured when possible by modified Simpson's method and was correlated with visual assessment [6], patients with ejection fraction <50% were considered to have systolic dysfunction.

Left ventricular end systolic diameter (LVESD), left ventricular end diastolic diameter (LVEDD), inter ventricular

septal wall thickness and left ventricular posterior wall thickness were recorded in millimeters according to American society of echocardiogram recommendations on M mode assessment[7,8], from these measurements left ventricular mass was measured according to Devereux formula and indexed in relation to body surface area [9,10] (left ventricular hypertrophy was considered when body mass index >130 gm/ m^2 in male and >100 mg/m^2 in female[11]), also left ventricular dilatation was assessed according to previous measurements (left ventricle was considered dilated when left ventricle volume >90 ml/m^2 [12]).

Left ventricle volume = $\frac{(LVEDD)^3 * 0.001047}{body\ surface\ area}$

Patients were divided into four groups according to echo study:
Group Inormal echocardiography.
Group IIsystolic dysfunction.
Group III left ventricular hypertrophy.
Group IV left ventricular dilatation.

Statistical analysis

The statistical significance for observed differences was assessed by student T- test and test of proportion to compare differences between variables. P value of less than 0.05 was considered statistically significant, P value of less than 0.001 was considered statistically extremely significant, P value of more than 0.05 was considered statistically not significant.

Results

The study involved 62 patients, 32 males and 27 females, their age ranged from 17 years to 63 years (mean (42.5±16), mean duration of dialysis was 12.3 ±9.4 months, the means of their systolic and diastolic blood pressure were (143.8±18 and 91.2±17 mmHg), their level of S. calcium, S. albumin and hemoglobin were low [2.0±0.6 mmol/l, 32±4 gm/l and 7.8 ±2gm/dl respectively].
Their mean ejection fraction, left ventricular mass index and left ventricular volume were 55.2±12%, 150.3 ±40gm/ m^2, and 78.3±31 ml /m^2 respectively as shown in table (1) , out of 62 patients there were 20 (30.3%) patients with normal echo study (G1) and 42 (67.7%) patients with abnormal echocardiography, 11 (17%) patients with left ventricular systolic dysfunction(G2), 39 (63%) patients with left ventricular hypertrophy (G3) and 17 (27%) had left ventricular dilatation (G4), out of the 42 patients with abnormal echocardiography there were 29 patients with one abnormality and 13 patients with more than one echocardiographic abnormality.
When patients with left ventricular disorders including left ventricular dysfunction, left ventricular hypertrophy and left ventricular dilatation compared with patients with normal echo they appeared to have statistically significant older age group, longer duration of dialysis with no significant difference regarding the sex as shown in table 2, 3and 4.

Out of 62 patients there were 18 diabetic patients, only 4 (22.4%) patients had normal echo, 14 (77.8%) patients had abnormal echo, 8 patients had one and 6 had more than one echo abnormality, systolic dysfunction occurred in 7 (39%) patients which was statistically significant when compared with incidence of systolic dysfunction in non diabetic renal failure, 11 (61.1%) patients had left ventricular hyper trophy and 4 (22.2%) patients had left ventricular dilatation,

both were statistically not significant when compared with non diabetic end stage renal failure as shown in table 6.

Table 1 Clinical, laboratory and echocardiographic data of all uremic patients

Parameter	Results
Age (year)	42.5±16
Sex M/F	32/27
Duration of dialysis (months)	12.3 ±8
Systolic blood pressure (mmHg)	143.8 ±18
Diastolic blood pressure (mmHg)	91.2 ± 17
S. calcium (mmol/l)	2.0 ±0.6
S. albumin (gm/l)	32± 4
Hemoglobin (gm/dl)	7.8±2
Ejection fraction %	55.2±12
Left ventricular mass index (gm/m^2)	150± 40
Left ventricular volume(ml/m^2)	78.3 ±31

Table 2 Compares different parameters between patients with normal echo (G I) and patients with systolic dysfunction (G II)

Parameter	Group I N. 20	Group II No. 11	P Value
Age	36.3±14	46.5±10	0.042
Sex M/F	11/9	7/4	0.64
Duration of dialysis (months)	6.5±5	16.2±6	0.0001
Systolic blood pressure (mmHg)	125.4±15	149.2±19	0.001
Diastolic blood pressure (mmHg)	80.8±9	97.2±17	0.003
S. calcium (mmol/l)	2.4±0.4	1.8±0.5	0.001
S. albumin (gm/l)	37.2±3	29.3±5	0.0001
Hemoglobin (gm/dl)	8.5±2	7.1±1.9	0.043

Table 3 Compares different parameters between patients with normal echo (G I) and patients with ventricular hypertrophy (G III)

Parameter	Group I N. 20	Group III No. 39	P Value
Age	36.3±14	44.9±9	0.008
Sex M/F	11/9	22/17	0.917
Duration of dialysis (months)	6.5±5	14.3±8	0.0002
Systolic blood pressure (mmHg)	125.4±15	157.6±16	0.00001
Diastolic blood pressure (mmHg)	80.8±9	100.7±11	0.00001
S. calcium (mmol/l)	2.4±0.4	1.9±0.4	0.00001
S. albumin (gm/l)	37.2±3	30.1±2	0.00001
Hemoglobin (gm/dl)	8.5±2	7.3±1.6	0.015

Table 4 Compares different parameters between patients with normal echo (G I) and patients with left ventricular dilatation (G IV)

Parameter	Group I N. 20	Group IV No. 17	P Value
Age	36.3±14	43.4±9	0.0001
Sex M/F	11/9	10/7	0.815
Duration of dialysis (months)	6.5±5	14.5±9	0.002
Systolic blood pressure (mmHg)	125.4±15	153.2±20	0.0001
Diastolic blood pressure (mmHg)	80.8±9	98.3±14	0.0001
S. calcium (mmol/l)	2.4±0.4	1.9±0.3	0.0002
S. albumin (gm/l)	37.2±3	31.3±4	0.0001
Hemoglobin (gm/dl)	8.5±2	6.8±2.4	0.024

Table 5 Shows the level of ejection fraction, left ventricular mass index and left ventricular volume of various groups.

Parameter	G1	G2	G3	G4
Ejection fraction %	61.3±10	40.2±6	55.5±5	54.3±4
Left ventricular mass index ($gm/m^{2)}$	111.3±17	157.5±30	181.7±42	179.5±23
Left ventricular volume (ml/m^2)	61.2±20	89.5±32	87.4±30	124.4±26

Table 6 Compares diabetic renal failure with non diabetic renal failure regarding systolic dysfunction, left ventricular hyper trophy and dilatation

Parameter	Diabetic renal failure No. 18	Non diabetic renal failure No. 44	P Value
Left ventricular systolic dysfunction	7	4	0.005
Left ventricular hyper trophy	11	28	o.851
Left ventricular dilatation	4	13	0.557

Discussion

Left ventricular disorders encountered in 67.6% of patients with end stage renal failure on haemodialysis in this study, other studies give various figures ranging from 71% to 85% [13, 14], slightly lower level in this study may be due to exclusion of patients with ischemic heart disease and thus this study agrees with the idea that in spite cardiovascular disease is the leading cause of death in uremic patients but coronary events alone are not the prevalent cause [15].

Left ventricular dysfunction occurred in 17% of patients in this study, other studies give various figures 15% [16], 20%[17,18] and 36% [19], left ventricular hypertrophy occurred in 63% of patient in this study, other studies give various results 46% [19], 55% [16], 70% [20], 95.5% [21]. While left ventricular dilatation

occurred in 27%, other study gives figure of 26.1% [16].

This study showed that these left ventricular disorders had significant relationship with age, they occurred more in older age group patients with longer duration of dialysis possibly due to progressive renal failure and it seems that haemodialysis is unable to slow the progression of these disorders and there are reports that renal transplant can regress them [22].

The level of mean systolic and diastole blood pressure in our patients was high reflecting that blood pressure is not well controlled; patients with left ventricular disorders had significantly higher blood pressure reflecting that high blood pressure is a predicator for left ventricular disorders specially left ventricular hypertrophy [16, 20, 23, 24].

This mandates an aggressive control of hypertension for regression of left ventricular hypertrophy with control of blood pressure has been demonstrated in various studies [24.25].

This study showed that patients with left ventricular disorders had lower level of serum calcium, similar result encountered in other study[16], low calcium level results in elevation of parathyroid hormone (secondary hyperparathyroidism), high parathyroid level is associated with myocardial hypertrophy and fibrosis as well as high coronary score [15] and there is positive relationship between parathyroid hormone and left ventricular hypertrophy, hyperparath-yroidism and malnutrition which are important factors influencing development of left ventricular hypertrophy in haemodialysis patients [26].

Hypoalbuminemia had been identified to be associated with left ventricular disorder, role of malnutrition (in addition to renal loss) as cause of it and development of left ventricular disorders is largely speculative [16].

This study showed that most of the patients were anemic and anemia was found to be significantly associated with left ventricular disorders and this is in agreement with other studies [16, 20,21,24].

So aggressive treatment of anemia is important to regress these abnormalities.

Diabetic patients with end stage renal failure on dialysis had more occurrence of left ventricular dysfunction despite exclusion of ischemic heart disease, thus carries worse prognosis and seems that diabetes in chronic renal failure is predictive for left ventricular disease [27].

Most of our patients didn't underwent echocardiographic examination prior to this study, echocardiography is valid non invasive test that can detect early left ventricular disorders specially left ventricular dysfunction which is an ominous sign because it predicts cardiovascular mortality as well as non fatal cardiovascular events[28] and it's early detection and treatment may retard the progression toward heart failure [10].

Specific recommendation have been issued by the national kidney foundation for the study of cardiomyopathy and the prevention of heart failure in patients with end stage renal failure and echocardiographic studies are indicated as a fundamental means for guiding risk stratification and treatment of these conditions [4].

Conclusions

1.Left ventricular systolic dysfunction, hypertrophy and dilatation are common in patients with chronic renal failure on haemodialysis .

2.Hypertension, anemia and hypocalcaemia are not well treated in our patients.
3.Older age group, longer duration of dialysis, hypertension, anemia, hypocalcaemia and hypoalbuminemia are risk factors for these disorders.
4.Left ventricular dysfunction occur more in diabetic patients with end stage renal failure on haemodialysis.

Recommendations

1.Aggressive treatment is required to control blood pressure, anemia and hypocalcaemia.
2.Uremic patient undergoing dialysis requires echocardiographic examination for early detection and treatment of left ventricular disorders.
3.Further studies are required to predict other risk factors for left ventricular disorders.

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