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Effect of Anemia on Left Ventricular Hypertrophy and Ejection Fraction in Maintenance Hemodialysis Patients

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Abstract: The present research aimed to consider the adverse effects of amenia on left venrticular function and structure in dialysis patients due to End-Stage Renal Disease (ESRD) undergoing regular hemodialysis. For patients complete blood count, serum Iron, total iron binding capacity and serum ferritin were measured. On the basis of septal thickness, the patients stratified into, no Left Ventricular Hypertrophy (LVH), mild, moderate and severe LVH. In this study a significant difference of Haemoglobin (Hb) and Haematocryt (Hct) between males and females with more values in the female group and a significant inverse correlation of serum ferritin with hemoglobin levels were found. A significant inverse correlation of Left Ventricular (LV) ejection fraction with duration of hemodialysis treatment was observed. A near significant inverse correlation of LV ejection fraction with serum ferritin was found, also a significant inverse correlation of LVH with LV ejection fraction was observed too. In present study female dialysis patients had more prominent anemia than males which implies more attention to anemia treatment in this group. We showed an inverse association of LV ejection fraction with serum ferritin. We also showed that duration of hemodialysis treatment have an adverse effect on progression of LVH. We concluded that anemia in conjunction with other important factors like duration of dialysis could aggravate the hypertrophy of LV.

Key words: Hemodialysis, anemia, left ventricular hypertrophy, left ventricular ejection fraction

INTRODUCTION

Cardiovascular disease is the principal cause of morbidity and mortality in dialysis patients[1]. The principal alterations responsible are left ventricular hypertrophy and arterial disease[2]. Left Ventricular Hypertrophy (LVH) is the consequence of combined effects of chronic hemodynamic overload and nonhemodynamic biochemical and neurohumoral factors characteristic of uremia. LVH is an independent risk factor for mortality in hemodialysis patients[2-4]. In recent years much progress has been made in understanding the pathogenesis of cardiovascular disease in the uraemic population[4]. Anaemia is a consistent finding in chronic renal disease, affecting up to 90% of patients and the central role of anaemia in the development of cardiovascular dysfunction is now well established[5,6]. Pathophysiologically chronic anemia, long-lasting flow/volume overload and increased cardiac work lead to progressive cardiac enlargement and left ventricular hypertrophy[7]. The risk of Coronary Heart Disease (CHD) increases when the anemia is not treated and recent studies have indicated that anemia in patients with chronic renal failure may predispose to ischemic heart disease, heart failure and premature death[7-9]. Therefore, the risk of CHD may be distinctly higher in people with renal insufficiency and concomitant anemia, when compared with people with renal insufficiency but without anemia and people with normal renal function[7-10]. A significant proportion of patients have established cardiovascular complications on initiation of dialysis, raising the possibility of early correction of anaemia as a strategy for preventing cardiovascular co-morbidities among renal patients[10-12]. It is thought that anaemia can increase the severity of heart failure and is associated with a rise in mortality, hospitalization and malnutrition. Anaemia can also further worsen renal function and cause a more rapid progression to dialysis than is found in patients without anaemia[10-13]. Partial correction of anemia with recombinant human erythropoietin likely reduces left

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ventricular mass and volume. Complete correction of anemia may prevent progressive left ventricular dilatation in patients with normal left ventricular volumes[3]. The present study aimed to consider the adverse effects of amenia on left venrticular function and structure in our hemodialysis patients.

MATERIALS AND METHODS

This cross-sectional study was conducted on patients with End-Stage Renal Disease (ESRD), who were undergoing maintenance hemodialysis treatment with acetate basis dialysate and polysulfone membranes. According to the severity of secondary hyperparathyroidism, each patient being treated for secondary hyperparathyroidism was given oral active vitamin D3 (Calcitriol), calcium carbonate and Rena-Gel capsules at various doses. According to the severity of anemia, patients were under IV iron therapy with Iron sucrose (venofer) at various doses after each dialysis session, all patients were under treatments of 6 mg folic acid daily, 500 mg L-Carnitine daily, oral Vitamin B-complex tablet daily and also 2000U IV Eprex (recombinant human erythropoietin (rHuEPO) for each patient after each dialysis session routinely. Exclusion criteria were active or chronic infection and using NSAID or ACE inhibitor drugs. The study was done in hemodialysis section of Hajar Medical, Educational and Therapeutic Center of Shahrekord University of Medical Sciences in Shahrekord of Iran. Blood samples were collected after an overnight fasting. For patients, complete blood count was measured using Sysmex-KX-21N Cell counter, within 30 min from taking the blood sampling. Levels of serum Iron, total iron binding capacity (TIBC) and serum ferritin (by radio immuno assay method; RIA) were measured using standard kits. On the basis of septal thickness, we stratified the patients into no LVH (septal thickness between 6-11 mm), mild (septal thickness between 11-15 mm), moderate (septal thickness between 15-18 mm) and severe LVH (septal thickness >18 mm). LVH measurements were done at the end diastolic phase[4]. Percent of cardiac ejection fraction between 55 to 75% was considered normal. The presence of cardiac chest pain was considered positive with its' typical presentation and past history of ischemic heart disease as well as its' dramatic response to nitroglycerine treatment[4]. Duration and doses of hemodialysis treatment were calculated from patients' records and the duration of each hemodialysis session was 4 h. For statistical analysis descriptive data are expressed as Mean±SD. Comparison between groups were considered using students' test. For correlations we used χ^2, Pearsons, spearman's rho, Kruskal-Walis and partial correlation tests. All statistical analysis were performed using the SPSS (version 11.5.00). Statistical significance was significant when $p<0.05$.

RESULTS

The total patients were 60 (F = 21 and M = 39), consisting of 44 non diabetic hemodialysis patients (F=15 and M=29) and 16 diabetic hemodialysis patients (F=6 and M=10). Table 1 shows the Mean±SD of age, the length of the time that patients had been on hemodialysis, dialysis dose and the results of laboratory tests. Mean±SD of age of total patients were 46±18 years. The length of the time patients had been on hemodialysis were 25±30 months(median:13.5 months). Mean±SD of hemoglobin and hematocrit of total patients were 8.9±2 g dL^{-1} and 28±6%, respectively. Mean±SD of LV ejection fraction of all patients were 48±10% (median: 50%). Mean±SD of diabetic and non diabetic group were 46±10 (median: 47.5%) and 48.6±11% (median: 50%), respectively. Stages of LVH in all patients were; stage one 30%, stage two 48.3%, stage three 21.7%. In

Table 1: Mean±SD, minimum and maximum of age, duration, dose and laboratory tests of total, non-diabetic and diabetic hemodialysis patients

Total patients	Minimum	Maximum	Mean±SD
n=60			
Age (years)	11	80	46±18
DH* (months)	2	156	25±30
Dialysis			
dose sessions	18	1584	219±321
Hb (g dL^{-1})	5	13	8.9±2
HCT %	14	42	28±6
Ferritin (ng dL^{-1})	27.00	2615.00	494±394
Iron (µg dL^{-1})	10.00	1515.00	295±391
TIBC (µg dL^{-1})	200.00	3363.00	976±622
Non diabetics			
n=44			
Age (years)	11	80	42.9±18
DH* (months)	2	156	29.8±35
Dialysis			
dose sessions	18	1584	258±367
Hb (g dL^{-1})	5	13	8.7±2
HCT %	15	42	27.5±6
Ferritin (ng dL^{-1})	27	2615	524±416
Iron (µg dL^{-1})	10	1010	271±334
TIBC	200	3363	908±672
Diabetics			
n=16			
Age (years)	27	79	54±16.7
DH* (months)	6	24	13±6
Dialysis			
dose sessions	54	216	114±52
TIBC	400	1803	1161±419
Hb (g dL^{-1})	5	13	9.4±2
HCT %	14	40	29±6.7
Ferritin (ng dL^{-1})	35	1106	409±320
Iron (µg dL^{-1})	11	1515	362±526

*Duration of hemodialysis treatment

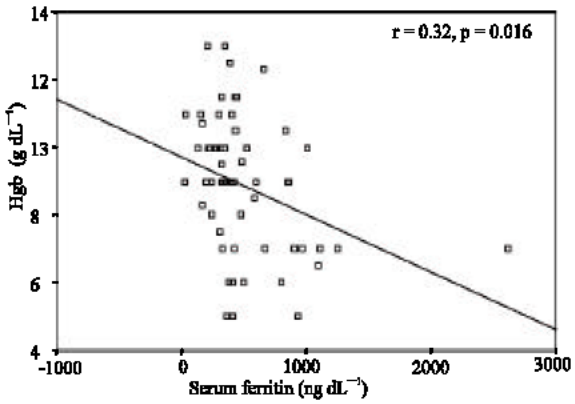

Fig. 1: Significant inverse correlation of serum ferritin with hemoglobin levels

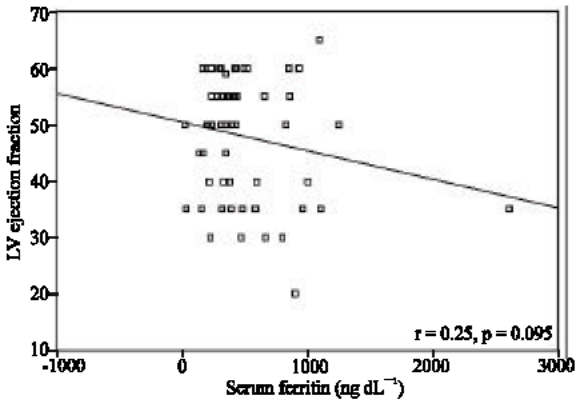

Fig. 2: Near significant inverse correlation of LV ejection fraction with serum ferritin

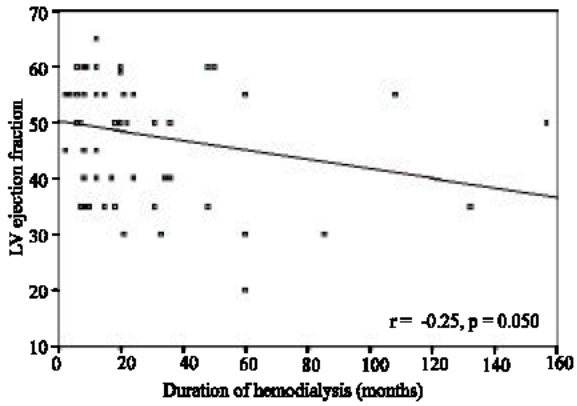

Fig. 3: Significant inverse correlation of LV ejection fraction with duration of hemodialysis

diabetic group stage of LVH were; Stage one 18.8%, stage two 56.3%, stage three 25%. In nondiabetic patients stage of LVH were ; Stage one:34.1%, stage two: 45.5%, stage three: 20.5%. Moreover 35% of total patients had cardiac chest pain, diabetics 56.3% and nondiabetics 27.3% had cardiac chest pain, respectively. In this study significant difference of Hb (9±2 vs 8±2 g dL^{-1}) (p= 0.053) and Hct (29± 6 vs 26± 5.5%) (p= 0.046) between male and female groups were seen. No significant difference of age, serum iron, TIBC and duration of hemodialysis treatment and also dialysis dose between males and females of total patients were observed. Non significant difference of serum ferritin, iron, TIBC, LV ejection fraction, Hb and Hct between diabetic and nondiabetic HD patients were also observed. In this study a significant inverse correlation of serum ferritin with hemoglobin levels was found (r = - 0.32, p = 0.016 and Fig. 1). A near significant inverse correlation of LV ejection fraction with serum ferritin was demonstrated too (r = - 0.22, p =0.095 and Fig. 2). Significant inverse correlation of LV ejection fraction with duration of hemodialysis treatment was demonstrated too (r = - 0.25, p =0.050 and Fig. 3). Statistical analysis on left ventricular hypertrophy and its correlation showed no significant correlation of LVH with gender, hypertension, diabetes mellitus and cardiac chest pain. No significant correlation of LVH with Hb, Hct, serum iron, TIBC, ferritin were demonstrated. Non significant correlation were found in LV ejection fraction with Hb, Hct, serum iron and TIBC. A significant inverse correlation of LVH with LV ejection fraction (r= - 0. 60, p<0.001) were found too.

DISCUSSION

Present study showed a significant difference of Hb, Hct between males and females with more values in females. A significant inverse correlation of serum ferritin with hemoglobin levels was found. A significant inverse correlation of LV ejection fraction with duration of hemodialysis treatment was observed. A significant inverse correlation of LVH with LV ejection fraction were found too. Jurkovitz *et al.*[14] on a total of 13, 329 participants conducted a study to evaluate the correlation of serum creatinin and anemia. The results have interaction between Hb concentration and serum creatinine (Scr) was significant. Among people with anemia and a Scr 1.2 mg dL^{-1} in women or 1.5 mg dL^{-1} in men was associated with a higher risk of Coronary Heart Disease (CHD) than those with normal Scr. In contrast, among those without anemia, this association was not noted. They concluded that high Scr is associated with almost a threefold risk of CHD among middle-aged people with anemia, whereas no increased risk is found in people with high Scr in the absence of anemia. Rasic *et al.*[15] in a one year followed up of 50 patients with end-stage renal disease by performing a serial echocardiography and

serial measurements of potential modifiable cardiovascular risk factors, showed that LVH is present in high percentage (72%) in uraemic patients, even at the beginning of hemodialysis treatment and this morphological abnormality is statistically significantly related to present anaemia near patients, other factors include hypertention and hyperparathyroidism. A recent analysis of the ARIC data found a 40% increased risk of CVD in subjects with anemia compared with patients with normal Hb[8]. Low Hb increases also the risk of death in patients with heart failure independent of renal function[9,15]. Other investigators have described a U-shaped relationship between hematocrit levels and risk of CVD[16-18]. The association between increased risk of CHD and high Scr in patients with anemia might be explained by an impairment in the physiologic mechanisms of adaptation to maintain the oxygen supply to the tissues in the presence of anemia. These mechanisms of adaptation are both nonhemodynamic and hemodynamic[7]. Nonhemodynamic mechanisms include increased erythropoietin production to stimulate erythropoiesis and increased oxygen extraction. In normal resting conditions, the nonhemodynamic factors can almost entirely compensate for Hb deficit[7]. However in the setting of kidney disease, erythropoietin production is impaired and therefore the only nonhemodynamic mechanism of compensation is an increase in oxygen extraction, which has a limited effect[19]. When the Hb concentration is <10 g dL^{-1}, nonhemodynamic factors become inadequate and increased cardiac output and blood flow begin to compensate for tissue hypoxia. There are three major components in the hemodynamic compensation[7]: increase in cardiac output; increase in preload as a result of higher venous return; and decrease in systemic vascular resistance as a result of arterial dilation, formation of collaterals, arteriovenous shunts, de novo angiogenesis and decrease in blood viscosity[7,20]. Anemia has also been identified as a risk factor for left ventricular growth in patients with mild to moderate renal insufficiency[6-21]. Left ventricular hypertrophy predisposes to heart failure or ischemic heart disease and ultimately premature death[6,9,21]. In this study female hemodialysis had more prominent anemia than males which implies more attention to anemia treatment in female hemodialysis patients. We showed an association between LV ejection fraction and serum ferritin. We also showed that duration of hemodialysis treatment have an adverse effects on progression of LVH. Thus we concluded that anemia might aggravate the LVH in conjuction with other important factors as mentioned one of them is duration of hemodialysis treatment.

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