Dear Sir,

Studies performed in anemic subjects and in humans with renal failure who received blood transfusions proposed that anemia is a hyperdynamic circulatory state characterized by increased contractility, stroke volume, cardiac output, cardiac index and preload [1]. Human recombinant erythropoietin (rhEPO) has enabled the study of hemodynamic and cardiovascular responses to the correction of the anemia of renal failure. But there are different results in these studies performed with rhEPO. Some authors reported an improvement in cardiac output and a fall in total vascular resistance after improvement of anemia with rhEPO [2,3], but others found a fall in cardiac index and an increase in systemic vascular resistance [4-7]. We investigated the effect of improvement of anemia with rhEPO on cardiac functions by echocardiographic measurements.

This study covered 25 patients (9 males, 16 females, mean age 46 ± 29 years). At first and in every month, some biochemical parameters (including blood urea nitrogen, creatinine, sodium, potassium, calcium phosphate, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase), serum iron and total iron-binding capacity, ferritin, vitamin B12, folic acid and some hormones [parathormone, testosterone, plasma renin activity (PRA), prolactin, angiotensin II, aldosterone] were measured. Every week, hematocrit (Hct), white blood cell, platelets and reticulocyte counts and bleeding time were measured. Blood pressures (BP) of patients were controlled by some antihypertensives (prazosin, α-methyldopa, calcium channel blockers). Primary diseases were chronic glomerulonephritis (8), hypertensive nephrosclerosis (2), tubulo-interstitial nephritis (9), diabetes mellitus of type 2 (5) and secondary amyloidosis (1). The dose of rhEPO was increased according to improvement of anemia. The patients were followed at least 6 months. Two-dimensional echocardiography was performed using an echocardiograph (model 7500, Toshiba, Tokyo, Japan) equipped with a linear array transducer (5.0-3.5 MHz). The following parameters were measured: myocardial thickness, internal dimension of the left ventricle and septal thickness, posterior wall thickness, thickness of the anterior wall, thickness of the free wall, thickness of the posterior wall, posterior wall thickness, left ventricular mass, left ventricular myocardial mass. We calculated the following parameters: systolic blood pressure, diastolic blood pressure, mean blood pressure, stroke volume, cardiac index, ejection fraction, left ventricular end diastolic volume, left ventricular end systolic volume, interventricular septal thickness, posterior wall thickness, left ventricular mass index, right ventricular mass index, left atrium area, left atrium volume, mitral valve orifice area, mitral valve area index, left ventricular wall thickness, left ventricular posterior wall thickness, left ventricular mass, left ventricular mass index, right ventricular mass index, left atrium area, left atrium volume, mitral valve orifice area, mitral valve area index, left ventricular wall thickness, left ventricular posterior wall thickness, left ventricular mass, left ventricular mass index, right ventricular mass index, left atrium area, left atrium volume, mitral valve orifice area, mitral valve area index, left ventricular wall thickness, left ventricular 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shortening; E/A = late diastolic filling/atrial contraction; AT = acceleration time; DT = deceleration time.
sional and Doppler echocardiography were performed at 0, 3 and 6 months according to the criteria of the American Echocardiographic Society.
Hct increased from 19.44 ± 3.78 to 27.08 ± 4.38%. BP and mean arterial BP
were unchanged at the end of 6 months. Total systemic resistance (TSR) increased but was not statistically significant. PRA decreased from 17.63 ± 14.95 to 9.43 ± 9.86 ng/ml/h (p < 0.02), but these were high levels. Angiotensin II and aldosterone levels also decreased but were not statistically significant. The measurements of echocardiography are shown in table 1. As can be seen, left ventricular mass, interventricular septal thickness diameter and left ventricular posterior wall diameter decreased at the end of 6 months. Global left ventricular systolic function was unchanged. Mean stroke volume, ejection fraction, cardiac index, fractional shortening and mean velocity of circumferential fiber shortening did not change significantly. At first, ejection fraction was below 50% in 5 patients. At 6 months, ejection fraction did still not reach 50% or more in these 5 patients. Diastolic function of the left ventricle changed statistically significantly: mean late diastolic filling/atrial contraction ratio decreased from 1.14 ± 0.41 to 0.92 ± 0.21 (p < 0.05). The late diastolic filling/ atrial contraction ratio increased in 24%, decreased in 70% and remained unchanged in the others. Some authors have noted an increase in BP in hemodialysis patients after therapy with rhEPO [8]. Increases in whole blood viscosity and reversal of hypoxia-induced vasodilation have been suggested as possible causes of increases in BP. However, while a rise in viscosity and TSR is a nearly universal finding in patients whose anemia is corrected with rhEPO, the development of hypertension is not. It has been suggested that the presence of a mismatch between increased TSR and reduced cardiac output identifies those who become hypertensive [8]. In our study, cardiac index and TSR were unchanged, but the levels of PRA, aldosterone and angiotensin II decreased at the end of 6 months. Thus, we can explain the unchanged BP at the 6th month.
We found lower measurements of left ventricular mass and left ventricular posterior wall diameter in our study. Reversal of left ventricular hypertrophy after therapy with rhEPO has been demonstrated in several studies [5, 8]. In our study, Hct increased from 19.44 ± 3.78 to 27.08 ± 4.38% (p < 0.001), the serum ferritin level decreased from 347.04 ± 274.60 to 199.64 ± 164.77 ng/ml (p < 0.02). We believe that the correction of anemia and a decrement of serum ferritin may be the cause of regression of ventricular hypertrophy. As a result, in our hemodialysis patients improvement of anemia with rhEPO regressed left ventricular hypertrophy, did not change left ventricular systolic function but slightly deteriorated diastolic function so that it is not yet known whether rhEPO will improve the long-term prognosis for cardiovascular status in hemodialysis patients.
References


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Ozakgun/Paydas/Demirtas/Sagliker
Erythropoietin and Cardiac Function