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Original article

Left ventricular hypertrophy in children, adolescents and young adults with sickle cell anemia

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ABSTRACT

Objective: The aims of this study were to estimate the frequency of left ventricular hypertrophy and to identify variables associated with this condition in under 25-year-old patients with sickle cell anemia.

Methods: A cross-sectional study was performed of children, adolescents and young adults with sickle cell anemia submitted to a transthoracic Doppler echocardiography. The mass of the left ventricle was determined by the formula of Devereux et al. with correction for height, and the percentile curves of gender and age were applied. Individuals with rheumatic and congenital heart disease were excluded. The patients were divided into two groups according to the presence or absence of left ventricular hypertrophy and compared according to clinical, echocardiographic and laboratory variables.

Results: A total of 37.6% of the patients had left ventricular hypertrophy in this sample. There was no difference between the groups of patients with and without hypertrophy according to pathological history or clinical characteristics, except possibly for the use of hydroxyurea, more often used in the group without left ventricular hypertrophy. Patients with left ventricular hypertrophy presented larger left atria and lower hemoglobin and hematocrit levels, reticulocyte index and a higher albumin:creatinine ratio in urine.

Conclusion: Left ventricular hypertrophy was observed in more than one-third of the young patients with sickle cell anemia with this finding being inversely correlated to the hemoglobin and hematocrit levels, and reticulocyte index and directly associated to a higher albumin/creatinine ratio. It is possible that hydroxyurea had had a protective effect on the development of left ventricular hypertrophy.

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Introduction

Sickle cell anemia (SCA) is a multisystemic disease characterized by acute episodes of pain and progressive lesions of target organs. It is one of the most common and most severe monogenic disorders in the world. In Brazil, it is estimated that 3500 children are born with sickle cell anemia each year, that is 1:1000 live births, and is thus a serious public health problem.[1] Cardiovascular disease is a frequent clinical manifestation of people with sickle cell anemia.

Eccentric left ventricular hypertrophy (LVH), dilation of the chambers, biventricular dysfunction, pulmonary hypertension and myocardial ischemia are the principal findings.[2–5] Patients with SCA frequently have severe anemia that results in increased cardiac output with minimal or no increase in cardiac frequency thereby causing dilatation of the left ventricle[6] correlated to the hemoglobin (Hb) level.[7,8] The dilated left ventricle adapts to the chronic volume overload by hypertrophy, thickening the heart muscle and stretching the myofibrils of the muscle. Hypertrophy allows the left ventricle to adapt to the chronic volume overload, initially preserving diastolic compliance and maintaining the filling pressure at normal levels.[9] The literature shows that LVH is a common condition in sickle cell anemia after the second decade of life.[10] Diagnosed by transthoracic Doppler echocardiography, the prevalence of LVH varies between 13 and 86%.[7,10–14] In chronic cases, LVH presents with diastolic[3,15,16] and systolic dysfunction.[3,15]

Given the high morbimortality, the present article aimed to estimate the frequency of LVH in children, adolescents and young adults with sickle cell anemia and determine variables associated to this condition.

Method

Study design and population

A cross-sectional study was conducted of patients between the ages of 7 and 25 with SCA as confirmed by electrophoresis, regularly treated in a referral center. All patients were in steady state, and were submitted to outpatient transthoracic Doppler echocardiography. The exclusion criteria were the presence of rheumatic or congenital heart disease. Patients were consecutively enrolled and allocated in two groups according to the presence or absence of LVH.

Transthoracic Doppler echocardiography

Echocardiographic examinations were performed using a Nemio® XG (Toshiba) device by one experienced echocardiographer. Patients were placed in the left lateral decubitus position without sedation to perform the echocardiographic measurements in parasternal and apical acoustic windows following the recommendations of the American Society of Echocardiography.[17] At least three cycles were analyzed for each variable. The electrocardiographic exam was performed concurrently with laboratory tests. The evaluation of the left ventricle was obtained using the variables: end diastolic thickness of the interventricular septum (IVS), end-diastolic thickness of the posterior wall of the left ventricle (LVPW), left ventricular end-diastolic diameter (LVDD) and left ventricular end-systolic diameter (LVSD). The relative wall thickness (RWT) was obtained using the formula: RWT = (IVS + LVPW)/LVDD. The left ventricular mass index (LVMI) was calculated using the formula proposed by Devereux et al.[18] in which:

$$\mathrm{LVMI}(g) = 0.8\{1.04[(\mathrm{IVS} + \mathrm{LVDD} + \mathrm{LVPW})^3 - {}^3\mathrm{LVDD}]\} + 0.6$$

Subsequently the result was corrected for the height[18,19] and applied to specific percentile curves for gender and age.[20] LVH was diagnosed when the LVMI was higher than the 95th percentile for gender and age.[20]

Demographic and clinical data

Data regarding the age, gender, anthropometry (weight, height), information regarding the diagnosis (age at diagnosis, electrophoresis results), previous use of hydroxyurea and pathological history (leg ulcers, gallstones, stroke, surgical splenectomy, priapism, acute chest syndrome, hospitalizations, transfusions and painful crises in the previous year) were collected through interviews and from medical charts.

Laboratory data

Data on the blood count, reticulocyte index (corrected by hematocrit), lactate dehydrogenase and total bilirubin levels, ferritin, serum creatinine and urea, albumin:creatinine ratio in urine and 24-hour creatinine clearance were collected during the week prior to the echocardiography in order to correlate them with LVH.

Ethical considerations

This study is part of clinical research in sickle cell anemia approved by the Research Ethics Committee of the Universidade Federal de Sergipe (number 0173.0.107.000-09). Patients over 18 years old and the guardians of under 18-year-old patients signed informed consent forms.

Data analysis

The results were analyzed using the Statistical Package for the Social Sciences for Windows version 17.0 (SPSS, Chicago IL). Categorical variables were analyzed using the chi-squared distribution or Fisher's exact test. The Student's *t*-test or Mann–Whitney test were used to compare numerical variables between the groups. A logistical regression model was used to evaluate the protective effect of hydroxyurea after the elimination of possible confusing variables. The level of significance was set for p-values <0.05.

Results

One hundred and nine patients with SCA were studied; 56 (51.4%) were male. SCA was diagnosed at a mean age of 69.28 ± 46.09 months and LVH was present in 41 (37.6%)