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Original article

Gated Myocardial Perfusion Scintigraphy in Children with Sickle Cell Anemia: Correlation with Echocardiography

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ABSTRACT

Objectives: The heart is one of the organs affected by sickle cell anemia (SCA). This prospective study has aimed to evaluate myocardial perfusion and left ventricle (LV) function in children with SCA by gated myocardial perfusion scintigraphy (G-MPS) and to compare the results with echocardiographic parameters.
Methods: Forty-three patients with SCA were evaluated by G-MPS and echocardiography. Myocardial perfusion and motion with thickening function were analyzed both visually and quantitatively. End-diastolic (EDV), end-systolic volumes (ESV), ejection fraction (EF), lung-to-heart (L/H) ratio were also calculated.
Results: None of the patients showed stress perfusion impairment in G-MPS. LV dilatation in 15 patients was observed both by G-MPS and echocardiography. EF values were within normal limits. Correlation between EF values calculated by two methods was not statistically significant. However, LV dilatation detected by both methods and EDV-ESV values in G-MPS were correlated to end-diastolic and end-systolic diameters calculated in echocardiography ($p<0.05$). M-Mode echocardiography revealed higher myocardial performance index (LV-MPI) in patients with LV dilatation. There was also a significant relationship between LV dilatation and frequent blood transfusions (>5/years) and acute chest syndrome ($p<0.05$).
Conclusion: Myocardial perfusion impairment in children with SCA is not frequently observed. Thus, performing the scintigraphy only in patients with cardiac symptoms should be considered. Since EF values of the children with SCA are not deteriorated in early stages, LV-MPI and LV dilatation should be considered as a significant parameter other than EF or perfusion data.

Gated-SPECT de Perfusión Miocárdica en Niños con Anemia Falciforme

Palabras clave:
Perfusión miocárdica
gammagrafía
ecocardiografía
anemia de células falciformes
niños

RESUMEN

Objetivo: El **c**orazón es uno de los órganos afectados por la anemia de células falciforme (SCA). El objetivo de este estudio prospectivo es evaluar la perfusión miocárdica y la función del ventrículo izquierdo (LV) en niños con SCA por la gammagrafía de perfusión miocárdica (G-MPS) y comparar los resultados con los hallazgos ecocardiográficos.
Métodos: Se evaluaron cuarenta y tres pacientes con SCA mediante estudios de G-MPS y ecocardiografía. La perfusión miocárdica y la función ventricular con la valoración de la motilidad y del engrosamiento se analizaron tanto de forma visual como cuantitativa. Se calcularon el EDV, ESV, EF, y el índice pulmón /corazón (L/H).
Resultados: Ninguno de los pacientes presentó deterioro de la perfusión post-estrés en el G-MPS. Se observó dilatación del LV en 15 pacientes, que también estuvo presente en el ecocardio. Los valores de EF se encontraban dentro de los límites normales. La correlación entre los valores de EF, mediante ambos métodos no fueron estadísticamente significativas. Sin embargo la dilatación del ventrículo izquierdo detectados por ambos métodos y los valores de EDV-ESV en la G-MPS se correlacionaron con los diámetros sistólico y diastólico final calculados por la ecocardiografía ($p<0,05$). La ecocardiografía en modo-M mostró mayor índice de rendimiento miocárdico (LV-MPI) en pacientes con dilatación del LV. También hubo una relación significativa entre la dilatación del ventrículo izquierdo y la frecuencia de transfusiones sanguíneas (> 5/año) y el síndrome torácico agudo ($p <0,05$).
Conclusión: El deterioro de la perfusión miocárdica en los niños con SCA no se observa con frecuencia. Debe considerarse el realizar la gammagrafía sólo en pacientes con síntomas cardíacos. Puesto que los valores de EF de los niños con SCA no se deterioran en las primeras etapas, el LV-MPI y la dilatación del ventrículo izquierdo deberían considerarse como un parámetro significativo.

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Introduction

Sickle cell anemia (SCA) is a chronic and congenital hematological disease which causes crucial destroys in many organs. Although cardiac problems do not seem to be frequently observed in children with SCA, even myocardial ischemia has been reported in literature.[1–3] Myocardial infarction and fibrosis were detected in 9.7% of postmortem examinations of adults and children with SCA.[4] Chronic anemia and iron overload are considered to be the possible causes of cardiac defects in SCA, although the exact reason is generally unknown. In recent literature, it has been suggested that cardiac abnormalities in children with SCA assumed to be related to disordered breathing, low asleep and waking oxygen saturations associated with left ventricle (LV) abnormalities.[5]

Finding out the myocardial problems in early stages is critical to prevent cardiac problems that might possibly develop later. Treadmill and echocardiographic examinations are not sufficient to detect myocardial ischemia in SCA patients.[6] In the field of nuclear cardiology, Tc-99m methoxy isobutyl isonitrile (MIBI) myocardial perfusion scintigraphy is a frequently and efficiently used method in order to demonstrate myocardial perfusion defects.[7] By using gated data, perfusion and the left ventricular function can be evaluated at the same time.[8] The aim of this prospective study is to evaluate myocardial perfusion and left ventricle functions with G-MPS in children with SCA and to compare the results with echocardiographic parameters.

Methods

Patients

In this study, we evaluated 43 consecutive children with SCA with a median age 12 years (ranged between 6 to 18 years). Fifteen of the patients were females; 28 were males. Children with diagnoses of homozygous SCA from the Pediatric Hematology Unit who were consulted to Pediatric Cardiology Unit and conducted to nuclear medicine department were evaluated prospectively between February 2007 and April 2009. Detailed physical examination, median levels of ferritin, pain crisis, history of splenectomy and hydroxyurea treatment as well as frequencies of transfusion, cerebrovascular accident, acute chest syndrome during the last year were recorded. The patients with the history of cerebrovascular accident and recurrent acute chest syndrome have been transfused every 3-4 weeks. Electrocardiography (ECG), echocardiography and Gated myocardial perfusion scintigraphy (G-MPS) were performed to all of the patients.

The exclusion criteria were not to have sickle-cell crisis during the last 3-months period, hemoglobin SC, hemoglobin S-thalassemia and the existence of other cardiac problems or chronic diseases. In accordance with the ethical standards laid down in the Declaration of Helsinki, the permission from the local ethics committee as well as the informed consent forms were obtained for this study (Local Ethical Committee B.30.2.MEÜ.0.20.05.04/347). Control cases were not included in the study because of the radiation effect.

Echocardiographic evaluation

A complete two-dimensional echocardiography was performed on each subject using an ultrasound imaging system with a size-appropriate transducer. Standard M-mode and Doppler echocardiography were performed in the supine and left lateral decubitus positions using a Vivid I echocardiography machine (GE Medical Systems Ultrasound, Tirat Hacarmel, Israel). Standard parasternal, apical, subxiphoid, and suprasternal views were used. The left ventricular end systolic and end diastolic dimensions (LVESD and LVEDD) were measured directly using M-mode echocardiography according to the recommendations of the American Society of Echocardiography.[9] Then; shortening fraction (SF) which is a quantitative measure of systolic function has also been calculated. As for the calculation of LVEDD *z* score, taking the literature into consideration, above + 2 SD values were accepted as a dilated ventricle.[10] On mitral flow, we measured maximum velocity of E (early flow velocity) and A (late flow velocity) waves and calculated E/A ratio. The myocardial performance index (MPI) of LV was calculated as the ratio of the summation of isovolumic contraction and relaxation time to the ejection time.[11] Higher MPI values have indicated worsening of combined systolic/diastolic function.

Gated myocardial perfusion scintigraphy

All patients underwent stress G-MPS. After 3 hours of fasting, a dose of Tc-99m MIBI scaled on the basis of the body surface area (mean 12 mCi, ranged between 8-15 mCi) was injected after the pharmacological stress testing by using dypridamole (140 μg/kg/min for 4 min). Thirty minutes after intravenous injection of Tc-99m MIBI, G-MPS imaging was acquired by a 90º configuration dual detector gamma camera (e-cam, Siemens Medical Systems, Germany) equipped with low-energy high-resolution collimators. The acquisition protocol of single photon emission computed tomography (SPECT) included; 64 projections with a 1.45 zooming factor (25 s/projection, 32 per detector, matrix size 64×64) over a 180° anterior arc divided into 8 frames per cardiac cycle. G-MPS images were reconstructed using back projection algorithm and a Butterworth filter with a cut-off 0.45 cycles per pixel and order 5. The rest study was omitted if the stress myocardial perfusion was interpreted as normal. None of the patients required sedation.

The images were evaluated by two nuclear medicine physicians visually as well as semi-quantitatively by the software programs, quantitative perfusion single photon emission computed tomography (QPS) and quantitative gated single-photon emission computed tomography (QGS) (Cedars-Sinai Medical Centre, Los Angeles, California USA). LV end-diastolic volume (LV-EDV), end-systolic volume (LV-ESV), ejection fraction (EF) parameters were also calculated by QGS. Index values of cardiac volumes (LV-EDVI and LV-ESVI) were derived as ml/m^2 by normalizing LV-EDV and LV-ESV according to body surface area (BSA) of the patients. In G-MPS, LV-EDVI over 75 ml/m^2 was accepted as dilatation depending on the LV-EDV reference values in relation to BSA.[12]

The perfusion, motion, and thickening scores were expressed as summed stress score (SSS), summed motion score (SMS), and summed thickening score (STS). The scores were obtained as a sum of all LV regions in a 20-segment model, on a 5-point scale for each segment between 0 and 5 for SSS (0: normal perfusion; 1: mildly reduced perfusion; 2: moderately reduced perfusion; 3: severely reduced perfusion; 4: absent uptake). A likewise scoring system was used for SMS (0: normal; 1: mild hypokinesis; 2: moderate hypokinesis; 3: severe hypokinesis; 4: akinesis; 5: dyskinesis) and STS (0: normal; 1: mildly impaired; 2: moderately impaired; 3: severely impaired; 4: absent thickening), as well. The LV EF was calculated using QGS program and was compared with the echocardiographic EF values. Lung-to-heart ratio (L/H), a sign of ventricular function deterioration, was also calculated by using 5×5 pixel size regions of interests over the lung and heart on anterior projection image. The L/H was derived by measuring and dividing the counts in the left upper lung by the counts over the myocardium.[13] The patients' radionuclide imaging results were compared to the clinical data and echocardiography.