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Assessment of the Myocardial Velocity by Tissue Doppler Imaging in Children of Sickle Cell Anemia

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Abstract

Background: Sickle cell anemia (SCA) is a formidable problem in India, and is more prevalent in Maharashtra. Cardiovascular events and complications are the leading cause of mortality and morbidity in patients with SCA. The aim of this study was to determine the issue Doppler Imaging (TDI) changes in left ventricular function in children suffering from SCA. *Methods and Results:* This case controlled study comprised of 20 cases of SCA, and 20 non-anaemic controls with normal haemoglobin and electrophoresis pattern. M-mode, Two-Dimensional, Doppler and Tissue Doppler Imaging (TDI) measurements of patients and controls were performed. In the study cases, age ranged from 5 years to 15 years with the mean age of 9.91 years. There were 12 males and 8 females in the study cases. Patients with SCA had significantly larger left atrial, and left ventricular dimensions. The ejection fraction and shortening fraction were lower in the cases, but the difference was not statistically significant. The LV tissue Doppler of the lateral annulus of mitral valve in SCD compared with control showed higher E′/A′ ratio and reduced S wave which was statistically insignificant ($p > 0.05$), similar finding were present at the level of interventricular septum and lateral annulus of tricuspid valve. *Conclusions*: TDI is a useful non-invasive technique to study the changes in cardiac structure and function. SCA in children results in a volume-overloaded heart with a significant increase in left ventricular dimensions.

Keywords: Sickle Cell Anemia; Tissue Doppler Imaging; Ventricular Function.

Introduction

Sickle cell anemia was first described in a west Indian student by Herrick in 1910. It is a significant health problem in India mainly in the central part of Maharashtra. The prevalence of SCA in different communities of Maharashtra ranges from 1.9% to 33.5%. Most of the SCA patient's has abnormal cardiac finding which are primarily the result of chronic anemia and the compensatory increased cardiac output. The disease is characterized by complications such as anemia, pulmonary hypertension, lungs, kidneys, spleen, and brain injuries due to deprived tissues and organs from oxygen-rich blood. The cardiac function in SCA is best evaluated by using echocardiographic modalities as two-dimensional, M-mode, Doppler, and TDI [1-4]. Doppler echocardiography is widely used to assess noninvasively the mitral and tricuspid flow for the assessment of diastolic function. TDI is a Doppler ultrasound modality that records regional systolic and diastolic velocities within the myocardium and time to peak myocardial velocities with high temporal resolution. It allows quantitative measurement of both systolic and diastolic velocities directly from the ventricular myocardium with the determination of the extent of mitral annular displacement in systole and diastole. It can be used at any point of the ventricular myocardium to give information on the regional wall motion. It can also be drawn upon in the assessment of ventricular

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dyssynchrony in biventricular pacing. The measurement of both systolic and diastolic components can be made simultaneously with Myocardial performance index (MPI) or Tei index [5-7]. It is used for the evaluation of the systolic and diastolic functions of the ventricle and is correlated with the index of the cardiac function in cardiac catheterization and magnetic resonance-derived right ventricular ejection fraction [8-9]. The assessment of peak systolic velocities of the ventricular myocardium with TDI is of incremental value to conventional echocardiography to assess global and regional ventricular performance in various clinical conditions [10]. TDI and transthoracic echocardiography are two useful tools to assess the risk of SCD. The present study was conducted to evaluate the cardiac functions and structure using TDI among children suffering from SCA compare to normal samples.

Material and Methods

This study was carried out in the Department of Pediatric, AVBRH hospital, Sawangi (Meghe), Wardha. It was a hospital based case-controlled study conducted from January 2015 to May 2017. The study comprised of 20 cases of sickle cell anemia (Hb SS), and 20 non-anaemic controls with normal haemoglobin and electrophoresis pattern. The control group was comparable in age and sex, free from cardiovascular disorder and not taking any cardioactive drugs. The study protocol was approved by the JNMC ethical institutional committee. Patients with SCA were excluded if they had a history of recent blood transfusion within three weeks, had hemoglobinopathy other than SCA, rheumatic heart disease, congenital heart disease, or advanced renal or hepatic failure. Detailed general and systemic examination was done in cases and controls with special emphasis were given for pulse, jugular venous pulse, blood pressure and presence of heart murmur. By using Phillip echocardiography machine, two-dimensional (2D), M-mode, Doppler and Tissue Doppler Imaging was performed.

The measurements of M-mode parasternal short-axis were conducted at end-diastole for interventricular septal thickness, LV posterior wall thickness and left ventricular diameter in diastole and systole. The fractional shortening and ejection fraction was estimated using M-mode and Simpson in the parasternal long- and short-axis views as well as in the apical four-chamber view. Also, the apical four-chamber view was used to record LV inflow velocities in which the peak flow velocities of the LV inflow in early diastole (E) and late diastole with atrial contraction (A) were measured. E/A velocity ratios were calculated for each cardiac cycle.

TDI was performed in the apical four-chamber view by placing a sample volume at three different site i) Lateral border of mitral valve annulus ii) Interventricular Septum and iii) Lateral border of tricuspid annulus. The Doppler beam was aligned as parallel as possible to the direction of the maximum annular motion. Peak systolic and diastolic velocities and timings of peak velocities at the LV and RV were assessed with TDI in all subjects. The following parameters were recorded: systolic velocity (S'), early diastolic velocity (E'), late diastolic velocity (A') and time intervals; isovolumetric contraction time (ICT), isovolumetric relaxation time (IRT) and ejection time (ET) at each site. The isovolumic relaxation time (IVRT') was measured from the end of the S' wave to the onset of the E' wave, and the isovolumic contraction time (IVCT') was measured from the end of the A' wave to the onset of the S' wave. The E/E' ratio was also calculated. Each TDI velocity or time interval was measured on 2-3 consecutive cardiac cycles and subsequently averaged. Then calculation of the mean E/E' (mitral inflow E wave/E' mitral annulus velocity) ratio was done. According to the E/E' ratio, patients were classified into: patients with E/E'≥ 15 (diastolic dysfunction), patients with E/E'≥ 8 but less than 15 (suspected diastolic dysfunction) and those with E/E'< 8 (without diastolic dysfunction). All data were obtained according to the recommendtions of the American Society of Echocardiography. The TDI Tei index is the IVCT plus IVRT divided by the ejection time (ET) and affords a simultaneous measurement of the atrioventricular inflow and ipsilateral semilunar outflow Doppler velocities [11-12].

Statistical Analysis

Data are expressed as mean± standard deviation (SD). The independent samples t-test was used to compare echocardiographic data between patients and controls. A value of $p < 0.05$ was considered statistically significant.

Results

In the study cases, age range was from 4 years to 15 years with the mean age of 7.91 years. There were 12 males and 08 females in the study group. On cardiovascular examination, mean heart rate was

82±11 beats per minute (bpm), mean blood pressure was 96±14/68±4 mmHg. On auscultation, 2 cases revealed an ejection systolic murmur heard maximally in 3rd left intercostal space parasternally. Patients with SCD compared with the control had a significant increase in the diameter of left atrium and left ventricle. There were no significant differences observed between the two groups for the left ventricle ejection fraction percentage. The ejection fraction and shortening fraction were lower in the cases, but the difference was not statistically significant. On Doppler study, 'E' and 'A' wave amplitude was higher in SCA cases as compared to the control which was not statistically significant. Standard Echocardiography parameters between cases and controls shows in Table 1. The LV tissue Doppler of the lateral annulus of mitral valve in SCD compared with control showed higher E'/A' ratio and reduced S wave ($p > 0.05$). The interventricular septum of tissue Doppler in SCD compared with control showed higher E'/A' ratio and reduced S wave ($p > 0.05$). In RV the tissue Doppler of the lateral annulus of tricuspid valve showed shorter S wave velocity higher E'/A' ratio as compared to control ($p > 0.05$). The results of the TDI study in the SCA cases and controls are depicted in Table 2. The isovolumic relaxation time (IVRT), isovolumic contraction time (IVCT), and Tei index were equal in both groups. Two patients had trivial tricuspid regurgitation without a significant pressure gradient.

Table 1: Standard Echocardiography parameters between cases and controls

Echocardiography Parameter	Cases (Means + SD)	Controls (Means + SD)	P Value
M-Mode			
LA	21.65± 3.81	18.36± 2.13	0.002
LVIVSd	9.61± 1.81	8.17± 3.21	0.236
LVIDd	35.65± 6.74	32.12± 2.31	0.000
Shortening Fraction	27.6± 3.08	28.7± 3.02	0.892
2-Dimension			
Ejection Fraction	59.90± 2.71	61.90± 4.65	0.984
Doppler			
Mitral E (cm/s)	115± 2.71	99± 11.12	0.991
Mitral A (cm/s)	67± 2.82	60± 1.23	0.123
Mitral E/A	1.84± 0.52	1.36± 0.51	0.999

Table 2: TDI derived parameters between cases and controls

TDI Parameter	Cases (Means + SD)	Controls (Means + SD)	P Value
TDI Lateral Mitral Annulus			
LV E' (cm/s)	17.12± 5.4	20.75± 6.2	0.983
LV A' (cm/s)	7.65± 2.60	11.05± 5.2	0.986
LV S' (cm/s)	12.1± 3.1	9.12±4.1	0.931
LV E' / A'	2.28± 0.61	2.19± 0.52	0.332
LV Tei Index	0.35± 0.07	0.32± 0.10	0.856
TDI Interventricular Septum			
Septal E' (cm/s)	12.9± 3.1	14.1± 2.13	0.876
Septal A' (cm/s)	6.62± 3.2	7.1± 1.21	0.728
Septal S' (cm/s)	9.4± 3.3	9.1± 1.22	0.562
Septal E' / A'	2.11± 6.1	2.07± 5.42	0.422
Septal Tei Index	0.33± 0.09	0.32± 0.06	0.379
TDI Lateral Tricuspid Annulus			
RV E' (cm/s)	16.2± 4.11	18.1± 1.72	0.993
RV A' (cm/s)	10.1± 5.91	10.2± 1.52	0.571
RV S' (cm/s)	13.4± 4.21	14.6± 1.23	0.825
RV E' / A'	1.87± 0.66	1.84± 0.28	0.416
RV Tei Index	0.38± 0.09	0.35± 0.11	0.874

Discussion

Sickle cell disease is an inherited disorder associated with significant morbidity. The SCD patients have abnormal hemoglobin in the RBCs, called hemoglobin S or sickle hemoglobin, because of adenine-to-thymine substitution in the sixth codon in the beta globin gene, replacing glutamic acid with valine in the beta-globin chain [13-14]. In SCA, the cardiovascular system is stressed by chronic anemia, recurrent small pulmonary artery occlusion, and myocardial hemosiderosis. Wali et al [15] reported that the dilated chamber in SCA was not associated

with any abnormality in systolic or diastolic ventricular function nor with significant hypertension. However, Lester et al [16] concluded that the major echocardiographic abnormality in SCA children was enlargement of left heart chambers; our study had similar findings. Kilinc et al [17] reported that mean left atrial dimension was increased in SCA group compared with controls ($p<0.001$), which is in concordance with the present study. Kingue et al [18] reported that the amplitudes of the mitral inflow 'E' and 'A' waves were increased, and the deceleration time (DT) was longer in the sickle cell group whereas in our study, 'E' and 'A' wave amplitude were increased in SCA cases as compared to the controls although the difference was not statistically significant. There were no abnormalities in the ejection fraction or shortening fractions. These results suggest early hemodynamic changes with progressive cardiac chamber dilation that become increasingly abnormal with growth. Notomi et al [19] assessed LV performance in 45 healthy controls by measuring rotational mechanics with TDI. In their study, LV performance increased significantly with age. Myocardial growth and an age-related increase in blood pressure may lead to greater myocardial velocities during systole in order to maintain adequate cardiac output. SCA is frequently complicated by pulmonary hypertension and cardiac involvement. Ferit Akgu et al [20] found that the LV functions were preserved in SCD patients with or without pulmonary hypertension and the RV diastolic function was disturbed only in SCD patients with pulmonary hypertension. The RV abnormal diastolic pattern may be in consequence of a rise in the RV afterload, secondary to pulmonary hypertension. Myocardial micro emboli may be caused by an ischemic area and diastolic abnormalities SCD patients, and these abnormalities are progressive with age. It should also be noted that low haemoglobin level and increased heart rate may worsen the cardiac disease in these patients [21].

TDI is an effective method for the evaluation of the cardiac function and myocardial velocities through the cardiac cycle. The Tei index is a simple parameter for the evaluation of the RV and LV functions and is correlated with the invasive measurements of the cardiac systolic and diastolic functions. TDI can record systolic and diastolic velocities during the same beat. No statistically significant changes found in cases as compare to controls in E'/A' ratio and S wave at the LV tissue Doppler of the lateral annulus of mitral valve. In patients with SCD, a chronic volume overload from prolonged anemia along with or without micro vasculopathy and myopathy, which affect all patients, may explain such abnormalities in echocardiographic examinations. Our SCA cases and controls had a normal Tei index. Prolongation of the ICT and IRT occurs in prolonged and chronic pathologic conditions such as increased LV load or an intrinsic LV myocardial dysfunction. A higher than normal Tei index is indicative of a reduced LV function. High-output state, which is seen in anemia, can also lead to heart failure. Lastly, the sickling process could directly affect the heart and induce myocardial ischemia and heart failure [5,21]. Chronic LV dysfunction in such patients maybe a significant determinant of the clinical outcome in acute states such as sickling crisis. The ejection fraction was within the normal limits in SCA cases, but it was lower than that of control group. Ghaderian M et al [22] in his study showed that Ea and Aa velocity in the mitral annulus and interventricular septum had no difference between the patients and controls (p value > 0.05), and nor was there any difference between the two groups as regards the Tei index, Ea/Aa, ejection fraction, and shortening fraction ($p > 0.05$). AboHadeed HM et al [23] reported that TDI technique appears to be more sensitive than conventional echocardiography in the early detection of myocardial dysfunction in children with SCA. This provides insights into the value of early screening and the potential for preventive therapy in children to avert cardiac morbidity and mortality in adults with SCA. The limitations of the present study was the small sample size.

Conclusion

TDI is a useful non-invasive technique to study the changes in cardiac structure and function. SCA in children results in a volume-overloaded heart with a significant increase in left ventricular dimensions. The evaluation of LV systolic and diastolic function via TDI did not indicate significant differences between SCD children compared to healthy controls.

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