ความผิดปกติทางหัวใจในผู้ป่วยโรคบีต้าธาลัสซีเมียฮีโมโกลบินอี ที่มีอาการรุนแรงและไม่รุนแรง

Cardiac abnormalities in mild to severe β thalassemia/HbE disease

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บทคัดย่อ

การเปลี่ยนแปลงทางหัวใจในผู้ป่วยโรค β thalassemia/HbE disease ได้มีการศึกษาแล้วบ้างในผู้ป่วยเด็กแต่ในขณะที่ข้อมูลของการเปลี่ยนแปลงทางหัวใจในผู้ป่วยเด็กโรคนี้ยังไม่มีการศึกษาละเอียด คณะผู้วิจัยได้ศึกษาความผิดปกติทางหัวใจในผู้ป่วยโรค β thalassemia/HbE disease จำนวน 48 คน มีอายุเฉลี่ย 12.5 + 4.4 (range, 2-23) ปี ผู้ป่วยทุกรายมีค่า left ventricular ejection fraction และ fractional shortening ปกติ และ left ventricular mass และ left ventricular free wall thickness ไม่เปลี่ยนแปลงจากการศึกษาปีก่อน ($p>0.05$) นอกจากนั้น Left ventricular diastolic function ซึ่งประเมินโดย mitral inflow พบว่า peak early mitral inflow velocity (E) และ peak late mitral inflow velocity (A) ไม่เปลี่ยนแปลงจากปีก่อน ($p<0.05$) การติดตามผู้ป่วยเหล่านี้เป็นเวลานาน ๆหลายปีมีความจำเป็นเพื่อจะศึกษาการเปลี่ยนแปลงของหัวใจในผู้ป่วยโรคนี้

Abstract

Follow-up study of cardiac involvement including echocardiographic studies in β thalassemia/HbE disease has been lacking. To prospectively follow-up cardiac abnormalities in mild to severe β thalassemia/HbE disease, we re-examined 48 patients with the use of echocardiography. The patients were aged 12.5 + 4.4 (range, 2-23) years. All patients had normal left ventricular ejection fraction and fractional shortening. In addition, patients had left ventricular mass and left ventricular free wall thickness comparable to previous studies ($p>0.05$). Peak early mitral inflow velocity (E) and peak late mitral inflow velocity (A) were also comparable with previous studies ($p>0.05$). Serial longer follow up of these patients is needed to address any diastolic abnormalities before the development of systolic dysfunction, which is the late sign of cardiac involvement of this disease.

คำสำคัญ: บีต้าธาลัสซีเมียฮีโมโกลบินอี ความผิดปกติทางหัวใจ การตรวจคลื่นเสียงสะท้อนหัวใจ

Keywords: β thalassemia/HbE disease, cardiac abnormalities, echocardiography

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Introduction

Thalassemia is an inherited hemoglobin disorder caused by impaired synthesis of the globin chains and resulting in chronic hemolytic anemia (Forsburg and Nathan, 1990; Engle et al., 1964). The severe form is thalassemia major and the milder form is thalassemia intermedia (Forsburg et al., 1990; Engle et al., 1964; Zurlo et al., 1989). Cardiac complications are important features of the clinical spectrum of thalassemia (Forsburg et al., 1990; Engle et al., 1964; Zurlo et al., 1989). They are the major causes of death and have been well documented in thalassemia major (Zurlo, De Stefano and Borgna-Pignatti, 1989). Although thalassemia major and thalassemia intermedia share common basic pathological mechanisms, cardiac involvement may be different in the latter because these patients generally have lower iron loads.

The β thalassemia/HbE disease seen in Thailand and Southeast Asia is generally classified as thalassemia intermedia. The purpose of the present study was to follow-up the severity of the cardiac involvement in β thalassemia/HbE disease.

Patients and Methods

The study population consisted of 59 patients with β thalassemia/HbE disease who were followed at the Department of Pediatrics of the Khon Kaen University from October 2002 to September 2003. Exclusion criteria were patients with rheumatic valvular heart disease or with congenital heart disease. Data on age, sex, hemoglobin level, serum ferritin, units of blood transfusion received, and durations of receiving desferrioxamine were collected. Chest roentgenogram, electrocardiogram and color Doppler echocardiography with Sonos 5500 were done in all patients. Of the 59 patients, 48 patients were re-examined a year later from October 2003 to September 2004. Data on age, sex, hemoglobin level, serum ferritin, units of blood transfusion received, duration of receiving desferrioxamine were re-collected. Electrocardiogram and color Doppler echocardiography with Sonos 5500 were done in all patients during the follow-up. Informed consent was obtained from each patient. Statistical analysis included mean, standard deviation and paired student t test.

Results

None of the 59 patients had clinical manifestations of congestive heart failure or pericarditis. Of the follow-up of the 48 patients a year later, electrocardiographic abnormalities were found in 4 (8.3%) (Table 1).

Echocardiographic findings of β thalassemia/HbE patients are shown in Table 2. The mean of left ventricular free wall thickness of the initial study was comparable to that of the follow-up study (0.6+0.1 vs 0.6+0.16 mm/M^2) ($p > 0.05$).

The average LV myocardial mass of the initial study was also comparable to that of the follow-up study (80+19 vs 81+19 g) ($p > 0.05$). In addition, comparable results were found between the initial study and the follow-up study including mitral E velocity (126+16 vs 125+15 cm/sec) ($p > 0.05$) and mitral A velocity (68+14 vs 69+10 cm/sec) ($p > 0.05$).

Discussion

The present study demonstrates that echocardiographic changes occurring in children with β thalassemia/HbE disease during the one-year

follow-up period were minimal. These comparable parameters also included peak early mitral inflow velocity (E) wave, peak late mitral inflow velocity (A) wave, E/A ratio, left ventricular free wall thickness and left ventricular myocardial mass.

Left ventricular fraction shortening and ejection fraction were normal in all patients. The failure to detect impaired ventricular systolic function can be explained by the fact that hemodynamic effects associated with anemia helped to maintain normal left ventricular ejection fraction and normal fractional shortening (Intragumtornchai et al., 1994).

The present study might not show any significantly changes in cardiac parameters as seen in others reports in adults since the mean age of our patients was only 12.5+4.4 years (Intragumtornchai et al., 1994; Seliem et al., 2002; Aessopos et al., 2001; Bosi et al., 2003; Kremastinos et al., 2001). Previous reports of adult patients with thalassemia intermedia from Greece, show that congestive heart failure developed in 5.4 % of patients aged 41.6 + 11.6 years (Aessopos et al., 2001). Pericarditis was found in 8.1% at a mean age of 25.7+14.4 years (Aessopos et al., 2001). All their adult patients had higher cardiac output than that of controls (9.34+2.28 vs 6.39+1.44 L/min; $p<0.001$). The patients in this study were also classified as thalassemia intermedia since they were not much dependent on blood transfusions. They still had no congestive heart failure and no pericarditis during this follow-up study.

The natural history of β thalassemia/HbE disease is still not fully understood, since it has a wide range of clinical severity (Intragumtornchai et al., 1994). This study has demonstrated the early cardiac changes occurring in pediatric patients who have β thalassemia/HbE disease and minimal changes were detected during a one-year follow-up study. Serial follow-up of these patients is needed to address any diastolic abnormalities before the development of systolic dysfunction, which is the late sign of cardiac involvement of this disease (Borow et al., 1982; Freeman et al., 1983).

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Table 1 Clinical and demographic findings of β thalassemia/HbE disease patients during the one-year follow-up.

Group		Initial study (59 cases)	Follow-up study (48 cases)
Age (yr) (mean ± SD)		1-22 (11.2 ± 4.5)	2-23 (12.5 ± 4.4)
Sex	Male	27	21
	Female	32	27
Body surface area (m^2)		1.0± 0.2	1.15 ± 0.2
Heart rate (beats/ min)		90 ± 10	88 ± 11
Mean arterial blood pressure (mm Hg)		70±12	73±12
Serum ferritin (ng/ml)		1066 ± 974	1050 ± 950
Hb level (mg %)		6.7 ± 1.2	6.8 ± 1.1
Regular Blood transfusion (cases)		40	32
Desferrioxamine (cases)		41	35
Abnormal Electrocardiograms		4	4

Table 2 Echocardiographic findings in patients with β thalassemia/HbE

Echocardiographic findings	Initial study (59 cases)	Follow-up study (48 cases)
LV free wall (mm/M^2)	0.6 ± 0.10	0.6 ± 0.16
RV free wall (mm/M^2)	0.5 ± 0.10	0.5 ± 0.15
IVS thickness (mm/M^2)	0.7 ± 0.2	0.7 ± 0.1
LVED d (mm/M^2)	4.5 ± 0.6	4.5 ± 0.6
LVES d (mm/M^2)	2.8 ± 0.5	2.8 ± 0.5
LV fractional shortening (%)	38 ± 5.1	39 ± 5.2
LV ejection fraction	56 ± 7	57 ± 5
LV myocardial mass (g)	80 ± 19	81 ± 19
Mitral E velocity (cm/sec)	126 ± 16	125 ± 15
Mitral A velocity (cm/sec)	68 ± 14	69 ± 10
Mitral E/A	1.9 ± 0.5	1.9 ± 0.5
Mitral DT of early inflow (ms)	141 ± 50	140 ± 60
Tricuspid E/A	1.5 ± 0.5	1.5 ± 0.5
Tricuspid DT of early inflow (ms)	135 ± 52	137 ± 51
Tricuspid regurgitation (mm Hg)	10 ± 5	10 ± 3