Myocardial disease in Egyptian Beta Thalassemia patients

Thesis

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List of Content

Subjects Page

List of Abbreviations

ECG	Electrocardiography
ECHO	Echocardiogram
EF:	Ejection fraction
EPO	*Erythropoietin*
FS	Fraction Shortening.
GLPS	Global longitudenal peak systolic strain.
GLPS A2C	Global longitudenal peak systolic strain two chambers apical
GLPS A4C	Global longitudenal peak systolic strain four chambers apical
GLPS AVG	Global longitudenal peak systolic strain average
GLPS LAX	Global longitudenal peak systolic strain longitudenal axis
HO-1	Heme-oxygenase1
HRV	Heart rate variability
IL	interleukin
IVSD	Interventricular septum diastole.
LPI	Labile plasma iron
LV	Left ventricular
LVIDd:	Left ventricle internal diameter diastole
LVPWD	Left ventricular posterior wall diastole
MnSOD	manganese-superoxide dismutase
MPs	microparticles
MRI	Magnetic resonance imaging
NO	Nitric oxide
NTBI	Non-transferrin-bound iron
PH	Pulmonary hypertension
ROS	Reactive oxygen species
TDI	Tissue Doppler imaging
TM	Thalassemia major
TNF	Tumor necrosing factor

List of Figures

List of Tables

Abstract

Background: The chronic transfusion, combined with extravascular haemolysis and increased intestinal absorption of iron in BTM patients, leads to significant haemosiderosis of all organs, including the heart. The new parameters of cardiac function, derived from two-dimensional speckle-tracking echocardiography could be useful for an early diagnosis of cardiac involvement in patients with thalassemia major. **Aim:** to detect early myocardial disease in beta thalassemia and to assess the effect of iron load on the myocardium by speckle tracking echocardiography correlating with the efficacy of iron chelation and other risk factors.

Methods: Thirty transfusion dependant β-TM patients were recruited. A detailed medical history (including transfusion, chelation, hepatitis C virus infection history) was gathered from the medical records. Laboratory investigations (CBC, liver function tests, markers of hemolysis), as well as calculation of mean serum ferritin in last 2years were done. Echocardiography (M mode and Speckle Tracking) was done to all patients, while MRI T2* and ECG holter were performed for patients with abnormal speckle echocardiography.

Results: Cardiac affection by speckled echocardiography (elevated longitudinal strain than 11%) was found in 33.3% of BTM patients. There were no significant differences between βTM patients with mean serum ferritin ≥2500 µg/L and those with serum ferritin <2500 µg/L as regard M mode echocardiographic parameters. Patients with mean serum ferritin > 2500 ng/mL in the last 2 years prior evaluation showed a significantly lower longitudinal strain

(GLPSLAX) (p=0.043) which is further proved by the significantly negative correlation with the mean serum ferritin (p=.002). There were no significant differences between both splenectomized and non splenectomized patients nor between patients on mono and those on combined chelation therapy as regard echocardiographic data (M mode,speckle). We did not find significant differences between patients with cardiac affection by speckled and those without as regard M mode echocardiographic data. When evaluating the cardiac MRIT2* of the 10 patients with proven myocardial affection by speckled echocardiography, we found that 9 out of 10 patients had low cardiac MRIT2* less than 20 ms and 3 out of 10 patients had low ejection fraction below 60 % .

Conclusion: An abnormal global longitudinal strain despite preserved LV systolic functions; with a significant negative correlation with mean serum ferritin; was observed among BTM patients. Magnetic Resonance Imaging T2* technique is still considered the reference standard in myocardial iron overload, its routine use is limited by its high costs, poor availability, yet speckle tracking echo techniques might be considered as an alternative effective method to detect early myocardial disease before evident systolic dysfunction.

INTRODUCTION

The thalassaemias are common genetic disorders worldwide and they constitute a major problem for patients, health providers and society. Beta thalassemia patients usually require regular blood transfusions to survive, however the chronic transfusion, combined with extravascular haemolysis and increased intestinal absorption of iron, leads to significant haemosiderosis of all organs, including the heart. ***(Mavrogeni et al., 2011).***

Cardiac complications such as heart failure and arrhythmias are the major causes of death in Beta Thalassemia patients accounting for up to 67% of death***. (Borgna et al.,2004).*** Iron cardiomyopathy is reversible, if chelation starts in time. Once heart failure develops, the prognosis is frequently poor. ***(Chouliaras etal ., 2009)***

The incidence of iron overload cardiomyopathy ranges from 11.4 to15.1% in Beta-Thalassemia major patients ***(li etal.., 2002)***. In the early stage, patients are usually asymptomatic.

Restrictive cardiomyopathy usually occurs before dilated cardiomyopathy, in accordance with diastolic dysfunction which normally happens before systolic dysfunction and overt heart failure. ***(De C et al., 2005).***

Speckle-tracking echocardiography is a new non invasive ultrasound imaging technique that allows for an objective and quantitative evaluation of global and regional myocardial function.(***Geyer H et al.,2011).***

The new parameters of cardiac function, derived from two-dimensional speckle-tracking echocardiography could be useful for an early diagnosis of cardiac involvement in patients with thalassemia major ***(Ines et al.., 2012).***

Currently cardiac MRI (CMR) has been known as a non- invasive technique of choice for monitoring iron overload in the heart ***(Mavrogeni et al., 2011)*** Cardiac T2* magnetic resonance identifies patients at high risk of heart failure and arrhythmia from myocardial siderosis in thalassemia major and is superior to serum ferritin and liver iron. (***Kirk et al., 2009)***