

Electro Cardiographic Assessment in Patients with Transfusion Dependant Beta Thalassemia Major Using Stress ECG and 24hrs ECG Monitoring

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا
إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

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List of Abbreviations

| Abb. | Mean |
|--------------|--|
| β | Beta |
| AHSP | Alpha Hb stabilizing protein |
| BM | Bone marrow |
| CMR | Cardiac magnetic resonance |
| CVS | Chorionic villous sampling |
| DBP | Diastolic blood pressure |
| DFO | Desferoxamine |
| DFT | Desferrithiocin |
| DM | Diabetes mellitus |
| EDV | End diastolic volume |
| EF | Ejection fraction |
| ESV | End systolic volume |
| FS | Fractional segment |
| HBED | Hydroxy benzyle ethylene diamine-diacetic acid |
| HCV | Hepatitis C virus |
| HDL | High density lipoprotein |
| HIC | Hepatic iron concentration |
| IFN | Interferon |
| IGF-1 | Insulin like growth factor-1 |
| IVSD | Inter ventricular septal diameter |
| LAD | Left atrial diameter |
| LDL | Low density lipoprotein |

| Abb. | Mean |
|--------------|---|
| LIC | Liver iron concentration |
| LPI | Labile plasma iron |
| LV | Left ventricle |
| LVEF | Left ventricle ejection fraction |
| LVIDd | Left ventricular intra diastolic diameter |
| LVPWd | Left ventricular posterior wall diameter |
| METs | Metabolic equivalent tasks |
| NTBI | Non transferrin bound iron |
| PH | Pulmonary hypertension |
| PVC | Premature ventricular contraction |
| PVR | Pulmonary vascular resistance |
| RDW | Red Cell distribution width |
| SBP | Systolic blood pressure |
| SVT | Supra ventricular tachycardia |
| TI | Thalassemia intermedia |
| TM | Thalassemia major |

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INTRODUCTION

Thalassemia is a genetic disorders in globin chain production. In individuals with β -thalassemia, there is either a complete absence of β -globin production (β° -thalassemia) or a partial reduction (β^{+-} thalassemia) (*Debaun and Vichinisky, 2007*).

Beta thalassemia usually become symptomatic as severe hemolytic anemia during 2nd 6 month of life, regular blood transfusion are necessary in these patients to prevent cardiac decompensation caused by anemia (*Eldor et al., 2002*).

Conventional management of β -thalassaemia major requires regular blood transfusions. This leads to excess iron accumulation, initially in the reticuloendothelial system and subsequently in all parenchymal organs, mainly heart, pituitary gland, pancreas and gonads, resulting in serious and sometimes fatal clinical complications (*Christoforidis et al., 2006*).

Transfusions are given on regular basis to maintain hemoglobin level above 10g / dl, which prevents progressive marrow expansion and cosmetic problems associated with facial bone changes and minimize cardiac dilation and osteoporosis (*Wonke et al., 2001*).

The major cause of morbidity and mortality in patients with beta thalassemia major is iron overload associated with chronic blood transfusion therapy, which can lead to iron deposition and damage to the heart, liver and endocrine organs and other organ failure. Iron toxicity is the leading cause of death in beta thalassemia major patients (*Wood et al., 2005*).

Vascular dysfunction with increased arterial stiffness and endothelial dysfunction has been demonstrated in patients with beta-thalassemia major (*Cheung et al., 2002*). Endothelial dysfunction as well as arterial stiffening is an important precursors for atherosclerosis (*Davignon and Ganz, 2004*), studies have also suggested a link between iron load and risk of atherosclerosis (*Timothy et al., 2007*).

Thalassemic (TM) patients are subjected to oxidative tissue injury because of continuous blood transfusions. It has been documented that circulating LDL from TM patients show marked oxidative modification that could represent an event leading to atherogenesis (*Brizzi et al., 2002*).

In recent years increasing evidence suggests that the oxidative modification of low-density lipoprotein (LDL) is the key step in the sequence of events leading to atherogenesis-related vascular alterations, so modified LDL