OXIDIZED LDL ANTIBODIES (OLDLAB) IN THALASSEMIC PATIENT

Thesis

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Dina Mohamed Foaad


Dedication
To:
My Dear Parents
Who gave me too much
And received too little
Dina


بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ وَكَانَ
فَضْلُ اللهِ عَلَيْكَ
عَظِيمًا
صدق الله العظيم
سورة النساء آية (١١٣)

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List Of Abbreviations

Abbrev.	Full term
ACAT	Acyl-CoA:cholesterol acyltransferase
AHSP	Alpha hemoglobin stabilizing proteins
APS	Antiphospholipid syndrome
ATIII	Anti thrombin III
ATP	Adenosine triphosphate
BCG	Bacillus calmette Guerin
BM	Bone marrow
BMI	Body mass index
BMT	Bone marrow transplantation
βTM	Beta thalassemia major
CBC	Complete blood count
CIM	Carotid intema thickness
CM	Chylomicrons
CMR	Cardiac magnetic resonance imaging
CVD	Cardiovascular disease
CVS	Chroinic villous sampling
DFO	Desferoxamine
DFT	Tridentate desferrithiocin
DM	Diabetes mellitus
EPO	Erythropoietin
FFA	Free fatty acids
GH-IGF-1	Growth hormone insulin like growth factor-1
GSH	Reduced Glutathione
HB	Hemoglobin
HBED	Hydroxybenzyl-ethylene diamine-diacetic acid
HBF	Hemoglobin F
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HDL	High density lipoprotein

List Of Abbreviations (Cont...)

Abbrev.	Full term
HIC	Hepatic iron concentration
HIV	Human immunodeficincy virus
HLA	Human leucocyte antigen
HPO	Bidentate hydroxypyrinones
ICL 670	Deferasirox
IFN	Interferon
IgA	Immunoglobulin A
IGF	Insulin like growth factor
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IVIG	Intravenous immunoglobulin
L1	Deferiprone
LDH	Lactate dehydrogenase
LDL	Low density lipoprotien
LIC	Liver iron concentration
LOX	Lactin like oxidized LDL
LPI	Labile Plasma Iron
LV	Left ventricle
LVEF	The left ventricular ejection fraction
m RNA	Messanger RNA
MRI	Magnetic resonance imaging
NTBI	Non-transferrin bound iron
OxLDL Ab	Oxidized LDL antibody
PCR	Polymerase chain reaction
PH	Pulmonary hypertension

List Of Abbreviations (Cont...)

Abbrev.	Full term
PIH	Pyridoxal Isonicotilloyl Hydrazone
PUFs	Polyunsaturated fatty acids
PVR	Pulmonary venous return
RBCs	Red blood cells
RDW	Red blood cell distribution width
ROS	Reactive oxygen species
s.TFR	Serum transferrin receptor
SD	Standered deviation
SPL	Splicing mutation
T4	Thyroxin hormone
TBARs	Thiobarbituric Acid Reactive Substances
TC	Total cholesterol
TG	Triglyceride
Th1	Type 1of T helper cells th 2 Type 2 of T helper cells
TI	Thalassemia intermedia
TM	Thalassemia major
TNF	Tumor necrosis factor
VLDL	Very low density lipoprotien
HSM	Hepatospelenomegaly

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 ***(Afroditi and Vassilios, 2006)***.

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

The major cause of morbidity and mortlaity 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 per 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 are internalized in monocyte-derived macrophages through cell surface scavenger receptors, an event that leads to foam