الأجسام المضادة للأكسدة
(OLABntibodies)
فى مرض السكرى النوع الأول

رسالة

توطئة للحصول على درجة الماجستير
فى طب الأطفال

مقدمة من

إنجى صفوت لويس
بكالوريوس الطب والجراحة

تحت إشراف

أ.د .محمد أبو الأسرار محمد البيومى عفيفى
أستاذ مساعد طب الأطفال
كلية الطب -جامعة عين شمس

د .نرمين حلمى محمود
أستاذ مساعد الباثولوجيا الإكلينيكية والكيميائية
كلية الطب -جامعة عين شمس

د .نيفين جمال أندراوس
مدرس طب الأطفال
كلية الطب -جامعة عين شمس

كلية الطب
جامعة عين شمس
~~٢٠١١~~٢٠١٢

OXIDIZED LOW DENSITY L-IOPROTEIN ANTIBODIES (OLABB) IN TYPE I DIABETES MELLITUS

Thesis

Submitted for Partial Fulfillment of the
Master. Degree in Pediatrics

Presented By

Engy Safwat Lewis
(M.B.B.Ch.)

Under the Supervision of

Dr. Mohamed Abo-El-Asrar Mohamed
Assistant Professor of Pediatrics
Faculty of Medicine - Ain Shams University

Dr. Nermine Helmy Mahmoud
Assistant Professor of Clinical and Chemical Pathology
Faculty of Medicine - Ain Shams University

Dr. Nevine Gamal Andrawes
Lecturer of Pediatrics
Faculty of Medicine - Ain Shams University

Ain Shams University
Faculty of Medicine
~~*2011*~~*2012*

First and Foremost thanks are to ALLAH, The compassionate and merciful, whose help is the main factor in accomplishing this work.

It is my pleasure to express my deepest thanks and gratitude to ***Dr. Mohamed Abo-ElAsrar Mohamed,*** Assistant Professor of Pediatrics, Ain Sams University for his great help and support, kind supervision and continuous encouragement. I am truly grateful for him.

I would like also to express my profound thanks and gratitude to ***Dr. Nermine Helmy Mahmoud,*** Assistant Professor of Clinical and Chemical Pathology, Ain Shams University for her constructive guidance, remarkable effort, and scientific assistance and whatever have been said, is little to express my respect and thanks to her.

I am truly indebted to ***Dr. Nevine Gamal Andrawes,*** Lecturer of Pediatrics, Ain Shams University for her meticulous supervision, encouragement, unlimited assistance and guidance during this work.

Last but not least, I would like to express my deep thanks and gratitude to all my dear ***Patients*** hoping them a good health.

Engy Safwat Lewis

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

List Of Contents

Title	Page No.
Introduction	1
Aim of the work	4
Review of literature	
• Diabetes mellitus	**Error! Bookmark not defined.**5
• Oxidized low density lipoprotein antibodies	56
Subject and methods	81
Results	89
Discussion	116
Summary	128
Recommendation	132
References	134
Arabic summary	——

List Of Tables

Tab. No.	Title	Page No.
Table (1):	Etiological classification of diabetes mellitus	6
Table (2):	Characteristic features of type 1 compared with type 2 diabetes in young people	8
Table (3):	The clinical and biological characteristic of different subtypes of type 1 diabetes.	10
Table (4):	Criteria for diagnosis of diabetes mellitus and impaired glucose	27
Table (5):	Classification of diabetic neuropathy.	35
Table (6):	Comparison between different types of insulin	42
Table (7):	Composition of the lipoproteins in plasma of humans.	64
Table (8):	Sex distribution between the three studied groups	102
Table (9):	Comparison between the three studied groups according to age.	103
Table (10):	Anthropometric measures of the three studied groups	104
Table (11):	Comparison between the three studied groups according to the laboratory findings	105
Table (12):	Comparison between group I and II regarding anthropometric measures and duration of DM	109
Table (13):	Comparison between the group I and group II according to laboratory findings	110
Table (14):	Correlation between OXLDL Ab and the studied parameters in the three groups	111

...matted
...matted
Field Code Changed
Field Code Changed
Field Code Changed
Field Code Changed
Field Code Changed
Field Code Changed
Field Code Changed
Field Code Changed
Field Code Changed
Field Code Changed
Field Code Changed
...matted
Field Code Changed
Field Code Changed
Field Code Changed
...matted
Field Code Changed
Field Code Changed
...matted
Field Code Changed
Field Code Changed
...matted
Field Code Changed
Field Code Changed
...matted
Field Code Changed
Field Code Changed
Field Code Changed
Field Code Changed
...matted
Field Code Changed

Table (1): Etiologic classification of diabetes mellitus 6

Table (2): Characteristic features of type1 compared with type 2 diabetes in young people: 7

Table (3): The clinical and biological characteristic of the different subtypes of type 1 diabetes: 8

Table (4): Criteria for the diagnosis of diabetes mellitus 15

Table (5): Complications of Diabetes 16

Table (6): The early changes are only detectable on careful clinical or laboratory examination. 20

Table (7): Classification and features of diabetic retinopathy. 20

Table (8): Methods for prevention of type 1 diabetes 23

Table (9): Factors determining the glycemic response to acute exercise in type 1 DM patients 33

Table (10): Types of insulin currently available 34

Table (11): Indications for the use of the pump in Children of different ages: 43

Table (12): Comparison between different types of insulin 56

Table (13): Composition of the lipoproteins in plasma of humans. 67

Table (14): Age of the studied groups 94

Table (15): Sex distribution between studied groups 95

Table (16): Comparison between the studied groups according to the age of the patients 96

Table (17): Comparison between the three studied groups according to the anthropometric measures 97

Table (18): Comparison between the three studied groups according to the laboratory findings 98

LIST OF TABLES (CONT…)

Tab. No.	.....	Title

Table (19): Comparison between the good metabolic control group and bad metabolic control group according to anthropometric measurements 102

Table (20): Comparison between the good metabolic control group and bad metabolic control group according to laboratory findings 103

Table (21): Comparison between the good control group and the healthy group according to studied parameters 105

Table (22): Comparison between the bad control group and the healthy group according to studied parameters 107

Table (23): Correlation between OLDL antibodies and the studied parameters in the three groups 109

Formatted: Font: (Default) Times New Roman, 12 pt, Complex Script Font: Times New Roman, 12 pt

Formatted: Font: (Default) Times New Roman, Complex Script Font: Times New Roman

Formatted: Font: (Default) Times New Roman, 12 pt, Complex Script Font: Times New Roman, 12 pt

List Of Figures

Fig. No.	Title	Page No.

Figure (1): Pathogenesis of type 1 diabetes..... 14

Figure (2): Triggering of beta-cell autoimmunity..... 17

Figure (3): The pathogenesis of islet cell destruction..... 22

Figure (4): Natural history of type 1a diabetes..... 24

Figure (5): Diabetic background retinopathy..... 33

Figure (6): The multifactorial pathogenesis of diabetic neuropathy..... 37

Figure (7): Contributing factors of diabetic management..... 40

Figure (8): Syringe and needle..... 44

Figure (9): Disposable insulin pen..... 44

Figure (10): Refillable insulin pen..... 45

Figure (11): Disposable insulin device with large dial..... 45

Figure (12): Insulin pump, showing an infusion set loaded into spring- Loaded insertion device..... 46

Figure (13): Insulin pump attached to its user with an infusion set..... 47

Figure (14): Islet cell transplantation..... 49

Figure (15): The medical equipment approach to an artificial pancreas..... 52

Figure (16): The Bio-artificial pancreas..... 53

Figure (17): Gene therapy using an adenovirus vector..... 54

Figure (18): Transport of cholesterol between the tissues in humans..... 61

Figure (19): Summary of the main events of lipid peroxidation and foam cell formation..... 76

Formatted: Justify Low, Indent: Before: 0 cm, Hanging: 2.59 cm, After: 2.22 cm, Space Before: 6 pt, Tab stops: 12.7 cm, Right,Leader: ... + Not at 12.68 cm

Formatted: Font: Bold, Complex Script Font: Bold

Formatted: After: 0 cm

Formatted: Font: 13 pt, Complex Script Font: 13 pt

LIST OF FIGURES (CONT...)

Formatted: Justify Low, Indent: Before: 0 cm, Hanging: 2.59 cm, After: 2.22 cm, Space Before: 6 pt, Tab stops: 12.7 cm, Right,Leader: ... + Not at 12.68 cm

Formatted: Font: Bold, Complex Script Font: Bold

Formatted: Font: Bold, Complex Script Font: Bold

Formatted: Font: Bold, Complex Script Font: Bold

Formatted: Font: Bold, Complex Script Font: Bold

Formatted: Font: Bold, Complex Script Font: Bold

Formatted: Condensed by 0.2 pt

Fig. No.	Title	Page No.
Figure (20):	Sex distribution between the three studied groups.	102
Figure (21):	Comparison between the studied groups according to the age of the patients	103
Figure (22):	Comparison between the three studied groups according to the anthropometric measures.	104
Figure (23):	Comparison between the three studied groups according to Hb and HbA1c.	106
Figure (24):	Comparison between the three studied groups according to TG, TC and OxLDL Ab.	107
Figure (25):	Comparison between the three studied groups according to LDL and HDL.	107
Figure (26):	Comparison between the good metabolic control group and bad metabolic control group according to anthropometric measurements.	109
Figure (27):	Comparison between the group I and group II according to PLT, TG, HDL, OXLDL antibodies.	110
Figure (28):	Correlation between OxLDL Ab and duration in group I.	112
Figure (29):	Correlation between OxLDL Ab and duration in group II.	112
Figure (30):	Correlation between HbA1C and OXLDL in group I.	113
Figure (31):	Correlation between HbA1C and OXLDL in the good control group.	113
Figure (32):	OxLDL Ab levels in group I	114

Figure (1): Progression from genetic susceptibility to overt type I diabetes 11

Figure (2): A possible mechanism for the immune destruction of pancreatic B-cells in IDDM 13

Figure (3): Clinical course of diabetic nephropathy 21

Figure (4): Insulin delivery devices 35

Figure (5): How Islet Cell Transplant surgery works 37

Figure (6): The artificial pancreas 38

Figure (7): The Exubera inhaler 40

Figure (8): The catheter at the end of the insulin pump is inserted through a needle into the abdominal fat of a person with diabetes. 42

Figure (9): An image of an insulin pump 58

Figure (10): Another example of insulin pumps of Medtronic 58

Figure (11): An image shows a miniature size of in vivo blood glucose sensor that is being developed 59

Figure (12): Transport of cholesterol between the tissues in humans 65

Figure (13): Summary of the main events of lipid peroxidation and foam cell formation. The OLDL particle is not only rapidly uptaken by macrophages via the scavenger receptor, but has also antigenic properties 81

Figure (14): Sex distribution between studied groups. 95

Figure (15): Comparison between the studied groups according to the age of the patients 96

List Of Figures (Cont...)

Fig. No. ..... **Title**

Figure (16): Comparison between the three studied groups according to the anthropometric measures. 97

Figure (17): Comparison between the three studied groups according to Hb, Duration of DM, WBC. 99

Figure (18): Comparison between the three studied groups according to PLT, RBC, TG, T. cholesterol and OXLDL. 99

Figure (19): Comparison between the three studied groups according to T3, T4 and C-peptide. 100

Figure (20): Comparison between the three studied groups according to T3, T4 and C-peptide. 100

Figure (21): Comparison between the good metabolic control group and bad metabolic control group according to anthropometric measurements 102

Figure (22): Comparison between the good metabolic control group and bad metabolic control group according to Hb, WBC, HbA1c, T3, T4 and C-peptide. 104

Figure (23): Comparison between the good metabolic control group and bad metabolic control group according to PLT, TG, HDL, OXLDL antibodies. 104

Figure (24): Comparison between the good control group and the healthy group according to Ht, BMI HB. 106

List Of Figures (Cont...)

Fig. No. ..... Title

Figure (25): Comparison between the good control group and the healthy group according to PLT, RBC, TG, T. cholesterol and OXLDL 106

Figure (26): Comparison between the bad control group and the healthy group according to Ht, BMI and Hb. 108

Figure (27): Comparison between the bad control group and the healthy group according to BG, TG, T. cholesterol and OXLDL antibodies. 108

Figure (28): Correlation between HbA1C and OXLDL in the bad control group. 110

Figure (29): Correlation between HbA1C and OXLDL in the good control group. 111

List Of Abbreviations

Abbrev.	Full term
αAAT	Alpha 1 antitrypsin
AGE	Advanced glycation protein
apo E1	Apolipoprotien E1
BCG	Bacillus calmette Guerin
BG	Blood glucose
BM	Basement membrane
BMI	Body mass index
CAD	Coronary artery Coronary artery disease
CBC	Complete blood count
CIM	Carotid intema intima thickness
CM	Chylomicrons
CSII	Continous subcutaneous insulin infusion
CVD	Cardio vascular disease
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
DPT1	Diabetes prevention trial 1
DSDS	Distal symmetrical polyneuropathies
DSPS	Distal symmetrical polyneuropathies
ER	Emergency
FDA	Food and Drug Administration
GLA	Gamma linolenic acid
HbB	Hemoglobin
HbA1c	Glycated hemoglobin
HDL	High density lipoprotein

Formatted: Spanish (International Sort)

Formatted: Spanish (International Sort), Subscript

Formatted: Spanish (International Sort)

Formatted: Line spacing: single

LIST OF ABBREVIATIONS (CONT...)

Abbrev.	Full term
HLA	Human leucocyte antigen
IC	Immune complexes ~~LDL – LOW density LIPOPROTIEN~~
ICA	Islet cell antibodies
IDDM	~~Indepentan~~Insulin dependent~~t~~ diabetes mellitus
IDL	Intermediate density lipoprotein
Ig M	Immunoglobulin M
IgG	Immunoglobulin G
IV	Intravenous
IVIG	Intravenous immunoglobulin
~~LP(~~LP (a)	~~Lipoprotein a~~Lipoprotein a
M	Mean
MHC	Major histocomatabitity complex
MNT	Medical nutrition therapy
~~**MNT**~~	~~Medical nutrition therapy~~
MODY	Maturity onset diabetes of the youth
NO	Nitric oxide
OxLDL	Oxidized low density lipoprotein
~~Antibodies low density lipoprotein antibodies~~	
OxLDL Ab	Oxidized LDL antibodies
PUFAs	Polyunsaturated fatty acids
r AVV	Recombinant adeno associated vir~~o~~us vector
SD	Standard ~~Slandered~~ deviation
SD~~S~~	Stable dimmers
SDS	Standard deviation score

Formatted: French (France)

Formatted: French (France)