AMYLIN AND ITS RELATION TO INSULIN AND LIPID PROFILE IN OBESE CHILDREN BEFORE AND AFTER WEIGHT LOSS

Thesis

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قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ
الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

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List of Contents

List of Abbreviations

ABCA1 ..... ATP-binding cassette A1

ACRP30..... Adipocyte Complement Related Protein of 30 kD

AgRP ..... Agouti gene related protein

AMY ..... Amylin

AN..... Acanthosis nigricans

ASIP..... Agouti-Signaling protein

BBS ..... Bardet-Biedl syndrome

BMI..... Body mass index

BP..... Blood pressure

CCK..... Cholecystokinin

CDC ..... Centers for Disease Control and Prevention

CETP ..... Cholesteryl ester transfer protein

cGMP..... Cyclic guanosine monophosphate

CGRP ..... Calcitonin gene related peptide

Chol ..... Cholesterol

CL–RAMP Calcitonin receptor-like receptor/ receptor activity-modifying protein

CMI ..... Comprehensive multidisciplinary intervention

COOH ..... Carboxyl group

C-peptide... Connecting peptide

CRP ..... C-reactive protein

CT ..... Calcitonin

DHEA-S..... Dehydroepiandrosterone-sulfate

DRG..... Diagnosis-related group

EDTA..... Ethylenediaminetetraacetic acid
ELISA..... Enzyme-linked immunosorbent assay
EMCL..... Extramyocellular lipid
FA ..... Fatty acid
FDA ..... Food and Drug Administration
FDA ..... Food and Drug Administration
FFA..... Free fatty acid
FGIR..... Fasting glucose/ insulin ratio
FPG..... Fasting plasma glucose
FSH..... Follicle-stimulating hormone
GI ..... Glycemic index
G-protein... Guanine nucleotide-binding protein
GRD..... Glycoregulation disorders
GSK-3..... Glycogen synthase kinase 3
HDL ..... High-density lipoprotein
HEK-293 ... Human embryonic kidney 293
HL ..... Hepatic lipase
HOMA..... Homeostatic model assessment
HSP-70..... Heat shock protein 70
HSPGs ..... Heparan sulfate proteoglycans
IAPP ..... Islet amyloid polypeptide
IDF..... International Diabetes Federation
IFG..... Impaired fasting glycemia
IGF-I..... Insulin growth factor 1
IGT ..... Impaired glucose tolerance

IMCL.....Intramyocellular lipid

IOM .....Institute of Medicine

IR .....Insulin Resistance

ISI .....Insulin sensitivity index

L-364718....CCK antagonist

LCAT.....Lecithin:cholesterol acyltransferase

LC-CoA.....Long-chain fatty acyl-CoA

LDL .....Low-density lipoprotein

LDLR.....Low-density lipoprotein receptor

LH.....Luteinizing hormone

LPL.....Lipoprotein lipase

LRP.....LDLR-related protein

LRP.....LDLR-related protein

MC3R.....Melanocortin receptor-3

MC4R.....Melanocortin 4 Receptor

MRI .....Magnetic Resonance Imaging

mRNA.....Messenger ribonucleic acid

MS ..... Metabolic syndrome

MTP.....Microsomal triglyceride protein

MUP.....4-Methylumbelliferyl Phosphate

NCEP/ATP III The third report of the National Cholesterol Education Program Adult Treatment Panel

NEFA.....Nonesterified fatty acids

NHANES...National Health and Nutrition Examination Study

NIBSC .....National Institute for Biological Standards and Control

NIDDM..... Non insulin dependent diabetes mellitus

NPY ..... Neuropeptide Y

OGTT ..... Oral glucose tolerance test

OSA ..... Obstructive sleep apnea

PCOS ..... Polycystic ovary syndrome

POMC ..... Pro-Opiomelanocortin

PSMF ..... Protein-sparing modified fast

PWS ..... Prader-Willi syndrome

PYY ..... Peptide YY

QUIKI ..... Quantitative insulin sensitivity check index

RAMP..... Receptor activity modifying protein

RER ..... Rough endoplasmic reticulum

sCT8-32 ..... Salmon calcitonin 8-32

SD..... Standard deviation

SER..... Smooth endoplasmic reticulum

SES..... Socioeconomic status

SFA ..... Saturated fatty acids

SI..... Insulin sensitivity index

SPSS..... Statistical Package for Special Science

SR-BI ..... Scavenger receptor class B, type I

SWM..... Structured weight management

T2DM ..... Type 2 diabetes mellitus

T3..... Triiodothyronine

T4..... Thyroxine

TBF..... Total body fat

TC ..... Total cholesterol

TCI..... Tertiary care intervention

TG..... Triglycerides

TNF..... Tissue necrotizing factor

TRLs..... Triglyceride-rich lipoproteins

TSH..... Thyroid-stimulating hormone

USDA..... United states Department of Agriculture

VLDL..... Very low-density lipoprotein

VMH..... Ventromdial hypothalamus

WC..... Waist circumference

WHO ..... World Health Organization

WLIP..... Weight loss intervention program

α-MSH..... α-melanocyte stimulating hormone

List of Tables

List of Figures

Introduction

Childhood obesity has reached epidemic levels in developed countries. Twenty five percent of children in the United States are overweight and 11% are obese ***(Whitaker et al., 1997)***. The frequency of obesity continues to rise in our country; ***Salem et al. (2002)*** reported that the prevalence of obesity was 14.7%-15.08% for male and female children adolescents.

Obesity is the most common cause of insulin resistance. Insulin resistance is the keystone of the "Metabolic syndrome" a major cardiovascular risk factor even in the absence of demonstrable glucose intolerance or diabetes ***(Bouchard, 2004)***. Moreover, it is associated with abnormal levels of blood lipids ***(Pi-Sunyer, 1993)***.

Amylin, also known as islet amyloid peptide, identified in 1987, is a naturally occurring hormone, released by the B cells of the pancreas and consists of 37 amino acids. It seems to decrease food intake through both central and peripheral mechanisms ***(Reda et al., 2002)***.

A role for amylin has been suggested in the pathogenesis of dyslipidemia and impaired glucose metabolism. Moreover, amylin can reduce chylomicron uptake, most probably by regulating lipoprotein receptors either directly or via modulation of insulin activity ***(Smith and Mamo, 2000)***.