Phagocytic Functions in Children with Simple Obesity and its Relation with Serum Leptin

Thesis

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List of Abbreviations

Abb.	Full term
AAP	American Association of Pediatrics
AgRP	Agouti-related peptide
AHO	Albright's Hereditary Osteodystrophy
ANC	Absolute neutrophil counts
ARC	Arcuate nucleus
AS	Alstrom syndrome
BBS	Bardet-Biedl syndrome
BDNF	Brain Derived Neurotrophic Factor
BMI	Body mass index
CCK	Cholecystokinin
CDC	Center for Disease Control
CSF	Cerebrospinal fluid
CVD	Cardiovascular disease
DMH	Dorsomedial nucleus
ER	Endoplasmic reticulum
FTO	Fat Mass and Obesity associated
GH	Growth hormone
GLP	Glucagon-like peptide
IFN	Interferon
IGF-1	Insulin-like growth factor 1
IgG	Immunoglobulin G
LAD1	Leukocyte adhesion deficiency1
LAGB	Laparoscopic adjustable gastric banding
LHA	Lateral hypothalamic area

Abb.	Full term
LIF	Leukemia inhibitory factor
MSH	Melanocyte-stimulating hormone
NK cells	Natural killer cells
NPY	Neuropeptide Y
NST	Nucleus of the solitary tract
PC1	Prohormone convertase 1
PHP1a	Pseudohypoparathyroidism 1a
PM	Plasma membrane
PMN	Polymorphonuclear
POMC	Pro-opiomelanocortin
PPAR	Peroxisome proliferator-activated receptors
PPHP	Pseudopseudohyoparathyroidism
PTHrP	Parathyroid hormone-related protein
PVN	Paraventricular nucleus
SES	Socioeconomic status
SNPs	Single Nucleotide Polymorphisms
SOCS	Suppressor of Cytokine Signaling
THC	Tetrahydrocannabinol
VAT	Visceral adipose tissue
VLEDS	Very low energy diets
VMH	Ventromedial hypothalamic nucleus
α-MSH	α-melanocyte-stimulating hormone

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Introduction

Body weight is regulated by numerous physiological mechanisms that maintain balance between energy intake and energy expenditure. Thus, any factor that raises energy intake or decreases energy expenditure by even a small amount will cause obesity in the long-term ***(Lustig, 2001).***

A child's weight status is determined using an age- and sex-specific percentile for BMI rather than the BMI categories used for adults because children's body composition varies as their age varies and varies between boys and girls. Obesity is defined as a BMI at or above the 95th percentile for children of the same age and sex ***(Barlow and Expert committee, 2007).***

Childhood obesity has more than doubled in children and tripled in adolescents in the past 30 years. The percentage of children aged 6–11 years in the United States who were obese increased from 7% in 1980 to nearly 18% in 2010. Similarly, the percentage of adolescents aged 12–19 years who were obese increased from 5% to 18% over the same period. In 2010, more than one third of children and adolescents were overweight or obese ***(Ogdenet, 2012).***

Childhood obesity has both immediate and long-term effects on health and well-being. Obese youth are more likely to have risk factors for cardiovascular disease, such as high cholesterol or high blood pressure. In a population-based sample of 5- to 17-year-olds, 70% of obese youth had at least one risk factor for cardiovascular disease ***(Daniels et al., 2005).***

Emerging data indicate an association between obesity and infectious diseases. Obesity may influence either the risk of getting an infection or the outcome of an infection once it is established. Obesity-related immune system dysregulation, decreased cell-mediated immune responses, impaired chemotaxis, dysregulated cytokine production, altered differentiation and intracellular killing by macrophages, obesity-related co-morbidities, respiratory dysfunction and pharmacological issues have been proposed as possible mechanisms ***(Huttunen and Syrjänen, 2013).***

Leptin is a 16 kDa protein synthesized mainly by adipose tissue and was originally identified as the gene defect responsible for the obesity syndrome. Circulating leptin levels are directly related to adipose tissue mass. High leptin levels signal the presence of sufficient energy stores to sites in the central nervous system, which respond

by reducing appetite and increasing energy expenditure, preventing severe obesity ***(Maffei et al., 1995).***

On the other hand, a pleiotropic role for leptin in mammalian physiology is clearly suggested by the complex syndrome exhibited by leptin-deficient and leptin receptor-deficient mice. Those mice are not only obese, but have abnormalities in reproductive function, hormone levels, wound repair, bone structure, and immune function ***(Fantuzzi and Faggioni, 2000).***

The structure of leptin and its receptor suggest that leptin is a member of the cytokine family. Leptin has a four-helix bundle similar to that of the long-chain helical cytokine family, which also includes IL-6, IL-11, IL-12, leukemia inhibitory factor (LIF), G-CSF, CNTF and oncostatin M. The leptin receptor is a cytokine receptor and belongs to the class I cytokine receptor family. The overall increase in leptin during infection and inflammation indicates that leptin is part of the immune response and host defense mechanisms ***(Gabay and Kushner, 1999).***

Leptin is found to be involved in regulation of fundamental effector functions of mononuclear phagocytes, which express receptors for this hormone. The regulation of mononuclear phagocytes by leptin is associated with

activation of the JAK/STAT signaling pathway, which leads to stimulation of phagocytosis, production of oxygen and nitrogen reactive species, and also to increase in secretion of pro-inflammatory cytokines ***(Shirshev and Orlova, 2005).***

Aim of Work

The aim of this study was to investigate the competence of phagocytic functions (intracellular killing) in obese children and its relation to their serum leptin.