

Study of Plasma Adiponectin level in Cases of Thyroid Dysfunction Associated with Body Weight Disorders

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List of Abbreviations

ATP	Adenosine
ARC	Arcuate nucleus
AMP	Adenosine monophosphate
ACRP30	Adipocyte complement related protein of 30KDa
ApM1	Adipose most abundant gene transcript-1
BMI	Body mass index
BAT	Brown adipose tissue
Ca²⁺	Calcium
CNS	Central nervous system
CART	Cocaine& amphetamine regulated transcript
CCK	Cholecystokinins
CSF	Cerebrospinal fluid
DIT	Diiodinated tyrosine
db/db mice	Diabetic mice
FT4	Free thyroxine
FNA	Fine needle aspiration
FABP	Fatty acid binding protein
GPCR	G-protein coupled receptor
GIT	Gastrointestinal tract
GTRS	Generalized thyroid gland resistance syndrome
GLP-1	Glucagon like peptide-1
GnRH	Gonadotropin releasing hormone
GBP28	Gelatin binding protein of 28KDa
HPT axis	Hypothalamo-pituitary thyroid axis
I	Iodide
ICAM-1	Intracellular adhesion molecule-1
KDa	Kilo Dalton
MIT	Monoiodinated tyrosine
MCR	Metabolic clearance rate
NIS	Sodium/Iodide symporter
Na	Sodium
NEFA	Non-esterified fatty acid
NTI	Non thyroid illness
NPY	Neuropeptide-Y

Ob gene	Obesity gene
ob/ob mice	Obese mice
PT axis	Pituitary thyroid axis
PR	Production rate
PAI-1	Plasminogen activator inhibitor-1
PVN	Paraventricular nucleus
rT3	Reversed triiodothyronine
RIA	Radioimmunoassay
RAIU	Radioactive iodine uptake
PPAR	Paroxysmal proliferator activator receptor
SNS	Sympathetic nervous system
S-TSH	High sensitivity thyrotropin
T4	Thyroxine
T3	triiodothyronine
TSH	Thyroid stimulating hormone
TTR	Transthyretin
TBG	Thyroxine binding globulin
TH	Thyroid hormones
TBPs	Thyroxine binding proteins
THBR	Thyroid hormone binding ratio
TNF-alpha	Tumor necrosis factor-alpha
TZDs	Thiazolidinediones
IRS-1	Insulin receptor substrate-1
UCP	Uncoupling protein
VCAM-1	Vascular cell adhesion molecule-1
WAT	White adipose tissue

INTRODUCTION

Thyroxine and triiodothyronine are two major hormones secreted from the thyroid gland and they have profound effects on the metabolic processes of the body (*Guyton,1992*). They are potent modulators of adaptive thermogenesis and can contribute to development of obesity (*Kortkiewski, 2002*).

Thyroid dysfunctions are often associated with minor changes in body weight and fat mass (*Kortkiewski, 2000*). It is well established that food intake as well as thermic effects of food is generally decreased in hypothyroidism. In contrast, a hyperthyroid state is associated with increased amount of food intake and increasing thermic effect of food. A consequence of this, body weight is on average decrease in hyperthyroidism by 15% (in comparison to the preceding euthyroid state) and hypothyroid patients weigh on average 15-30% more (*Kortkiewski, 2002*).

One of the important effects of T₃ is its influence on the family of uncoupling proteins (UCP 1, 2 ,3). UCP is a proteolytic thermogenic molecule that uncouples proton entry from ATP synthesis and contributes significantly to adaptive thermogenesis. In humans, the most important is UCP-3 expressed in deep white abdominal adipose tissue, abdominal organs and muscles. UCP-3 levels are decreased

three-fold in hypothyroidism and increased six-fold in hyperthyroidism (***Kortkiewski, 2002***).

Adipose tissue is a specialized connective tissue that functions as the major storage site for fat in the form of triglycerides. Adipose tissue is found in mammals in two forms: white, and brown adipose tissue. Most adipose tissue is white (***Albright & Stein, 1998***).

Adipose tissue has an active role as an endocrine and paracrine organ (***Mohamed Ali et al., 1998***). Of the hormones secreted by white adipocytes are interleukin-6, leptin, tumor necrosis factor-alpha (TNF-alpha) plasminogen activator inhibitor-1 (PAI-1) and Adiponectin (***Brayhaun et al., 2001***).

In Graves thyrotoxic patients, regardless of the thyroid status, adipose tissue secretion of interleukin-6, TNF-alpha, or PAI-1 is markedly increased in comparison with euthyroid subjects (***Wahrenberg et al., 2002***).

Thyroid hormones regulate the expression of leptin mRNA, and the secretion of leptin by adipocytes in vitro (***Yoshida et al., 1997***). It was stated that thyroid states modulate the serum leptin concentration independent of body mass index, with a small increase in thyrotoxicosis, and a small decrease in hypothyroidism (***Diekman et al., 1998***).

Introduction & Aim of The Work (3)

Adiponectin is a 244 amino acids protein synthesized and secreted exclusively by the adipose tissue (***Fernandez et al., 2003***). It is abundant in human plasma, accounting approximately for 0.01% of total plasma proteins (***Arita et al., 1999***).

One of the most interesting features of adiponectin is that in contrast to adipocytokines, which are markedly up regulated in obesity, its adipose tissue expression and plasma concentration are reduced in overweight and obese subjects (***Beltowski, 2003***), and type 2 diabetic patients (Hotta, et al. 2001). Adiponectin has anti-inflammatory and insulin sensitizing properties (***Stefan et al., 2001***).

A study aimed to explore the interaction between thyroid and adrenal cortex on the adiponectin/ insulin sensitivity relationship was done and it was observed that there is an association between circulating adiponectin concentration and free T3, which persists after adjustment for additional co-variables (***Fernandez et al., 2003***)

On the other hand, ***Santini et al., (2004)*** had performed a study to evaluate the relationship between thyroid status and adiponectin. They found that metabolic changes associated with thyroid dysfunction are not related to variations in serum levels of adiponectin, although the thyroid dysfunction is associated with metabolic changes that affect mass and function of adipocyte (***Santini, et al., 2004***).

AIM OF THE WORK

The aim of our work is to study the relationship between thyroid dysfunction associated with body weight disorders and plasma adiponectin level.

The Thyroid Gland

Glands of the body are of two kinds: exocrine and endocrine. Thyroid gland is one of the largest endocrine organs that secretes its hormones into the extracellular space around the gland, hence carried away by the blood. The thyroid gland is composed of large number of follicles (acini), filled with colloid. The major constituent of this colloid is a large glycoprotein and thyroglobulin (*Tortora, 1995*).

Anatomy of the thyroid gland:

The thyroid, the largest gland in the body, weighs about 20 grams with the right lobe larger than the left lobe. Adult size is reached at the age of 15 years. The two lateral lobes lie anterior to the thyroid cartilage and are connected by a small isthmus located just below the cricoid cartilage.

The lobes are divided by fibrous septae into pseudolobes composed of spherical structures called follicles. A dense capillary network surrounds the follicles which are richly innervated by sympathetic and parasympathetic nerve endings (*Wolfgang H., 1996*).

The accessory thyroid glands, separate masses of thyroid tissue. They are not uncommonly found near the

hyoid bone, in the tongue, in the superior mediastinum, or beneath the sternomastoid muscle (**Mc Minn, 1994**).

Two pairs of vessels constitutes the abundant arterial blood supply, namely the superior and inferior thyroid arteries, they supply the gland with a normal rich flow of blood (4-6 ml/min/g). In diffuse toxic goiter, blood flow rates may exceed IL/min (**Larsen, 1998**). A fifth artery, the thyroid ima, present in 3% of individuals, arises from aorta (**Mc Minn, 1994**).

The thyroid gland is drained by a venous plexus forming a superior thyroid vein at the upper pole of the gland, middle thyroid vein from the middle of the lobes both of them enter the internal jugular vein, and inferior thyroid veins form a plexus in front of the cervical part of the trachea, draining isthmus and lower poles directly to innominate vein (**Mc Minn, 1994**).

The lymphatics follow the arteries. From upper pole of thyroid gland, they enter the antero-superior group of deep cervical lymph nodes. From the lower pole, they enter the postero-inferior group. A few pass downward into the pre-tracheal nodes (**Ekholm, 1995**).

The thyroid receives innervations from both sympathetic fibers arise from the cervical ganglion, and parasympathetic fibers derived from the vagus and reach the