Clinical Nutrition xxx (2014) 1–5

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Relationship between thyroid hormones, resting energy expenditure and cardiometabolic risk factors in euthyroid subjects

Angela Spadafranca*, Chiara Cappelletti, Alessandro Leone, Laila Vignati, Alberto Battezzati, Giorgio Bedogni, Simona Bertoli

International Center for the Assessment of Nutritional Status (ICANS), University of Milan, Italy

ARTICLE INFO

Article history:
Received 6 May 2014
Accepted 21 July 2014

Keywords:
Resting energy expenditure
Indirect calorimetry
Thyroid stimulating hormone
Tetraiodothyronine
Triiodothyronine
Metabolic syndrome

SUMMARY

Background & aims: Whereas hypothyroid subjects have a decreased resting energy expenditure (REE), it is unknown whether REE is associated with TSH in euthyroid subjects. It is also uncertain whether there is an association between cardiometabolic risk factors and TSH among euthyroid subjects. The primary aim was to test whether REE and TSH are associated in euthyroid subjects. The second aim was to evaluate the association between TSH and cholesterol, HDL-cholesterol, triglycerides, glucose and blood pressure.

Methods: 885 Caucasian euthyroid subjects (75% women) aged 18–79 years and with a median body mass index of 28.6 kg/m^2 were consecutively studied at our Research Center. REE was measured using a canopy-equipped indirect calorimeter. Multivariable regression of 25th, 50th and 75th percentiles was used to evaluate the association between the outcomes (REE, cholesterol, HDL-cholesterol, triglycerides, glucose and blood pressure) and the predictors (TSH, FT4 and FT3) controlling by gender, age and body mass index.

Results: REE was not associated with TSH, FT4 and FT3 at any percentile. On the contrary, a positive association between TSH and triglycerides was evident at all percentiles. A positive association between FT3 and HDL-cholesterol was also present but only at the 75th percentile.

Conclusions: REE is not associated with TSH in euthyroid subjects. It is however positively associated with triglycerides confirming the findings of recent population studies.

1. Introduction

Thyroid hormones regulate energy homeostasis by acting both in peripheral tissues and the central nervous system [1,2]. Overt hypothyroidism is associated with decreased resting energy expenditure (REE) and weight gain while hyperthyroidism is associated with increased REE and weight loss [3,4]. Even if patients undergoing treatment for hypothyroidism show measurable changes of REE with small changes in levothyroxine dosage [5], the relationship between thyroid hormones and REE in euthyroid subjects is widely unknown. A lack of association between REE and TSH has been reported in euthyroid subjects with severe obesity [6] but no data are now available on the REE-TSH association in non-obese euthyroid subjects.

Hypothyroidism is associated with an increase of many cardiovascular risk factors, i.e. dyslipidemia, hyperglycemia and hypertension, and may predispose to atherosclerosis [7,8]. It is however uncertain whether cardiovascular risk factors are associated with TSH among euthyroid subjects. In the largest study of lipid profile performed so far in euthyroid subjects, Meisinger et al. found a positive association between TSH and triglycerides that was independent from gender and a positive association between TSH and cholesterol in women [9]. Similar findings were recently reported by Garduño-Garcia et al. [10] in a Hispanic population, together with an association between TSH and insulin and HOMA-IR but not with glucose [10].

We performed a large cross-sectional study to evaluate the REE-TSH relationship among euthyroid subjects and to evaluate also the association of TSH with total cholesterol, HDL-cholesterol, triglycerides, glucose and blood pressure.

* Corresponding author. International Center for the Assessment of Nutritional Status (ICANS), Via Botticelli 21, 20133 Milano, Italy. Tel.: +39 02 50316652; fax: +39 02 50316191.
E-mail address: angela.spadafranca@unimi.it (A. Spadafranca).

http://dx.doi.org/10.1016/j.clnu.2014.07.014
0261-5614/

Table 1
Measurements of the study subjects.

	Women ($n = 664$)			Men ($n = 221$)			Total ($n = 885$)		
	P_{25}	P_{50}	P_{75}	P_{25}	P_{50}	P_{75}	P_{25}	P_{50}	P_{75}
Age (years)	36	45	55	39	47	57	37	46	55
Weight (kg)	64.8	72.8*	82.8	83.7	93.0	103.4	67.4	77.6	90.1
Height (m)	1.57	1.62*	1.66	1.71	1.75	1.81	1.59	1.64	1.71
BMI (kg/m^2)	25.1	27.9*	32.0	27.6	30.1	33.6	25.8	28.6	32.4
Waist (cm)	82	91*	100	99	106	116	85	95	104
REE (Kcal/day)	1281	1388*	1509	1644	1802	1956	1320	1460	1650
REE: weight (Kcal/kg)	17.4	18.8	20.7	18.1	19.2	20.4	17.6	19.0	20.6
TSH (mU/l)	1.26	1.76	2.46	1.23	1.71	2.21	1.26	1.74	2.40
FT4 (pg/ml)	9.50	10.6*	11.9	9.90	11.1	12.1	9.60	10.8	12.0
FT3 (ng/ml)	2.77	3.05	3.37	2.99	3.29	3.56	2.80	3.10	3.42
Cholesterol (mg/dl)	186	210	237	183	207	235	185	210	237
HDL-cholesterol (mg/dl)	51	60*	71	40	45	53	47	57	68
Triglycerides (mg/dl)	64	86*	119	85	121	173	68	94	131
Glucose (mg/dl)	84	90*	97	89	97	106	85	92	100
Systolic BP (mm Hg)	110	120*	130	120	130	140	110	120	130
Diastolic BP(mm Hg)	70	75*	80	75	80	90	70	80	85

*$p < 0.001$ *vs.* males at P_{50} regression.
Abbreviations: $P_{25} = 25^{th}$ percentile; $P_{50} = 50^{th}$ percentile; $P_{75} = 75^{th}$ percentile; BMI = body mass index; REE = resting energy expenditure from indirect calorimetry; TSH = thyroid stimulating hormone; FT4 = free thyroxine; FT3 = free triiodothyronine, BP = blood pressure.

2. Subjects and methods

2.1. Study design

We consecutively studied euthyroid subjects who came to ICANS (International Center for the Assessment of Nutritional Status) voluntarily between January 2008 and December 2011 to obtain an assessment of nutritional status and cardiometabolic risk. Inclusion criteria were age ≥18 years and presence of euthyroidism. Euthyroidism was operationally defined as a value of TSH between 0.2 and 4.2 ng/ml. Exclusion criteria were psychiatric disease, cancer and chronic disease (e.g. heart failure). The institutional review board approved the study procedures and each subject provided written informed consent. The study was carried out according to the Declaration of Helsinki.

Clinical examination, anthropometry, indirect calorimetry and blood samples for laboratory examinations were performed on the same day.

2.2. Clinical examination and anthropometry

All subjects underwent a clinical examination before being enrolled into the study. Anthropometric measurements were taken by the same operator following international guidelines [11]. Weight was measured to the nearest 100 g and height to the nearest 0.1 cm using a balance with incorporated stadiometer (SECA 711, SECA, Hamburg, Germany). BMI was calculated as weight (kg)/stature $(m)^2$ and classified according to the World Health Organization [12]. Waist circumference was measured at the midline between the last rib and the iliac crest [12].

2.3. Indirect calorimetry

REE was measured using an open-circuit ventilated-hood system (Sensor Medics Vmax29, Sensor Medics, Anaheim, CA) in the post-absorptive state (≥12 h from fasting) and in a thermo-neutral environment (24–26 °C). The subjects lying in a horizontal position remaining awake for at least 20 min prior to perform the measurement. At least 30 min of respiratory gas exchange data were collected with the first 10 min being discarded to allow acclimation of the subject [13]. REE was calculated as the average of at least 20 min of gas exchange using Weir's equation [14].

2.4. Laboratory measurements

Fasting cholesterol, HDL cholesterol, triglycerides and glucose were measured using an enzymatic method (Cobas Integra 400 Plus, Roche Diagnostics, Rotkreuz, Switzerland). Fasting TSH, FT4 and FT3 were measured using immunoenzymatic method (Cobas E 411, Roche Diagnostics, Rotkreuz, Switzerland). Blood pressure was measured by a physician using a random-zero mercury sphygmomanometer following JNC 7 guidelines [15].

2.5. Metabolic syndrome

The metabolic syndrome (MS) was diagnosed using the harmonized international definition [16]. Large waist was defined as waist circumference ≥102 cm in men and ≥88 cm in women, low HDL-cholesterol as HDL-cholesterol <40 mg/dl in men and <50 mg/dl in women, high triglycerides as triglycerides ≥150 mg/dl, high blood pressure as systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg, and high glucose as glucose ≥100 mg/dl. MS was defined as 3 or more of the above components.

2.6. Statistical analysis

Continuous variables are reported as 25^{th}, 50^{th} and 75^{th} percentiles because of non-Gaussian distributions. Categorical variables are reported as counts and percentages. All continuous variables besides age were winsorized using a tail of 0.01. This implies that values under the 1st or over the 99^{th} internal percentile were put equal to the 1st or 99^{th} percentile, respectively. Winsorization limits the influence of outliers and increases the generalizability of the results [17,18]. Between-gender comparisons of continuous variables were performed using univariable regression of the 50th percentile of the outcome with gender (0 = female; 1 = male) as predictor [19]. Multivariable regression of 25^{th}, 50^{th} and 75^{th} percentiles was used to evaluate the association between the outcomes [REE (kcal/day), total cholesterol (mg/dl), HDL-cholesterol (mg/dl), triglycerides (mg/dl), glucose (mg/dl), systolic blood pressure (mm Hg) and diastolic blood pressure (mm Hg)] and the predictors [TSH (mUI/l), FT4 (pg/ml) and FT3 (ng/ml)] using gender (0 = female; 1 = male), age (years/10) and BMI (kg/m^2) as covariates [19]. We used multivariable running plot sand multivariable fractional polynomials to test whether the relationship

Please cite this article in press as: Spadafranca A, et al., Relationship between thyroid hormones, resting energy expenditure and cardiometabolic risk factors in euthyroid subjects, Clinical Nutrition (2014), http://dx.doi.org/10.1016/j.clnu.2014.07.014