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Thyroid hormones and lipid metabolism in a group of patients over seventy

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Abstract. – **Numerous studies have suggested a marked correlation between thyroid functionality indices and lipid metabolism. In this trial we assessed the functional parameters of 165 individuals over 70, 87 women and 78 men, correlating the serum values of T3, T4, FT4, TSH with cholesterol, triglycerides, HDL, Apo-A and Apo-B levels.**

The correlation was performed over the whole population studied and subsequently, after dividing the population by sex and age (3 age groups: A, 70-75; B, 76-80; C, over 80) in the individual groups. In the population as a whole, we have observed a statistically significant correlation between T4/cholesterol (P=0.0001); T3/cholesterol (P=0.06); T4/triglycerides (P=0.0001); T3/triglycerides (P=0.09); T4/HDL (P=0.0001); T4/Apo-A (P= 0.02); T3/Apo-A (P=0.008); T4/Apo-B (P=0.0001). Analysis by gender shows a statistically significance between the female and male sexes in the correlation between T3/cholesterol (P=0.001); T3/triglycerides (P=0.06); T4/cholesterol (P=0.0001) and T4/triglycerides (P=0.0001). When the data were analyzed by age, in Group A (75-80) there was no statistically significant correlation, whereas in Group B (76-80) there has been an increase in significance in the correlation between T3/cholesterol (P=0.006); T3/triglycerides (P=0.001); T3/Hdl (P=0.08); T3/Apo-A (P=0.0001); T3/Apo-B (P=0.08); T4/cholesterol (P=0.00001) and); T4/Apo-A (P=0.0001). On the other hand in the Group C age group (over 80) this significance is considerably lower. Maybe this decrease of correlations should be attributed to a global savings of the older organisms, or to a process of natural selection.

Key Words:

Thyroid hormones, Lipid metabolism, Elderly.

Introduction

A general correlation between blood levels of thyroid hormones (T3, T4, FT4), thyroid stimulating hormone (TSH) and lipid metabolism in general is well estabished. Numerous studies on this subject, nearly all confirm the presence of an inverse relationship between thyroxin serum levels and cholesterol[1,2,3].
Other studies demonstrate the influence of iodothyronine on the catabolism of the Very Low Density Lipoprotein (VLDL), showing are increase in LDL and VLDL fractions in untreated hypothyroidism[4,5].

The increase in LDL and VLDL seems to depend from a decrease in the oxidative capacity of fatty acids, reflected in a reduction of their catabolism[4,6]. Various studies conducted on the effect of thyroid hormones on apoproteins A1, A2 and B, show an increase in apo-A1, apo-A2 and apo-B in hypothyroidism, although in a non conclusive manner[3,7,8,9,10].

As decribed by Muls et al., as early as 1984, there is an evident direct correlation between apo-A_1 and apo-A_2 with T4 and above all a strong inverse correlation between apo-B and T4[11].

The data concerning a definite correlation between thyroid hormones and triglyceride is more controversial[3].

Indeed, several studies indicate a modest relationship between triglyceride increase and hypothyroidism, although even this modest significance has resulted in continuing investigations.

In vitro and in vivo studies have also been performed to study the effects of thyronine on serum lipids[12,3,13,14].

In vitro it has been observed that thyroid hormones stimulate oxidation of fatty acids and increase the release of fatty acids by adipose tissue into the blood stream[12,15]. Several studies have demonstrated thyroxin's regulatory action on fatty acid mobilisation,

through interaction with the catecholaminergic system, mainly through modulation of the lipolytic action of epinephrine[3,16]. Moreover, other trials demonstrate the inhibitory effect of insulin on lipolysis, thus manifesting a lipogenous effect[13,17].

In vivo effects are demonstrated by the experiment by Schjeide et al[14]. These Authors, have observed obese hypothyroidism in chickens for 36 weeks, noting a highly significant increase in all lipid moieties, above all triglycerides and phospholipids, and not associated with an adequate increase in apoproteins A1 or B. The variation of the relationship beetween thyroid lipids and age are proven by a recent study on a population of older women[19].

In this study Bauer et al. demonstrate that high TSH in 9.704 older white women is associated with a deleterious change of serum lipids, with an increase of lipid abnormalities.

In the present study we aim to assess, in continuation of our trials on lipoproteins and dyslipidemic disorders in geriatric individuals, the correlation between thyroid functionality indices and lipid metabolism indices in the elderly.

Materials and Methods

We studied 165 patients; 78 males and 87 females, with a mean age of 76.3 ± 1.8 years. The body weight was 60 ± 4 Kg in males, 54 ± 3 in females. Patients were divided into three groups (A, B, C) according to age: group A consisted of patients years of age under 76 (n = 64); group B consisted of patients between 76 and 80 years old (n 57); group C consisted of patients over 80 years of age (n = 44). All data was correlated to the sex variable.

Inclusion criteria was the absence of clear thyroid pathology. Moreover, we excluded patients with a family history of dyslipidemia, smokers, patients with a pharmacological history of intake of hypolipaemic drugs, corticosteroids, diuretics or insulin. We also excluded also subjects with alcohol intake. In the patients we measured thyroid functionality indices in the blood, that is T3, T4, TSH and FT4, using the following analysis kits: for T3 – T3-I-125 Pantex kit; for T4 – T4-I-125 thyroxin Pantex kit; for FT4 – FT4-I-125 RIA, BINAX kit; for TSH – NML-LES kit, TSH-I-125-IRMA (Organon Teknika).

We also assessed lipid serum levels[20] (cholesterol, triglycerides, HDL, Apo A, Apo B) adopting enzymatic colorimetric method using Choles-cinet and Trigli-cinet (Sclavo) diagnostic kits for the free moiety of cholesterol and triglycerides, and, for HDL, adopting deproteinisation with a precipitant reagent using the Boehringer Mannheim diagnostic kit, and subsequently measuring the complex using the above-mentioned Choles-cinet (Sclavo) enzymatic colorimetric diagnostic method.

The Apoproteins were measured by immuno-chemical reaction adopting the N-Apolipoprotein test diagnostic kit using nephelometer (Boehring).

For statistical analysis a linear correlation was performed (Pearson's Test). Student's *t* test was performed for all thyroid functionality parameters (T3, T4, TSH and FT4) and the lipid metabolism parameters (cholesterol, triglycerides, HDL, Apo-A, Apo-B).

Results

T3 values were between 1.290 and 0.830 ng/ml, with a mean of 1.331 ± 0.512 ng/ml; T4 values were between 39.560 and 168.030 ng/ml, with a mean of 87.096 ± 28.469 ng/ml; TSH values were between 0.040 and 12.950 mU.I./ml, with a mean of 1.239 ± 1.344 mU.I./ml and finally FT4 values were between 0.220 and 11.830 ng/dl, with a mean of 1.491 ± 0.979 ng/ml.

These data, illustrated in Table 1, reflect our reference population which was euthy-

Table I. General data from the population studied (165 patients, 87 females 78 males).

Mean values ± 1 SD of the studied population
T3 = 1.331 ± 0.512 ng\ml
T4 = 87.09 ± 28.46 ng\ml
TSH = 1.239 ± 0.97 µUI\ml
FT4 = 1.491 ± 0.979 ng\dl
Cholesterol = 197 ± 61 mg\dl
Triglycerides = 156 ± 45 mg\dl
H D L = 56 ± 22 mg\dl
APO A = 1.435 ± 0.206 mg\dl
APO B = 0.998 ± 0.407 mg\dl

roid with mean values within normal limits for a geriatric population.

Serum values of cholesterol ranged between 86 and 369 mg/dl, with a mean of 197 ± 61 mg/ml, a value that would seem higher in the female sex compared to male sex (235 vs. 154 mg/ml).

Triglyceride serum levels ranged between a minimum of 71 mg/dl and a maximum of 276 mg/dl, with a mean value of 156 ± 45 mg/dl, with a higher value in women than in men (184 vs. 124 mg/ml).

The HDL lipoproteic moiety in our groups was between 22 and 123 mg/dl, with a mean value of 56 ± 22 mg/dl.

Apo-B values were between 0.330 and 2.460 mg/dl, with a mean value of 0.998 ± 0.407 mg/dl.

Correlation With Thyroid Status

Cholesterol

Our data indicated a significant negative correlation between cholesterol and T4 (R =-0.596: P=0.0001) and T3 (R=-0.436: P=0.06).

There did not seem to be any statistically significant correlation with TSH and Free T4 (R=-0.031 and –0.088; P=N.S. for both).

Triglycerides

There was a significant negative correlation between triglycerides and T3 T3 (R=-0.334: P=0.09) and T4 (R=-0.406: P=0.0001).

There did not seem to be any statistically significant correlation with TSH and FT4 (R=-0.058 and 0.046: P=N.S. for both).

HDL

There was a significant positive correlation between HDL and T4 (R=0.420: P=0.001). There did not seem to be any statistically significant correlation with T3, FT4 and TSH (R=-0.272;-0.122;0.015: P=N.S. for all).

Apo A

There was a positive correlation between Apo A and T4 levels (R=0.345: P=0.02) and T3 levels (R=0.320: P=0.008). There was no significant statistical correlation with FT4 and TSH (R=-0.014;-0.055: P=N.S. for both).

Apo B

There was a statistically significant negative correlation Apo B and T4 (R=-0.369: P=0.0001) whereas there seemed to be no correlation with T3, FT4 and TSH (R=-0.216;0.002;-0.046: P=N.S. for all values).

Gender

There was a statistically significant negative correlation between T4 and cholesterol in the 87 female individuals compared to the 78 males. This trend would seem to be confirmed for T3/cholesterol, for T3/triglyceride and T4/triglycerides relationships (P=0.0001).

All the other parameters studied revealed correlations of statistically little significance in terms of the sex variable, compared to values obtained for the population as a whole (See Table VI).

Age

The results for the three groups (A, B, C) overlapped those obtained for our population as a whole. In the first group (A) correlation values were almost identical to those of the whole population. However, in the second group (B) there was a statistically significant correlation between T4 and higher cholesterol (R=-0.672: P=0.00001), a statistically more significant correlation also for T3/Apo A (R=-0.403: P=0.0001) and T4/Apo A (R=-0.461: P=0.0001).

In the third group (C) the correlation values tended to be lower for all parameters observed: the relation between T4 and cholesterol remained significant, but less marked (R=-0.348: P=0.001), and the levels of statistical significance, though qualitatively maintaining the same correlation trend, tended to be lower for all parameters observed (see Table V).

Discussion

The data we obtained would seem to concur with current literature and confirm the existence of a lipolytic action of iodiothyronine, and particulargy of T4. The lipolytic action would seem greater against cholesterol and the triglycerides.

Table II. Mean Values ± 1 SD of the studied parameters in groups A, B and C.

	Group A 64 patients 31 M 33 F	***Group Bx 64 patients 25 M 32 F***	***Group C 44 patients 22 M 22 F***
T 3	1.332 ± 0.263 ng\ml	1.240 ± 0.62 ng\ml	1.670 ± 0.73 ng\ml
T 4	84.20 ± 22.31 ng\ml	88.15 ± 31.90 ng\ml	91.78 ± 32.94 ng\ml
TSH	1.290 ± 1.22 UI\ml	1.210 ± 1.01 UI\ml	1.202 ± 0.55 UI\ml
FT4	1.480 ± 1.020 ng\dl	1.620 ± 0.831 ng\dl	1.339 ± 1.111 ng\dl
Cholesterol	202 ± 61 mg\dl	210 ± 49 mg\dl	173 ± 77 mg\dl
Triglycerides	171 ± 34 mg\dl	159 ± 69 mg\dl	130 ± 38 mg\dl
HDL	49 ± 25 mg\dl	52 ± 71 mg\dl	71 ± 46 mg\dl
APO A	1.492 ± 0.121 mg\dl	1.450 ± 0.310 mg\dl	1.449 ± 0.150 mg\dl
APO B	1.002 ± 0.251 mg\dl	1.010 ± 0.459 mg\dl	0.977 ± 0.490 mg\dl

Table III. Linear correlation analysis of Pearson's correlation coefficient (R) of parameters studied.

	T3	***T4***	***TSH***	***FT4***
Cholesterol	- 0.436	- 0.596	- 0.031	- 0.088
Triglycerides	- 0.334	- 0.406	- 0.406	- 0.046
HDL	0.272	0.420	- 0.122	0.015
APO A	0.345	0.320	- 0.055	- 0.014
APO B	- 0.216	- 0.369	- 0.046	0.002

Table IV. Levels of significance of correlated parameters in the population studied.

	T3	***T4***	***TSH***	***FT4***
Cholesterol	0.06	0.0001	NS	NS
Triglycerides	0.09	0.0001	NS	NS
HDL	NS	0.0001	NS	NS
APO A	0.008	0.02	NS	NS
APO B	NS	0.0001	NS	NS

Table V. Significance of correlated values in the age-matched classes.

	Group	***T3***	***T4***	***TSH***	***FT4***
	A	0.01	0.0001	NS	NS
Cholesterol	B	0.006	0.0001	NS	0.08
	C	0.08	0.001	NS	NS
	A	0.01	0.0001	NS	NS
Triglycerides	B	0.001	0.0001	NS	NS
	C	NS	0.001	NS	NS
	A	NS	0.0001	NS	NS
HDL	B	0.08	0.001	NS	NS
	C	NS	0.06	NS	NS
	A	0.001	0.02	NS	NS
APO A	B	0.0001	0.0001	NS	NS
	C	0.06	NS	NS	NS
	A	NS	0.0001	NS	NS
APO B	B	0.08	0.0001	NS	NS
	C	NS	0.001	NS	NS

Table VI. Significance (P) of sex-correlated values.

		Cholesterol	*Triglicerides*	*HDL*	*APO A*	*APO B*
T3	F	0.006	0.001	NS	0.008	NS
	M	0.01	0.006	NS	0.006	NS
T4	F	0.0001	0.0001	0.0001	NS	0.0001
	M	0.001	0.002	0.0001		0.001
TSH	F	NS	NS	NS	NS	NS
	M	NS	NS	NS	NS	NS
T4	F	NS	NS	NS	NS	NS
	M	NS	NS	NS	NS	NS

HDL also seems to suffer from this degradation action of thyroid hormones, and the positive correlation is due to the increase in both T3 and T4[21,22].

Apo-A would seem to increase as a result of the direct action of the iodiothyronines, whereas Apo-B seems to decrease[22].

This is undoubtedly a favourable antiatherogenous effect on the part of iodiothyronine. The differing relationship between lipid profile and thyroid hormones that exists between sexes is interesting. It would seem that in women over seventy there is a decrease in lipolysis and an increase in liposynthesis, due to a natural depletion of estrogenic hormone formation that characterises a greater quantity of substrate because of cholesterol synthesis[23].

Data concerning age-related variations are interesting. Our data confirm that metabolic pathways involved in "management" of lipids, at a certain age are less subject to influence by thyroid hormones[14].

This reduction of significativity levels in studied parameters, shown in older age, seems to be due to a general tendency of the effect of thyroid hormone on the lipidic intracellular metabolism in patients over 80 years of age.

Moreover in over 80 years old patients the serum levels of cholesterol take in the global population an J-Shaped curve, in which the higher incidence of mortality is in high limit and in low limit of the curve related global population considered.

Whether this tendency is age-related or whether there is a natural selection that allows the healthy individual to reach old age more easily, thus guaranteeing genetic predominance over environmental conditions, and therefore senescence itself[24,25,26,27].

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