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DUOX2, a new player on the scene of thyroid hormones

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Abstract

Introduction. *Thyroid disorders have very high frequency both in Romania and around the world. Nowadays new parameters are needed to diagnose thyroid disease. Clinicians need new parameters, with rapid determination, low cost, high affinity and specificity.*

The aim *of our study was to investigate possible relationships between thyroid hormones (TH), TSH and DUOX2, and thus a possible involvement of oxidative stress (OS) in thyroid malfunction.*

Material and methods. *The study included 66 patients (men and women), divided on 2 lots: 33 patients with hypothyroidism and 33 patients with hyperthyroidism. The control group was represented by 33 healthy volunteers. All the participants, patients and controls, provided the informed consent to participate in the study.The parameters analyzed were serum TSH, FT4, FT3 and DUOX2.*

Results. *Our results showed that in hypothyroidism patients we have lower levels of TH, and higher level of DUOX2. This suggest an accumulation of enzyme, unused for synthesis. In the meantime, in hyperthyroidism group we can observe a lower level of serum DUOX2, due to massive synthesis of TH.*

Conclusions. *We can assume that DUOX2 has a crucial role in TH and, by producing hydrogen peroxide, an important role in OS. Additional studies are still needed in order to establish whether DUOX2 should be regarded as useful OS biomarker in thyroid pathology.*

Keywords: thyroid, thyroid hormones, dual oxidase, oxidative stress

INTRODUCTION

Thyroid disorders have very high frequency both in Romania and around the world. Nowadays new parameters are needed to diagnose thyroid disease. Parameters that highlight the exact place where the normal synthesis circuit is interrupted. This is necessary for the development of new targeted treatments that act on the affected structure and thus ensure a higher success rate. Clinicians need new parameters, with rapid determination, low cost, high affinity and specificity. The thyroid follicle is the functional structure responsible for thyroid hormone (TH) biosynthesis, thyroxine(T4) and triiodothyronine (T3) (1,2).

Equilibria, biological variation, homeostatic interrelations and set points between thyroid stimulating hormone (TSH), FT4, and FT3 become relevant for the observed expression of multivariate normality and stability in thyroid health (1). All three routine thyroid parameters (THS, FT4, FT3) must be viewed together in order to create an appropriate image of the possible thyroidal affection (3).

A number of chemical reactions are fundamental for TH synthesis, and one of these reactions is the oxidation of the substrate in the presence of

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hydrogen peroxide and a peroxidase enzyme that catalyzes the process, thyroperoxidase (TPO). The hydrogen peroxide necessary for TH biosynthesis is generated at the apical surface of the thyrocyte through a controlled reaction catalyzed by 2 members of the NADPH oxidases family, dual oxidase 1 (DUOX1) and dual oxidase 2 (DUOX2) (4-6).

The aim of our study was to investigate possible relationships between TH, TSH and DUOX2, and thus a possible involvement of oxidative stress (OS) in thyroid malfunction (7).

MATERIAL AND METHODS

The study included 66 patients (men and women), divided on 2 lots: 33 patients with hypothyroidism and 33 patients with hyperthyroidism. The control group was represented by 33 healthy volunteers. All the participants, patients and controls, provided the informed consent to participate in the study.

The parameters analyzed were serum TSH, FT4, FT3 and DUOX2. Measurement of serum TSH, FT4 and FT3 was performed using an automatic immunoassay system (IMMULITE 1000, Siemens Germany). Measurement of serum DUOX2 was performed using ELISA technique and assay kit from Abbexa UK.

TABLE 1. *Experimental data obtained in control group and hypothyroidism group*

Parameter	Control group	Hypothyroidism group	p
TSH (µUI/ml)	1.80±0.62	23.81±5.1	0.01
FT3 (pg/ml)	2.32±0.35	2.86±0.8	0.01
FT4 (ng/dl)	1.30±0.23	1.20±0.16	0.01
DUOX2 (ng/ml)	2.98±0.87	7.33±3	0.01

TABLE 2. *Experimental data obtained in control group and hyperthyroidism group*

Parameter	Control group	Hyperthyroidism group	P
TSH (µUI/ml)	1.80±0.62	0.04±0.02	0.01
FT3 (pg/ml)	2.32±0.35	4.14±1.03	0.01
FT4 (ng/dl)	1.30±0.23	2.47±0.9	0.01
DUOX2 (ng/ml)	2.98±0.87	2.65±0.7	0.01

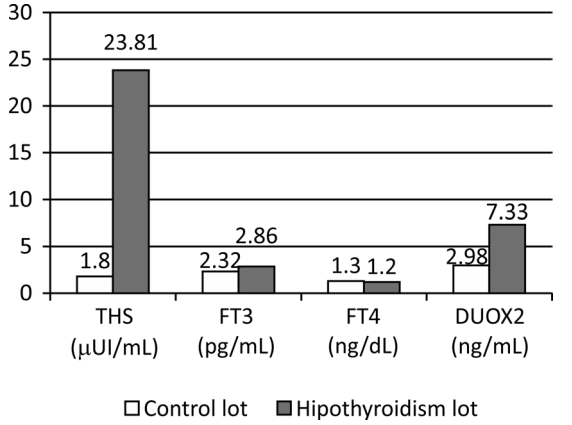

FIGURE 1. *Experimental data obtained in control group versus hypothyroidism group*

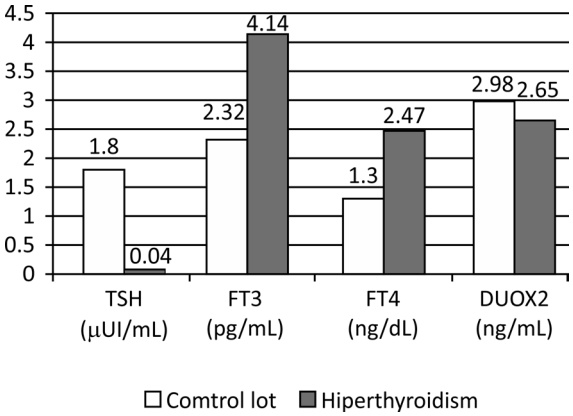

FIGURE 2. *Experimental data obtained in control group versus hyperthyroidism group*

Statistical analysis comparison between the two studied groups was done with Student's t test for parametric parameters.

RESULTS

Our experimental data is highlighted in Table 1 and Table 2 and represented in Figures 1 and 2. Our results showed that the patients with high levels of TSH 23.81 ±5.1 µUI/ml have increased levels of DUOX2 7.33± 3 ng/ml, compared with the levels in control group: TSH 1.80±0.62 µUI/ml and DUOX2 2.98±0.87 ng/ml; r^2=0.1.

Patients with very low levels of TSH 0.04 ±0.02 µUI/ml have lower levels of DUOX2 2.65± 0.7ng/ml, compared to the levels in control group TSH 1.80±0.62 µUI/ml and DUOX2 2.98±0.87 ng/ml; r^2=0.06.

DISCUSSIONS

Our results showed that in hypothyroidism patients we have lower levels of TH, and higher level of DUOX2. This suggest an accumulation of enzyme, unused for synthesis. In the meantime, in hyperthyroidism group we can observe a lower level of serum DUOX2, due to massive synthesis of TH.

We can assume that DUOX2 has a crucial role in TH and, by producing hydrogen peroxide, an important role in OS. It is known that DUOX are essential for TPO catalyzed hormone synthesis (7,8). Previous studies demonstrated that hydrogen peroxide generated by DUOX, inhibit TPO activity due to oxidative damage to the enzyme. If DUOX activity is increased, and the TPO activity is reduced, thyroid tissue could be harmed because hydrogen peroxide is less consumed by the TPO system and produced in higher amounts by DUOX. Reactive oxygen species (ROS) accumulate, leading to oxi-

dative damage of the thyroid gland (8-11). Other studies associated OS with both hyperthyroidism and hypothyroidism however, the mechanisms are different: low availability of antioxidants in hypothyroidism and increased ROS production in hyperthyroidism. It is demonstrated in many studies the involvement of OS in numerous pathologies, and thyroid disorders are among them (12,13). Some hyperthyroidism complications in target tissues are caused by OS (14,15).

CONCLUSIONS

In conclusion we can confirm the importance of DUOX2 in thyroid disfunction, based on the significant correlation between levels of TSH and DUOX2 (r^2=0.1 for hypothyroidism lot; r^2=0.06 for hyperthyroidism lot), and thus the involvement of OS in thyroid malfunction.

Additional studies are still needed in order to establish whether DUOX2 should be regarded as useful OS biomarker in thyroid pathology.

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