

Nutritionals Nutraceuticals Functional Foods Dietary Supplements

NuFFooDS

perspectives on science & business
Spectrum

Volume 4 | Issue 10 | June 2017 | ₹ 100

www.nuffoodsspectrum.in

52 pages including cover

ASIA - Fastest Growing Processed Food Market



41

Fluctuating funding
for 'Recession-Proof' food
and nutraceutical start-ups

44

ASLI NAKLI –
Calling for action



Dr Sanjay Agrawal
Leading Pharmaceutical
Consultant and Editor-in-
Chief of IJM Today

Nutraceuticals and Thyroid disorders

It is well known that oxidative stress (OS), defined as an imbalance between radicals and antioxidant defense, is implicated as a pathophysiological mechanism of different diseases and is a topic of growing interest. Cell injury is a consequence of OS; recognized targets are DNA, lipids and proteins, which react with hydroxyl radicals to form specific products. Especially in the field of cardiovascular diseases, the role of OS has been reevaluated, even if the therapeutic aftermath is still debated. Antioxidant defenses include enzymatic and non-enzymatic molecules and they are modulated by hormones, which regulate their synthesis and turnover.

Both hypothyroidism and hyperthyroidism can be associated with OS, moreover thyroid hormone (TH)-induced oxidative damage could be a factor responsible for the progression of heart failure, as suggested by the benefit of T3 administration on antioxidant systems in rat heart after pharmacological-induced hypothyroidism. However, few data exist on the possible diagnostic role of antioxidant measurements; in this review we examine thyroid regulation of antioxidants and OS in cardiac physiology and disease; then we speculate on the situation of low-T3 syndrome (also called "non-thyroidal illness", NTIS), a condition present in chronic disease. This hormonal situation reflects a compensatory mechanism, but the need of replacement therapy is matter of discussion. Therefore the evaluation of OS parameters could represent a further insight into the pathophysiology of NTIS

Thyroid Hormones and Oxidative Stress Previous studies suggested that the hypermetabolic state of hyperthyroidism is associated with an increase in free radical production, while the hypometabolic state of hypothyroidism symmetrically leads to a reduced free radical production. Indeed both hyperthyroidism and hypothyroidism are associated with enhanced oxidative stress involving enzymatic and non-enzymatic antioxidants. Furthermore, some complications of

hyperthyroidism are specifically related to the oxidative stress in target tissues.

Thyroid hormones influence lipid composition of rat tissues and therefore the susceptibility to oxidative stress. However, there is specificity in tissue response, and differential effects of T3 and T4 are possible, as previously review. In rat liver, T3-induced hyperthyroidism was found to be associated with altered lipid-peroxidation indices, including elevated levels of thiobarbituric acid reactive substances (TBARS) and hydroperoxides. On the contrary, no change in TBARS was observed in homogenized livers from rats made hyperthyroid by administration of T4 over a 4-week period. As regards testis, no significant change was observed in lipid peroxidation (evaluated as TBARS or hydroperoxides) of hyperthyroid adult rats, but hyperthyroidism promoted protein oxidation rate as indicated by an enhanced content of protein-bound carbonyls.

Thyroid Hormones, Antioxidants and the Heart ROS have been indicated as both detrimental and protective, via different pathways, for cardiac myocyte functions,





Thyroid hormones exert a key role in the modulation of antioxidant systems and OS is demonstrated both in hyper- and hypothyroidism. In the field of hypothyroidism, a debated question is the treatment of NTIS

electrophysiology and pharmacology. ROS effects on contractility are well recognized in literature, but recently also cardiac excitability has been investigated. ROS influence sarcolemmal and mitochondrial ion channels, which are responsible for cardiomyocyte excitability. It is known from the literature that oxidative stress is involved in the clinical course of different cardiopathies and in general it is involved in negative outcomes in cardiovascular disease. ROS have a crucial role in the genesis of atherosclerosis inducing vascular smooth muscle cell (SMC) growth and proliferation, oxidation of LDL, reduction of NO bioavailability, and vascular inflammation, which are characteristic features of the disease.

Indeed in Amiodarone treated subjects the drug invariably alters the indexes usually employed to measure thyroid function; in this situation CoQ10 correlates with the metabolic state better than with thyroid hormone levels themselves. The possible explanations for the very low CoQ10 levels in hyperthyroid patients include: decreased synthesis related to competition for tyrosine, which is a common substrate for CoQ or thyroxine synthesis, even if this hypothesis is disconfirmed by experimental data in animals; increased CoQ10 utilization, due to the increased stimulation of energy metabolism; increased degradation; decreased levels of carriers in serum, since it has been

demonstrated that the release of VLDL from liver is decreased in hyperthyroid states; similar mechanisms can be invoked to explain high CoQ10 levels in hypothyroid patients. An important index of body antioxidant defense is the antioxidant capacity of blood plasma, which is studied more and more frequently. Representing the functional sum of antioxidants present in plasma, it is a measure of the extracellular antioxidant barrier. In a recent work, TAC was determined during cardiovascular bypass surgery in patients with coronary heart disease: TAC decreased during surgery, but no further decrease in TAC was observed during reperfusion, indicating that it is a relatively stable parameter of the antioxidative barrier of the body.

Some analogies do exist with another situation of NTIS, the chronic obstructive pulmonary disease (COPD). In patients with COPD, evaluating lung parameters and antioxidant parameters are important because of a possible involvement of OS in NTIS. COPD is a complex condition, which cannot be considered a lung-related disorder, but rather a systemic disease also associated to increased oxidative stress. Articles evaluated thyroid hormones and antioxidant systems, the lipophilic CoQ10 and total antioxidant capacity (TAC) in COPD patients to reveal the presence of a low-T3 syndrome in COPD and investigated the correlation between thyroid hormones, lung function parameters and antioxidants. The evaluation of CoQ10 was particularly interesting, also for the energetic role of this molecule, which is a component of the mitochondrial respiratory chain, as above stated; its concentrations were also corrected for cholesterol, due to its lipophilic nature.

CONCLUSIONS

In conclusion thyroid hormones exert a key role in the modulation of antioxidant systems and OS is demonstrated both in hyper- and hypothyroidism. In the field of hypothyroidism, a debated question is the treatment of NTIS. Even if in the literature data are conflicting, our data suggest considering NTIS as a real hypothyroidism at tissue level and not only as an adaptive response to the conditions mentioned above. In particular, CoQ10 levels seem to be a reliable index of thyroid hormone effects; moreover, OS is a mechanism to be underlined in the physiopathology of NTIS and, again, it can reflect a condition of hypothyroidism. The question of usefulness of replacement therapy is complex and based on standardization of different factors involved: the choice of hormone (T4 or T3); the route of administration (oral or intravenous); and the definition of clinical endpoints, due to the complexity of clinical models with different interfering factors. When the molecular mechanisms underlying low T3 levels are better understood, it may be possible to choose which patients are likely to benefit from replacement therapy as well as the appropriate schedule of treatment. **NS**