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Editorial

Thyroid Hormones and Tissue Oxidative Stress

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Thyroid hormones affect the growth, development, and metabolism of vertebrates [1] and are considered the major regulators of homeostasis. One of the main effects of thyroid hormones is the stimulation of the cellular metabolism that is normally accompanied by an increase in reactive oxygen species (ROS) production. Consequently, when plasma levels of thyroid hormones increase, oxidative injury of hormone target tissues develops because of the alteration in the antioxidant pro-oxidant- balance [2]. The analysis of the content of low molecular weight antioxidants and of the activities of antioxidant enzymes in tissues from hyperthyroid rats shows that they are tissue dependent [3]. Although the levels of single antioxidants are generally independent of the extent of oxidative damage [3], the global antioxidant capacity and ability to counteract an oxidative insult are always reduced in hyperthyroid tissues [3]. In the cells, ROS arise from different sources, including cytosolic oxidases, peroxisomes, mitochondria, endoplasmic reticulum, and lysosomes. However, despite disagreeing opinions, mitochondrial respiratory chain, being the site of oxidative phosphorylation, which utilizes about 90% of the oxygen consumed by the cells, is considered the most important source of ROS production [4]. The determination of mitochondrial ROS release by respiring mitochondria shows that hyperthyroidism increases such a release in skeletal muscle, liver and heart [5-7]. It is conceivable that the increased ROS release is due to the well-known capacity of thyroid hormones to induce increases in the respiratory chain component content [8,9]. The idea that such an increase also involves the autoxidizable carrier content, has been demonstrated determining the mitochondrial ROS release using combinations of respiratory substrates and inhibitors of respiratory chain, which render the ROS release dependent on the concentration of the autoxidizable component located between the site of electron ingress and the site of the block of the respiratory chain [5-7]. The thyroid hormone- induced increase in components of mitochondrial chain is further confirmed by the hormone capacity to induce up regulation of factors involved in the transcription of nuclear genes codifying for component of the respiratory chain, the nuclear respiratory factors 1 and 2 (NRF1 and NRF2) and the coactivator of peroxisomal proliferator activated protein 1 (PGC1) which regulates the action of NRF 1 and 2 [10]. Interestingly, the increase in components of respiratory chain such as the cytochromes, which can interact with H_2O_2 generating the ·OH radical, remarkably affect the capacity of hyperthyroid mitochondria to remove exogenous H_2O_2 [11]. Indeed, although the mitochondria levels of antioxidants able to react with H_2O_2 generating reactive species are lower, the whole mitochondrial capacity of hyperthyroid mitochondria to remove H_2O_2 is higher than euthyroid mitochondria. Because there is an extensive interplay among the various cellular sources of ROS, this can explain the remarkable oxidative damage by which are affected mitochondria of hyperthyroid tissues. The mitochondrial oxidative damage is responsible for mitochondrial dysfunction, and the administration of an antioxidant such as vitamin E attenuates both mitochondrial oxidative damage and dysfunction [12]. Interestingly some complications of hyperthyroidism are due to thyroid hormone induced oxidative stress in target tissues and the antioxidant supplementation can have beneficial effects [12] even if more studies are necessary to better define the mechanism of antioxidant protection.

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