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Thyroid dysfunction and physical activity: clinical and therapeutic implications

Abstract

Thyroid dysfunctions and, in particular, hypothyroidism are complex diseases characterized by signs and symptoms that may have a significant negative impact on quality of life and performance in the course of physical activity. The exercise intolerance in conditions of untreated hypothyroidism is multifactorial and is dependent on the functional limitations of the various system organ class. Thyroid hormones preserving the functions of cardiovascular, respiratory and muscle systems during relaxation and during exercise and they are responsible for the limitation of exercise tolerance in conditions of hypothyroidism.
Adequate hormone replacement therapy in conditions of hypothyroidism, in addition to improving the quality of life, helps to achieve good results during physical activity. However, exercise intolerance in patients with overt hypothyroidism and in patients with subclinical hypothyroidism, is not always reversible following an appropriate hormone replacement therapy.
In fact, in these patients there is a loss of tolerance to physical activity, consequently they perform a lower physical activity resulting deterioration in the quality of life. These patients do not enjoy the psychophysical benefits who instead are available to individuals who practice regular physical activity. In general an active lifestyle based on regular physical activity of aerobic type is recommended in all subjects, in particular in patients with hypothyroidism as it can improve the quality of life regardless of the condition of hypothyroidism

Key words: thyroid - physical activity - hypothyroidism

Riassunto

Le disfunzioni tiroidee e, in particolare, l'ipotiroidismo sono malattie complesse caratterizzate da segni e sintomi che possono aver un impatto notevolmente negativo sulla qualità della vita e sulla performance in corso di attività fisica. L'intolleranza all'esercizio fisico in condizioni di ipotiroidismo non trattato è multifattoriale e dipende dall'insieme di limitazioni funzionali dei diversi apparati. Gli ormoni tiroidei preservando le funzioni cardiovascolari, respiratorie e muscolari a riposo e durante l'esercizio rappresentano il fattore limitante per la tolleranza all'esercizio in condizioni di ipotiroidismo. Un'adeguata terapia ormonale sostitutiva in condizioni di ipotiroidismo, oltre a migliorare la qualità della vita concorre a garantire buoni risultati sportivi durante l'attività fisica. Tuttavia, l'intolleranza all'esercizio nei pazienti con ipotiroidismo conclamato e, in misura minore, in pazienti con ipotiroidismo subclinico, non è sempre reversibile in seguito ad una adeguata terapia ormonale sostitutiva. Infatti, in tali pazienti si assiste ad una minor tolleranza all'attività fisica che porta a sua volta ad una minor attività fisica praticata con conseguente peggioramento della qualità della vita in tali pazienti in quanto viene meno il beneficio psico-fisico di cui si giovano i soggetti che praticano un'attività fisica regolare. In generale uno stile di vita attivo basato su una regolare attività fisica di tipo aerobio è raccomandata in tutti i soggetti ed in particolare in pazienti con ipotiroidismo in quanto in grado di migliorare la qualità della vita indipendentemente dalla condizione di ipotiroidismo.

Parole chiave: tiroide – attività fisica – ormoni tiroidei

Introduction

The thyroid is an endocrine gland, located in the anterior region of the neck, that through the synthesis and secretion in the circulation of 2 hormones, triiodothyronine (T3) and thyroxine (T4), plays an extremely important physiological role: it directly influences skeletal and brain development, participates in the regulation of body metabolism and in the development of skin, hair system and genital organs. Thyroid hormones are produced by the thyroid follicular cells in response to the pituitary hormone TSH, whose production is in turn regulated by the hypothalamic hormone TRH. The secretion of thyroid hormones is pulsatile and follows a circadian rhythm; the highest levels of T3 and T4 are reached during the night and early morning, while the lowest levels are reached between 12 am and 9 pm.

Action of thyroid hormones

Thyroid hormones in the foetus and infant are indispensable for the normal growth and for the maturation of various organs, while in the adult they condition the function of each organ and tissue through a generalized increase in metabolic processes. In particular, thyroid hormones:

- - directly regulate the **basal metabolic rate** through the increase in oxygen consumption at rest, of the production of heat and of energy expenditure (as a result of the increase in mitochondrial oxidative metabolism and respiratory enzymes). In fact, in normal conditions, O2 consumption is about 250 ml / min, in conditions of hypothyroidism it drops to 150 ml / min and increases to 400 ml / min in conditions of hyperthyroidism;
- - promote glycogenolysis and gluconeogenesis (through an increase in hepatic glucose production and the synthesis of the enzymes involved in its oxidation);
- - stimulate lipolysis (using fat as energy) and lipogenesis (adipose tissue synthesis), with a predominant effect on lipolysis and a consequent increase in the availability of fatty acids, whose oxidation generates ATP, used for thermogenesis;
- - increase protein synthesis and therefore have a trophic effect on the muscle;
- - regulate the growth and differentiation of the central nervous system during foetal life and during the first weeks of life;
- - increase myocardial contractility (inotropic positive effect), heart rate (positive chronotropic effect) and venous return to the heart; they are therefore essential for the functioning of the heart;
- - have a key role in skeletal development, in fact: they stimulate endochondral ossification, linear growth and maturation of the epiphyseal centers, promote maturation and activity of chondrocytes in the cartilage of foil growth, in adults, accelerate bone remodeling with major effect on reabsorption.

Thyroid hormones also have other various metabolic effects: they increase intestinal motility, promote the absorption of cyanocobalamin (vit. B12) and iron, increase the synthesis of erythropoietin, renal blood flow and glomerular filtration, stimulate the endogenous production of other hormones (GH), have a permissive role in reproductive functions and regulate the trophism of skin and skin adnexa. A dysfunction of the thyroid gland results in two well-defined clinical syndromes:

- *hypothyroidism*: clinical syndrome deriving from a deficiency of thyroid hormones in tissues that leads to a general reduction of all the body's metabolic processes;
- *hyperthyroidism*: morbid condition deriving from increased serum concentrations of the free fractions of thyroid hormones which leads to a general increase in metabolic processes.

Effects of thyroid hormones on the osteomuscular apparatus

The action of thyroid hormones at muscular level

Thyroid hormones control the production of energy and many aspects of neuromuscular physiology through the modulation of contractile protein synthesis and the regulation of transmembrane ion fluxes.
In particular:

- hey regulate the synthesis of myosin heavy chains (through the increase of the alpha-isoenzyme and the reduction of the beta-isoenzyme, resulting in a prevalence of type II fibers, with high ATPase activity and contractile efficiency);
- they increase Ca-ATPase (enhancement of the uptake of calcium in the sarcoplasmic reticulum with increased plasma contractility);
- they increase Na / K-ATPase (increased sodium efflux with enhancement of contraction and increased consumption of O2 and thermogenesis).

In general, the effects of thyroid dysfunctions on the osteomuscular apparatus result in a reduced effort tolerance. In hypothyroidism this is due to a reduced cardio-vascular reserve (reduction of VO2 max, reduced cardiac output, increased lactate), to a reduced pulmonary reserve, to an altered distribution of blood flow and a reduction in substrate oxidative capacity. The mechanisms underlying the reduced muscular efficiency are attributable to the increase in slow fibers (type I), to an altered oxidative function with a consequent reduction of ATP and phosphocreatine, to the decrease of intracellular pH and to the early glycogen depletion. In hyperthyroidism, instead, the decrease in effort tolerance depends on an increase in the rate of blood flow and cardiac output at rest and on a decreased efficient use of O2, of the anaerobic threshold, of the contractile reserve and of work capacity.
These effects are the consequence of an increase in cardiac frequency and output. These metabolic effects

translate clinically in weakness, asthenia, exertional dyspnea and exercise intolerance in hypothyroid patients. In hyperthyroid patients, instead, physical activity leads to events like: resting tachycardia, reduced effort tolerance, muscle weakness (especially of proximal muscles and extensors), reduction of muscle mass.

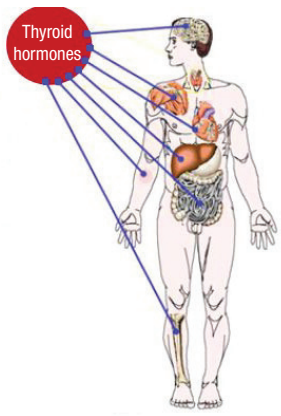
Effects of exercise on the thyroid function

In addition to determining a number of beneficial effects on the cardiovascular system, physical exercise also influences a wide range of endocrine and metabolic functions. Because of the known influence of thyroid hormones on the cardiovascular system, various studies have been conducted to examine the variations of the thyroid function and other endocrine glands during exercise. The lack of consistency of these studies resides in different aspects: wide variety of types of exercise put in relation to the thyroid function, individual variability and non-homogeneity of the conditions of the initial thyroid function.

In particular Smallridge et al. presented a study in which three different conditions of exercise were evaluated (sedentary, amateur runners and marathon runners); in these categories no significant differences of thyroid function in baseline conditions and after TRH stimulation (TRH test) were detected. The only significant difference concerned, in fact, prolactin baseline levels dosed in the immediate post-exercise phase and one hour after the end of the exercise, which were lower in sedentary subjects than in those who carried out regular physical activity, while no significant differences were found among amateur runners and athletes, because also the peak of prolactin after TRH stimulation resulted higher in this second group. This study seems to show that, while the effects of physical activity on thyroid hormones are negligible, exercise would, however, influence other hormones, in particular prolactin, whose values are modified by physical activity, without any modulation due to the intensity of physical activity. Some authors have in fact suggested that intermittent hyperprolactinemia produced by exercise can play a role in the amenorrhea often found in young female athletes (1). Also according to other authors, a short duration exercise would only have a modest influence on the hypothalamic-pituitary-thyroid axis: it has been demonstrated, in fact, that low workloads do not determine changes in TSH nor during exercise or during the subsequent 24 hours (2); while in case of submaximal prolonged exercise, other studies show a continuous increase in TSH levels both during the exercise and in the 15 minutes after its end. The significant increase in TSH, which can be observed after prolonged physical stress, is most likely due to the minor peripheral level of thyroid hormones, widely used at tissue level, with a consequent stimulation (through the physiological feedback pathways) of the TRH synthesis at the hypothalamic level and consequently of the TSH at the pituitary level. This has been demonstrated in a study conducted in Norway in which high plasma levels of T3, T4, TSH and of the protein that binds thyroid hormones (TBG) have been highlighted in cross-country skiing athletes immediately after a performance: the plasma levels of T3, T4 and TSH went back within the initial limits only several days after the end of the exercise session (2). Therefore, while an intense but short physical activity is not able to determine significant modifications of plasma levels of thyroid hormones, prolonged training sessions lead to a marked increase in the levels of T3 and T4 as a result of the action of the positive feedback on the hypothalamic-pituitary-thyroid axis. Prolonged physical activity can therefore influence the biosynthetic activity of the thyroid gland and increase the levels of T3 and T4 without however producing the toxic effects that occur in case of hyperthyroidism. Some studies, however, have demonstrated a reduction in circulating T3, probably as a result of the increased peripheral conversion in reverse T3 (3).

It should also be considered that physical activity, does not directly condition the thyroid activity, but indirectly affects the synthesis and the production of thyroid hormones by modifying the nutritional status. Since it regulates energy metabolism, the thyroid function is in fact affected greatly by the nutritional status: its activity is reduced in conditions of negative energy balance, such as during fasting, in which the production of thyroid hormones and tissue sensitivity to these hormones decrease. This represents a defense mechanism that reduces tissue metabolism in order to limit energy consumption. In fact, according to Uribe et al. (4) the activity of the hypothalamic-pituitary-thyroid axis is reduced in conditions of negative energy balance, but the effect of chronic exercise on the axis is controversial and not well-known at the hypothalamic level.

Signs and symptoms of hypothyroidism



Central Nervous System: loss of memory, poor concentration and deafness

Pharynx: hoarseness

Heart: bradycardia and pericardial effusion

Musculature: delayed relaxation of reflex

Extremities: feeling of cold

Lungs: shortness of breath and pleural effusion

Intestine: constipation and ascites

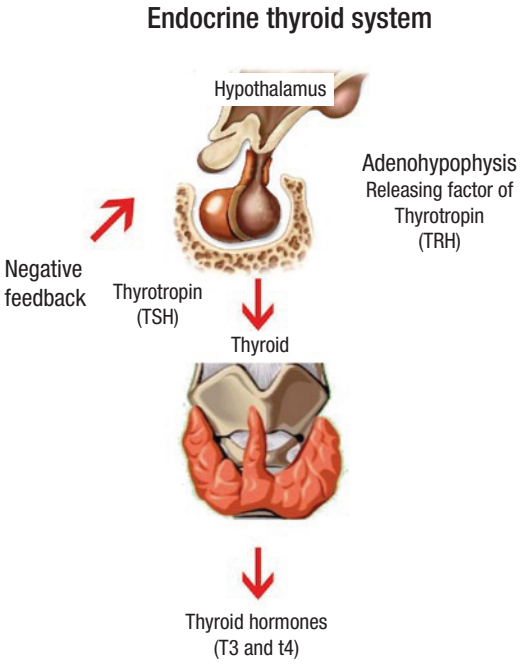
Reproductive system: menorrhagia

Skin: paresthesia and myxedema

Hair Loss

Hypothyroidism and physical activity

Hypothyroidism is a complex disease characterized by signs and symptoms that may have a considerably negative impact on quality of life and performance (5) during physical activity. Exercise, in fact, requires the coordinated functioning of heart, lungs, peripheral circulation and muscles. Since they preserve cardiovascular, respiratory and muscle functions at rest and during exercise (6), thyroid hormones represent the limiting factor for exercise tolerance in conditions of hypothyroidism. In general, a proper replacement therapy in conditions of hypothyroidism, in addition to improving the quality of life helps to guarantee good results in sports during physical activity. However, a significant number of patients continues to experience reduced physical performance even during adequate hormone replacement therapy (3); however, there are no randomized clinical studies that have assessed reduced exercise tolerance in hypothyroid patients adequately treated with levo-thyroxine. In a recent review of the literature (3) it has been shown that exercise intolerance in conditions of untreated hypothyroidism is multifactorial and dependent on the functional limitations of the different apparatuses (cardiovascular, cardiopulmonary, pulmonary, musculoskeletal, neuromuscular). In addition, exercise intolerance in patients with overt hypothyroidism and, to a lesser extent, in patients with subclinical hypothyroidism, is not always reversible following an adequate hormone replacement therapy (7). This analysis showed that the condition of hypothyroidism can lead to significant negative effects on physical well-being, both in untreated patients and in those adequately treated with Levo-thyroxine, making them more intolerant to exercise than healthy subjects. According to this review, there are contradictory data on the effects of physical activity in patients with primary hypothyroidism and what emerges is that hypothyroidism is associated with a worse quality of life and consequently with less physical well-being, both in treated patients and in those not adequately treated with Levo-thyroxine. In particular, these patients have a lower exercise tolerance that, in a vicious circle, leads to less physical activity and to the loss of the benefits which instead are observed in all those who do regular exercise. In general, an active lifestyle based on regular physical aerobic activity is recommended for all subjects, even in patients with hypothyroidism who nonetheless benefit from regular physical activity. The potential physical limitations that are observed in hypothyroid patients and in those treated with replacement therapy do not represent an impediment to a regular physical activity. It is important that sports physicians and endocrinologists work together to limit the negative effects of thyroid dysfunction, without excluding regular physical activity and promoting an active lifestyle with all the benefits that it entails.



Conclusions

Regular physical activity proved to be one of the main factors that can reduce mortality and cardiovascular comorbidities. Limited exercise sessions on a regular basis represent the best non-pharmacological therapy to prevent and reduce complications of cardiovascular diseases. Subjects with thyroid dysfunction represent a particular subgroup that despite the known limitations (asthenia, easy fatigue etc.) benefit from regular physical activity in terms of quality of life and psychophysical well-being.

Important messages: reassure patients that there are no contraindications to regular physical activity in case of a worse performance with respect to subjects with a normal function; involve sports physicians in therapeutic decisions; promote physical activity as one would do among subjects without thyroid dysfunction.

However, there are still significant gaps in the knowledge of the metabolic mechanisms in subjects with thyroid dysfunction who do exercise. Research in this area must provide answers through controlled studies linking physical performance to thyroid hormone status.

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