36 - EFFORT INTOLERANCE IN SUBCLINICAL HYPOTHYROIDISM: IMPLICATIONS IN PHYSICAL TRAINING PRESCRIPTION

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INTRODUCTION

The Hypothyroidism is a syndrome characterized by clinical and biochemistry manifestations in consequence of the deficiency of thyroid hormones. The Subclinical Hypothyroidism (SH) is a minimum dysfunction of thyroid where the patient presents high level of serum thyroid-stimulating hormone (TSH) and normal concentrations of triiodotyronine (T3) and free thyroxine (T4) (BIONDI & COOPER, 2008). Its prevalence can get to 20%, depending on the population and age investigated, being more frequent in old women (SURKS et al., 2004). One of the main characteristics of patients with SH is the intolerance to effort (KAHALY, 2000; KAHALY, KAMPMANN & MOHR-KAHALY, 2002). Literature reviews demonstrate that even minimum alterations in the function of thyroid can have relevant cardiovascular consequences, increasing the risk of development of cardiovascular illnesses and mortality (OCHS et al., 2008). The effect of the SH on the cardiovascular system is well registered in literature and the condition of euthyroidism, reached for the levothyroxine replacement (L-T4), can revert, in the majority of the cases, the observed cardiovascular abnormalities in these patients (KAHALY, 2000; KLEIN & DANZI, 2007; BIONDI & COOPER, 2008;). On the other hand, few studies had investigated the exercise response in patients with SH, especially in relation to the analysis of the functional capacity and the effect of the hormonal replacement, having contradictory results (PLOUGH et al., 1996; KAHALY, 2000; BRENTA et al., 2003; CARACCIO et al., 2005; MAINENTI et al., 2009).

The present study examines the main cardiovascular alterations decurrent of the SH and their implication in the functional capacity of these patients, providing directions for future research. Article search was made in the Medline database (Keywords: Subclinical Hypothyroidism; Physical exercise; Functional capacity) and references of relevant articles, books and summaries, published from January,1995 to June, 2010.

PHYSIOLOGICAL ACTION OF THE THYROID HORMONES IN THE CARDIOVASCULAR SYSTEM

To facilitate the comprehension of the impact of hypothyroidism in the functional capacity, it is necessary to understand the action of thyroid hormones in the cardiovascular system. The thyroid hormones control the expression of certain genes of the myocardium, regulating the calcium availability that affects systolic and diastolic function. The main genic transcriptions regulated by these hormones are related to proteins of the sarcoplasmatic reticulum: Activator ATP-ase Calcium (Ca2+-ATP-ase - SERCA2) and Fosfolamban, that are essential in the regulation of the transient of calcium in systole (calcium release) and in diastole (retaken of calcium) of the myocardium (MOOLMAN, 2002). The Fosfolamban regulates the action of the SERCA2 (inhibiting), mechanism for which the beta-adrenergics agonists exert a positive inotropic function in the heart (KLEIN & DANZI, 2007). This phosphorization is important as for the event of diastole as to provide the necessary amount of calcium for its subsequent release in systole (MOOLMAN, 2002). The thyroid hormones also act directly and indirectly in tonus of the smooth vascular peripheral muscle, inhibiting the mechanism of platelet aggregation in vitro. As result of the direct action of these hormones, there was capillary vasodilatation, that leads to the reduction of the peripheral resistance, the increase of the cardiac debit and the maintenance of the mean arterial blood pressure, favoring the cellular metabolism and intervening, consequently, in the pulmonary gas exchange. In the presence of the hypothyroidism, it has an inversion of these physiological effects.

Therefore, the thyroid hormones act directly on the cardiovascular system, regulating the contractility and cardiac relaxation (central mechanism) as well as vascular tonus (peripheral mechanism). Functional capacity is the consequence of the integrated action of the pulmonary, cardiovascular and muscular systems response to the exercise, any alteration in this gear causes impact in its efficiency (WASSERMAN et al., 2005).

Organic-functionary dysfunctions in patients with Subclinical Hypothyroidism and Implications in the Functional Capacity

As previously seen, cardiac phenotype is extremely sensible to the changes in the level of hormones of thyroid. In the SH, it Klein is resultant of a reduced action of thyroid hormones in such a way in the heart as in the peripheral vascular ways (KLEIN & DANZI, 2007). In this in case that, the modified levels of T3 and T4 promote dysfunctions in diverse physiological parameters, as observed in Table 1.

Table 1: Organic and Functional Alterations in Subclinical Hypothyroidism Patients

System	Organic and Functional Alterations
Cardiovascular and Hemodynamic	↓ Cardiac Contractility (Left Ventricular Systolic Dysfunction) ↓ Heart Rate ↓ Cardiac Output ↑ Peripheral Vascular Resistance ↓ Systolic Blood Pressure ↓ Heart Rate Variability ↑ Pre-ejection Period (Left Ventricular Diastolic Dysfunction) ↑ Arterial Stiffness
Metabolic and Muscular	↓ Mitochondrial Enzymatic Activity ↓ Oxidative metabolism capacity ↓ Insulin Sensitivity ↑ Serum cholesterol levels (Dyslipidemia)

(Adapted according to BIONDI et al., 1999; KAHALY, 2000; PALMIERI et al., 2004; REUTERS et al., 2006; MAINNENTI et al., 2007; BIONDI & COOPER, 2008; CABRAL et al., 2009)

The lesser myocardial contractility, the impaired systolic function, the diastolic dysfunction and the increased systemic vascular resistance are the main organic-functional alterations observed in patients with SH. In reason of these alterations, there is a low supply and extraction of the oxygen to the active muscles during the exercise because of the lesser cardiac output and blood flow resistance, respectively, compromising the efficiency of the gas exchanges in the muscle. According to KAHALY et al. (2002), the inadequate cardiovascular support seems to be one of the main involved factors in the intolerance to the effort in the SH. It can be said that the reply to the effort reflects the organic-functionary alterations already observed in resting in these patients. The clinical evaluation and of the muscular function discloses that patients with SH present greater frequency and higher scores for myalgia complaints, beyond weakness and reduction of the force of the scapular and pelvic waist, when compared to the group of healthy individuals (REUTERS et al., 2006). In fact, transversal studies demonstrate minor performance during the exercise and worse functional capacity indicators in patients when compared the healthy people (Table 2).

Table 2: Studies on Exercise Response in Subclinical Hypothyroidism Patients

Study	Exercise Response in SH x Control Group	Exercise Response after L-T_4 Replacement
AREM et al. (1996)		↑Systolic function (Small improvement)
MONZANI et al. (1997)	↓Muscular metabolism ↑ Lactate Accumulation	
KAHALY (2000)	↓Systolic function, ↓ O_2 Pulse, ↓$\dot{V}O_{2máx}$, ↓Vital capacity, ↑ Lactate Accumulation, ↓ Work Capacity at AT	↑Systolic function, ↑O_2 Pulse, ↑$\dot{V}O_{2máx}$, ↑ Vital capacity, ↑ Work Capacity at AT
BRENTA et al. (2003)	↓ Diastolic function	↑Systolic and Diastolic Function at peak (not significant)
CARACCIo et al. (2005)	↓$\dot{V}O_{2peak}$, ↑Accumulation of Lactate, ↑HR ↓Tolerance to the effort	No Change
MAINENTI et al. (2007; 2009)	↓Expired fraction of O_2 ↓Duration in the Effort Test ↓Amplitude of Variation of the SBP ↓Recovery of the DBP	↓$\dot{V}O_2$, ↓$\dot{V}E$ and ↓HR for the same submaximal intensity
XIANG et al. (2009)	↑Endothelial function, $\dot{V}O_{2máx}$ after-training	
AMATI et al. (2009)	↓ Insulin Sensitivity No alteration in the $\dot{V}O_{2peak}$ after-training	
AKCAKOYUn et al. (2009)	↓Longitudinal Left Ventricular Function No change SBP, DBP and HR	
AKCAKOYUN et al. (2010)	SBP, DBP, HR, Effort Tolerance (No change) ↓ Recovery Time After-Exercise ↓ Chronotropic response	

(SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; AT: Anaerobic Threshold; VO_2: Oxygen Uptake).

It is verified that patient with SH when compared to healthy people or the euthyroid controls have the following characteristics in response to exercise: lesser peak oxygen uptake ($\dot{V}$O2pico), decreased anaerobic threshold (AT), lesser oxygen upatke and workload in AT, greater accumulation of lactate, greater heart rate (HR) and O2 for same workload, decreased vital capacity and efficiency of the oxidative metabolism. Moreover, the recovery of the physiological parameters after the exercise is slower in the patients. Recent studies had used the ergospirometry as a method to measure the functional capacity, that supplies differentiated information related to the exercise response, making possible higher agreement of the intolerance to the effort in the SH. Despite of its importance, however, its use in the evaluation of these patients is recent and needs more attention. New studies are necessary, once the reduced sample size and the different exercise protocols used. Moreover, only two studies had investigated the behavior of the physiological variable during the recovery in patients with SH (MAINENTI et al., 2007; AKCAKOYUN et al., 2010).

EFFECT OF THE HORMONAL REPLACEMENT WITH LEVOTHYROXINE (L-T4) IN THE FUNCTIONAL CAPACITY

One of the alternatives to revert the observed cardiovascular alterations in patients with subclinical hypothyroidism is the hormonal replacement with Levothyroxine (L-T4). According to some authors, the return to the euthyroidism condition reverts the observed cardiovascular alterations in these patients. However, a consensus in literature does not exist still on the general recommendation of the L-T4 replacement, having to be analyzed each case, considering the risk of progression of the illness and cardiac complications (BIONDI & COOPER, 2008; PALMIERI et al., 2004; SURKS et al., 2004). The studies disclose that the diastolic and systolic function during the effort improves after the drug therapy, once the abnormality of the left ventricular contractility function of the are corrected and the diastolic function normalized (AREM et al., 1996; KAHALY, 2000; BRENTA et al., 2003), being able to improve the endothelial function, preventing or reverting atherosclerosis and the coronary arterial illness (BIONDI & COOPER, 2008). However, few randomized and controlled studies exist, that use control-placebo and make the comparison of the values of the cardiac performance in the exercise daily pre and post-treatment, besides reduced sample number and different methodologies. The efficiency of the replacement of L-T4 in improving the functional capacity and the tolerance to the physical effort in the patients with SH is argued in literature. Some studies confirm this hypothesis (KAHALY, 2000), while others reject it (CARACCIO et al., 2005) or demonstrate only fast improvement (AREM et al., 1996; BRENTA et al., 2003); third still confirm benefits only in submaximum effort (MAINENTI et al., 2009).

Therefore, new studies are necessary to elucidate the real impact of the L-T4 on functional capacity of patients with SH. After the beginning of the treatment, the reevaluation vary of six months to one year, counted from the normalization of the hormone levels (reach of the euthyroid state). The main physiological processes that can explain the better performance in the exercise after the TSH normalization are the increase of the myocardial contractility and the improvement of the vascular function, probably due to regularization of the activity of some enzymes influenced by thyroid hormones (MONZANI et al., 2001; RAZVI et al., 2007). Thus, the impact of the replacement of L-T4 on the cardiopulmonary performance to the exercise in patients

with HS is still controversial. The sample size, the lack of a control group and the use of different ergometers as well as the graduation of TSH level are possible causes for the contradictory results in available articles.

EXERCISE PRESCRIPTION FOR SUBCLINICAL HYPOTHYROIDISM PATIENTS

In the bibliographical revision carried out only one study was found on the effect of the physical training in SH patients (XIANG et al., 2009). After six months of aerobic training, the patients showed improvements in endothelial function. From some evidences raised in the present study, it is possible to identify characteristics and functional abnormalities in SH patients similar to cardiac and pulmonary patients. In this direction, at the moment of the exercise prescription to these patients, the Physical Education professionals must be intent to following characteristics of the exercises program: type: aerobic and/or resistance exercise; intensity: moderate, being able to be monitored by the subjective perception of effort; frequency: 3-5 times a week; duration: at least 30 minutes for session. Special attention must be given on the hydration. Another important aspect is that about 40% of the patients with SH present diastolic hypertension, and depending on the pressure levels for times they take medication antihypertensive (SURKS et al., 2004). The professional also must be aware to the risk of falls due to the characteristic of muscular weakness and the biggest resistance to the insulin, what can provoke slight hypoglycemia.

FINAL CONSIDERATIONS

Patients with subclinical hypothyroidism present a series of cardiovascular commitments in the rest and during the exercise, having similar limitations to the observed ones in other chronic deseases, as low the tolerance to the effort. There are promising results of L-T4 replacement in the improvement of the observed organic-functionary alterations; however, the drug therapy by itself seems not to be enough for the improvement of the functional capacity of these patients. Under the health point of view, the limited functional capacity observed in the SH can restrict the daily activities or even hinder that they get physically active, compromising the life quality of these patients. Therefore, the practice of physical exercises must be stimulated in this population, recognizing the importance of mapping ventilatory response parameters in effort. It makes possible an adjusted, individualized and more appropriated training prescription. There is a lack of available literature of relative information to the effect of the physical training in the SH and scientific recommendations for physical exercise prescription for this special population. Thus, it is recommended to the Physical Education professionals the use of lines direction of prescription similar to those for cardiac patients. New researches must be developed trying to investigate the effect of the physical training in the functional capacity of patients with SH, as well as follow-up studies of these patients throughout the time, looking for important physiological variables for the diagnosis and prognostic of the illness.

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EFFORT INTOLERANCE IN SUBCLINICAL HYPOTHYROIDISM: IMPLICATIONS IN PHYSICAL TRAINING PRESCRIPTION ABSTRACT

ABSTRACT

The subclinical hypothyroidism (SH) is characterized by cardiovascular and metabolic alterations that compromise the capacity of exercise accomplishment. The intolerance to the effort is the main characteristic of these patients. Studies disclose that the hormonal replacement with levothyroxine (L-T4) revert these alterations, but the evidences are insufficient in relation to the improvement of the functional capacity. In general, patients with low tolerance to the effort present a slower response during the exercise and recovery. The present study examines the main cardiovascular alterations decurrent of the SH and its implication in the functional capacity, providing directions for future research. There is a lack of studies on the response to the exercise in these patients. Thus research is necessary that can give support to the physical exercise prescription for patients with SH.

KEYWORDS: Hypothyroidism; Physical Exercise; Functional Capacity.

L'INTOLÉRANCE AUX EFFORTS HYPOTHYROÏDIE SUBCLINIQUE: IMPLICATIONS POUR L'ORDONNANCE DES EXERCICES PHYSIQUES

RÉSUMÉ

Hypothyroïdie Subclinique (HS) la est caractérisée par cardio-vasculaire et métaboliques qui sapent la capacité à effectuer pour l'exercice. L'intolérance à l'effort est la principale caractéristique de ces patients. Les études montrent que le traitement hormonal substitutif avec lévothyroxine (L-T4) revient ces amendements, mais la preuve est insuffisante pour l'amélioration de capacité fonctionnelle. En général, les patients avec une faible tolérance à présenter une réponse plus lente pendant l'année et sur le recouvrement. Cette étude examine les principales maladies cardio-vasculaires changements découlant de la HS et sa participation à la capacité fonctionnelle, fournissant directions pour la recherche future. Trouvé-si une pénurie d'études sur la réponse d'exercer chez ces patients et la nécessité de nouvelles recherches qui peuvent sous-tendent la prescription des exercices physiques pour les patients avec le SH.

MOTS-CLÉS: Hypothyroïdie; L'exercice Physique; Capacité Fonctionnelle.

INTOLERANCIA AL ESFUERZO EN HIPOTIROIDISMO SUBCLÍNICO: IMPLICACIONES PARA LA PRESCRIPCIÓN DE EJERCICIOS FÍSICOS

RESUMEN

El hipotiroidismo subclínico (HS) se caracteriza por alteraciones cardiovascular y metabólicas que comprometen la capacidad de ejercicio. La intolerancia al esfuerzo es la principal característica de estos pacientes. Estudios revelan que el reemplazo hormonal con levotiroxina (L-T4) reverti estas alteraciones, pero las evidencias son insuficientes en relación con el mejoramiento de la capacidad funcional. En general, los pacientes con baja tolerancia al esfuerzo presente una respuesta más lento durante el ejercicio y la recuperación. La presente estudio analiza las principales alteraciones cardiovasculares decurrentes del HS y su implicación en la capacidad funcional, proporcionando direcciones para futuras investigaciones. Hay una falta de estudios sobre la respuesta al ejercicio en estos pacientes. Por lo tanto investigación es necesario que puede dar apoyo al prescricion del ejercicio físico para pacientes com HS.

PALABRAS CLAVE: Hipotiroidismo; Ejercicio Físico; Capacidad Funcional.

INTOLERÂNCIA AO ESFORÇO NO HIPOTIREOIDISMO SUBCLÍNICO: IMPLICAÇÕES PARA A PRESCRIÇÃO DE EXERCÍCIOS FÍSICOS

RESUMO

O hipotireoidismo subclínico (HS) é caracterizado por alterações cardiovasculares e metabólicas que comprometem a capacidade de realização de exercício. A intolerância ao esforço é a principal característica destes pacientes. Estudos revelam que a reposição hormonal com Levotiroxina (L-T4) reverte estas alterações, mas as evidências são insuficientes em relação à melhoria da capacidade funcional. Em geral, pacientes com baixa tolerância ao esforço apresentam uma resposta mais lenta durante o exercício e na recuperação. O presente estudo examina as principais alterações cardiovasculares decorrentes do HS e sua implicação na capacidade funcional, provendo direções para futuras pesquisas. Constatou-se uma carência de estudos sobre a resposta ao exercício nestes pacientes e a necessidade de novas pesquisas que possam dar suporte a prescrição de exercícios físicos para pacientes com HS.

PALAVRAS-CHAVE: Hipotireoidismo; Exercício Físico; Capacidade Funcional.