122 - SUBMAXIMAL EXERCISE-RECOVERY CHRONOTROPIC RESPONSE OF SUBCLINICAL HYPOTHYROIDISM PATIENTS TREATED WITH LEVOTHYROXINE

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INTRODUCTION

The cardiovascular system is strongly influenced by thyroid hormone action. According to Dillman (1990), the deficiency of these hormones may change the myocardial function, reducing the activity of the enzymes involved in the regulation of calcium fluidity to myocytes and in the expression of contractible proteins.

Subclinical hypothyroidsm (SH) is defined as a condition in which the levels of (TSH) thyrothrophine are elevated , associated to normal levels of the thyroid hormones T4 (thyroxine) and T3 (triiodothyronine) and their respective free functions (KAHALY; DILLMANN, 2005). Although the term “subclinical” is used in order to elucidate that this is a disease essentially based upon changing's of biochemistry order, literature reveals, more and more, the presence of evidences and symptoms of Overt Hypothyroidism (OH) in patients with HS (RODONDI *et al.,* 2005).

Biondi *et al.* (2002) revised the effects of HS in cardiovascular system and mentioned, among others, the enlargement of the pre-ejection period and of the vascular periferic resistance and the diminution of the contraction of myocardial, of cardiac output, and the fraction of ejection in effort. Besides, Rodondi *et al*. (2006) certified in a study of metanalyses, an association between SH and the enlargement of risk of development of coronarian disease.

Considering the possibility of occurrence of changings in cardiovascular response in this group of patients, this study aims to evaluate the heart rate (HR) response in the three first minutes of exercise-recovery, before and after six months of recovering from the euthyroidism condition, through replacement with levothyroxine.

MATERIALS AND METHODS

Sample

Seventeen inactive women aged between 31 and 54 years have participated voluntarily of this study, that presented two dosages of TSH above the superior limit of normality (4,0 mUI/i), with a minimum interval of four weeks, associated to normal levels of T4 l (0,8- 1,9 ng/dL). At least one dosage was accomplished at the Laboratory of Clinical Pathology / Section of Hormones of Clementino Fraga Filho Hospital of Federal University of Rio de Janeiro (HUCFF/UFRJ). The patients were divided randomly into two groups: treatment with levothyroxine (n=9) and observation (n=8).

The following criterions of exclusion were adopted to the participation in the study: the using of drugs and substances that interferes in thyroid function, the presence of diseases, even the steady ones that may change the circulating levels of thyroid hormones and previous replacement with levothyroxine.

Protocol

Patients were led to the Laboratory of Physiology of Exercise of EEFD- UFRJ, were the evaluation of cardiopulmonary capacity took place through ergospirometry. In this case, it was used a treadmill (ECAFIX EG 700.2), and it was adopted the Modified Balke's protocol. The eletrocardiographics evidences (Medical Diagnostic Workstation (MDW) - Cardio Control 2000/ 2001) were processed in real time. The values of heart rate (HR; bpm) observed in the first, second and third minutes of exercise-recovery were considered in the analyses.

The interruption of the test occurred for the asking of the patient or because of the apparition of symptoms that could prevent its proceeding and/ or could represent risk to the patient. The line of direction of American College of Sports Medicine (ACSM, 2003) was observed to the control of limiting symptoms. Patients were evaluated in two moments: basal and after a six month intervention (replacement with levothyroxine), or observation.

Ethical Committee

This study was approved by the Ethical Committee of HUCFF/ UFRJ. All subjects gave their written consent and the protocol was approved by the local ethics committee.

Statistical Analysis

Results were expressed trough descriptive measures (mean ± standard-deviation). It was used the Mann-Whitney test to compare the mean values inter groups and to the comparison intra groups after 6 months of intervention or observation it was used the Wilcoxon test. The level of significance adopted was of 5% and the statistical treatment was accomplished in the software SPSS13.0 *for Windows*.

RESULTS

The groups showed comparable concerning the variables smoking and the menopause presence (chi-square test; p 0,05). Differences statically significant as for variables ageing, weight and Body Mass Index (BMI) were not observed.

Table 1 - Mean values (± standard-deviation) of the general characteristics of the sample

Variables	Treatment (n = 9)	Observation (n = 8)	p-value
Age (years)	43,1 ± 6,6	45,5 ± 5,6	0,47
TSH (mU/l)	8,0 ± 2,6	7,3 ± 1,9	0,67
T4L (ng/dl)	1,1 ± 0,2	1,0 ± 0,3	0,67
Weight (kg)	71,0 ± 14,5	65,3 ± 11,3	0,39
BMI (m/kg^2)	28,3 ± 5,2	25,2 ± 2,9	0,85
Menopause (yes; %)	29,4	33,3	0,49
Smoking (yes; %)	11,8	22,2	0,92

Table 2 - Mean values (± standard deviation) of heart rate (bpm) in the first, second and third minutes of exercise-recovery - Basal Evaluation - Treatment and Observation Groups

Time (minute)	Treatment (n = 9)	Observation (n = 8)	p-value
First	128,0 ± 22,9	127,9 ± 12,5	0,81
Second	114,4 ± 15,2	114,4 ± 17,6	0,50
Third	110,8 ± 13,4	109,1 ± 15,1	0,61

Concerning HR and considering the observed results in initial analyses (basal), it was observed that behavior of this variable in the three first moments of recovering considered in the study, showed similar between groups , without the evidence of significant statistically differences (Table 2). However, when the results were observed after six months of intervention or observation, it was noticed that the group that had received replacement of levothyroxine presented reduction of FC in all considered moments of recovering, especially at the first minute, while the group of observation maintained similar average values, accordingly to Table 3.

Table 3 - Mean values (± standard deviation) of heart rate (bpm) in the first, second and third minutes of exercise-recovery - Basal Evaluation and 6 months of treatment or observation - Treatment and Observation Groups

	Treatment (n = 9)			Observation (n = 8)		
	Basal	**6 months**	**p-value**	**Basal**	**6 months**	**p-value**
First	128,0 ± 22,9	117,0 ± 17,5	0,06	127,9 ± 12,5	129,0 ± 19,8	0,46
Second	114,4 ± 15,2	107,0 ± 14,4	0,14	114,4 ± 17,6	113,6 ± 21,6	0,34
Third	110,8 ± 13,4	105,7 ± 12,8	0,23	109,1 ± 15,1	110,1 ±18,7	0,50

DISCUSSION

The recovering of FC after vigorous effort is a recognized indicator as an important predictor of morbidities and mortalities, above all, those associated to cardiovascular system (Nilsson *et al.,* 2007). An inefficient recovering (slower) indicates a diminished answer of cardiovascular system and autonomous nervous system after effort especially of parasympathetic activity (kizilbash *et al*., 2006).

Literature registers that individuals with HS may present deteriorations in their cardiovascular system such as the enlargement of the pre-ejection period and of peripheric vascular resistance as well as the diminishing of contractibility of the myocardium (Biondi *et al*., 2002). However, studies have demonstrated that the treatment with replacement of levothyroxine may cause positive effects in the improvement and in the control of them and other evidences and symptoms characteristic of HS (MONZANI *et al*., 2001).

Up to this moment, there were not found studies that examined the effect of the treatment with replacement of levothyroxine in the recovering of FC after effort. Thus, our results suggest that levothyroxine, as well as in the other cardiovascular parameters investigated in the literature, seems perform, too, a positive effect in this indicator.

It is relevant to add that, although significative statistic differences may have not been found, the results observed in this work have a great clinical relevance since the individuals under treatment presented lower values of FC after 6 months of euthyroidism condition.

CONCLUSION

In the present study, the treatment with replacement of levothyroxine seems to have been favorable to improvements in the recovering of FC response after effort in patients with HS after 6 months of euthyroidism condition, with important influence in the first minutes after effort.

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SUBMAXIMAL EXERCISE-RECOVERY CHRONOTROPIC RESPONSE OF SUBCLINICAL HYPOTHYROIDISM PATIENTS TREATED WITH LEVOTHYROXINE

ABSTRACT

Subclinical hypothyroidism (SH) is defined as a condition in which the levels of (TSH) thyrothrophine are elevated , associated to normal levels of the thyroid hormones T4 (thyroxine) and T3 (triiodothyronine) and their respective free functions.

Although many studies about these patients group are done, little is known about exercise-recovery heart rate (HR). Objective: Considering the possibility of occurrence of changings in cardiovascular response in this group of patients, this study aims to evaluate the heart rate (HR) response in the three first minutes of exercise-recovery, before and after six months of recovering from the euthyroidism condition, through replacement with levothyroxine. Methods: A total of 17 patients was randomly divided into two groups: treatment (n=9; 43,1 ± 6,6 years) and observation (n=8; 45,5 ± 5,6 years). Patients were submitted to a cardiopulmonary test, performed in a treadmill, using Modified Balke´s protocol, in two moments: basal and after six months of treatment or observation. It was used the Mann-Whitney test to compare the mean values inter groups and to the comparison intra groups after 6 months of intervention or observation it was used the Wilcoxon test (p=0,05). Results: Both groups presented similar mean HR values in the first evaluation. However, when we analyzed results after six months of intervention or observation, we observed that the group that received levothyroxine presented lower values of HR in all minutes of exercise-recovery considered in the present study. The observation group maintained the same mean values of HR. Conclusion: Patients treated with levothyroxine presented a better HR exercise-recovery, especially during the first minute.

KEY-WORDS: Subclinical hypothyroidsm, Heart Rate and Levothyroxine

RéCUPéRATION DE LA FRéQUENCE CARDIAQUE APRÈS L'EXERCICE DES PATIENTES AVEC SUBCLINIQUE HYPOTHYROIDSM TRATADOS AVEC LEVOTHYROXINE

RÉSUMÉ

Le Subclinique hypothyroidism (SH) est définie comme un état où les niveaux de thyrothrophine (TSH) sont élevées et ils sont associées à des niveaux normaux de la hormones thyroïdiennes (T4-thyroxine ; T3-triiodothyronine) et aussi a leurs fonctions respectives. Bien que de nombreuses études sur ces patients sont déjà fait, on sait peu de choses sur la récupération de la fréquence cardiaque (FC) aprés le l'exercice. Objectif: Cette étude vise évaluer la response de la fréquence cardiaque dans les trois premières minutes de récupération du exercisce, avant et après six mois en lequelle les patientes sont maintenu dans le état de *Euthyroidism* estabile par le intervention avec *levothyroxine*. Méthodes: Un total de 17 patients ont été aléatoirement divisés en deux groupes: *traitement* (n=09; 43,1 ±6,6 ans) et d'*observation* (n=08; 45,5 ±5,6 ans). Les patients ont été soumis à un test cardiopulmonaire, exécutée dans un tapis roulant en utilisant le protocole de Balke modifié, en deux moments: basale et après six mois de traitement ou de l'observation. On a utilisé le test de *Mann Whitney* pour comparer les résultats entre les groupes et pur comparer le resultats intra-groupes, après 6 mois d'intervention ou d'observation, on a utilisé le test de *Wilcoxon* (P = 0,05). Résultats: Les deux groupes ont présenté des valeurs de FC moyennes similaires aux de la première évaluation. Les résultats, au bout de six mois d'intervention ou d'observation, ont montré que le groupe qui a reçu levothyroxine a présenté valeurs de FC plus baisse dans toutes les minutes de recouvrement envisagées dans la présente étude. Le groupe d'observation a maintenu les valeurs de FC similaires à la première évaluation. Conclusion: Les patients traités par levothyroxine ont présenté un meilleur recouvrement de la FC, en particulier pendant la première minute. Apré le exercice.

MOTS-CLES: Subcliniques Hypothyroidsm, Fréquence Cardiaque, Levothyroxine.

COMPORTAMIENTO DE LA FRECUENCIA CARDIACA EN LOS TRES PRIMEROS MINUTOS DE RECUPERACIóN, DE PACIENTES TRATADOS CON LA LEVOTIROXINA

RESUMEN

Subclínica hypothyroidism (SH) se define como una condición en la que los niveles de thyrothrophine (TSH) son elevados, asociado a los niveles normales de las hormonas tiroideas (T4-tiroxina; T3-triyodotironina) y sus respectivas funciones libre. Aunque muchos estudios acerca de estos pacientes se realizan, poco se sabe sobre el recuperación de la frecuencia cardiaca (FC) después de lo ejercicio. Objetivo: Este estudio tiene como objetivo evaluar el comportamiento de la FC en los tres primeros minutos de recuperación, antes y después de seis meses en que les pacientes estaban en la condición de *Euthyroidism*, con la medicación *levotiroxina*. Métodos: Un total de 17 pacientes se dividieron al azar en dos grupos: tratamiento (n=09; 43,1 ±6,6 años) y de observación (n 0; 45,5 ±5,6 años). Los pacientes fueron sometidos a una prueba de esforzó, realizado en una estera rodante, con el protocolo de *Balke* modificado, en dos momentos: basal y después de seis meses de tratamiento o de observación. Se utilizó la prueba de *Mann-Whitney* para comparar los valores medios entre los grupos. Para la comparación dentro de los grupos, después de 6 meses de la intervención u observación, se utilizó la prueba de *Wilcoxon* (p =0,05). Resultados: Ambos grupos presentaron valores similares de FC al de la primera evaluación. Sin embargo, cuando analizamos los resultados después de seis meses de la intervención u observación, se observó que el grupo que recibió levotiroxina presentan valores más bajos de FC en todos los minutos de recuperación que considerarse en el presente estudio. El grupo mantiene la observación de los valores de la media de FC después do tratamiento. Conclusión: Los pacientes tratados con *levotiroxina* presentaron una mejor recuperación de la FC, especialmente durante el primer minuto.

PALABRAS CLAVE: Subclínica Hypothyroidsm, Frecuencia Cardiaca, Levothyroxine.

RESPOSTA CRONOTRÓPICA PÓS-ESFORÇO SUBMÁXIMO EM PACIENTES COM HIPOTIROIDISMO SUBCLÍNICO TRATADOS COM REPOSIÇÃO DE LEVOTIROXINA

RESUMO

O Hipotireoidismo Subclínico (HS) é definido como uma condição onde os níveis de TSH (tireotropina) encontram-se elevados, associados aos níveis normais dos hormônios tiroidianos T4 (tiroxina) e T3 (triiodotironina) e de suas respectivas frações livres. Apesar de muitos serem os estudos acerca dos indivíduos acometidos pelo HS, pouco se sabe em relação ao comportamento da freqüência cardíaca (FC) no período pós-esforço neste grupo de pacientes. Objetivo: Analisar o comportamento da FC nos primeiros três minutos da recuperação pós-esforço em pacientes com HS, antes e após um período de seis meses de eutireoidismo estável pela reposição hormonal (levotiroxina) em pacientes com HS. Métodos: Foram avaliadas 17 pacientes, divididas randomicamente em dois grupos: tratamento (n=09; 43,1 ± 6,6 anos) e observação (n=08; 45,5 ± 5,6 anos). As pacientes foram submetidas a duas avaliações ergoespirométricas, em esteira, com o protocolo de Balke modificado, realizadas no período pré-tratamento e após 6 meses de restauração do eutireoidismo ou de observação. Para a comparação das médias, utilizou-se o teste Wilcoxon (intra grupos) e Mann-Whitney (inter grupos) (SPSS 13.0 *for Windows*), adotando como significativo o valor de p = 0,05. Resultados: Os dois grupos apresentaram comportamento similar no estágio basal. Entretanto, ao analisarmos os resultados após 6 meses de intervenção ou observação, foi observado que o grupo que recebeu reposição (levotiroxina) apresentou redução da FC em todos os momentos da recuperação considerados, enquanto que o grupo de observação manteve valores médios semelhantes. Conclusão: Pôde-se verificar um melhor comportamento da recuperação da FC do grupo tratamento, sendo esta mais evidente no 1º minuto após o esforço.

PALAVRAS-CHAVES: Hipotireoidismo Subclínico, Frequência Cardíaca, Levotiroxina.