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Heart rate recovery to sub maximal exercise in patients with subclinical hypothyroidism – an observational study

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Abstract

Introduction: Exercise intolerance is typical characteristic of the subclinical hypothyroidism.
Purpose: Evaluation of heart rate responses to sub maximal exercise in subclinical hypothyroidism.
Materials and Method: Twenty three subclinical hypothyroids and thirty age, sex and BMI matched euthyroid controls were selected. Sub maximal exercise was performed using Bruce protocol using 75% target heart rate in treadmill. Heart rate recovery to sub maximal exercise was done using ECG lead II.
Results: Compared to Euthyroid controls, Subclinical Hypothyroidism (SCH) show a significant increase in warm up period heart rate. (p=0.05). There is a significant increase in the heart rate during recovery period at both 1st and 2nd minute in SCH when compared to controls. (p=0.03, 0.01), negative correlation exist between TSH level and 1st minute heart rate recovery.
Conclusion: We conclude that subjects with Subclinical hypothyroidism, shows a delayed heart rate recovery in response to a sub maximal exercise.

Keywords: Parasympathetic tones, Basal metabolic rate, Physical Exertion, Exercise tolerance, Hypothyroidism

Introduction

Subclinical hypothyroidism (SCH) is the term used to describe patients with normal free thyroxin (T_4) and free triiodothyronin (T_3) and thyroid stimulating hormone (TSH) levels of more than 5 mIU/L, with generally no obvious symptoms of hypothyroidism.[(1)] Thyroid hormones are mandatory for various processes that are essential for human metabolism. The cardiovascular system is one of the most important targets of thyroid hormones and is very sensitive to a minimal decrease of circulating thyroid hormones.[(2)] There may be alterations in both myocardial function and changes in lipoprotein profile which results in increased risk of atherosclerosis, coronary heart disease, and myocardial infarction.[(3)] In asymptomatic patients, cardiac structure and function may remain normal at rest, but moderate to severe exercise may bring out hidden abnormalities.[(4)] These include reduced exercise stroke volume, reduced left ventricular ejection fraction, mild prolongation of pre ejection period, impaired exercise tolerance, lower maximum power output and maximal Oxygen consumption (VO_2), and higher heart rates with increasing workload.[(5,6)] SCH may impair left ventricular diastolic function, alter endothelial function, increase the C-reactive protein level, and thus increase the risk of atherosclerosis.SCH does result in a small increase in low-density lipoprotein, cholesterol and a decrease in high-density lipoprotein, changes that enhance the risk for development of atherosclerosis and coronary artery disease.[(7,8)]

Flow-mediated vasodilatation, a marker of endothelial function, is significantly impaired in SCH, and decreased heart rate variability, a marker of autonomic activity, suggests hypo functional abnormalities in the parasympathetic nervous system.[(9)] Heart rate recovery (HRR) which is one of the indicators of cardiovascular fitness is mainly thought to be due to parasympathetic reactivation and has been shown to be a remarkable complement to a medical assessment of an individual. Recovery of the heart rate immediately after exercise is mediated by vagal reactivation,[(10)] with slow heart rate recovery (HRR) being a predictor of all cause mortality and sudden death.[(11)] HRR ≤12 beats per minute (bpm) at 1st minute for upright position, ≤18 bpm at 1st minute for supine position and ≤ 22 bpm at 2 minutes for sitting position are considered abnormal.[(12)]

Lower exercise tolerance is an outstanding SCH characteristic. During maximal and submaximal exercises, patients with SCH showed lower efficiency of cardiopulmonary response to effort.[(13,14,15)] Results are conflicting during recovery.[(16)]

Studies have shown that HR and SBP during exercise and recovery in asymptomatic subclinical hypothyroid patients may differ from euthyroid controls.[(17,18)] Data on the relation between subclinical thyroid disease (SCTD) and heart rate during exercise are limited& as of our knowledge there is no work done to assess the correlation between TSH levels and HRR in hypothyroid patients.

Materials and Method

The above study conducted in the department of physiology after obtaining the ethical clearance from the institutional ethical committee. 23Subjects who are

diagnosed as subclinical hypothyroid with TSH more than 5.5 mIU/L with normal free T_3 and T_4 in the age group of 30-50 years of both the genders attending the medicine O.P.D selected as subjects randomly. Sample size was calculated with the help of formula based on incidence in population with the previous references.[19]

$n= 2(Z_a+Z_{1-\beta})^2 \sigma^2/\Delta^2$

With $p<0.05$ as acceptable and a study with 80% power; following values were: $Z\alpha$, is 1.96. $Z1-\beta$ is 0.8416. The standard deviation would be approximately $1.2(\sigma)$ calculated from the previous studies. The value of Δ is 1.0

$n=2(1.96+0.8416)^2(1.2)^2/ (1.0)^2$

n= 23

The subjects explained regarding the procedure and written informed consent taken.30 age and sex matched controls with normal T_3, T_4, and TSH, selected from general population served as controls. (n=30)

Exclusion criteria: Subjects with overt hypothyroidism, hypertension, ischemic or valvular heart disease, arrhythmia, previous vascular surgery, heart failure, respiratory disease, pulmonary hypertension, hepatic or renal dysfunction, diabetes mellitus, significant neurological or psychological disease and smokers were excluded.

Study protocol: Exercise testing

Patients were instructed not to have coffee, tea or cola 12 hours before the tests. They were asked to come to the physiology laboratory at 9.0am after having a light breakfast. Detailed history took on standard proforma about age& clinical features. Reports of investigation (T_3, T_4, and TSH) collected.

Exercise protocol: participants asked to relax for 10 minutes. At the end of 10 minutes basal HR recorded by ECG instrument in lead II. Instrument – ECG instrument with paper speed of 25mm/sec was used for above test. (BPL, Cardiart 6208 View. BPL Limited, Bannerghatta Road, Bangalore). Instrument: TREADMILL (SCHILLER, at-10 Plus, 12 Channel ECG Unit).

All the subject underwent exercise treadmill test according to Bruce protocol. A warm up period for 1 min included. Predicted peak heart rate calculated as (220-age in years). Target heart rate 70% of Predicted peak heart rate. The protocol included a graded exercise pattern on a treadmill which started at a speed of 2.7 km/hr with 10% grade, increased after 3 min to second stage at 4.0 km/hr with 12% grade. This level is comparable to moderate submaximal exercise. HR recorded at each grade till stoppage of exercise using treadmill. Participants were, instructed to stop exercise if they achieve their target heart rate. They were also instructed to stop exercise if they experience any symptoms related to angina, light headedness, confusion, and fatigue or if there were signs of cyanosis, change in heart rhythm or failure of testing equipment. During post exercise recovery phase, HR recorded for each min for a period of 2 minute. Heart rate recovery (HRR) was taken as the difference between maximum HR and the HR at specified time period after recovery.

HRR 1st Minute = maximum Heart Rate – Heart rate at 1st minute of recovery period.

HRR 2nd Minute= maximum Heart Rate – Heart rate at 2nd minute of recovery period.

Statistical analysis: HRR response to submaximal exercise between hypothyroidism and euthyroid done by using unpaired T test. Intergroup analysis was done by using paired T test using SPSS software version 20.

Results

This is a cross-sectional study done on 23 subclinical hypothyroid patients (n=23) and 30 healthy euthyroid controls (n=30). Table 1 shows the demographical characteristics of the SCH and controls. The mean age group of SCH and controls were 34.78±5.23 and 36.16±7.92 years & BMI were 23.56±3.1and 21.22±2.14kg/mt^2 respectively.

Table 2 shows the heart rate responses to exercise between controls and SCH. There is no significant difference in basal heart rate between SCH and controls. But there is a significant increase in warm up period heart rate in SCH when compared to controls. (p=0.05). There is no difference in heart rate during Ist stage, IInd stage of exercise between SCH and controls. There is a significant increase in the heart rate during recovery period at both 1st and 2nd minute in SCH when compared to controls. (p=0.03, 0.01) Graph 1 demonstrates the heart rate responses to exercise between SCH and controls. Table 3 shows that HRR 1st minute and HRR 2nd minute is significantly lower in SCH when compared to controls. (p=0.03, 0.04). Graph 2 demonstrates the correlation between TSH levels and HRR in SCH & controls.

Table 1: Demographical characteristics of the Euthyroid and subclinical hypothyroid. (SCH)

	Euthyroid (n=30)	SCH (n=23)	T value	P value
Mean age (Years)	36.16±7.92	34.78±5.23	0.988	0.12
Gender Male Female	 12 (40%) 18 (60%)	 10(43%) 13(57%)		
BMI (Kg/mt^2)	21.22±2.14	23.56±3.12	-1.041	0.30

BMI: Body Mass Index, values are expressed as Mean±SD.

Table 2: Cardiovascular response to exercise between euthyroid and subclinical hypothyroid. (SCH)

Parameter	Euthyroid (n=30)	SCH (n=23)	T value	P value
Basal heart rate	80.67±3.84	78.75±2.10	1.730	0.089
Warm up (1 min)	90.34±5.23	93.22±7.23	-1.274	0.05*
Exercise				
1. Ist stage	111.76±7.89	110.87±8.90	0.245	0.34
2. IInd stage	132.52±7.70	134.21±9.08	-0.165	0.87
Recovery				
1. Ist miute	98.90±6.56	113.65±4.53	-2.188	0.03*
2. 2nd minute	82.44±4.22	94.76±7.66	-3.575	0.01*

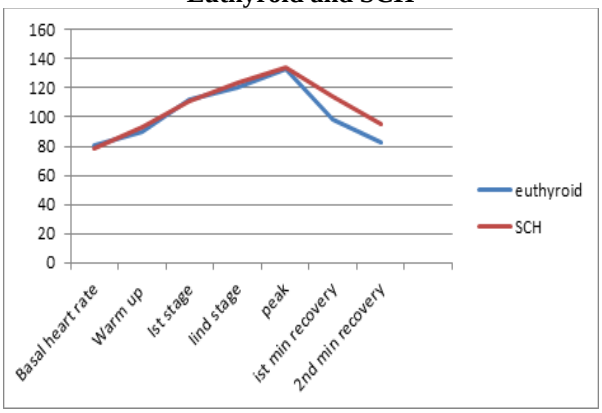
Values are expressed as Mean±SD, p<0.05 considered significant *

Table 3: HRR in Euthyroid Vs subclinical hypothyroid. (SCH)

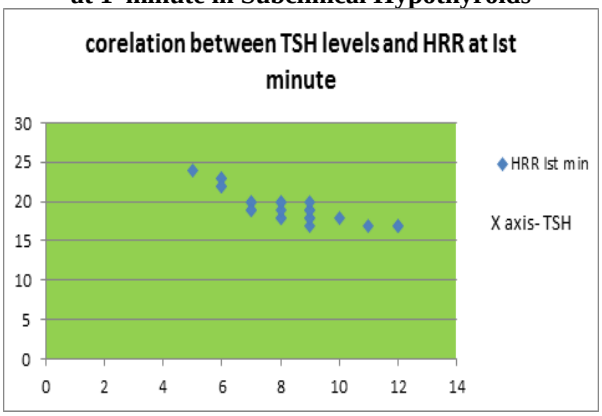
	Euthyroid (n=30)	SCH (n=23)	T value	p value
HRR at 1st minute	33.62±3.23	20.21±2.89	2.363	0.03*
HRR at 2nd minute	50.08±6.90	40.45±4.87	1.876	0.04*

Values are expressed as Mean±SD, p< 0.05 considered significant.

Graph 1: Heart rate responses to exercise in Euthyroid and SCH



Graph 2: correlation between TSH levels and HRR at 1st minute in Subclinical Hypothyroids



Discussion

This study provided a comprehensive comparison of exercise and recovery pattern between subclinical hypothyroid patients and euthyroid controls. In this study, for both groups the HR increased during exercise and remained so, even after 2 min of recovery. Also, in comparison to controls, SCH patients had a higher HR at warm up exercise, while no difference was observed in 1st stage and IInd stage of exercise. The increased heart rate in the first minute of exercise has previously been suggested as a novel autonomic marker that helps in accurate diagnosis of high risk CAD patients.[20] In another study by Akcakoyun et al, there was no significant change in HR at rest or during exercise between groups, whereas HRR was significantly lower during exercise testing in subclinical hypothyroid patients compared to control and chronotropic incompetence was found in patients.[17] results were similar to our study, where we found no significant difference in basal HR, and also during exercise but decreased HRR in SCH. Similarly, Mainenti *et al*., reported the lower values of HR for patients at the end of test.[16] Sunita et al showed SCH and euthyroid had normal HR and BP at rest, heart rate and BP increased with exercise and remained high even after 5 min of recovery from exercise. HR was higher in SCH at 1 min of exercise & no significant changes in HRR.[18] Our study demonstrated a significant reduction in HRR in SCH when compared to euthyroids. It has been suggested that a delayed decrease in HR during 1 and 2 min recovery of graded exercise, may be a reflection of decreased vagal activity and is a powerful predictor of overall mortality.[21]

Conclusion

We conclude that subjects with subclinical hypothyroidism will show a delayed heart rate recovery to sub maximal exercise.

References

1. Cooper DS, "Subclinical hypothyroidism" N Engl J Med 2001;345:260–265.

2. Klein I, Ojamaa K, "Thyroid hormone and the cardiovascular system" N Eng J Med 2001;344:501-509.
3. Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC, "Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: The Rotterdam study" Ann Intern Med 2000;132:270–278.
4. Kahaly GJ, "Cardiovascular and atherogenic aspects of subclinical hypothyroidism." Thyroid 2000;10:665-679.
5. Mishra TK, Routray SN, Das S, Behera M," Left ventricular dysfunction in patients with subclinical hypothyroidism and its reversibility after hormone therapy." J Assoc Physicians India 2005;53:943–946.
6. Caraccio N, Natali A, Sironi A, Baldi S, Frascerra S, Dardano A, et al. "Muscle metabolism and exercise tolerance in subclinical hypothyroidism: A controlled trial of levothyroxine." J Clin Endocrinol Metab 2005;90:4057–4062.
7. Rodondi N, den Elzen WP, Bauer DC, Cappola AR, Razvi S, Walsh JP, et al. "Subclinical hypothyroidism and the risk of coronary heart disease and mortality". JAMA 2010;304:1365-1374.
8. Biondi B, Cooper DS," The clinical significance of subclinical thyroid dysfunction." Endocr Rev 2008;29:76-131.
9. Galetta F, Franzoni F, Fallani P, Rossy M, Carpi A, Rubello D, et al. "Heart rate variability and QT dispersion in patients with subclinical hypothyroidism." Biomed Pharmacother 2006;60:425-430.
10. Imai K, Sato H, Hori M, Kusuoka H, Ozaki H, Yokoyama H et al. "Vagally mediated heart rate recovery after exercise is accelerated in athletes but blunted in patients with chronic heart failure." J Am Coll Cardiol 1994;24:1529–1535.
11. Jouven X, Empana J-P, Schwartz PJ, Desnos M, Courbon D, Ducimetière P. "Heart-rate profile during exercise as a predictor of sudden death". N Engl J Med 2005;352:1951–1958.
12. Dimopoulos S, Manetos C, Panagopoulou N, Karatzanos L Nanas," The prognostic role of heart rate recovery in health and disease." Austin journal of cardiovascular disease and atherosclerosis 2015;2:1-10.
13. Caraccio N, Natali A, Sironi A, Baldi , Frascerra S, Dardano A ,et al." Muscle metabolism and exercise tolerance in subclinical hypothyroidism: a controlled trial of levothyroxine". J Clin Endocrinol Metab 2005;90:4057–4062.
14. Mainenti MR, Teixeira PF, Oliveira FP, Vaisman M, "Effect of hormone replacement on exercise cardiopulmonary reserve and recovery performance in subclinical hypothyroidism." Braz J Med Biol Res 2010;43:1095–1101.
15. Xiang GD, Pu J, Sun H, Zhao L, Yue L, Hou J." Regular aerobic exercise training improves endothelium-dependent arterial dilation in patients with subclinical hypothyroidism." Eur J Endocrinol 2009;161:755–761
16. Mainenti MR, Teixeira FS, Oliveira FP, Vaiman M, "Impact of subclinical hypothyroidism in cardiopulmonary response during effort and its recovery." Arq Bras Endocrinol Metab 2007;51:1485–1492.
17. Akcakoyun M, Emiroglu Y, Pala S, Kargin R, Guler GB, Esen O, et al. "Heart rate recovery and chronotropic incompetence in patients with subclinical hypothyroidism." Pacing Clin Electrophysiol. 2010;33:2-5.
18. Sunita, Aarti Sood Mahajan, AK Jain, NP Singh, TK Mishra, " Heart rate and blood pressure response to exercise and recovery in subclinical hypothyroid patients." Int J Appl Basic Med Res 2013;3:106–110.
19. Prashant K, Supriya B, "Sample size calculation." Int J Ayurveda Res 2010;1:55-57.
20. Fletcher GF, Froelicher VF, Hartley LH, Haskell WL, Pollock ML," Exercise standards. A statement for health professionals from American Heart Association." Circulation 1990;82:2286–2322.
21. Falcone C, Buzzi MP, Klersy C, Schwartz PJ, "Rapid heart rate increase at onset of exercise predicts adverse cardiac events in patients with coronary artery disease." Circulation 2005;112:1959–1964.