Article

Relationship of Thyroid Hormones with Heart Rate Variability

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Abstract

Background: Altered thyroid functions are associated with variation in autonomic regulation of cardiovascular activity. Cardiac Autonomic Nervous Activity (CANA) can be assessed quantitatively by analysis of Heart Rate Variability (HRV). **Objective:** To observe the relationship between CANA with altered TSH and FT_4. **Methods:** This cross sectional study was carried out in the Department of Physiology, BSMMU, Dhaka between1st July 2007 and 30th June 2008 on 60 patients with excess thyroid hormone (group B, aged 30-50 years). Based on treatment, 30 untreated newly diagnosed patients were designated as group B_1 and 30 patients under treatment with antithyroid drugs for at least 2 months were included into group B_2 in order to observe the effect of treatment. All these patients were selected from the Out Patient Department of Endocrinology wing of Department of Medicine, BSMMU, Dhaka. Sociodemographically matched 20 apparently healthy euthyroid persons were selected for comparison (group A). To confirm thyroid status, serum TSH and serum FT_4 levels were measured by AxSym system and some of the spectral HRV parameters i.e.mean R-R interval, mean heart rate, variance, LF n.u, HF n.u and LF/HF ratio were assessed by recordings of ECG for 5 minute (short term) with a polyrite. For statistical analysis Pearson's correlation coefficient (r) test was used. **Results:** With serum TSH level, the LF n.u. power and LF/HF ratio showed significant ($p<0.05$) positive correlations but HF n.u. power showed significant ($p<0.05$) negative correlation in group B_1. But these three parameters showed non significant correlations with TSH in the other two groups (A, B_2). Similarly with serum TSH level, variance and mean R-R interval showed negative and mean HR showed positive correlation in group B_1. In group A, all these parameters were positively correlated whereas in groupB_2, RR interval and variance were positively and mean HR was negatively correlated. All these correlations were statistically non significant. With serum FT_4 levels, mean R-R and HF n.u. were negatively and mean heart rate, LFnu, LF/HF were positively correlated in all three groups but variance showed positive in group A and negative correlation in B_1 and B_2. All these correlations were statistically non significant. **Conclusion:** From this study it can be concluded that changes in autonomic nervous regulation are related to altered serum level of TSH and FT_4 in hyperthyroids.

Key words: HRV, LF, HF, RR interval, Hyperthyroid

J Bangladesh Soc Physiol. 2010 June; 5(1): 20-26
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http://www.banglajol.info/index.php/JBSP

Introduction:

Deviation of normal thyroid hormonal status has influence on cardio-vascular system. Changes of serum thyroid hormone levels are related to alteration in CANA. [1,2]

Hyperthyroidism demonstrated lower turnover rate of catecholamines.[3,4] Beta-receptor blockers increase sympathetic activity in hyperthyroid patients.[2,5-8] In hyperthyroidism there is alteration of catecholamine binding

receptors or change in affinity or mechanism of action. [8-11]

The vagal effect on heart rate is reduced in hyperthyroids. [12-15] Moreover there is sympathovagal imbalance in hyperthyroidism. [16] It has also been shown that excess thyroid hormone decreases peripheral resistance, enhances heart rate, contractility and cardiac output. [6,17-20] The thyroid hormone has direct effect on exaggeration of sinus nodal rhythmicity. [21,22] Moreover, it also reduces the excitability of cardiac parasympathetic nerves in CNS.

Power spectral analysis of HRV demonstrates the CANA, which is highly accepted for detection of sympatho-vagal imbalance. [23] Many researchers have observed that sympatho-adrenal axis is changed in hyperthyroid patients. Again, others reported exaggerated sympathetic efferent outflow in hyperthyroids. [8,16,25,26]

On the other hand researchers also reported that hyperthyroidism determines the degree of reduction of vagal efferent. Therefore, heart rate is mediated by relative hypersympathetic tone. [14] At the same time, observation of hyperactivity of SA node was reported in hyperthyroid patients. [14,21]

A variation in the heart rate, that is higher rate in hyperthyroids was reported by some researchers.[12] Again, some investigators had observed lower heart rate in hyperthyroids after treatment. It has also been reported that lower R-R interval in untreated hyperthyroid patients indicates reduced parasympathetic regulation.[13, 14,21,27,28]

Lower values in time domain measures of HRV of untreated hyperthyroids was observed by many researchers.[16,24,29] Some studies reported lower value of variance in untreated hyperthyroids[8,14,16,30] and some observed higher value of this parameter in treated hyperthyroid patients.

Some investigators had observed lower LF and HF power in untreated hyperthyroids than those of healthy control. [14,31]

LF n.u. and HF n.u. were higher in untreated hyperthyroid patients in comparison to healthy control group.[14] Similarly, higher LF/HF ratios in untreated hyperthyroids compared to euthyroids and treated hyperthyroid were reported by many researchers[8,14,16,29.]

Hyperthyroidism is one of the common endocrine disorder in Bangladesh. Different cardiovascular and metabolic disorders may be associated with this excess thyroid hormone status. Now a day, it is quite possible to prevent the development of different systemic complications and return the life expectancy to normal. But no such study yet was under taken to observe the relationship of HRV measures with the thyroid hormones in hyperthyroidism.

Therefore, this study was carried out to assess the CANA in hyperthyroid patients in order to find out the correlation of HRV parameters with thyroid hormones. It is expected that the outcome of this study may be useful in searching the relations of these hormones with CANA, so that early treatment can be helpful for the patients.

Methods

This cross sectional study was carried out in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University from 1st July 2007 to 30th June 2008. to observe the relationship between CANA and excess thyroidal activity in hyperthyroid patients. For this, 60 hyperthyroid patients (group B) with age ranged from 30-50 years were selected. On the basis of treatment, they were divided into group B_1 consisting of untreated patients on their 1st day of diagnosis and group B_2 consisting of patients treated for at least 2 months. For comparison, 20 age and sex matched apparently healthy euthyroid subjects (group A) were also studied. The study group was selected from the Out Patient Department of Endocrinology, BSMMU, Dhaka. Subjects with history of any heart diseases, hypertension, diabetes mellitus, renal diseases, psychiatric disorders, hyperthyroidism due to

exogenous L-thyroxine, pregnancy and smoking were excluded from the study. After selection, the subject was informed about the aims, objectives and detail procedure of the study before examination and collection of blood sample. He or she was encouraged for voluntary participation and was allowed freedom to withdraw from the study whenever he or she liked, even after participation. If he or she agreed to enroll to the study, informed written consent was taken from him / her. Then the subject was prepared for the study by giving advice to have their meal by 9:00 pm, free from any physical or mental stress, not to take sedatives or any drugs affecting central nervous system and had a good sleep at night before the day of examination. He or she was advised to avoid tea or coffee at breakfast and was asked to attend the Department of Physiology of Bangabandhu Sheikh Mujib Medical University between 9:00 a.m. to 11:00 a.m. on the day of examination. Then the subject was taken to Autonomic Nerve Function Test Laboratory and detail history was taken. Then his / her thorough physical examinations were done and all informations were recorded in a prefixed questionnaire. Then he or she was kept under complete bed rest in supine position for 15-20 minutes in a cool and calm environment. During this period the subject was advised not to talk, eat or drink and also not to perform any physical or mental activity, even sleep. Then all preparations for recording of the Heart Rate Variability parameters were made by connecting the channels of ECG and Pulse to a polygraph for 5 minutes (short term). After recording of HRV parameters, 5 ml of venous blood was drawn from the subject. Serum TSH and serum FT_4 levels were measured by AxSYM system [25]. Heart Rate Variability parameters in both time domain and frequency domain method (in short term) were collected from Polygraphic recording.Mean RR interval,Mean HR,Variancea for time domain and LF nu,HF nu,LF/HF for frequency domain were measured For statistical analysis Pearson's correlation coefficient (r) test was done.

Results

Anthropometric details of all the groups are presented in Table I. Groups were matched for age, sex and height. The median body weight and BMI were significantly ($p<0.001$) lower in group B_1 compared to those of group A and B_2. But no significant differences of these values were observed between group A and B_2.

The median value of TSH was significantly lower ($p<0.001$) and FT_4 was higher ($p<0.001$) in group B_1 and B_2 than those of A. Again though FT_4 was significantly ($p<0.001$) lower in group B_2 than that of B_1 but TSH levels were almost similar in both the groups. (Table II).

With serum TSH level, all the parameters of HRV showed positive but nonsignificant except LF n.u. and LF/HF ratio, which showed negative correlation in group A. Again LF n.u. and LF/HF ratio showed positive and significant ($p<0.05$) whereas HF n.u showed negative but significant ($p<0.05$) correlation with serum TSH in group B_1. Once more mean R-R interval and variance established nonsignificant and negative but mean heart rate showed positive correlation with the same parameter in the same group. Moreover in group B_2 all the HRV parameters showed positive but nonsignificant except mean heart rate and HF n.u, which were negatively correlated with serum TSH (Table III).

Once more all the parameters of HRV showed positive but nonsignificant correlation in all the groups except mean heart rate and HF n.u. in group A, mean R-R interval , variance and HF n.u in group B_1 and mean R-R interval and HF n.u in group B_2 , which showed negative correlation, with serum FT_4 level (Table IV).

Table I : Anthropometric measures in different groups (n=80)

Groups	Age(years)	Sex	Height(cm)	Weight(kg)	BMI(kg/m^2)
A(n=20)	38.5[a]39.15[b]	M= 8F= 12	160[a]160[b]	53.5[a]54.1[b]	20.87[a]21.00[b]
B_1(n=30)	35.5[a]38.87[b]	M=10F= 20	157[a]160[b]	43[a]46.05[b]	17.77[a]17.83[b]
B_2(n=30)	41[a]40.8[b]	M=14F=16	159[a]161[b]	49.5[a]52.77[b]	20.02[a]20.13[b]
Statistical analysis					
Groups			P value		
A vs B_1	0.882 [ns]	M=0.637 [ns]F= 0.106 [ns]	0.904 [ns]	0.000***	0.000***
A vs B_2	0.366 [ns]	M=0.201 [ns]F= 0.336 [ns]	0.448 [ns]	0.475 [ns]	0.212 [ns]
B_1 vs B_2	0.251 [ns]	M=0.414 [ns]F= 0.505 [ns]	0.478 [ns]	0.000***	0.000***

Data were expressed as [a]median and [b]mean. For statistical analysis, ***= p<0.001, ns= p>0.05.

Table II: Serum TSH and FT_4 level in different groups (n=80)

Groups	TSH(mIU/L)	FT_4(pmol/L)
A(n=20)	3.11[a]2.79[b]	10.25[a]10.81[b]
B_1(n=30)	0.01[a]0.023[b]	51.03[a]51.35[b]
B_2(n=30)	0.01[a]0.022[b]	25.06[a]30.39[b]
Statistical analysis		
Groups	P value	
A vs B_1	0.000***	0.000***
A vs B_2	0.000***	0.000***
B_1 vs B_2	0.627 [ns]	0.000***

Data were expressed as [a]median and [b]mean. For statistical analysis, ***= p<0.001, ns= p>0.05.

Table III: Correlation of heart rate variability parameters with serum TSH level in different groups (n = 80).

Parameters	Groups					
	A		B_1		B_2	
	r	p	r	p	r	p
Mean R-R interval	+ 0.000[ns]	1.000	- 0.299 [ns]	0.108	+ 0.163 [ns]	0.388
Mean Heart rate	+ 0.022 [ns]	0.926	+ 0.249 [ns]	0.184	- 0.185 [ns]	0.329
Variance	+ 0.219 [ns]	0.353	- 0.028 [ns]	0.882	+ 0.156 [ns]	0.410
LF n.u.	- 0.209 [ns]	0.377	+ 0.363 *	0.049	+ 0.081 [ns]	0.670
HF n.u.	+ 0.205 [ns]	0.386	- 0.381 *	0.038	- 0.059 [ns]	0.757
LF/HF	- 0.204 [ns]	0.388	+ 0.433 *	0.017	+ 0.018 [ns]	0.926

Statistical analyses were done by Pearson's correlation coefficient (r) test.
* = p<0.05, ns = not significant, n = number of subjects.

Table IV: Correlation of heart rate variability parameters with serum FT_4 level in different groups (n = 80).

Parameters	Groups					
	A		B_1		B_2	
	r	p	r	p	r	p
Mean R-R interval	- 0.124 ns	0.604	- 0.052 ns	0.785	- 0.126 ns	0.509
Mean Heart rate	+ 0.152 ns	0.524	+ 0.039 ns	0.836	+ 0.157 ns	0.406
Variance	+ 0.048 ns	0.841	- 0.079 ns	0.677	- 0.308 ns	0.098
LF n.u.	+ 0.187 ns	0.430	+ 0.019 ns	0.921	+ 0.225 ns	0.232
HF n.u.	- 0.188 ns	0.428	- 0.026 ns	0.889	- 0.283 ns	0.130
LF/HF	+ 0.150 ns	0.528	+ 0.137 ns	0.470	+ 0.226 ns	0.230

Statistical analyses were done by Pearson's correlation coefficient (r) test.
ns = not significant, n = number of subjects.

Discussion

The present cross sectional study was undertaken to observe the relationship between both time domain and frequency domain measures of HRV like mean R-R interval, mean heart rate, variance, LF n.u. power, HF n.u. power and LF/HF ratio and excess thyroid hormone and lower level of TSH and very high FT_4 levels in patients with hyperthyroidism. More over, all these correlations were also observed in healthy age and sex matched adults.

It has been suggested that along with the CNS manifestations, excess thyroid hormones usually affect every single cell of human body and results in exaggerated manifestations of hyperadrenergic state and all of them have impact on heart rate. Thyroid hormones cause increased sinoatrial nodal activity. [17] In addition, these hormones potentate the metabolic activity, oxygen consumption in peripheral tissue and b receptors activities.[20]

In this study, sympathetic hyperactivity might be the cause of HRV dysfunction in the hyperthyroid patients of the present series which is further supported by the positive relationships of LF n.u. power with serum FT_4 level. Again contribution of decreased modulation of parasympathetic activity is likely to occur in both the groups of hyperthyroid patients of the present study . The negative correlations of some parameters with serum FT_4 level are also in favor of this statement. At the same time, the sympathovagal balance is shifted towards sympathetic dominance in hyperthyroid patients of the present series, which is supported by the positive correlation of LF/HF ratio with serum FT_4 level. All these findings are less pronounced in treated hyperthyroids than that of untreated hyperthyroids. So, it may be plainspoken that treatment improves the conditions.

However, the exact mechanisms involved for the impairment of cardiac autonomic nervous activity in hyperthyroids of the present series can not be elucidated from this type of study. Assessment of serum or urinary catecholamines levels may be helpful to establish the involvement of neuroeffector mechanisms both centrally and peripherally in the hyperthyroid patients of the present series.

Conclusion

Heart rate variabilties are closely related with the hormones related to thyroid function in hyperthyroid state of patients and following treatment may return the patients' condition towards almost normal.

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