Article

Heart Rate Variability in Hyperthyroidism

Kabir R[1], Begum N[2], Ferdousi S[3], Begum S[4], Ali T[5]

Abstract

Background: Hyperthyroidism is associated with altered cardiac autonomic nervous activity (CANA). Heart Rate Variability (HRV) analysis is a promising technique to quantify CANA and therefore can be done in hyperthyroidism. **Objective:** To observe the HRV parameters in patients with hyperthyroidism to find out the influence of excess thyroid hormone on cardiac autonomic nervous activities. **Method:** The cross sectional study was carried out on 60 hyperthyroid patients (groupB)aged 30-50 years in the Department of Physiology, BSMMU, Dhaka from 1st July 2007 to 30th June 2008. Age and sex matched 20 apparently healthy euthyroids were also studied for comparison (group A). On the basis of treatment, they were further divided into group B_1 consisting of 30 untreated newly diagnosed patients and group B_2 consisting of 30 hyperthyroid patients treated with antithyroid drugs for at least 2 months. The patients were selected from the Out Patient Department of Endocrinology, BSMMU, Dhaka. To assess thyroid status, serum TSH and serum FT_4 levels were measured by AxSym system and time domain measures of HRV such as mean R-R interval, mean heart rate, SDNN and RMSSD were assessed from 5minute(short term) ECG recording by a polygraph. For statistical analysis Mann-Whitney U test was done. **Results:** Mean R-R interval was significantly ($P<0.001$) lower but mean heart rate was significantly ($P<0.001$) higher in untreated patients than those of treated and euthyroids subjects. These values were found almost similar when compared between euthyroids and treated hyperthyroids. Similarly SDNN and RMSSD were significantly lower in untreated hyperthyroids than both euthyroids ($P<0.001$) and treated hyperthyroids ($P<0.01$). **Conclusion:** This study concluded that decreased vagal modulation on heart rate may occur in hyperthyroidism, which may be restored following adequate treatment of the disease.

Keywords: HRV, R-R Interval, Heart rate, RMSSD, Hyperthyrodism

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For author affiliations, see end of text.

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Introduction

Deviation from normal thyroid status has profound influence on all body systems including cardiovascular system. Changes in serum thyroid hormone levels are usually associated with alteration in autonomic regulation of cardiovascular activity.[1,2]

It has been reported that the parasympathetic regulatory effect on heart rate is reduced in hyperthyroid patients.[3-6] Moreover, parasympathetic blocker reduces vagal activity that determines autonomic imbalance in hyperthyroidism.[7]

Several investigators reported higher sympathetic tone with impaired parasympathetic modulation and consequent tachycardia in hyperthyroid patients.[3, 8-15]

Clinical features of hyperthyroidism are similar to that of excess catecholamines but studies demonstrated lower turnover rate of catecholamines.[16,17] Some investigators reported increased sympathetic activity in hyperthyroid patients with beta-receptor blocking drugs.[2,8,18-20] There may be alteration of catecholamine binding and affinity for receptors in presence of thyroid hormone excess.[20-24]

The thyroid hormone has direct effect on exaggeration of sinus nodal rhytmicity.[10,25] Moreover, it also reduces the excitability of cardiac parasympathetic nerves in CNS. Though cardiac autonomic impairment results in excess mortality, only a few studies have assessed the autonomic nerve function status in hyperthyroidism.[26]

Several researchers have explored the cardiac autonomic nervous activity in hyperthyroid patients. It has been reported that sympatho-adrenal axis is changed in these groups of patients. Again, some researchers reported exaggerated sympathetic efferent outflow in hyperthyroids.[7,20,27,28]

Heart rate variability is the result of cardiac autonomic nervous modulation on intrinsic cardiac automaticity. HRV analysis is used to detect the magnitude of the individual components of the autonomic control of the heart. Analysis of the R-R interval variation is used to assess the cardiac parasympathetic activity in healthy adults.[29]

Lower R-R interval variability and higher heart rate in untreated hyperthyroid patients but lower heart rate in hyperthyroids after treatment has been reported by many researchers [3,5,28,30] Researchers investigating HRV in hyperthyroids found lower SDNN and RMSSD in untreated hyperthyroids.[7,26,31]

Hyperthyroidism is one of the common endocrine disorders in Bangladesh. Different cardiovascular and metabolic disorders may be associated with hyperthyroidism. Though most of them remain unnoticed, it is possible to prevent the development of such complications. Several studies on cardiac autonomic nerve dysfunction in diabetes mellitus[32], renal failure[33], aging[34], obesity[35] and post-menopausal women[36] were conducted by conventional method but no such data on hyperthyroidism by analysis of HRV is yet available in our country.

Therefore, this study was carried out to assess the autonomic nerve function status in hyperthyroid patients. It is expected that the outcome of this study may be useful in screening of autonomic nerve function disorder in hyperthyroidism so that early treatment can be done to minimize risk of its complications.

Methods

This cross sectional study was carried out to observe the HRV by time domain method in 60 hyperthyroid patients with age ranged from 30-50 years in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University from 1st July 2007 to 30th June 2008. Hyperthyroid patients were divided into B_1,untreated patients on their 1st day of diagnosis and B_2, 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. All the subjects were free from heart diseases, hypertension, diabetes mellitus, renal diseases, psychiatric disorders, hyperthyroidism due to exogenous L-thyroxine, pregnancy and smoking.

After selection, the subject was thoroughly 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 / 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. to11:00 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 / 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)[27]. 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. Heart Rate Variability parameters in time domain method like mean R-R interval, mean Heart Rate, SDNN (standard deviation of N-N interval) and RMSSD (square root of mean squared difference of successive NN intervals) were collected from Polygraphic recording. Data were expressed as mean and median. For statistical analysis Mann-Whitney U test was used.

Results

Anthropometric details of the subjects 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 group B_2.

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

Groups	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)
A	38.5^a	160^a	53.5^a	20.87^a
(n=20)	39.15^b	160^b	54.1^b	21.00^b
B_1	35.5^a	157^a	43^a	17.77^a
(n=30)	38.87^b	160^b	46.05^b	17.83^b
B_2	41^a	159^a	49.5^a	20.02^a
(n=30)	40.8^b	161^b	52.77^b	20.13^b
Statistical analysis				
Groups	P value			
A vs B_1	0.882 ^{ns}	0.904 ^{ns}	0.000***	0.000***
A vs B_2	0.366 ^{ns}	0.448 ^{ns}	0.475 ^{ns}	0.212 ^{ns}
B_1 vs B_2	0.251 ^{ns}	0.478 ^{ns}	0.000***	0.000***

Data were expressed as ^{a}median and ^{b}mean.
***= $p<0.001$, ns= $p>0.05$.

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

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***

Mean and median values of mean R-R interval and HR were significantly ($p<0.001$) lower in group B_1 than those of group A and B_2. But no statistically significant differences of these values were found between group A and group B_2. The median SDNN and RMSSD were significantly lower in group B_1 than those of group A ($p<0.001$) and group B_2 ($p<0.01$). However, no statistical significant differences of SDNN and RMSSD were observed between groups A versus B_2.

Table III: Heart rate variability parameters in different groups (n=80)

Groups	Mean R-R interval (Sec)	Mean H.R (Beats/min)
A(n=20)	$0.74^a 0.802^b$	$81.5^a 76.7^b$
B_1(n=30)	$0.57^a 0.562^b$	$106^a 106.7^b$
B_2(n=30)	$0.74^a 0.825^b$	$81^a 75.5^b$
Statistical analysis		
Groups	P value	
A vs B_1	0.000***	0.000***
A vs B_2	0.464 ns	0.571 ns
B_1 vs B_2	0.000***	0.000***

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

Table IV: Heart rate variability parameters (short term) in different groups (n=80)

Groups	SDNN(ms)	RMSSD(ms)
A(n=20)	$32.42^a 37.63^b$	$37.62^a 49.14^b$
B_1(n=30)	$13.62^a 16.06^b$	$9.81^a 16.06^b$
B_2(n=30)	$20.91^a 33.25^b$	$17.76^a 38.29^b$
Statistical analysis		
Groups	P value	
A vs B_1	0.000***	0.000***
A vs B_2	0.223 ns	0.216 ns
B_1 vs B_2	0.004**	0.004**

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

Discussion

In the present study, heart rate variability (HRV) like mean R-R interval, mean heart rate, SDNN, RMSSD were measured by time domain method to assess cardiac autonomic nervous activity in patients with hyperthyroidism. Serum TSH and FT_4 levels were also measured to determine their thyroid hormone status. All these parameters were compared with healthy age and sex matched adults. The autonomic nerve function status assessed by these HRV parameters in healthy subjects were almost similar to the findings reported by the investigators from different countries.[5-7,20,31,37]

In this study, all subjects were matched for age and sex. Serum TSH level was significantly lower and FT_4 was significantly higher in both untreated and treated hyperthyroid patients compared to healthy control. The BMI was found significantly lower in untreated hyperthyroids in comparison to both healthy control and treated hyperthyroids. All these changes were due to the disease process involved

Significantly lower mean R-R interval and higher HR were found in untreated hyperthyroids compared to those of healthy and treated hyperthyroids. However, statistically no significant differences of these values were observed between treated hyperthyroids and healthy control. Similar findings were also observed by several investigators from different countries.[4-7,10,15,20,28,30,31] The values of SDNN and RMSSD were found significantly lower in untreated hyperthyroids compared to those of both healthy control and treated hyperthyroid patients. But statistically no significant differences of these values were observed between healthy euthyroids and treated hyperthyroids.[7,26,31,37]

It has been suggested that lower values of SDNN and RMSSD denote decreased high frequency component of HRV which is suggestive of decreased cardiac vagal modulation [38].

It has been suggested that reduced cardiac vagal effects in hyperthyroidism may be attributed to interference of peripheral neuroeffector mechanism and central inhibition of cardiac baroreflex reducing vagal discharge.[30] Though, some studies[39] observed the presence of increased sympathetic tone in hyperthyroidism but others[6] found the normal levels of catecholamine or even reduced in hyperthyroidism.

Along with the CNS manifestations, excess thyroid hormones usually affect every single cell of human body and results in exaggerated manifestations as hyperadrenergic state and all of which have impact on heart rate. Thyroid hormones also cause increased intrinsic activity of SA node.[21] In addition, these hormones potentiate the metabolic activity, oxygen consumption in peripheral tissue and beta receptors activities.[15]

Many researchers have observed R-R interval, heart rate, SDNN, RMSSD in hyperthyroids and found cardiac autonomic dysfunction in them.[5,7,20] In the present study, hyperthyroid patients are most likely to be suffered from cardiac autonomic dysfunction as there are signs of decreased HRV indicated by lower values of mean R-R interval, mean Heart Rate, SDNN and RMSSD. More marked changes of all these values in untreated hyperthyroids than treated hyperthyroids also are in support of these findings. On the other hand, improvement of cardiac autonomic nerve function state in treated hyperthyroids in this study suggests that treatment may improve this dysfunctional state.

However, the exact mechanisms involved for the impairment of cardiac autonomic nervous activity in hyperthyroids 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

Cardiac autonomic nerve dysfunction may occur in hyperthyroid patients and proper treatment of the patients may improve the condition.

Author affiliations

***1.** Md. Rasel Kabir, Assistant professor, Department of Physiology, ZH SikderWomen Medical College, Dhaka. Email:raselkabir623@gmail.com

2. Noorzahan Begum, Professor Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh. Email: noorzahanbeg@ yahoo.com

3. Sultana Ferdousi, Assistant Professor, Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh. Email: sferdousiratna@ gmail.com

5. Sultana Ferdousi, Assistant Professor, Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh. Email: sferdousiratna@ gmail.com

6. Afroza Begum, Assistant Professor,(cc) Department of Community Medicine, Shahid Sohrawardy Medical college, Dhaka

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