

Power Spectral Analysis of Heart Rate Variability In Hypothyroidism

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Abstract

Background: Hypothyroidism is one of the common clinical problems with high incidence in women particularly in older age. It has profound effect on metabolic processes in almost all tissue of the body and heart is particularly sensitive to thyroid hormone action. Power spectral analysis (PSA) is useful to determine the cardiac autonomic regulation by assessing sympathovagal balance. **Objectives:** To assess the cardiac autonomic nervous activity by power spectral analysis of heart rate variability in patients with hypothyroidism. **Method:** This cross sectional study was carried out in the Department of Physiology, Banghabandhu Sheikh Mujib Medical University from 1st July 2008 to 30th June 2009 on 60 female patients of 30-50 years with hypothyroidism (group B). For comparison, 30 age sex matched apparently healthy euthyroid subjects (group A) were also studied. Based on treatment, hypothyroid patients were divided into B₁ (patients on their 1st day of diagnosis, before starting of treatment) and B₂ (patients with medication for 12-18 months). The patients were selected from the Out Patients Department of Endocrinology, BSMMU. Serum TSH and FT₄ levels of all subjects were measured by AxSYM system. To perform power spectral analysis of HRV Total Power (TP), Low Frequency (LF), High Frequency (HF), LF norms (nu), HF norms (nu) and LF/HF ratio were assessed by a Polyrite. For statistical analysis of data, Independent Sample t test, One Way ANOVA and Pearson's correlation coefficient test were done as applicable. **Results:** The mean serum TSH (38.16 vs 2.18; 2.04) was significantly higher and FT₄ (5.12 vs 15.13; 15.08) was significantly lower (p<0.001) in group B₁ than those of group A and B₂. The mean values of all the spectral parameters of HRV in euthyroid subjects were within normal range. In untreated hypothyroid patients the mean values of TP (77.11 vs 2702.87; 2683.73), HF power (56.68 vs 342.02; 437.34) HF nu (24.79 vs 36.35; 34.55) were found significantly (p<0.001) lower LF/HF (1.7±0.3, 3.16±.84 and 1.93±.58) and LF nu (75.32 vs 63.71, and 65.90) were significantly (p<0.001) higher and in comparison to both euthyroids and treated patients. **Conclusion:** Alteration in cardiac autonomic nervous activity characterized by reduced vagal modulation and higher sympathetic activity may occur in the hypothyroid patients..

Keywords: HRV, LF HF LF/HF Hypothyroidism

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Introduction

The thyroid gland is the largest endocrine gland of our body, produces two major hormones, thyroxine and triiodothyronine. These hormones play vital role in metabolism, profound effect on sensitivity of tissues to catecholamine, stimulates O₂ consumption of most of the cells in the body,

necessary for normal growth and maturation and therefore affects every organ and organ system.^{1,2}

Hypothyroidism is one of the common endocrine disorder in our country. About 3% of the general population are hypothyroids. The incidence is

more in women particularly in older age but men are also affected.³

Hypothyroidism may be associated with different cardiovascular and metabolic disorders including autonomic nerve function disorders which are evident by the changes in cardiac autonomic nervous activities (CANA). Increased sympathetic and decreased parasympathetic activities are the usual findings in hypothyroids. Increase in sympathetic activity possibly be due to TRH which directly stimulates sympathetic outflow within the CNS.⁴ Dysfunction of ANS may also affect various other organs.

Heart rate variability is the result of intrinsic cardiac automaticity and an indicator of the interaction between cardiac sympathetic and parasympathetic activity⁵. It has been reported that increase in sympathetic and decrease in parasympathetic activity may reduce beat to beat variability⁶.

Power spectral analysis of HRV can demonstrate the definite impairment in cardiac autonomic control, by its ability to detect sympatho-vagal imbalance^{5,7}. Power spectral components for HRV analysis includes Total power, VLF power, LF power, HF power, HF norm, LF norm and LF/HF ratio⁵.

Several studies reported Lower values of total power, HF power and LF power in untreated hypothyroids than those of euthyroids⁸⁻¹¹.

Again, higher LF norm and lower HF norm in untreated hypothyroid patients in comparison to healthy control was also reported by some investigators^{8,9,12}. Cacciatori et al. Galetta et al. observed higher LF/HF ratio in untreated hypothyroids than those of euthyroids and also treated patients⁹⁻¹⁰.

Though most of the time they remain unnoticed, it is possible to prevent the development of various complications related to autonomic dysfunction in thyroid dysfunction. In our country, heart rate variability by power spectral analysis was investigated in hyperthyroids¹³. In addition, several studies on autonomic nerve function in some clinical condition and health

such as diabetes mellitus, aging process, obesity and post-menopausal women were done by conventional method¹⁴⁻¹⁷ However, no published data is yet available on hypothyroidism by power spectral analysis.

Therefore, the present study was undertaken to assess the autonomic nerve function status in hypothyroid patients by power spectral analysis of HRV. This study may be useful in screening of autonomic nerve function status in hypothyroidism in order to minimize hypothyroid related complications.

Methods

This cross sectional study was carried out to observe the HRV by time domain method in 60 hypothyroid female patients (group B) with age ranged from 30-50 years in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University from 1st July 2008 to 30th June 2009. For comparison 30 age and sex matched apparently healthy euthyroid subjects (group-A) were also studied. Hypothyroid patients were further subdivided according to treatment received into B₁, i.e. untreated hypothyroid patients and B₂ i.e. treated patients achieving euthyroid status. The patients were selected from the Out Patient Department of Endocrinology, BSMMU and the controls were selected from the same area near to hospital by personal contact. All the subjects were free from heart disease, hypertension, diabetes mellitus, chronic renal failure, psychic disorders, and smoking.

After selection, the subject was thoroughly informed about the aim, objectives and detail procedure of the study before examination and collection of blood sample. They were encouraged for voluntary participation and were allowed freedom to withdraw from the study whenever she liked even after participation. If she agreed to enroll to the study, informed written consent was taken from them. For examination the subjects were advised to have their meal by 9:00 pm on previous night, to remain free from any physical or mental stress, not to take any drugs affecting central nervous system and to have a good sleep at night before the examination

day. The subject were advised to avoid tea or coffee at breakfast and to attend the Autonomic Nerve Function Test Laboratory

Between 9:00 to 11:00 a.m. on the day of examination. Then the subject was interviewed and detail history regarding personal history, drug history, past medical history was taken to exclude exclusion criteria. Then thorough physical examinations and anthropometric parameters like height, weight, BMI, were taken and the information were recorded in a prefixed questionnaire. Then the subjects were kept under complete bed rest in supine position for 20 minutes in a cool and calm environment. During this period she was advised not to talk, eat or drink and also not to perform physical or any mental activity, even sleep. Then all preparations for recording of the Heart Rate Variability parameters were made by connecting the channels to a transducer for ECG to a computerized polygraph and 5 minutes recording was taken in resting supine position. Data were obtained by software analysis of the power spectral band of the HRV⁵. After the recording is over, 5ml of venous blood was drawn from the subject .The serum level of thyroid hormone was measured by Microparticle enzyme Immuno Assay(MEIA) method. Data were expressed as mean ± SD. For statistical analysis, Independent Sample t test and one way ANOVA were used as applicable.

Results

All the subjects were matched for age and BMI and no statistically significant differences were observed among them. (Figure 1)

The mean serum TSH was significantly higher (p<0.001) and FT₄(5.12vs 15.13; 15.08) was significantly lower(p<0.001) in group B₁ than those of group A and B₂ but no statistically significant differences were observed regarding both FSH and FT₄ when compared between group A and B₂ (Table I).

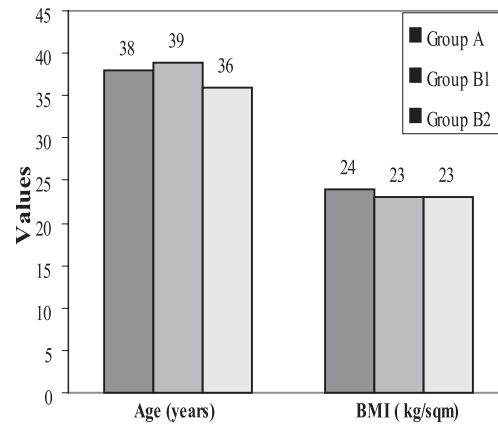


Figure 1: Age and BMI in different groups (n=90)

Table I: Serum TSH and FT₄ levels in different groups (n=90)

Groups	TSH(mIU/L)	FT ₄ (pmol/L)
A(n=30)	2.18±1.04	15.13±4.21
B ₁ (n=30)	38.16±30.50	5.12±1.89
B ₂ (n=30)	2.04±1.01	15.08±3.95

Statistical analysis:

Groups	P values	
A vs B ₁ vs B ₂	0.000***	0.000***
A vs B ₁	0.000***	0.000***
A vs B ₂	0.608 ^{ns}	0.964 ^{ns}
B ₁ vs B ₂	0.000***	0.000***

Data were expressed as mean ±SD. *** = P<0.001. ns = P>0.05

The mean values of all the spectral parameters of HRV in euthyroid subjects were within normal range. In untreated hypothyroid patients the mean values of TP, HF power, HF nu were found significantly (p<0.001) lower but LF/HF ratio and LF nu were significantly (p<0.001) higher and in comparison to both euthyroids and treated patients. Again, no statistically significant differences were observed when all these parameters were compared between group A and B₂. (Table II &Table III)

Table II: Power Spectral HRV Measures in Different groups(n=90)

Groups	Total Power(ms ²)	LF %(ms ²)	HF power(ms ²)
A(n=30)	2702.87±1297.89	14.65±10.7	342.02±362.15
B ₁ (n=30)	1177.11±584.04	17.87±11.5	56.68±50.76
B ₂ (n=30)	2683.73±1275.87	14.8±12.3	437.34±410.47

Statistical analysis:

Groups			
A vs. B ₁ vs. B ₂ ^a	0.000***	0.825 ^{ns}	0.000***
A vs. B ₁ ^b	0.000***	0.844 ^{ns}	0.000***
A vs. B ₂ ^b	0.954 ^{ns}	0.698 ^{ns}	0.344 ^{ns}
B ₁ vs. B ₂ ^b	0.000***	0.576 ^{ns}	0.000***

Data were reported as mean ± SD. Statistical analysis were done by One way ANOVA^a and Independent sample 't' test^b. LF = Low frequency, HF = High frequency, ms² = squared millisecond.

Table III: Power Spectral HRV Measures in Different groups(n=90)

Groups	LFnu	HFnu	LF/HF
A(n=30)	63.71±4.07	36.35±4.12	1.7±0.3
B ₁ (n=30)	75.32±4.85	24.79±4.89	3.16±.84
B ₂ (n=30)	65.90±5.23	34.55±4.67	1.93±.58

Statistical analysis:

Groups			
A vs. B ₁ vs. B ₂ ^a	0.000***	0.000***	0.000***
A vs. B ₁ ^b	0.000***	0.000***	0.000***
A vs. B ₂ ^b	0.161 ^{ns}	0.105 ^{ns}	0.982 ^{ns}
B ₁ vs. B ₂ ^b	0.000***	0.000***	0.000***

Data were reported as mean.±SD. Statistical analysis were done by One way ANOVA^a and Independent sample 't' test^b.

LFnorm.= LF power in normalized unit, [(LF/total power-VLF)×100] HF norm.=HF power in normalized unit, [(HF/total power-VLF)×100] LF/HF= ratio of low frequency and high frequency.

Group A: Apparently healthy Euthyroids.(control)

Group B : Hypothyroid (study group)

B₁ : Untreated .

B₂ : Treated.

Discussion

In last decade several investigators had assessed cardiac autonomic activity by power spectral analysis of HRV from the ECG recoding in Hypothyroid patients^{8,-11,18-20}.

Different power spectral components of HRV has been used as marker of cardiac autonomic activity. The task force guideline for HRV analysis have demonstrated the interpretation of these parameters to understand the status, behavior

and the balance between sympathetic and parasympathetic due to their continuous interaction⁵. The total power represents the total variability of R-R interval and is the result of the total cardiac autonomic nervous activities and hormonal activities on heart. Therefore its lower value indicates lower modulation of the cardiac autonomic nervous activities on heart⁵.

Two major component of spectral band, HF power and HF norm reflect the parasympathetic modulation on the heart⁵ and LF power represents the sympathetic activity on the heart; though, some investigators claimed that it is also under some parasympathetic contribution whereas LF norm emphasizes the controlled & balanced behavior of the sympathetic nervous system⁵.

The cardiac sympathetic and parasympathetic activities are always in interaction. The LF/HF ratio can be considered as a marker of their sympatho vagal balance.

The values of spectral components of HRV in euthyroid subjects in this study were comparable to those reported by the various investigators from different countries^{18,21,23,24} and also from our country.¹³⁻¹⁷

In this study no significant differences were observed in all these parameters when compared between euthyroid and treated patients with their almost euthyroid status.

In the present study, significantly lower total power in untreated hypothyroid is consistent to the findings of some other studies⁹⁻¹¹

Again, significantly lower values of HF power and HF norm in untreated hypothyroid indicating their reduced vagal modulation of heart compared to euthyroid and treated hypothyroid patients who obtained euthyroid status. Similar observations were also made by some researchers^{8-10,12}.

A conflicting picture regarding LF power and LF norm in hypothyroidism is available from various studies. Some showed an increase, some showed

a decrease and some others found no change in LF in hypothyroid compared to euthyroid subjects.

In the present study though higher but statistically not significant value of LF and significantly higher values of LF norm in untreated in hypothyroid is in contrast to those researchers^{8,12}, who found significantly lower LF and LF norm in hypothyroids but LF norm is comparable to some studies⁹.

LF/HF ratio was found significantly higher in hypothyroids compared to control and euthyroid treated hypothyroid patients in this study. This finding is consistent to the observations made by some researchers^{9,10,25} but contradicts to other investigator's findings^{8,12}.

Findings from research articles analyzing HRV showed that various authors have proposed several mechanisms with physiological background for the observed changes of power spectral components in the deficient state of thyroid hormone in human or in animal model experiment.

It has been suggested that increased sympathetic and decreased vagal modulation might occur in hypothyroidism^{9,10,26}. But decreased HR is one of the important feature of hypothyroid which is attributed to desensitization of receptor and also due to cardiac chronotropic response to adrenergic stimulation despite evidence of sympathetic overactivity. It has also been suggested that decreased binding of catecholamine with alpha and Beta receptors in cardiac myocytes might be responsible for cardiovascular changes in Hypothyroids¹⁰. Several investigator suggested that though plasma catecholamines are increased in hypothyroidism but overall depression of adrenergic responses at cardiac and peripheral level indicates desensitization both at the receptor or post receptor site^{9,10,21,23,24, 26}.

In this study, higher values of LF power, LF norm are suggestive of presence of sympathetic over

activity in the hypothyroid patients of the present series. However, decreased values of total power, HF power and HF norm revealed reduced vagal tone in these groups of patients. Moreover, shifting of sympatho vagal balance towards sympathetic predominance in this study is also in favor of sympathetic over activity in hypothyroid patients.

Conclusion

Alteration in cardiac autonomic nervous activity characterized by reduced vagal modulation and higher sympathetic activity may occur in the hypothyroid patients.

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