Article

Heart Rate Variability in Patients with Essential Hypertension

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Abstract

Background: Essential hypertension may be associated with altered cardiovascular autonomic nerve function. Heart Rate Variability (HRV) analysis is an important tool for quantitative measurement of autonomic nerve activity. **Objective:** To assess the cardiac autonomic nerve function status in essential hypertension by analyzing time domain measures of heart rate variability. **Methods:** This cross sectional study was carried out in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University from 1st July 2008 to 30th June 2009.For this purpose, 60 hypertensive male patients with age ranged between 40-60 years (group B) were enrolled from the Out Patient Department of Cardiology, BSMMU, Dhaka. Based on treatment received, hypertensive patients were subdivided into group B_1 i.e.untreated patients on their 1st day of diagnosis and group B_2 i.e.patients with antihypertensive therapy. For comparison, 30 age & sex matched apparently healthy normotensive subjects (group A) were also studied as control group. Time domain measures of Heart Rate Variability (HRV) such as Mean RR intervals, Mean HR, SDNN & RMSSD were assessed by a Polygraph machine to observe both sympathetic and parasympathetic nerve function status. For statistical analysis of data, Independent sample t-test, One-way ANOVA test, were used as applicable. **Results:** Mean R-R interval SDNN and RMSSD were significantly ($P<0.01$) lower but mean heart rate was significantly ($P<0.01$) higher in untreated hypertensive patients than those of normotensive subjects. But differences in all these 4 parameters when compared between control and treated hypertensive patients were found statistically non significant. **Conclusion:** Impaired cardiac autonomic nerve function characterized by sympathetic overactivity may occur in hypertensive patients.

Key words: Mean RR, SDNN,RMSSD, hypertension

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Introduction

Hypertension is an emerging health problem in Bangladesh among the cardiovascular diseases. The prevalence rate of hypertension is very high and more than 20% of the adults in Bangladesh have hypertension.[1] In essential hypertension no specific medical cause can be found to explain patient's condition. The adverse effects of hypertension principally involve the blood vessels, the retina, the heart, and the kidneys including the central nervous system.[2]

Evidence from studies of both animals and humans suggested that autonomic nervous system plays a crucial role in the development of hypertension.[3] The arterial baroreflex mechanism regulates blood pressure through reflex effects on the heart, resistance vessels and renal excretion of sodium and water.[4]

There is evidence that faulty noradrenaline reuptake in the cardiac sympathetic nerves amplify the sympathetic neural signal in essential hypertensive patients.[5]

Essential hypertension is treated with drugs which themselves modify the sympatho-parasympathetic balance.[6,7]

The heart rate variability analysis is a powerful tool in assessment of the cardiac autonomic nerve function. It is an accurate, reliable, reproducible, yet simple to measure and to process. The source of information for HRV is a continuous beat-by-beat measurement of interbeat intervals.[8]

Time domain method records the heart rate at any point in time or the intervals between successive QRS complex in a continuous ECG record. Common simple time domain variables include the mean normal-to-normal QRS complex (NN) interval and the mean heart rate. Statistical time domain variables include the standard deviation of the NN interval (SDNN) and the square root of the mean squared differences of successive NN intervals (RMSSD).

Several investigators from different countries reported that mean R-R interval was significantly lower and mean heart rate was significantly higher in untreated hypertensive patients than those of healthy control.[9-13] However, some of the investigators failed to find any significant differences of these parameters between these two groups.[11,14]

Again, a number of studies also documented lower values of SDNN and RMSSD in both untreated and treated hypertensive groups compared to those of normotensive subjects.[10-17]

Hypertension is one of the common cardiovascular problems in our country. Large number of people in our population are affected with hypertension remains unnoticed, which subsequently present with various complications. In addition to metabolic factors, many studies have documented sympathetic hyperactivity as the principal underlying cause for hypertension. Therefore, qualitative measurement of cardiac sympathetic nerve activity along with cardiovagal balance may throw some light on the role of autonomic modulation to develop hypertension and also change in the autonomic activity after treatment with antihypertensive therapy. Therefore, the present study was carried out to observe the autonomic nerve function status in untreated and treated hypertensive patients analyzing HRV by time domain method.

Methods

This cross sectional study was carried out on 60 male hypertensive patients with age ranged from 40-60 years (group B) in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University from July 2008 to June 2009. Based on treatment, hypertensive patients were subdivided into group B_1 i.e untreated patients on their 1st day of diagnosis and group B_2 i.e. patients with antihypertensive medication. For comparison, 30 age, sex and BMI matched apparently healthy normotensive subjects (group A) were also studied. The study group was selected from the Out Patient Department of Cardiology, BSMMU, Dhaka and the control group was selected by personal contact. Both the groups were free from heart diseases, secondary hypertension, diabetes mellitus, renal diseases and psychic disorders.

After selection, the subject was thoroughly informed about the objectives and detail procedure of the study before examination and collection of blood sample. They were encouraged for voluntary participation and allowed freedom to withdraw from the study whenever they like even after participation. If they 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 the previous night, to remain free from any physical or mental stress, not to take sedatives or any drugs affecting central nervous system and to have a good sleep at night before the day of examination. The subjects were also asked to avoid tea or coffee at breakfast and to attended the Autonomic Nerve Function Test Laboratory in the Department of Physiology of Bangabandhu Sheikh Mujib Medical University

between 9:00 to11:00 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 for exclusion criteria. Then thorough physical examinations and anthropometric measurement including height and weight were taken.and BMI was calculated. All information were recorded in a prefixed questionnaire. Then he was kept under complete bed rest in supine position for 15-20 minutes in a cool and calm environment. During this period subject 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 of ECG and a 5 minutes recording was taken in resting supine position and the HRV parameters were studied by time domain method.

Heart Rate Variability parameters in time domain method such as 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 assessed by Polygraph (RMS Polyrite D, version 2.2) and for statistical analysis Mann-Whitney U test, Chi-square test and Pearson's correlation coefficient test were done as applicable.

Results

All the groups were matched for age and BMI (Table I).

The mean resting pulse rate($p<0.05$) systolic (SBP) and diastolic (DBP) blood pressures($p<0.001$) were significantly higher in group B_1 than those of group A and B_2. But statistically no significant differences were observed when these parameters were compared between group A and group B_2 .(Table II)

The mean R-R interval was significantly lower($p<0.01$) and mean heart rate was significantly ($p<0.01$) higher in group B_1 compared to group A. But no statistical significant differences were found in these parameters when compared between group B_1 and group B_2.Again no significant differences were found when compared between A and B_2.

Table I: Age and BMI in different groups (n=90)

Groups	Age (years)	BMI (kg/m^2)
A(n=30)	48.37±8.03	24.46±3.28
B_1(n=30)	49.77±7.70	25.37±2.93
B_2(n=30)	48.13±6.24	23.47±4.16

Statistical analysis

Groups	p values	
A vs B_1 vs B_2 [a]	0.651 [ns]	0.115 [ns]
A vs B_1 [b]	0.493 [ns]	0.263 [ns]
A vs B_2 [b]	0.900 [ns]	0.308 [ns]
B_1 vs B_2 [b]	0.370 [ns]	0.05 [ns]

Data were expressed as mean ± SD. Statistical analysis were done by One-way ANOVA[a] and Independent sample t-test [b]

BMI= Body Mass Index, ns = $p>0.05$, n = number of subjects.
Group A: Apparently healthy normotensive (control).
Group B: Hypertensive(study group)
B_1-Untreated. B_2 : Treated.

Table II: Resting Pulse Rate and BP in different groups (n=90)

Groups	Pulse (bpm)	SBP (mm of Hg)	DBP (mm of Hg)
A(n=30)	71.23±7.28	112.67 ±10.73	74.43±8.71
B_1(n=30)	77.30±10.22	156.33 ±16.18	101.50±8.63
B_2(n=30)	74.4±9.09	117.83 ±14.24	78.33±10.20

Statistical analysis

Groups	P values		
A vs B_1vs B_2 [a]	0.036*	0.000***	0.000***
A vs B_1 [b]	0.010*	0.000***	0.000***
A vs B_2 [b]	0.142 [ns]	0.118 [ns]	0.117 [ns]
B_1 vs B_2 [b]	0.250 [ns]	0.000***	0.000***

Data were expressed as mean ± SD. Statistical analysis were done by One-way ANOVA[a] and Independent sample t-test [b] SBP = Systolic blood pressure, DBP= Diastolic blood pressure.
*** = $p<0.001$, ** = $p<0.01$, * = $p<0.05$, ns = $p>0.05$, n= number of subjects.

Mean SDNN and RMSSD were significantly ($p<0.001$) lower in group B_1 compared to group A and B_2 except SDNN which is though lower than B_2 but statistically not significant. Again these values were significantly ($p<0.001$) lower in B_2 than those of group A. (Table-III).

Analysis of Correlations of HRV measures with blood pressure showed that he mean R-R interval was negatively correlated in group B_1(r=-0.089) but positively correlated in group A(r=+0.233) and B_2 (r=+0.070) with SBP.(Table IV).

But with DBP, this parameter showed negative(r=-0.137, r=-0.151) correlation in group B_1 and B_2 whereas positive (r= +0.015) correlation in group A.(Table V).

Again, the mean HR showed positive correlation in group B_1(r= +0.074) and negative correlations in group A(r= -0.029) and B_2 (r= -0.283) with SBP(Table IV). Again, with DBP it was positively (r= +0.244) correlated in group $B_1$and A(r= +0.137), but negatively correlated(r=-0.079) in group B_2 (Table V). All these relationships were statistically nonsignificant.

Table III : Time domain measures of HRV in different groups (n=90)

Groups	Mean R-R interval (Sec)	Mean HR (bpm)	SDNN (ms)	RMSSD (ms)
A (n = 30)	0.9±0.15	71.13±7.37	65.58±17.07	32.33±4.92
B_1(n = 30)	0.79±0.2	76.97±9.12	49.82±6.38	20.03±2.63
B_2(n = 30)	0.8±0.15	72.70±8.75	51.99±7.70	23.37±3.11

Statistical analysis

Groups	p values			
A vs B_1 vs B_2 [a]	0.007**	0.025*	0.000***	0.000***
A vs B_1 [b]	0.003**	0.008**	0.000***	0.000***
A vs B_2 [b]	0.019 *	0.456 [ns]	0.000***	0.000***
B_1 vs B_2 [b]	0.648 [ns]	0.070 [ns]	0.239 [ns]	0.000***

Data were expressed as mean ± SD.
Statistical analysis were done by One-way ANOVA[a] and Independent sample t-test [b]
R-R = Interval between successive QRS complex (sec), HR = Heart rate.
SDNN=Standard deviation of NN interval.
NN = Intervals between adjacent QRS complexes from SA node depolarization.
RMSSD=Square root of mean squared differences between adjacent NN intervals,
ms=millisecond, ms^2=squared millisecond.
*** = $p<0.001$, * = $p<0.05$ ns = $p>0.05$, n= number of subjects.

Table IV: Correlation of heart rate variability measures with SBP in different groups (n = 90).

HRV measures	Groups					
	A		B_1		B_2	
	r	p	r	p	r	p
Time domain:						
Mean R-R interval	+ 0.233	0.215 [ns]	- 0.089	0.639 [ns]	+ 0.070	0.712 [ns]
Mean HR	-0.029	0.881 [ns]	+ 0.074	0.698 [ns]	- 0.283	0.129 [ns]

Table V : Correlations of heart rate variability measures with DBP in different groups (n = 90).

HRVmeasures	Groups					
	A		B_1		B_2	
	r	p	r	p	r	p
Time domain:						
Mean R-R interval	+ 0.015	0.935 ns	- 0.137	0.470 ns	-0.151	0.426 ns
Mean HR	+0.137	0.471 ns	+ 0.244	0.194 ns	- 0.079	0.677 ns

Statistical analyses were done by Pearson's correlation coefficient (r) test.
SBP= Systolic Blood Pressure
DBP= Diastolic Blood Pressure
ns = p>0.05 , n = number of subjects

Discussion

In the present study, findings of the time domain HRV parameters in healthy control group were almost similar to those reported by the various investigators from different countries[10-14] and also from our country [18-20]

In this study, the mean resting pulse rate and resting systolic and diastolic blood pressures were found significantly higher in untreated hypertensive patients in comparison to that of healthy normotensive and treated hypertensive groups. But these values showed no statistically significant difference between healthy normotensive and treated hypertensive groups

Similar type of findings was also reported by the various investigators from different countries[3,11,13,14,21]

Significantly lower mean R-R interval and significantly higher mean heart rate were observed in untreated hypertensive patients than those of healthy control. Similar findings were also reported by researchers from different countries[9-13]

Again, in this study, the mean values of SDNN and RMSSD were found significantly lower in untreated hypertensive patients compared to healthy control. Similar significant change in these two parameters in hypertensive patients were also reported by [10-17]

Again, in untreated hypertensive patients mean R-R interval was negatively correlated whereas mean HR was positively correlated with both SBP and DBP. The correlations were statistically not significant. No report was available to compare these findings.

Investigators suggested that essential hypertension is commonly neurogenic and attributed to sympathetic overdrive. They also suggested that several factors are responsible for the changes of autonomic nerve function activities associated with essential hypertension. Presence of autonomic nerve dysfunction may leads to arterial hypertension.[9,11,14,22]

More over in essential hypertension, there is increased rate of sympathetic nerve firing and also increased density of sympathetic innervations. Furthermore, co-transmission of adrenaline in cardiac sympathetic nerve along with impaired removal of noradrenaline from the synaptic cleft might also be the contributory factors for sympathetic over activity in essential hypertension.[5]

Again some investigators recommended that b adrenergic mediated vasodilation might have some contribution in the sympathetic overdrive in essential hypertension[23-25]

In the present study, decreased values of SDNN,RMSSD indicating decreased HRV and

lower RR interval and higher HR are suggestive of decrease vagal modulation and higher sympathetic activity in essential hypertension. This is further supported by negative correlation of RR interval and positive correlation of HR with systolic and diastolic blood pressure.

Conclusion

From the result of this study it can be concluded that impaired cardiac autonomic nerve function characterized by sympathetic overactivity may occur in hypertensive patients.

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