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Cardiac autonomic functions in hypertensive and normotensive subjects: a comparative study

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Abstract

Background

Hypertension, is considered one of the principal risk factors for cardiovascular disorders, increases the mortality. Dysfunction of the autonomic nervous system (ANS) is closely associated with this clinical condition. Heart rate variability (HRV) is a biomarker and noninvasive tool for the quantitative estimation of cardiac autonomic function. The aim of the study was to assess the cardiac autonomic nerve function status in hypertensive patients by analyzing time domain measures of HRV.

Methods

Equal numbers (n=50, in each group) of hypertensive and normotensive male subjects (40-60 yrs) were participated in this study. Electrocardiogram (ECG) was recorded and time domain measures of HRV such as mean RR intervals, mean heart rate (HR), Standard Deviation of Normal-Normal (SDNN) interbeat interval (ms), root mean square successive differences (RMSSD) and percentage of differences between adjacent normal RR interval > 50 msec (pNN50%) were assessed as an indicative of ANS function status. Statistical analysis was done by using unpaired t-test.

Results

Significant reduction was observed in SDNN, RMSSD, pNN50% amongst hypertensive subjects compared to normotensives.

Conclusion

Impaired cardiac autonomic nerve function characterized by sympathetic over activity and reduced vagal activity was found amongst hypertensives. A decrease in the baroreceptor reflex increases risk for occurrence of cardiac arrhythmias in future. So cardiac ANS tests could be considered as diagnostic criteria for the hypertensives and early detection, can increase curability and save lives.

Key words

Autonomic nervous system, heart rate variability, hypertension, sympatho-vagal imbalance, time domain

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Cardiac autonomic functions in hypertension

Background

Hypertension is the most common disease, which doubles the risk of cardiovascular morbidity and mortality. It accounts for 20-50% of all deaths [1]. Hypertension damages blood vessels, retina, heart, kidneys and nervous system [2]. Several factors involved in hypertension and most of them remain unknown. Genetic factors play a crucial role, comprised of approximately 40-60% of cases. Environmental factors include high salt intake, heavy consumption of alcohol, obesity and lack of exercise *etc.* [3]. There are several biomarkers available for the detection of hypertension [4]. Numbers of hypertensive patients are increasing in developed countries such in the USA, but in many low and middle-income countries rate is faster [5]. A systematic review and meta-analysis by Nupane *et al*. discussed the hypertension prevalence rate for several Asian countries - Bangladesh: 17.9%; Bhutan: 23.9%; India: 31.4%; Maldives: 31.5%; Nepal: 33.8%; Pakistan: 25%; and Sri Lanka: 20.9% [6]. A recent study from Kerala, India shows that higher prevalence of hypertension [7].

The autonomic nervous system plays a crucial role in regulation of blood pressure (BP) and HR, thus may be an important pathophysiological factor in development of hypertension [8]. Regulation of BP is controlled via baroreflex mechanism through reflex effects on the heart, resistance vessels and renal handling of sodium and water excretion [9]. Earlier research showed that faulty noradrenaline reuptake among patients of essential hypertension increases sympathetic response [10]. Sympatho-parasympathetic balance is the most common choice of treatment for these patients [11, 12]. Overall cardiac health and balance between sympathetic and parasympathetic control on the cardiac activity can be analyzed by HRV. This is an index of cardiac autonomic regulation [13, 14]. So HRV is considered as a very useful, accurate, reliable, reproducible, noninvasive biomarker of cardiac autonomic function [14]. The HRV indicates the oscillations in the interval between consecutive heart beats (RR interval), also oscillations between consecutive instantaneous heart rates [15]. To be clearer, HRV indicates the degree of balance in sympathetic and vagus nerve activity. A decrease in HRV is an indicative of incapability in the ANS or sinoatrial node's responsiveness, may indicate the presence of physiological malfunction [16]. HRV analysis can be done in two forms: time domain and frequency domain measures. Time domain measures are the means and standard deviations of R-R intervals recorded by the continuous ECG, where NN (normal to normal) represents all R-R intervals [17]. In essential hypertension, ANS plays an imperative role in diagnosis, so the present research was aimed to compare HRV between hypertensive and normotensive subjects.

Material and Methods

Study Period

The research work was done in the Department of Physiology, JJM medical college, Davanagere, Karnataka, India, in the period June 2010 to June 2012.

Study design and the participants

Informed written consent was obtained from the subjects willing to participate voluntarily in this study. Experimental procedure was explained and they were assured to withdraw themselves at any level of this research due to any inconveniences. Subjects were advised to have dinner by 9:00 pm regularly and a sound sleep at night. This practice followed to prevent physical and mental stress. They were instructed not to take sedatives, any drugs, avoid tea or coffee at breakfast which could influence the study parameters. Subjects attended neuro-physiology lab of JJM medical college, between 9.00 am - 11.00 am. Detailed medical history and thorough clinical check up was done to find out duration of hypertension, family history, previous drug history and habits of smoking, alcoholism *etc*. Then subjects were instructed to take rest in supine position for 15-20 minutes in a cool and calm environment.

Data collection

BP, ECG, Time domain measures of HRV was measured by the principal investigator. BP was measured by a mercury sphygmomanometer. A standard adult size cuff measuring 23 cm by 12 cm was used for all subjects. Three readings were taken in supine position and average of second and third were used for the study. Subjects were rested in the same position for at least 10 minutes, after which resting ECG (digital ECG system) was recorded with the subjects remaining supine for 5 minutes.

Multiple recordings of the ECG were taken by using additional filter settings. By using calculation tools, automated analysis; reports were generated automatically and saved. Instantaneous heart rates at RR intervals were continuously plotted using Niviqure software (operating system: Microsoft windows 7).

Time domain measures of HRV such as mean RR intervals, mean HR, SDNN (ms), RMSSD, Triangular interpolation of NN interval histogram(Hz) (TINN) and pNN50% were assessed to observe both sympathetic and parasympathetic nerve function status.

Inclusion criteria

Equal numbers (n=50 in each group) of hypertensive (diagnosed cases) and normotensive male subjects (age group of 40-60 years), who wanted to participate voluntarily, were considered.

ISSN 2321-5291
Medical Science 2016; June, Vol-4(2):320-324
Cardiac autonomic functions in hypertension

Exclusion criteria

Female subjects were not included because they were very less in number. History of smoking and alcoholism, drug treatment (except antihypertensives) were excluded. Several other factors were considered to set up as exclusion criteria like secondary arterial hypertension, congestive cardiac failure, symptomatic coronary artery disease, atrial fibrillation, diabetes mellitus *etc*.

Ethical committee approval

Approval was taken before experiment from the Institutional research ethics board. All guidelines, ethics and confidentiality maintained throughout this research work. This study was performed according the declaration of Helsinki (latest version).

Sample size calculation

Hypothesis testing for two means (equal variances) formulae was used to find out the sample size in both the groups.

In a pilot study done prior to the study showed Standard deviation of SDNN (ms) in normotensive = 10.2, Standard deviation of SDNN (ms) in hypertensive = 9.1, Mean difference = 6. Effect size = 0.622, Alpha Error(%) = 5, Power(%)= 85, sided = 2, required sample size per group was 47. But we have collected 50 per group [18, 19].

Outcome variable

HR (bpm), Systolic BP (mm Hg), Diastolic BP (mm Hg), SDNN (ms), RR (ms), pNN50%, RMSSD, RR Δ Index, TINN (ms).

Explanatory variables

Explanatory variable was blood pressure [normotensive and hypertensive].

Data management and statistical analysis

The collected data was analyzed by using the software statistical package for the social sciences (SPSS) for windows version 16.0 (SPSS Inc; Chicago, II, USA). Statistical analysis was done by using unpaired t-test. The results were expressed as Mean±SD. Student's t-test was performed for two group comparisons. $p<0.05$ was considered as statistically significance [Table - 1].

Results

Subjects in two groups were matched for age, HR and BP. Among hypertensives mean age was more compared to normotensives. Significant increase in HR, systolic BP and diastolic BP was observed in hypertensive subjects. Time domain measures of HRV such as mean SDNN (ms), RR intervals, PNN50% and RMSSD showed a statistically significant reduction amongst hypertensives.

Table - 1 Time domain analysis of HRV between normotensive and hypertensive subjects

Measurements	Normotensive subjects (Mean±SD)	Hypertensive subjects (Mean±SD)	P value
SDNN (ms)	66.96±10.01	59.16±9.54	0.000†
RR (ms)	949.15±140.38	848.39±166.82	0.001†
pNN50%	6.19±2.74	1.60±2.04	0.000†
RMSSD	30.92±12.40	18.99±11.49	0.000†
RR Δ Index	0.07±0.02	0.05±0.01	0.000†
TINN (ms)	301.84±198.90	128.84±79.38	0.000†

†P<0.01 statistically significant

Discussion

Hypertension is considered as the most common non communicable disorder which affects several systems of our body, including cardiovascular system. It is a big concern due the devastating effects of its chronic complications. Cardiac function is regulated by various intrinsic and extrinsic mechanisms. Over the years, HRV got importance because it is noninvasive and reproducible measure of ANS dysfunctions of underlying cardiovascular pathology, including coronary artery disease, hypertension, chronic heart failure (CHF) and myocardial infarction (MI) [20-23].

Heart rate in hypertension

Epidemiological evidences past six decades confirmed that elevated resting heart rate (RHR) associated with increased risk cardiovascular mortality, both in the general population (with or without risk factors), and in patients suffering from Cardiovascular disorders [24, 25]. In this study there was significantly increased HR amongst hypertensives compared to normotensives corroborating earlier works [26-28]. Fast RHR is significantly correlated with higher BP and increased HR is prospectively related to the development of hypertension. Increased sympathetic tone manifested by higher heart rate is common among hypertensives [29].

Time domain analysis of HRV

Our study showed a statistically significant reduction in SDNN (ms) in hypertensive subjects compared to normotensives supported by other researchers [30-35].

There was significantly reduced RR (ms) interval in hypertension. Similar findings were documented by Pavithran P *et al*. [9]. In our study RMSSD was significantly reduced in hypertensives. This was supported by the findings of Park SB *et al* and Tabassum R *et al*. [34, 35].

Decreased SDNN, RMSSD values indicated reduced HRV and lower RR interval and higher heart rate are suggestive of decreased vagal modulation and higher sympathetic activity in essential hypertension.

ISSN 2321-5291
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Cardiac autonomic functions in hypertension

In our research pNN50% showed significant reduction among hypertensives. Past workers also reported the same [30-33]. pNN50% is a sensitive measure of parasympathetic activity; so a drop in pNN50% among hypertensive subjects, strongly supports a decreased vagal tone. Our study showed significantly reduced RR Δ index and TINN (ms) value amongst hypertensives. RR Δ index and TINN (ms) represents the parasympathetic activity and their significant reduction is a strong indicative of hypertension.

Conclusion

HRV can be used as a clinically efficient tool for the detection and evaluation of cardiac autonomic function. Our study showed that HRV is significantly reduced in hypertensive patients compared to normotensives, indicating a decrease in the baroreceptor reflex and sympatho-vagal imbalance characterized by sympathetic over activity and lower vagal modulation. Since reduced HRV is associated with cardiac arrhythmias so this is always a risk factor for hypertensives. HRV can be used for early detection of cardiac arrhythmias which may save lives and future complications.

Limitations & future scope of the study

It is strongly recommended, conducting broad spectrum multi-centric studies in future with a large number of study population including females.

Abbreviations

Autonomic nervous system (ANS), blood pressure (BP), electrocardiogram (ECG), heart rate (HR), Heart rate variability (HRV), percentage of differences between adjacent normal RR interval > 50 msec (pNN50%), root mean square successive differences (RMSSD), Standard Deviation of Normal-Normal (SDNN), Triangular interpolation of NN interval histogram (TINN)

Competing interests

Authors declare that they do not have any competing interest.

Authors' contribution

Mangala Gowri SR, Vinay G designed the study, interpreted the data, drafted the manuscript, and revised it. Mangala Gowri SR conducted the research; Vinay G helped in the data formulation and analyzing. All authors critically revised the manuscript and finally approved it for publication.

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ISSN 2321-5291
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