A Comparative Study of Heart Rate Variability During Deep Breathing in Normotensive and Hypertensive Subjects

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ABSTRACT

Background: Autonomic neuropathy in hypertensives leads to impaired regulation of blood pressure (BP) and heart rate variability (HRV). Heart Rate Variability with Deep Breathing (HRVdb) test is a simple, non-invasive & sensitive measure of cardiac autonomic function. Objective: To compare the heart rate variability in normotensive and hypertensive subjects and to evaluate heart rate variability during deep breathing (HRVdb) as a tool to assess cardiovascular autonomic regulation, for clinical and research purposes. Material and Methods: The study included 50 normotensive and 50 hypertensive male subjects matched for age and BMI. HRV parameters: Mean RRI; RMSSD; LF; LFnu; HF; HFnu and LF/ HF ratio were analysed. One minute deep breathing test was employed and the mean of the heart rate differences in 6 breath cycles was analyzed. Results: The time & frequency domain measures of HRV were reduced in hypertensive group. HRVdb showed significant difference in the hypertensive group than in the normotensive group. Conclusion: Reduced HRVdb in the hypertensive group, indicates impaired regulation of the cardiovascular autonomic function. A reduction in HRV is associated with an increased risk of cardiac morbidity and mortality. HRVdb can be used as a simple bedside procedure to assess cardiovascular autonomic regulation and also as a simple non-invasive tool for clinical and research studies for the assessment of the neural control of heart rate.

KEYWORDS: Heart Rate Variability, Deep breathing, Autonomic Nervous System, Hypertension.

INTRODUCTION

The heart has rich innervations from both the limbs of the autonomic nervous system (ANS). The heart rate and its fluctuations reflect changes in cardiac autonomic control[1] Heart Rate Variability (HRV) refers to the beat to beat alterations in heart rate. HRV conventionally describes the beat-to-beat fluctuations in the heart rate or the variations in consecutive RR intervals. HRV is primarily due to the changing modulation of vagal and sympathetic control of the heart and may therefore be considered as an estimate of autonomic heart rate control[2] This neural link creates the basis of assessment of cardiac autonomic regulation through measurement of HRV[1]. Thus measurements of HRV provide a non-invasive tool for assessing autonomic control of the heart rate [3, 4].

Hypertension is the most common human cardiovascular disease, characterized by systolic blood pressure (SBP) of more than 140 mmHg and/or diastolic blood pressure (DBP) of >90 mmHg [5]. In more than 95% of cases, a specific underlying cause of hypertension cannot be found and such patients are said to have essential hypertension. The pathogenesis of essential hypertension is not clearly understood but is believed to be due to renal, neurogenic, vascular and genetic factors; in reality it has a multifactorial aetiology [6]. Worldwide it is estimated to cause 7.1 million premature deaths each year and 4.5% of the disease burden[7].

ANS plays a fundamental role in the control of arterial blood pressure and heart rate and therefore, may be
considered an important pathophysiological factor in the development of arterial hypertension [8]. Measurements of HRV might assess progressive alterations in the sympatho-vagal balance observed in essential hypertension[9]. Studies have reported decreased HRV among hypertensives[10]. Research into HRV and respiration over the past 150 years has led to the insight that HRVdb is a highly sensitive measure of parasympathetic cardiac function [11].

Thus the present study is planned to determine whether HRVdb is reduced in hypertensive subjects and also to assess whether HRVdb can also be used as a simple non-invasive procedure to evaluate cardiac autonomic regulation for clinical and research purposes.

MATERIALS AND METHODS

Selection of the Subjects: The present study was conducted in the Department of Physiology, Navodaya Medical College, Raichur, Karnataka. 50 normotensive and 50 hypertensive male subjects, belonging to the age group of 30-60 years, attending the Medicine OPD were selected. The study protocol was approved by the Institutional Ethical Committee.

Inclusion Criteria: In the normotensive group, subjects with normal BP, normal ECG & in good health as evaluated by general physical examination without any known respiratory, cardiovascular illness, or any disorder which can interfere the autonomic responses were included. In the hypertensive group known hypertensive on treatment with normal ECG were included.

Exclusion Criteria: Subjects with diabetes mellitus, symptomatic coronary disease, congestive cardiac failure, arrhythmias, any systemic illness and those with h/o tobacco & alcohol consumption were excluded.

Study Design: The study protocol was explained to the subjects and consent was obtained. During first visit anthropometric parameters, Body Mass Index (BMI), heart rate (HR) and blood pressure (BP) in supine rest and ECG were recorded. Each subject is given specific dates to visit autonomic laboratory. A day before the test subjects were advised to have their dinner before 9:00 pm and to refrain from any kind of stress. Also instructed not to have coffee, tea and cola 12 hours before the tests and to have light breakfast two hours before the tests. In the laboratory the subject is asked to relax in supine position for 30 minutes and then the tests were performed using ECG V: 52 [HRV analysis software], manufactured by NIVIQURE Meditech Pvt Ltd, Bengaluru. ECG V: 52 is a Computerized Data Acquisition System used in conjunction with PC/Laptop.

Heart Rate Variability Analysis: Recording was standardized and instructions followed as per the guidelines of Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology [12]. A chest lead ECG was recorded using ECG V: 52 for 5 minutes in supine rest with eyes closed, which is simultaneously analyzed by the software.

Beat-to-beat variations in instantaneous heart rate were derived offline using a rate-detector algorithm. Briefly, a 5-min ECG was acquired at a sampling rate of 1000 Hz during supine rest with the subjects breathing normally at 12–18 per min. RR intervals were plotted using the ECG V: 52 software.

An RR series was extracted using a rate-detector algorithm after exclusion of artefacts and ectopic. A stationary 256 second RR series was chosen for analysis. In the time domain, the standard deviation of normal-to-normal RR intervals (SDNN) was taken as an index of overall HRV. The RR series was resampled at 4 Hz, the mean and trend removed, a Hann window applied and the 1024 data point series transformed by fast Fourier transformation. Low frequency (LF) and high frequency (HF) spectral powers were determined by integrating the power spectrum between 0.04 and 0.15 Hz and 0.15 and 0.4 Hz respectively. Spectral powers are expressed in absolute units of milliseconds squared. LF and HF powers are also expressed in normalized units.

Heart Rate Response to Deep Breathing: The subject is trained to breathe deeply at a rate of 6 breaths/minute in supine position. Then he is asked to breathe deeply, steadily and slowly for 1 minute at the rate of 6 breathes/minute (5 seconds inspiration and 5 seconds expiration duration, of each cycle of one minute) while ECG was continuously recorded. The heart rate change with deep breathing (deep breathing difference) was then expressed as the mean of the differences between the maximal and minimal heart rate in 6 respiratory cycles.

Deep Breathing Difference (DBD) = Mean of Heart Rate Difference in 6 Breath Cycles.

Statistical Analysis: All data is expressed as Mean ± SD. Student ‘t’ test used to compare the data of normotensive and hypertensive subjects. Mann-Whitney test used to analyze HRV. p value < 0.05 considered statistically significant and p value < 0.01 as highly significant.

RESULTS

Subjects of both the groups were matched for age and BMI (Table-1). Even though the BMI was found to be higher in hypertensives (22.04±2.77) as compared to normotensives (21.2±1.8) it was statistically non significant. The resting heart rate, systolic blood pressure and diastolic blood pressure were higher in hypertensive group (Table-2). The time domain measures of HRV i.e., the Mean RRI (RR Interval) and RMSSD and also the frequency domain measures of HRV i.e., the LF (Low Frequency); HF (High Frequency); HF nu (High Frequency normalized units) and the LF; HF were reduced in the hypertensive when compared with the normotensive subjects and were found to be statistically significant in the present study (Table-3). In the present study HRVdb is reduced in the hypertensive group (17.84±3.58) as compared to normotensive group (27.28±7.63) and was statistically significant with a p value <0.0001 (Table-4).
Table 1: Baseline Characteristics of Subjects.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Normotensive Group</th>
<th>Hypertensive Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.3 ± 7.71</td>
<td>50.2 ± 7.6</td>
</tr>
<tr>
<td>Height (cms)</td>
<td>169.4 ± 4.84</td>
<td>168.06 ± 3.99</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>60.94 ± 5.79</td>
<td>62.1 ± 6.54</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>21.22 ± 1.8</td>
<td>22.04 ± 2.77</td>
</tr>
</tbody>
</table>

Table 2: Resting Cardiovascular Parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normotensive</th>
<th>Hypertensive</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate (bpm)</td>
<td>73.34 ± 13.42</td>
<td>79.39 ± 13.56</td>
<td>&lt; 0.03*</td>
</tr>
<tr>
<td>SBP mmHg</td>
<td>127.0 ± 8.23</td>
<td>139.1 ± 12.45</td>
<td>&lt; 0.0001*</td>
</tr>
<tr>
<td>DBP mmHg</td>
<td>79.8 ± 6.2</td>
<td>83.7 ± 3.96</td>
<td>&lt; 0.0003*</td>
</tr>
</tbody>
</table>

Table 3: Heart Rate Variability Parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normotensive</th>
<th>Hypertensive</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RRI</td>
<td>848.76 ± 158.52</td>
<td>765.72 ± 64.36</td>
<td>&lt; 0.004*</td>
</tr>
<tr>
<td>RMSSD</td>
<td>42.74 ± 37.72</td>
<td>24.48 ± 4.73</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>LF</td>
<td>991 ± 123.17</td>
<td>465.86 ± 41.68</td>
<td>&lt; 0.0001*</td>
</tr>
<tr>
<td>LFnu</td>
<td>68.03 ± 3.84</td>
<td>62.1 ± 7.97</td>
<td>&lt; 0.0001*</td>
</tr>
<tr>
<td>HF</td>
<td>471.64 ± 51.223</td>
<td>241.91 ± 15.26</td>
<td>&lt; 0.0001*</td>
</tr>
<tr>
<td>HFnu</td>
<td>32.35 ± 1.84</td>
<td>28.10 ± 2.15</td>
<td>&lt; 0.0001*</td>
</tr>
<tr>
<td>LF/HF</td>
<td>2.12 ± 0.31</td>
<td>1.93 ± 0.20</td>
<td>&lt; 0.0001*</td>
</tr>
</tbody>
</table>

Table 4: HRV-db in Normotensive & Hypertensive Subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normotensive</th>
<th>Hypertensive</th>
<th>p value</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRV-db</td>
<td>27.28 ± 7.63</td>
<td>17.84 ± 3.58</td>
<td>&lt; 0.0001</td>
<td>Significant</td>
</tr>
</tbody>
</table>

DISCUSSION

The present study showed that the measures of HRV are significantly reduced in hypertensive subjects relative to their age & BMI matched normotensive counterparts. The presence of reduced HRV in hypertensive subjects is consistent with the hypothesis that impaired regulation of the ANS plays a role in the pathogenesis of hypertension. Because changes in blood pressure affect autonomic tone and vice versa, HRV measures differ in hypertensive subjects when compared with those with normal blood pressure [13]. The time domain methods are used to investigate recordings of short durations, whereas the frequency domain methods are usually able to provide results that are more easily interpretable in terms of physiological regulations [12].

Time Domain Measures: Mean RRI (RR Interval) which measures the sum of the levels of parasympathetic and sympathetic influences was lower in hypertensive as compared to normotensives. Similar statistically significant results of reduced mean RRI in the hypertensives were obtained in studies done by Asuman H. Kaftan et al [14] and Gianfranco Piccirillo et al [15]. RMSSD (square root of the mean of the sum of the squares of differences between adjacent NN intervals) is an estimate of high-frequency variations in heart rate in short-term NN recordings, reflects an estimate of parasympathetic regulation of the heart [16]. RMSSD is lower in the hypertensive group than in the normotensive group (p < 0.01). The time domain methods are used to investigate recordings of short durations. Time domain methods record the heart rate at any point in time or the intervals between successive QRS complexes in a continuous ECG record. In the present study, decreased values of mean RRI and RMSSD indicating decreased HRV are suggestive of decreased vagal modulation and higher sympathetic activity in essential hypertension [17].

Frequency Domain Measures: Low Frequency (LF) component is believed to be a marker of the sympathetic modulation, was found to be reduced significantly in the hypertensive group. High Frequency (HF) Component a major contributor of the efferent vagal activity was lower in hypertensives as compared to normotensives. This result is in accordance with studies conducted by Gianfranco Piccirillo et al [15] and R Virtanen et al [18]. HF is also known as a 'respiratory' band because it corresponds to the NN variations caused by respiration, the respiratory sinus arrhythmia (RSA). The heart rate is increased during inhalation and drops during exhalation. Deep and even breathing causes an increase in the amplitude of HF peak on power spectrum.

However if respiration rate drops below nine breaths per minute this peak moves into LF frequency range and still represents parasympathetic regulatory activity [16] Harald M. Stauss et al [19] report that HF component is exclusively mediated by the cardiac parasympathetic nervous system, while LF component can be mediated by both divisions of the autonomic nervous system. Thus the
finding of reduced LF in the present study may be consequent to the reduction observed in the parasympathetic activity in hypertensive individuals [19].

**Low Frequency normalized units (LF nu)** measure minimizes an effect of changes in very low frequency power and emphasizes changes in sympathetic regulation. **High Frequency normalized units (HF nu)** minimizes an effect of changes in very low frequency power and emphasizes changes in parasympathetic regulation [20]. LFnu & HFnu components are reduced in the hypertensive group. Identical reduction in the hypertensive group were also found in various other studies[14, 21]. The representation of LF and HF in normalized units emphasizes the controlled and balanced behaviour of the two divisions of the autonomic nervous system. **Low Frequency /High Frequency (LF/HF)** measure indicates overall balance between sympathetic and parasympathetic systems [16].

The LF/HF ratio which is the ratio of the extent of fluctuations of the sympathetic tone to that of the parasympathetic tone was reduced in hypertensives as compared to normotensives in the present study. Similar results were found in other studies[14, 15]. Higher values reflect domination of the sympathetic system, while lower ones indicate domination of the parasympathetic system. However, when deep and even breathing occurs at rates less than nine breaths per minute, the elevation of this parameter reflects increase of parasympathetic regulation due to the effect of respiratory sinus arrhythmia [16].

Thus the low and high frequency components and their ratio would provide a model to evaluate broadly, the dynamic changes of the sympathetic balance. Essential hypertension is commonly neurogenic and attributed to sympathetic overdrive and may be associated with parasympathetic inhibition. It has also been suggested that increased rate of sympathetic nerve firing and also increase in density of sympathetic innervations might cause sympathetic over activity in hypertensive patients. The co transmission of adrenaline in cardiac sympathetic nerve along with impaired removal of nor adrenaline from the sympathetic cleft might also be the contributory factors for sympathetic over activity in essential hypertension [22].

**Heart Rate Variability with Deep Breathing (HRVdb)**: HRVdb represents a very sensitive measure of parasympathetic cardiac function and thus is an important component of the battery of cardiovascular autonomic function tests used in clinical autonomic laboratories. Deep breathing magnifies HRV with respiration, allowing for methods to assess HRV with respiratory cycles [11]. In the present study HRVdb is reduced in the hypertensive group (17.84 ±3.58) as compared to normotensive group (27.28±7.63) and was statistically significant with a p value < 0.0001. J.Srinivasa et al found significant decrease in the mean HRV with deep breathing in the hypertensive signifying blunted parasympathetic cardiac control in the hypertensives [23,24].

Fouad and colleagues found a similar linear relationship between HRVdb and parasympathetic cardiac control, leading them to conclude that HRVdb is an accurate index of cardiac vagal tone [11]. Deep breathing induced changes in heart rate occur because of alterations in cardiac parasympathetic activity and when this system is impaired deep breathing leads to decrease in HRV. Three mechanisms are generally proposed to explain the modulation of heart rate associated with respiration:

1. A direct influence of medullary respiratory neurons on cardio motor neurons;
2. An indirect influence on heart rate of blood pressure changes secondary to respiratory movements that are mediated via arterial baroreceptors or atrial stretch receptors;
3. A reflex response to lung inflation mediated by thoracic stretch receptors, most likely from the lungs and chest wall.

In most autonomic disorders, parasympathetic function is affected before sympathetic function, so HRVdb provides a sensitive screening measure for parasympathetic dysfunction in many autonomic disorders[25]

**CONCLUSION**

The present study concludes that sympathetic balance may be altered towards sympathetic predominance in essential hypertension which is supported by markedly decreased parasympathetic activity. Also heart rate variability during deep breathing can be used as a simple bedside non-invasive tool to assess cardiovascular autonomic regulation.

**REFERENCES**


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