SPECTRAL ANALYSIS OF HEART RATE VARIABILITY IN BRONCHIAL ASTHMA PATIENTS

JITENDRA GUPTA, AMITABH DUBE, VIRENDRA SINGH AND R. C. GUPTA

Department of Physiology,
SMS Medical College,
Jaipur – 302 004

(Received on November 5, 2011)

Abstract: The study was carried in the Departments of Physiology and Medicine at S.M.S. Medical College, Jaipur. Thirty patients of bronchial asthma, aged 20-30 years attending outpatient clinics of S.M.S. Hospital and thirty healthy volunteers were recruited in the present study for spectral analysis of Heart Rate Variability (HRV) using impedance peripheral pulse in the right forearm. Two spectral components were recorded namely high frequency (HF) component (0.15–0.4 Hz), an indicator of vagal efferent activity and low frequency (LF) component (0.04–0.15 Hz), replicator of composite sympatho-vagal interplay. These components were analyzed as LF nu (Low Frequency normalized unit), HF nu (High Frequency normalized unit) and LF/HF ratio. Low frequency component in absolute units of the asthmatic patients differed insignificantly (P>0.05) from LF of the subjects, whereas the same calculated as normalized units was found to be significantly low in the patient group (P<0.01), as compared to that of the control group. The High Frequency (in absolute units) index of HRV was significantly high in asthmatics (P<0.01) as compared to the HF (absolute units) of controls. Similar trend was observed in the normalized units of HF (P<0.01). LF/HF ratio was not significantly different in patient and control groups (P>0.05). It was concluded that a significantly raised central vagal outflow and a concomitant significantly low central sympathetic efferent could be appreciated in asymptomatic asthmatic patients as compared to that in the control group. This deranged sympathovagal interplay with parasympathetic dominance could be a plausible pathophysiological mechanism leading to airway obstruction, the hallmark of bronchial asthma.

Key words: bronchial asthma heart rate variability autonomic functions

INTRODUCTION

The cardiovascular and respiratory autonomic efferent fibers have common central origin (1) and hence the altered cardiovascular and respiratory responses may

*Corresponding Author: Dr. Jitendra Kumar Gupta, M.D., 10/1/2, Sector 10, Vidhyadhar Nagar, Jaipur – 302 023; E-mail: drjitendra@gupta007@gmail.com
reflect the abnormalities of the autonomic nervous system. Therefore, to evaluate the autonomic functions in asthmatics, different noninvasive, safe and easily reproducible cardiovascular autonomic reflex function tests were used (2).

The measurement of Heart Rate Variability (HRV) is a relatively new powerful noninvasive methodology which can evaluate and measure the neuro-cardiac function that reflects heart-brain interactions and both cardiac and autonomic nervous system (ANS). Reduced HRV has thus been used as a marker of reduced vagal activity.

The integrity of the autonomic nervous system has been tested in vivo in various disorders (3, 4, 5, 6). Similar procedures have been adopted by a few workers (7, 8) to evaluate the autonomic status in bronchial asthma. The introduction of HRV analysis, especially the identification of power of low frequency band of HRV spectral function with the activity of sympathetic nervous system, and power of its high frequency band with activity of parasympathetic nervous system, has opened up new avenues for ANS assessment. The present study so undertaken evaluated the power spectral density of HRV in Bronchial Asthma patients.

The present study was undertaken in order to evaluate the HRV profile of Bronchial Asthma patients of local resident population in the backdrop of the past studies so done on the subject. It was an attempt to get a better appreciation of the behavior of HRV in the patients under study.

This study was also undertaken to resolve the dilemma of the quality/quantity of sympatho-vagal inter play at the bronchial musculature axis.

MATERIAL AND METHODS

The study was carried in the Departments of Physiology and Medicine, S.M.S. Medical College, Jaipur. Thirty patients of bronchial asthma attending outpatient clinic of S.M.S. Hospital and thirty healthy volunteers were studied. After obtaining prior informed written consent, patients in the age group between 20 to 30 years with history and clinical features of bronchial asthma as defined by the American Thoracic Society (1962) were included in the study (9). A detailed history and thorough physical examination was carried out in all the subjects, to exclude other cardiopulmonary disease. The patients so selected were not taking any drug modulating the autonomic nervous system or cardiac rate for the preceding two weeks (except beta-agonist aerosols in the event of an exacerbation, preferably at least six hours prior to the test). Patients with any associated cardiopulmonary illness or other disease condition known to produce autonomic neuropathy were excluded from the study, as those with a history of respiratory infection over the preceding six weeks.

Heart rate variability (HRV) is assessed by measuring the variability in heart rate as evaluated through electrical signals generated from the heart (ECG) or by the peripheral pulsations which are depicted through principals of photoplethysmography with equal or similar sensitivity & specificity (10, 11, 12, 13, 14).

Routine investigations were done in all
subjects to exclude other cardiopulmonary diseases including respiratory infections. For short term analysis of HRV, Impedance Peripheral Pulse in the right forearm was recorded in the supine position for 5 minutes after 15 minutes of supine rest as per the International Protocol (AIIMS, 2006) (15). The Impedance Peripheral Pulse wave signals were continuously amplified, digitized, and stored in the computer for offline analysis in Frequency Domain. The detection of ‘C’ wave was done by software developed indigenously by Bhabha Atomic Research Center (BARC) incorporated in the medical analyzer module of NIVOMON and was taken to obtain the cardiac interval (R - R Interval) as C occurs within 150 milli-seconds of the R wave (16). All recordings were visually examined and manually corrected if required. Abnormal beats and areas of artifacts were automatically and manually identified and excluded from the study. The Power spectral densities (PSD) were plotted in ms²/Hz against preset frequencies. Power of the spectral bands are calculated in ms² (absolute power) and in normalized units (n.u.) (17).

**Statistics**

Statistical analysis was performed using SPSS version 17. The comparison of HRV indices between the two study groups (Asymptomatic bronchial asthma patients and age matched controls) were evaluated using Levene’s test for equality of variance, ‘t’ values were calculated taking equal variance assumed.

**RESULTS**

The present study evaluated power spectral analysis of HRV in frequency domain among asthmatic patients and compared it with the age and sex matched controls.

We observed significantly low VLF component of HRV in asthmatic group as compared to control group (P<0.05).

Our results regarding LF Component showed that when measured in absolute units, there is no statistically significant difference (P>0.05) between the patient and

<table>
<thead>
<tr>
<th>TABLE I: Comparison of anthropometric and PSD profile of patients and control.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Male/Female Sex Ratio</td>
</tr>
<tr>
<td>Height (cms)</td>
</tr>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>Respiratory Rate(breaths/min)</td>
</tr>
<tr>
<td>Heart Rate (beats/min)</td>
</tr>
<tr>
<td>VLF (Very Low Frequency) in ms²</td>
</tr>
<tr>
<td>Low Frequency (LF) in ms²</td>
</tr>
<tr>
<td>High Frequency (HF) in ms²</td>
</tr>
<tr>
<td>Low Frequency (LF) (in normalized units, n.u.)</td>
</tr>
<tr>
<td>High Frequency (HF) (n.u.)</td>
</tr>
<tr>
<td>LF/HF Ratio</td>
</tr>
</tbody>
</table>
control group; however in asthmatics LF n.u. values were significantly lower (P<0.01) as compared to controls.

The HF component in the present study depicted significantly high value in asthmatics as compared to control whether measured in absolute (P<0.01) or normalized units (P<0.01).

LF/HF ratio did not register significant difference (P>0.05) between asthmatic and control group.

Table – I depicts the comparative evaluation of anthropometric and power spectral density measures of asthmatics patients with age and sex matched controls.

DISCUSSION

The study was conducted to evaluate sympathetic, parasympathetic activity and their interplay in asymptomatic bronchial asthma patients and to compare it with the age matched controls, by measurement of the variation in resting heart rate using frequency spectrum analysis of HRV.

The Mean VLF (probable representative of tissue-based rennin-angiotensin system and endothelial functions) (15) component of HRV was evaluated in frequency domain. The difference between asthmatic and control groups was statistically significant (P<0.05). The above findings were indicative of suppressed peaks and amplitude of tissue-based rennin-angiotensin system and endothelial functions in asthmatic patients, the significance of which needs to be elaborated further.

Statistical comparison of the Mean Absolute LF component of HRV between asthmatic and control groups shows that the difference was not significant (P>0.05).

However the statistical comparison of Low Frequency (n.u.) component of HRV between the same groups shows a significantly low LF n.u. component (P<0.01) in the asthmatic patients.

Our findings of LF component of HRV analysis, which represents effectively sympathetic activity modulation (18, 19), showed that in asthmatic patient, LF (n.u.) component is less than that of the control group, whereas absolute LF component was not significantly different.

In our study the HF component (index of parasympathetic activity) (18, 19) was also evaluated.

In the patient group mean absolute HF component was significantly high (P<0.01) than the control group.

The mean HF (n.u.) component of HRV of asthmatics was again significantly high (P<0.01), as compared to the control group.

Our findings regarding HF component of HRV showed that it was higher in asthmatics as compared to controls whether measured in absolute or normalized units. As the HF component represents unquestionably the parasympathetic drive, it establishes that vagal tone is greater in asthmatics as compared to that of controls.

In our study the mean value of LF/HF
ratio, an index which approximately equilibrates the sympathetic and parasympathetic activities and denotes an effective interplay between them, was also calculated. The patient and control group did not register a significant difference on Levene’s Test of Equality of Variances (P>0.05).

Hence, it can be deduced from the above observations that a probable compromised central sympathetic outflow and enhanced vagal tone in asthmatics lead to an imbalance in sympato-vagal interplay at the periphery and an increased propensity to airway obstruction, an essential feature of bronchial asthma.

Garrard et al (20), Fujii et al (21), Pichon et al (17) and Ostrowska-Nawarycz et al (22) also designed a similar study on asymptomatic and symptomatic asthmatic patients and compared the findings of sympathetic and parasympathetic activity with the age matched control group. These studies using HRV analysis also did not report any intra or post recording complications. So, it can be stated without reservation from our study as well, that HRV is an absolutely safe and useful non-invasive method for assessing numerous disease states including bronchial asthma in which modulation of autonomic nervous system need to be evaluated.

Our findings considering LF component were consistent with that of Pichon et al (17) and Garrard et al (20). Pichon et al (17) measured LF (n.u.) of test group and found it to be 79±21 n.u.; while for the control group it was 89±9.0 n.u. Garrard et al (20) also observed that LF(n.u.) component was significantly low in both asymptomatic (P<0.002) and acute (P<0.02) asthma patient as compared to control. The results of the present study are consistent with those observed by Pichon et al (17) and Garrard et al (20), who also reported similar results corroborating the fact that sympathetic activity represented by LF (n.u.) component is significantly low in asthmatics as compared to controls.

Pichon et al (17) measured mean absolute L.F. component in test and control group and found it to be 921±1,014 ms² and 1,063±1,121 ms² respectively. The said values do not differ significantly. Fujii et al (21) also could not establish any significant difference in the absolute LF band between the controls and asthmatics. Our results in LF component of HRV expressed either in absolute and normalized units agree with that of the aforesaid authors.

The findings regarding HF component have been reported by Pichon et al (17). The mean absolute HF component as tabled by them was in the range of 243±300 ms² observed in asthmatics, as compared to that in control group (188±405 ms²), the difference of which was not statistically significant. In contrast, the mean HF (n.u.) component of test group was significantly high of the order of 21±21 n.u., while the same for control group was 11±9 n.u.

Ostrowska-Nawarycz et al (22) reported, at resting conditions, a growing tendency for HF component of HRV spectra together with greater intensity of asthma, i.e., with increasing intensity of clinical signs and symptoms of asthma, the HF component of
HRV also increases in magnitude. Their observation showed that in youth group with moderate asthma, the HF component (40.8±14.0 n.u.) at rest was significantly high (P<0.05) than in the age matched control group (30.8±10.7 n.u.). Similar findings were also reported by Fujii et al (21) and Kazuma et al (23).

In the present study, the HF component of HRV spectra, expressed either in absolute or normalized units, was found to be significantly high in asthmatics, which further endorses the fact that an enhanced central vagal tone, as exemplified by high HF index of HRV, is instrumental in the pathogenesis of bronchial asthma.

Our findings regarding mean LF/HF ratio also correlates with that of Pichon et al (17). They reported mean LF/HF ratio in the test group to be 7.8±6.6; while for control group it was 14.5±15.0, which was not significantly different. Fujii et al (21) also documented similar findings in asthmatic and control groups.

Hence, it can be deduced from the above observations that a probable compromised central sympathetic outflow and enhanced vagal tone in asthmatics lead to an imbalance in sympatho-vagal interplay at the periphery and an increased propensity to airway obstruction, an essential feature of bronchial asthma. The fine interplay between sympathetic and the vagus, as exemplified by the measures of HRV in Frequency Domain namely LF, HF (both expressed in absolute and normalized units) & LF/HF ratio, seems to be deranged and further elaboration and validation is needed for HRV to become an effective diagnostic and prognostic clinical indicator in patients of bronchial asthma.

**Conclusion**

The present study delineated a significantly raised central parasympathetic outflow and a concomitant significantly low central sympathetic outflow in asymptomatic asthmatic subjects as compared to that observed in control group. This deranged sympathovagal interplay with vagal dominance at the expense of a decreased sympathetic outflow could be a plausible pathophysiologic mechanism leading to airway obstruction, the hallmark of Bronchial Asthma. Hence, HRV could serve as a potential non-invasive tool in monitoring the patients of bronchial asthma.

**REFERENCES**


