Original Article

Autonomic Function Tests in Prehypertensive Young Adult Males of Uttarakhand Region

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Abstract

Pre-hypertensives are at increased risk for rise in blood pressure and cardiovascular morbidities. Autonomic dysfunction is both a cause and effect of high blood pressure. Considering its serious prognosis the current study was undertaken with an aim to assess autonomic functions in pre-hypertensive young adult males.

Male volunteers of 20-40 years were divided into normotensives (n=44) and clinically healthy pre-hypertensives (n=44). They were subjected to anthropometric measurements, Heart Rate variability (HRV) analysis along with Standard Isometric Handgrip Test (HGT) and Sinus arrhythmia test.

Analysis showed a significant increase in sympathetic activity among prehypertensives characterized by lower rise in DBP (mmHg) in response to HGT: [11.27±3.76 mmHg vs 23.95±6.29 mmHg, (p<0.05)]. Parasympathetic activity was significantly decreased among prehypertensives (HFnu: 30.02±14.43 vs 41.62±14.91, p<0.05); E/I ratio: 1.20±0.10 vs 1.32±0.10, p<0.05). Sympathovagal balance showed prominent sympathetic activity (2.85±1.78 vs 1.75±0.98; (p<0.01) among prehypertensives. Salt intake among prehypertensives was significantly higher than normotensives (21.2±1.2 gm/day vs 9.0±0.5 gm/day: P<0.001).

Conclusion: Autonomic dysfunction is evident in prehypertensives with an enhanced sympathetic activity, decreased parasympathetic activity and an altered sympathovagal balance in prehypertensives, salt intake was found on a higher side. Thus lifestyle changes in the form of balanced diet and moderate exercise may be advised to attenuate the risk progression of prehypertension to hypertension.

Introduction

People suffering from hypertension worldwide are approximately 1 billion and it is responsible for 7.1 million deaths each year. According to WHO,
prehypertension is responsible for approximately 62% of cardiovascular disease (CVD) and 49% of ischemic heart disease (IHD) (1). Thus, WHO along with Joint National Committee (JNC VII) have categorized prehypertensives as individuals with systolic pressure of 120-139 mm Hg and/or a diastolic pressure of 80-89 mm Hg. The aim of this reclassification is to limit the rate of progression of pre hypertension to hypertensive levels (15% in the next 5 years once diagnosed) Individuals in prehypertensive category are at increased risk for rise in blood pressure and sudden coronary death, myocardial infarction, stroke (1). Longitudinal data from Framingham Heart Study (2) have suggested that high normal BP (prehypertension) is associated with a more than twofold increase in relative risk from CVD among prehypertensives as compared to normotensives. Factors identified in this progression included age, weight gain and obesity. Autonomic imbalance and sympathetic overactivity has been consistently reported by a lot of studies which increases vasoconstrictor tone of the systemic vasculature. This will ultimately results in the development of essential hypertension. Few evidences of sympathovagal imbalance in prehypertensives have been reported by G K Pal earlier (3). He also emphasized that male gender, parental history of hypertension and obesity might have a role to play in the genesis of pre-hypertension (4, 5). However, these notions are still less documented in as the precise mechanism elucidating autonomic dysfunction is still unclear. Considering the serious prognosis of pre hypertension, the current study was undertaken in prehypertensive individuals to assess autonomic functions in prehypertensive adult males. As a newly formed hilly state of India with a high salt intake population & rising prevalence of hypertension by recent NHFS-3 (National Family Health Survey-3) survey an additional rationale for identifying factors associated with prehypertensives is to advise them healthcare measures/recommend lifestyle changes (6).

Methods

The clearance from institutional ethical committee was obtained and the study was conducted in the Department of Physiology, Himalayan Institute of Medical Sciences (HIMS), Swami Ram Nagar, Dehradun, over a period of 12 months. It was a cross sectional analytical study conducted on a representative group of residents, employees and students of HIHT University.

The sample size for each group was calculated as 44. The formula for comparing the difference of means between the groups was used with $\alpha=0.05$, power ($\beta$) = 80% and effective size (es) = 0.6 which gives sample size $n=44$ (7). Volunteers (20-40 years) were selected from a representative group of residents, employees and students of HIHT based on the JNC criteria of hypertension (1). They were divided into two groups; Group I (Controls): Normotensive and clinically healthy volunteers, Group II (Cases): Prehypertensive and clinically healthy volunteers. Exclusion criteria was history of diabetes mellitus, endocrine disorders, renal diseases, diagnosed CVD, smokers, alcoholics, obesity, disabled following written informed consent from the subjects for inclusion in the study.

Anthropometric parameters were assessed at the time of entry. Volunteers were subjected to and familiarized with the procedure of all the tests. They were asked to report in the department in the morning between 9:00 am and 10:00 am preferably without heavy meals and a good sleep. Data was collected at the point of entry by data recording questionnaire. Salt intake was calculated as sodium intake by food analysis using a recall method by food frequency questionnaire (8) tailored to the regional dietary habits & grouping was done on basis of similarity profile. Value of Sodium intake was calculated using NIN guidelines (9) in cooked food, salt packet consumed and published recipe for readymade food. Non-invasive techniques (e.g. HRV, handgrip dynamometer) were used to record the variables so as to avoid discomfort or harm to the subjects.

Data acquisition for HRV and Respiratory sinus arrhythmia test was done using window based computerized polygraph i.e. physiopac (PP-8-Medicaid systems; Include Welch’s Periodogram; Spectral Window’s width: 1024; Spectral Window’s overlap: 512; Sampling rate: 1000 samples/sec). Standardized protocol was followed to acquire data for the HRV & Sinus arrhythmia. Volunteers were
instructed to avoid nicotine, caffeine and any kind of physical exercise in the last 24 hours. Recording was done at an ambient temperature of 25°C. Following a rest of 15 minutes, recording of HR was done for 5 minutes for HRV analysis. Heart Rate variability (HRV) parameters of Low frequency (LF) power (nu), High frequency (HF) power (nu) and LF/HF Ratio were then noted. Baseline heart rate and respiration was recorded in sitting position from ECG and stethographic respiratory tracings respectively for 1 minute using computerized polygraph machine. Respiratory sensors consist of strain gauze sensitive to stretch with Velcro straps that are strapped around the chest. It shows expansion and contraction of the chest cage as a rise and fall signal on the screen. The subject was asked to take slow and deep inspiration (5 seconds each) followed by slow and deep expiration (5 seconds each) such that each breathing cycle lasted for 10 seconds. Six such cycles were recorded. E/I ratio i.e. Ratio of average RR interval during expiration to average RR interval during inspiration in six cycles of deep breathing was then calculated from ECG and respiratory tracings (10). Handgrip Dynamometer (PP-105-INCO Ambala) was used for measurement of isometric force and sustained static exercise stimulation. Baseline BP and HR was recorded in sitting position. The subject then held the dynamometer in the non-dominant hand, with the arm by the side of the body. The pointer on the dial of the dynamometer was adjusted at zero and the base rested on the palm. Maximum Voluntary Contraction (MVC) was recorded prior to the test by asking the subject to squeeze the dynamometer with maximum isometric effort, and maintained it for at least 5 seconds. No other body movement was allowed. The subject was then asked to press handgrip dynamometer at 30% of MVC for 3 minutes. The alteration in the BP and HR just before the release of hand grip was taken as the index of response to hand-grip test. Difference in diastolic BP just before release was used for analysis (10).

Data Management & Statistical Analysis: Statistical Analysis was done using SPSS (Statistical Package for the Social Sciences, version 17). The variables analyzed were anthropometric parameters, and autonomic functions. Independent two sample 't' test was used for comparing the means for the above mentioned parameters between the normotensives and pre hypertensives. Pearson correlation was used to study the correlation between the above mentioned parameters. Multiple Linear Regression analysis was done to evaluate the predictor of Resting SBP and DBP after adjusting the effect of age, BMI, LF/HF ratio, E/I ratio and ADBP among prehypertensive.

Results

The study conducted with an aim to assess autonomic functions in prehypertensive adult males found no significant difference when demographic parameters of age, weight, height, BMI and WHR were compared between prehypertensive and normotensive groups. This showed the homogeneity of selection of subjects. The cardiovascular parameters of baseline SBP, baseline DBP, pulse pressure and mean arterial pressure were found significantly low in the normotensive group as compared to prehypertensive groups (p<0.001).

Table I shows comparative demographic, anthropometric and cardiovascular parameters among normotensives & pre hypertensives. No significant difference was observed for demographic and anthropometric parameters between the two groups.
significant decline in E/I Ratio was also observed in prehypertensive (1.20±0.10) when compared with normotensive group (1.32±0.10) (p<0.05). This indicates parasympathetic withdrawal among prehypertensives resulting in an increase in heart rate during expiration and thus shortening of RR interval.

Table III shows Pearson correlation analysis which was done to assess the strength of association of various factors PR, BMI, WHR, SBP, DBP, SI, LF/HF Ratio, E/I Ratio with each other among prehypertensives. Salt intake (SI) was significantly & positively correlated with SBP (r=0.5; P= 0.001), DBP (r=0.63; P<0.001), Pulse Rate (r=0.37 ; P=0.01) among prehypertensive. It was positively related with LF/HF ratio (r=0.22) but relation was not significant (P =0.06). Salt intake was significantly & positively correlated with SBP (r=0.49; P<0.001) & DBP (r=0.63: P=.01) in normotensives. E/I ratio was significantly declined in E/I Ratio was also observed in prehypertensive (1.20±0.10) when compared with normotensive group (1.32±0.10) (p<0.05). This indicates parasympathetic withdrawal among prehypertensives resulting in an increase in heart rate during expiration and thus shortening of RR interval.

In respiratory sinus arrhythmia test, a statistically significant decline in E/I Ratio was also observed in prehypertensive (1.20±0.10) when compared with normotensive group (1.32±0.10) (p<0.05). This indicates parasympathetic withdrawal among prehypertensives resulting in an increase in heart rate during expiration and thus shortening of RR interval.

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### Table II: Autonomic function analysis among normotensives & prehypertensives.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameter</th>
<th>Group I (Normotensives) n=44</th>
<th>Group II (Prehypertensives) n=44</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Low Frequency (LF) Power (nu)</td>
<td>57.3±15.43</td>
<td>66.46±15.10**</td>
</tr>
<tr>
<td>2.</td>
<td>High Frequency (HF) Power (nu)</td>
<td>41.62±14.91</td>
<td>30.02±14.43***</td>
</tr>
<tr>
<td>3.</td>
<td>LF/HF Ratio</td>
<td>1.75±0.98</td>
<td>2.85±1.78***</td>
</tr>
<tr>
<td>4.</td>
<td>Difference in DBP (ΔDBP) (mmHg)</td>
<td>23.95±6.29</td>
<td>11.27±3.76***</td>
</tr>
<tr>
<td>5.</td>
<td>E/I Ratio</td>
<td>1.32±0.10</td>
<td>1.20±0.10***</td>
</tr>
</tbody>
</table>

Data presented as mean±SE; * mark indicates comparison b/w group I & II; *P<0.05; **P<0.01; ***P<0.001, E: Expiration, I: Inspiration.

### Table III: Pearson correlation of BMI, WHR, PR, SBP, DBP, SI, LF/HF Ratio, E/I Ratio with each other among prehypertensives (n=44).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>BMI (Kg/m²)</th>
<th>WHR (Ratio)</th>
<th>PR (Beats/min)</th>
<th>BSBP (mmHg)</th>
<th>BDBP (mmHg)</th>
<th>SI (g/day)</th>
<th>LF/HF Ratio</th>
<th>E/I Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (Kg/m²)</td>
<td>1</td>
<td>r = 0.032</td>
<td>r = 0.230</td>
<td>r = -0.181</td>
<td>r = -0.051</td>
<td>r = -0.111</td>
<td>r = 0.195</td>
<td>r = -0.31*</td>
</tr>
<tr>
<td>WHR (Ratio)</td>
<td>1</td>
<td>r = 0.206</td>
<td>r = 0.013</td>
<td>r = 0.263</td>
<td>r = 0.103</td>
<td>r = -0.123</td>
<td>r = -0.027</td>
<td>r = -0.167</td>
</tr>
<tr>
<td>PR (Beats/min)</td>
<td>1</td>
<td>r = 0.393**</td>
<td>r = 0.546**</td>
<td>r = 0.393**</td>
<td>r = 0.546**</td>
<td>r = 0.378*</td>
<td>r = 0.009</td>
<td>r = -0.253</td>
</tr>
<tr>
<td>BSBP (mmHg)</td>
<td>1</td>
<td>r = 0.824**</td>
<td>r = 0.500**</td>
<td>r = 0.824**</td>
<td>r = 0.500**</td>
<td>r = 0.180</td>
<td>r = -0.079</td>
<td>r = -0.079</td>
</tr>
<tr>
<td>BDBP (mmHg)</td>
<td>1</td>
<td>r = 0.639**</td>
<td>r = 0.223</td>
<td>r = 0.639**</td>
<td>r = 0.223</td>
<td>r = 0.223</td>
<td>r = 0.052</td>
<td>r = -0.052</td>
</tr>
<tr>
<td>Salt Intake (g/day)</td>
<td>1</td>
<td>r = 0.22</td>
<td>r = 0.22</td>
<td>r = 0.22</td>
<td>r = 0.22</td>
<td>r = 0.135</td>
<td>r = 0.031</td>
<td>r = 0.031</td>
</tr>
<tr>
<td>LF/HF Ratio</td>
<td>1</td>
<td>r = 0.02</td>
<td>r = 0.02</td>
<td>r = 0.02</td>
<td>r = 0.02</td>
<td>r = 0.02</td>
<td>r = 0.02</td>
<td>r = 0.02</td>
</tr>
</tbody>
</table>

r = Pearson’s correlation coefficient, *P<0.01; **P<0.001; BMI (Body mass index), WHR (Waist hip ratio), PR (Pulse rate), BSBP (Baseline SBP), BDBP (Baseline DBP), LF/HF (Low frequency/High frequency).
negatively correlated to BMI ($r=-0.31$; $P=0.02$). Pulse rate is also positively related to SBP ($r=0.39$) & DBP ($r=0.54$) and relation is highly significant ($p<0.001$). LF/HF ratio was positively related to salt intake in normotensives and the relation was significant ($r=0.41$; $P=0.003$).

Multiple Regression analysis for DBP & predictors like age, BMI, WHR, salt intake, LF/HF ratio & E/I ratio estimated that age significantly ($p=0.002$) contributed to rise in DBP ($R^2=.31$; $\beta$ coefficient = 0.54). Also LF/HF ratio contributed significantly ($p=0.03$) to rise of DBP($R^2 = 0.56$, $\beta$ coefficient = 0.29) in prehypertensives. Regression analysis for SBP and it’s predictors showed that BMI significantly ($p=0.003$) contributed to rise in SBP ($R^2 = 0.29$; $\beta$ coefficient = 0.55) in prehypertensives.

Discussion

Our study revealed higher levels of weight, BMI and WHR in prehypertensive group as compared to normotensive group. This is in accordance to studies by Bracho. M et al and Kotpalliwar M. K. et al exhibiting weight, BMI, WHR and waist circumference as significant predictors of prehypertension (11, 12, 13). We found a rise of 0.3 mmHg in both SBP and DBP with every 1 kilogram increase in weight which is in concordance with Framingham Study which showed 10% rise in body weight with 7 mmHg rise in SBP (14). Also, every 1 kg excess body weight lost is associated with decreases of 0.3 mmHg and 0.4 mmHg in SBP and DBP, respectively (15). In Egypt, Azza Mohamed Sarry El-Din et al percentages of the hypertensive individuals increased with age and degree of obesity emerged as an important risk factor for hypertension (16).

Autonomic function analysis of our study revealed an increased sympathetic activity and sympathovagal imbalance among pre-hypertensives. G K Pal et al elucidated increased LF and LFnu and LF-HF ratio along with decreased HF and HFnu ($p<0.001$) in prehypertensive subjects (17, 18). In Turkey, similar findings of significantly altered LFnu, HFnu and LF/ HF values were observed by M. TolgaDoðru et al suggesting that subjects with high-normal BP have raised sympathetic activity (increased LFnu) and diminished parasympathetic activity (HFnu), thus are more likely to develop hypertension (19).

Alteration of sympathovagal balance (SVB) is a known fact in prehypertension and LF-HF ratio is a sensitive indicator of SVB. Thus, an increase in LF-HF ratio among prehypertensives was not only due to an increase in sympathetic activity but also due to diminished parasympathetic activity. Furthermore, resting pulse rate was significantly higher in our results among prehypertensives indicating a considerable decrease in vagal tone as lower resting heart rate is a good index of higher parasympathetic activity. Many pathophysiologic mechanisms were proposed to explain the relationship between high blood pressure and sympathetic over activity. One theory by Thornton et al suggested that blunted reflex response of heart rate and lumbar sympathetic nerve activity to volume expansion indicates impaired cardiopulmonary volume receptor function (20). Also, chronic elevation of blood pressure associated with episodic hypoxia and increased peripheral resistance is associated either deficiency of nitric oxide release or production (21).

In our study, a significantly lower $\Delta DBP$ in prehypertensive group showed high baseline SNS activity. To the best of our knowledge we couldn’t find any evidence supporting diminished $\Delta DBP$ among prehypertensives but Ewing DJ et al tracing the natural history of diabetic autonomic neuropathy cited $\Delta DBP$ of less than 10 mmHg during isometric exercise as abnormal (22). The autonomic changes in our results were similar to the aforementioned diabetic autonomic dysfunction. But our findings were in contrast with Pal G K et al which showed a significant increase in $\Delta DBP$ with rise in blood pressure; $p<0.001$ (10).

Our results exhibiting a significant decline in E/I Ratio in pre hypertensives were in accordance with Wu J S et al which found reduced E/I ratio among prehypertensives ($p<0.001$) (23). Similar diminution of E/I ratio ($p<0.001$) among pre hypertensive offspring of hypertensive parents was shown in a study by G K Pal et al (10). Sinus arrhythmia mainly results from spillover of signals from the medullary respiratory center into the adjacent vasomotor center.
causing alternate increase and decrease in the heart rate during inspiratory and expiratory cycles of respiration (18). A decline in parasympathetic vagal activity among pre hypertensives increases heart rate during expiration thus reducing the E/I ratio. We found daily salt intake significantly higher (P<0.001) in prehypertensives. It was higher in quantity than the study conducted in hilly population of Tehri-Garhwal by Saxena P. et al with 22% of hypertensives consuming salt >8 gm/day (24). Mean dietary salt intake in urban south India was 8.5 g/d (25). Cutler JA found an average lowering of 76 mmol/L sodium per day associated with a 1.9/1.1 mm Hg reduction in BP in patients with prehypertension (26). In yet another study adjusted hazard ratios for patients with a high salt diet (≥6 g/d) were 1.57 (95% confidence interval [CI], 1.17-3.31; P=.018) for hypertension. It means pre hypertensives have 57% more chances of landing into hypertension as compared to normotensives (27), Attenuation of functional nephrons with age offset Na+ balance of body causing secondary increase in the blood pressure. High salt intake affects the cortisol metabolism & subsequent vascular changes in normotensive persons may lead to future probability of high blood pressure in them. However dietary salt intake effect on blood pressure may be heterogeneous based on genetic variability in salt sensitivity of individuals.

To summarize, autonomic dysfunction is evident in higher salt intake prehypertensives with an enhanced sympathetic activity, decreased parasympathetic activity and an altered sympathovagal balance as compared to normotensives.

Limitations of our study included use of physiopac (PP-8-Medicaid systems) which has restrained our ability to edit recordings. Results might not be generalized to other parts of the country as sample population exclusively comprised of residents, employees and students of HIHT University representing Uttarakhand region. Thus, weight reduction, deep breathing exercises and HRV biofeedback technique are some of the ways suggested to reduce blood pressure along with lifestyle changes in the form of balanced diet and moderate exercise may be advised to attenuate the risk progression of prehypertension to hypertension.

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References


