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RESEARCH ARTICLE

A comparative study of autonomic reactivity in normotensive and pre-hypertensive young adult Indian males

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ABSTRACT

Background: Hypertension is a non-communicable disease of major concern. Research evidence from both, animal and human studies, indicates that deranged autonomic function may contribute to development and sustenance of hypertension. **Aims and Objectives:** To study the progressive changes in autonomic reactivity, this study was planned to compare autonomic reactivity in normotensives and pre-hypertensives. **Materials and Methods:** A total of 60 (30 normotensives and 30 pre-hypertensive) young adult males participated in this study. Parasympathetic reactivity tests (expiration/inspiration ratio, 30/15 and IV/II ratios) were done using single-channel student physiograph machine. Sympathetic reactivity was tested by cold pressor test and handgrip dynamometry test. **Results:** There was a statistically significant increase in sympathetic reactivity by handgrip dynamometry test in pre-hypertensive participants as compared to normotensive. Furthermore, a decrease in parasympathetic reactivity was found in pre-hypertensives compared to normotensives, although values were not significant statistically. **Conclusion:** As the blood pressure increases, sympathetic reactivity increases while parasympathetic reactivity gradually decreases. These autonomic changes may underlie the development of human hypertension.

KEY WORDS: Autonomic Nervous System; Hypertension; Blood Pressure; Hand Strength; Cold Pressor Test

INTRODUCTION

Hypertension is a non-communicable disease of major concern. It is reported as the fourth cause of premature deaths in industrialized and seventh in unindustrialized countries.[1] Research evidence from both, animal and human studies, indicates that deranged autonomic function may contribute to development and sustenance of hypertension.[2–7] Increasing evidence suggests that increased blood pressure (BP) in young adults might be related with persistent hypertension, and increased cardiovascular disease and death in later life.[8]

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Prehypertension has emerged as a common predisposing factor for hypertension as well as cardiovascular complications.[9] First, in 2003, the term "prehypertension" was explained as systolic BP (SBP) of 120–139 mmHg and/or diastolic BP (DBP) of 80–89 mmHg.[10] The prevalence of such prehypertension is 32.3% in urban India, with males (36%) being significantly more affected than females (28.1%). Prehypertension may progress to clinical hypertension in a relatively short span of time. However, the pathogenesis of this syndrome is still unclear.[11]

Autonomic dysfunction can be both a cause and an effect of raised BP. Pre-hypertensives are at a higher risk of

developing hypertension and cardiovascular complications with subsequent increased morbidity and mortality.[12] Considering the serious outcomes of prehypertension, the present study was planned to evaluate autonomic reactivity in pre-hypertensive Indian males.

MATERIALS AND METHODS

The present study was conducted at the Department of Physiology, Smt. B.K. Shah (SBKS) Medical Institute and Research Center, Sumandeep Vidyapeeth University, Piparia-391760, Waghodia, Gujarat, India. After prior ethical approval from the Institutional Ethics Committee of SBKS MI and RC, a total of 60 undergraduate medical and paramedical students of Sumandeep Vidyapeeth voluntarily participated and were enrolled to this study. Thirty normotensives and 30 pre-hypertensive participants were selected as per JNC VII guidelines[10] using stratified random sampling according to the following criteria:

Inclusion and Exclusion Criteria

Those participants who agreed to give a written informed consent, who were 17–24 years of age, male participants who were right handed (for uniformity), and who were normotensive and pre-hypertensive as per JNC VII guidelines[10] were included in this study. Following were excluded – underweight (body mass index [BMI] <18.5), overweight (BMI >24.99), on any drug treatment that can affect BP or autonomic functions, on any yoga/exercise/diet/other regime, suffering from any metabolic disorder specially, diabetes mellitus and/or thyroid disorder, any cardiovascular or neuropsychiatric disorder, any known illness affecting or involving autonomic nervous system, smokers, and/or alcoholics.

After taking the written informed consent and recording their full particulars, height, weight, and resting BP of each participant were measured using standard protocol.

Resting BP Measurement

Participant was instructed to sit comfortably in a chair, keeping feet on the ground while arms were supported at the heart level, for a minimum of 5 min. SBP and DBP (in mm of mercury) were measured with the help of a mercury sphygmomanometer (PERFECT, India). An average of three such measurements was taken as the resting BP.[10]

BMI

BMI was derived from following formula:[13]

BMI = Weight (in kg)/Height^2 (in m^2)

All the measurements were performed between 9.30 am and 11.00 am in a separate examination room. Subjects were asked to abstain from coffee, tea, or cola for 12 h before the experiment. A light breakfast was allowed 2 h before the study. The temperature of examination room was maintained between 23 and 25°C. They were allowed to adapt the experimental and environmental conditions for 1 h. During that period, detailed history taking and physical examination were performed. The procedure of the tests was elucidated to the participants beforehand and informed consents were taken. The following measurements were carried out in all the subjects:

Resting Heart Rate

The subject was asked to lie comfortably for about 15–20 min. The continuous electrocardiography (ECG) was recorded from standard limb leads for complete 1 min using the single-channel student physiograph machine (INCO, Ambala, India) (paper speed 25 mm/s). The total number of R waves on the recordings in 1 min was counted and taken as resting heart rate.

Mean BP (MBP)

MBP was derived from the following formula: MBP = Diastolic BP + 1/3 Pulse Pressure.

Parasympathetic Reactivity Tests

Heart rate variation with deep breathing (expiration/inspiration ratio [E/I])

The subject was explained about the test properly. Participant was instructed to lie restfully in supine position for 1 min with the ECG limb leads connected to the physiograph machine. During this period, continuous lead-II ECG was recorded. After a verbal command, the subject started to breathe in and out deeply and continuously, six breaths per minute (5 s for inspiration and 5 s for expiration each). The point of beginning of inspiration and point of beginning of expiration were marked on ECG paper.

E/I Ratio = Longest R-R interval while Expiration/Shortest R-R interval while Inspiration

Heart rate variation during supine to standing position (30:15 ratio)

After making the subject lie down in supine position for about 5 min, he/she was instructed to stand up erect as rapidly as possible with the ECG limb leads connected to the physiograph machine. During this period, continuous lead-II ECG was recorded and the time of standing was marked on the recording.

30:15 Ratio = maximum R-R interval about 30th beat during standing/minimum R-R interval about 15th beat during standing

Valsalva ratio (IV/II ratio)

Each subject performed Valsalva maneuver by blowing in a mouth piece that was attached to a mercury manometer (against closed glottis) and maintained a 40 mm Hg pressure for 15 s. Continuous ECG was obtained 1 min before the maneuver (resting period), during maneuver (strain period, for 15 s – Phase II), and 1 min after strain period (Phase IV).

Valsalva Ratio = Longest R-R interval post strain (up to 20 beats)/shortest R-R interval during strain

Sympathetic Reactivity Tests

BP changes to isometric exercise (hand grip test)

Participant was asked to sit comfortably and BP was measured at a few minutes' intervals. Test was started only after consistent BP readings were recorded. Isometric exercise was performed using hand grip dynamometer. First, the subject gripped the dynamometer maximally with their dominant arm (all the subjects were right handed). Three such trials were performed successively and the highest value was recorded as maximum voluntary contraction (MVC. After interval of 5 min, handgrip exercises were again done, but this time sustained steadily by participant at 30% MVC for minimum of 2 min. During this procedure, SBP and DBP were recorded at every 30 s intervals with the help of mercury sphygmomanometer from non-exercising arm. Maximum rise in SBP and DBP was considered as the index of response. After the exercise, the BP was recorded till it came down to normal level.

BP changes to cold stimulation (cold pressor test [CPT])

Participant was asked to sit comfortably and BP was measured at a few minutes' intervals. Test was started only after consistent BP readings were recorded. Participant was then instructed to submerge his hand in a container with ice-cold water. Temperature of water was maintained at 4–6°C throughout the experiment with the help of a mercury thermometer. The SBP and DBP were measured in other arm at 30 s intervals for 2 min period. After 2 min, participant was permitted to take out his hand and a towel was provided for rewarming. Throughout the procedure, participants were reassured over and over again. The maximum increases in the SBP and DBP were recorded as a response to cold stimulation. After the test, BP was recorded till it came down to normal level.

The collected data were entered into MS Excel 2010 and analyzed using SPSS (Statistical Package for the Social Sciences), version 20. The unpaired Student's t-test was used to compare the mean of various parameters between normotensive and pre-hypertensive groups. $P < 0.05$ was considered statistically significant and < 0.01 was considered highly statistically significant.

Table 1: Anthropometric variables of the study participants

Parameter	Normotensive (Mean±SD)	Pre-hypertensive (Mean±SD)	*P* value
Age (years)	18.37±0.81	18.57±0.77	0.33
Weight (kg)	52.65±4.80	53.42±3.79	0.49
Height (meters)	1.58±0.06	1.57±0.05	0.49
BMI (kg/m^2)	21.14±1.49	21.79±1.61	0.11

Unpaired Student's *t*-test

RESULTS

Table 1 shows anthropometric data while Table 2 shows resting cardiovascular variables of study participants. Parasympathetic and sympathetic variables of the study participants are depicted in tables 3 and 4, respectively. Sympathetic reactivity was found to be increased in the pre-hypertensive group [Table 4] as evidenced by SBP reactivity to handgrip dynamometry test ($P < 0.05$). SBP reactivity in

Table 2: Resting cardiovascular variables of the study participants

Parameter	Normotensive (Mean±SD)	Pre-hypertensive (Mean±SD)	*P* value
R-HR (bpm)	76.00±4.76	80.60±5.33	< 0.01
R-SBP (mmHg)	111.47±4.95	121.13±8.48	< 0.01
R-DBP (mmHg)	72.27±3.51	81.27±4.38	< 0.01
R-MBP (mmHg)	85.33±3.50	94.56±3.64	< 0.01

Unpaired Student's *t*-test. R-HR: Resting heart rate, R-SBP: Resting systolic blood pressure, R-DBP: Resting diastolic blood pressure, R-MBP: Resting mean blood pressure

Table 3: Parasympathetic variables of the study participants

Parameter	Normotensive (Mean±SD)	Pre-hypertensive (Mean±SD)	*P* value
E/I ratio	1.59±0.20	1.55±0.18	0.42
30/15 ratio	1.32±0.18	1.27±0.13	0.22
IV/II ratio	1.42±0.32	1.35±0.17	0.29

Unpaired Student's *t*-test

Table 4: Sympathetic variables of the study participants

Parameter (post-test minus pre-test values)	Normotensive (Mean±SD)	Pre-hypertensive (Mean±SD)	*P* value
SR-C (mmHg)	18.07±5.21	20.93±9.77	0.16
DR-C (mmHg)	15.00±5.09	17.33±5.44	0.09
SR-H (mmHg)	17.87±4.20	21.67±9.37	< 0.05
DR-H (mmHg)	14.20±5.47	16.87±5.91	0.07

Unpaired Student's *t*-test. SR-C: Systolic blood pressure reactivity to cold pressor test, DR-C: Diastolic blood pressure reactivity to cold pressor test, SR-H: Systolic blood pressure reactivity to handgrip dynamometry test, DR-H: Diastolic blood pressure reactivity to handgrip dynamometry test

response to CPT, DBP reactivity in response to CPT, and DBP reactivity to handgrip dynamometry test were also increased, however, values were not significant statistically [Table 4]. Parasympathetic reactivity was found to be decreased in the pre-hypertensive group [Table 3], but values were insignificant statistically.

DISCUSSION

There was a progressive decrease in parasympathetic modulation of cardiac autonomic function from normotensive to pre-hypertensive group as evidenced by Table 3 although this finding was statistically insignificant. Similar results were found by Wu *et al*.[13] and Narhare *et al*.[14] This could possibly be due to a hemodynamic shift from normal BP to prehypertension that leads to an increased cardiac output but normal peripheral resistance.[15] Such increase in cardiac output is reported to be associated with elevated sympathetic tone with a decrease in parasympathetic supply to heart.[4,15]

Table 4 shows comparison of sympathetic function tests performed on the study participants. The handgrip exercise increases both BP and heart rate.[16-22] Brorson *et al*.[22] have reported that handgrip exercises at 30% of MVC increase both SBP and DBP in normotensives as well as hypertensives. Aoki *et al*.[23] have reported that handgrip exercise increases BP, especially in borderline hypertensives. We confirmed that handgrip exercise increased BP in both normotensive and pre-hypertensive participants. Many studies indicate a great response of BP pre-hypertensives and borderline hypertensives.[24-27] The great response of arterial strips to vasoactive stimuli in young spontaneously hypertensive rates[28-30] suggests an increased response of the arterial muscles in subjects with essential hypertension.[28,31] Thus, the increased BP found in our study may be due to such great response. CPT produces an increase in BP in healthy individuals.[32-38] In the early period of this test, cardiac output increases with only small rise in sympathetic nerve activity in muscle, but in the late period of the test, an increase this activity increases peripheral resistance.[32,39] Furthermore, pulse pressure rises, mostly in the end.[34] Our results are also in agreement with these findings. We found an increase in BP response to CPT in pre-hypertensives. These findings are in agreement with many previous studies.[38-40] Persons with hypertension have been reported to show greater changes in BP during different types of stress than normotensives.[41] Such hyper reactors to CPT, especially with a sluggish recovery rate, might be more prone to develop essential hypertension in later life.[42] Zbrozyna *et al*.[43] suggested that as young hypertensives are unable to habituate to persistent renal vasoconstriction in response to cold pressure test, they show exaggerated rise in BP during CPT. Thus, there was a progressive increase in sympathetic autonomic function from normotensive to pre-hypertensive group.

Limitations and Directions for Future Research

Ours was a cross-sectional study, and hence, its findings require confirmation by a longitudinal follow-up study. Data collection was done mainly by physiograph, but computerized instruments (e.g., Powerlab) could have generated more reliable data. Family history of hypertension was not taken into consideration which may affect the autonomic function status of participants. Gender role was not taken into consideration in this study as we studied only male participants. Autonomic functions may vary amongst males and females.[44] Similar study on a larger sample size can be more informative.

CONCLUSION

As the BP increases, sympathetic reactivity increases while parasympathetic reactivity gradually decreases. These autonomic changes may underlie the development of human hypertension.

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