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Original Article

Study on Cardiovascular Autonomic Function Tests on Young Healthy Males and Females

Anirban Bhowmick[1], Kaushik Samajdar[2], Arup Bandyopadhyay[3]

[1]Assistant Professor, Department of Physiology, MGM Medical College, Kishanganj, Bihar, India, [2]Professor and Head, Department of Physiology, North Bengal Medical College, Siliguri, West Bengal, India, [3]Professor and Head, Department of Physiology, MGM Medical College, Kishanganj, Bihar, India

Abstract

Background: Autonomic neuropathy is a common complication of several systemic disorders like diabetes mellitus. To combat that its early detection is essential. However, to understand the pathophysiological states, there should first be a standardization of these values in normal healthy adult people, and our venture in this study is prompted by this need. We have also deliberately used multiple simple tests without using any costly equipment keeping in mind the large poor community of crores in developing countries and more so in a rural and semi-urban base in India.

Materials and Methods: Heart rate (HR) and blood pressure (BP) responses in the following situations were noted as cardiovascular function tests: Supine position, at rest, standing position from supine, tilted supine position (head up tilt), valsalva maneuver, isometric exercise, and cold pressor test. The parameters recorded were HR, systolic BP (SBP), diastolic BP (DBP), and mean arterial BP (MABP). Before doing each test time was given for the physiological parameters such as BP and HR to come to the basal value.

Results: The results show that the mean ± standard deviation for mean blood pressure and HR changes in head up test 0.785 ± 5.32 and 0.267 ± 4.997, respectively, in males and 0.267 ± 3.976 and 0.450 ± 5.349, respectively, in females. Vasoconstrictor reserve 3.67 ± 2.844 in males and 1.78 ± 1.993 in females. SBP rise and DBP rise during cold exposure test 2.844 ± 5.262 and 1.552 ± 4.629, respectively, in males and 0.450 ± 3.445 and −0.225 ± 3.238, respectively, in females. While the valsalva ratio (VR) was highly significant and SBP, DBP rise during cold exposure was significant. VR 1.241 ± 0.067 in males and 1.119 ± 0.039 in females was highly significant. Tachycardia ratio 1.266 ± 0.071 in males and 1.144 ± 0.044 in females was highly significant. Standing BP and HR from supine position 0.1185 ± 3.746 and 1.600 ± 3.563, respectively, in males was significant and 2.429 ± 3.213 and 1.794 ± 3.853, respectively, in females was not significant ($P > 0.05$ means statistically not significant, $P < 0.05$ significant and $P < 0.01$ highly significant).

Conclusion: We have prepared through our study standardized normal values of various data related to autonomic functions among healthy young adults in eastern India. It is seen from this study that parasympathetic responses showed that maximum responses were more in case of males. Sympathetic responses showed that maximum responses were more in males and in some cases more in females. Studies involving larger population should be employed with sophisticated methods of analysis of HR variability and with more specific tests to validate our observations.

Key words: Cardiovascular autonomic function tests, Cold pressor tests, Vasoconstrictor reserve, Valsalva ratio, Tachycardia ratio

INTRODUCTION

The term autonomic nervous system (ANS) was coined by Langley a century ago.[1] It was meant for controlling most of the visceral activities which were involuntary and could not be easily modified, hence called "autonomic." It maintains internal homeostasis by regulating cardiovascular, thermoregulatory, gastrointestinal, genitourinary, exocrine, and pupillary functions.[2]

ANS can be studied noninvasively and reproducibly by a battery of well-accepted autonomic function tests. In general, the tests are designed to assess cardiovagal, adrenergic and sudomotor functions.[3,4]

In this study, it is tried to evaluate the cardiovascular autonomic functions and their correlations, if any in

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Corresponding Author: Arup Bandyopadhyay, Department of Physiology, MGM Medical College, Kishanganj, Bihar, India.
Email: Arupbanerjee1953@gmail.com

healthy young males and females in basal states as well as in physiological stressful conditions.

MATERIALS AND METHODS

Materials and methods used in the study were as follows.

Study Setting and Design

This was an institutional cross-sectional study which was conducted in the Department of Physiology, North Bengal Medical College and Hospital (NBMCH), West Bengal, India.

Study Duration

This was studied over a period of 1 year starting from April 2013 to April 2014.

Study Population

A total of 85 students in the 1st year MBBS class of NBMCH, West Bengal, India, were studied after taking proper informed consent from them.

Sampling Design

The 1st year students were divided into two groups, i.e., males and females. Then from each group, students were taken as per inclusion and exclusion criteria.

Inclusion Criteria

Students in the 1st year MBBS class both males and females of NBMCH were included in our study after taking history followed by doing a general examination.

Exclusion Criteria

Any students found having major past or any existing cardiovascular or neurological illness, history of taking any long-term medication or having any addiction were excluded from the study. Female students during bleeding phase of menstrual cycle were also excluded.

Parameters Studied

Heart rate (HR) and blood pressure (BP) responses in the following situations were noted as cardiovascular function tests:

1. Supine position, at rest,
2. Standing position from supine,
3. Tilted supine position (head up tilt),
4. Valsalva maneuver,
5. Isometric exercise,
6. Cold pressor test.

Study Tools

This consists of standard clinical tools including:

a. Electrocardiography (ECG) machine (BPL, CARDIART 108T DIGI),
b. Mercury sphygmomanometer,
c. Stethoscope,
d. Tilt table,
e. Ice and cold water,
f. Thermometer,
g. Dynamometer.

Method of Study

Permission was taken at first from the principal and ethics committee, NBMCH.

Collection of Data

Every volunteer was explained about the purpose and procedure of the study, and a written consent was taken from each one of them. They were made familiar with equipment and instructed to discontinue the test if they faced any discomfort and report immediately. The tests were done after a light breakfast in the morning.

Procedure Employed

The parameters recorded were HR, systolic BP (SBP), diastolic BP (DBP), and mean arterial BP (MABP). Before doing each test time was given for the physiological parameters such as BP and HR to come to the basal value.

Supine position

Keeping the patient fully relaxed in supine position for 10-20 min, radial pulse rate was counted for 1 min with simultaneous auscultation of heart sounds to get the resting HR and also by doing ECG (counting the R-R interval in ECG). Basal BP was measured in this condition by palpatory and auscultatory method.

Standing position

From the supine position, with the BP cuff and the ECG monitor attached the patient was instructed to stand up abruptly. Within 15 s of standing, HR and BP were recorded. The measurements repeated after 1 min, 2 min, and 3 min time. The mean HR was calculated as the average of the longest and shortest R-R interval.

Tilted supine position (response to head-up tilt)

The subject was placed supine over the tilt table for 10 min and after that with the ECG leads and BP cuff connected, the head end of the table was inclined upward to an angle of 70° with horizontal plane.[5] The immediate response of HR and BP was noted.

Valsalva maneuver

It is a test done to assess the low and high-pressure baroreceptor integrity. Changes in the arterial BP and HR were noted to assess the response to valsalva maneuver.

The subject was instructed properly before the procedure. Then, with continuous ECG monitoring, the subject was asked to exhale forcefully for about 15-20 s against resistance of 40 mmHg in an open loop system. The BP of each subject was measured during the Valsalva maneuver and also immediately after that. The continuous ECG was taken 1 min before (resting period), during the procedure (15 s, strain period), and 1 min subsequent to strain period. The VR, the ratio of the maximum R-R interval during expiratory phase (Phase II) to the minimum R-R interval during the relaxation phase (Phase IV, within 20 beats) was calculated. The tachycardia ratio (TR) was also calculated.

VR = Longest R-R interval after Valsalva/shortest R-R interval during Valsalva

TR = Shortest R-R interval during Valsalva/longest R-R interval after Valsalva

Isometric exercise

During sustained isometric exercise the BP increases due to increase in peripheral resistance and also increases in cardiac output (CO). The subject was instructed to perform hand grip in a dynamometer giving as much pressure as he/she could apply for 3-4 s which was maximum voluntary contraction. Then, he/she was instructed for a sustained hand grip exercise maintaining a pressure of 30% of maximal activity for 1 min with that dynamometer.[21] The shortest R-R interval during the exercise and the longest R-R interval while relaxed (within 5 beats) are determined. The change in DBP from the basal value was recorded. Vasoconstrictor reserve was calculated then.

Vasoconstrictor reserve = (Maximum diastolic pressure at the end of 1 min of sustained isometric hand grip–baseline diastolic pressure)

It evaluates mainly the sympathetic function.

Cold pressor test

After proper instructions, the subject was asked to submerge one of the upper limbs in very cold water (at or below 4°C) in a container for 60 s. The BP and HR were recorded at 30 s, 60 s, 90 s, and 120 s of submersion of the limb.

Plunging the limb in cold water raises the BP reflex by stimulation of the sympathetic system.

Statistical Analysis

- Statistical analysis was performed using statistical software 'SPSS version 16.0' (SPSS Corp, Chicago, IL, USA).
- Comparison among males and females form their basal state to various stressful conditions were tested using paired *t*-test while comparison of similar tests between two genders was done using unpaired *t*-test.

RESULTS

Results of our study are given in the following charts (Tables 1 and 2) and diagrams (Figures 1-3).

DISCUSSION

Among the various functions done by ANS, one of the most important fields is its effect on chorionic villus sampling (CVS). There are also different effects of it on CVS between the genders. Clinical and experimental evidence suggest that gender difference has a significant influence on the ANS activities including that on the CVS. Gender difference in the incidence and clinical course of a range of CVS responses such as BP, CO, HR, and other variables are also well recognized. Studies of Huikuri *et al.* have shown that females have decreased baroreceptor responsiveness as compared to males. Furthermore, hormone replacement therapy has got favorable effect on baroreceptor responsiveness suggesting that hormonal factors may have some role in autonomic modulation.[6] Baroreflex sensitivity is decreased in women as compared with men, but tonic vagal regulation

Table 1: Comparative study of sympathetic functions on the sample

Parameters	Mean±SD		*P* value	Significance
	Males	Females		
Head up tilt test				
MBP	0.785±5.32	0.267±3.976	0.616	Not significant
HR	0.267±4.997	0.450±5.349	0.871	Not significant
Vasoconstrictor reserve	3.67±2.844	1.78±1.993	0.001	Highly significant
Cold exposure test				
SBP rise	2.844±5.262	0.450±3.445	0.016	Significant
DBP rise	1.522±4.629	−0.225±3.238	0.050	Significant

SD: Standard deviation, MBP: Mean blood pressure, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 2: Comparative study of parasympathetic functions on the sample

Parameters	Mean±SD		*P* value	Significance
	Males	Females		
VR	1.241±0.067	1.119±0.039	0.000	Highly significant
TR	1.266±0.071	1.144±0.044	0.000	Highly significant
Standing BP	0.1185±3.746	2.429±3.213	0.003	Significant
Standing HR	1.600±3.563	1.794±3.853	0.810	Not significant

VR: Valsalva ratio, SD: Standard deviation, BP: Blood pressure, HR: Heart rate, TR: Tachycardia ratio

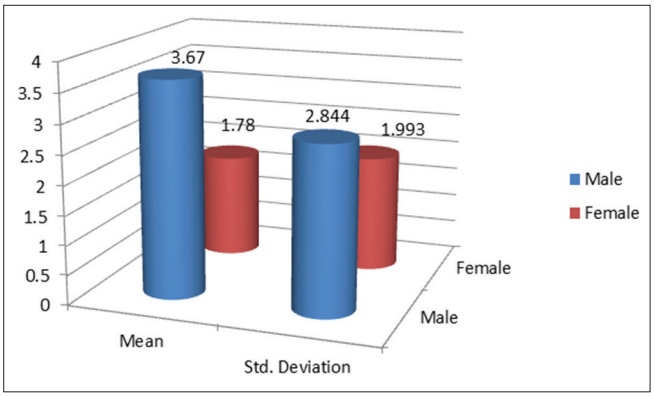

Figure 1: Comparison of the vasoconstrictor reserve of males and females during isometric exercise testing

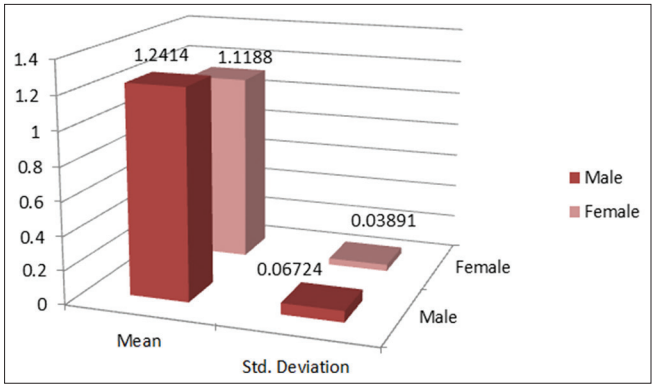

Figure 2: Comparison of valsalva ratio among genders

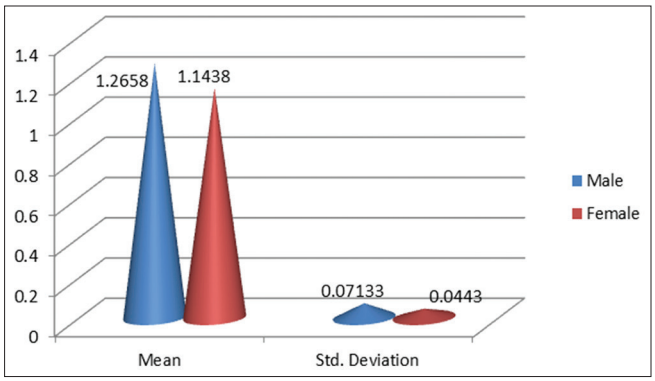

Figure 3: Comparison of tachycardia ratio among genders

of HR is augmented. Baroreflex sensitivity and HR variability are higher in postmenopausal women who are on estrogen replacement therapy compared with those without therapy suggesting that hormonal factors may partly explain the sex-related differences in autonomic modulation of HR.[7]

Outcome after myocardial infarction is worse for women than men[8-10] while women with nonischemic cardiomyopathy have improved survival. In addition, to the well-known difference in age of presentation of coronary heart disease women are more likely to suffer from Raynaud's phenomenon and to experience presyncopal and syncopal episodes.[11,12]

In this study, we found mean blood pressure (MBP) decreased during standing in both genders (though the decrement was more in females) while the HR increased in both genders (increment more in females). In the study, the decrease in BP was significant in females ($P < 0.03$) but increase in HR was not significant in females ($P > 0.05$).

In a study conducted by Narhare *et al.*, decrease in MBP was more in male during standing posture from supine state.[22]

In this study during isometric exercise test, done by a hand grip dynamometer it was found that there was less vasoconstrictor reserve in case of females than their male counterparts. Moreover, the difference was of significant value ($P < 0.01$).

A similar study was conducted by Pramanik and Singh showed that in the normal persons SBP and DBP increased after 1 min of handgrip test. However, the rise in SBP in females was not significant. In females with occasional postural hypotension, the vasoconstrictor reserve was significantly less ($P < 0.05$) than in the control females. Result indicated less reserve in females compared to their male counterparts.[13] The study corroborates our observations.

In another study from Amritsar,[14] sympathetic activity was compared by galvanic skin resistance (GSR), cold pressor response, and handgrip test. Result showed SBP and DBP rise was more in the case of males in all age groups than female counterparts during handgrip test. However, the results were statistically insignificant.

In still another study by Mehta *et al.*[15] hand grip response showed that the rise in SBP was more in case of males ($P < 0.5$) and DBP rise was more in case of females ($P < 0.01$).

In a study in 1993 in Finland[16] on males and females it was observed that the HR response to the Valsalva maneuver was greater in females of more than 50 years age than males of same age. The DBP response to isometric handgrip was higher in males of <50 years age than females of same age.

During an upright tilt, or for that matter while standing, a person's cardiovascular system has to adjust itself to prevent a significant portion of the blood volume from pooling in the legs. These adjustments consist of an increase in DBP, MBP and HR, and peripheral vascular resistance which is mainly due to increase sympathetic outflow by the effect of baroreflex activation due to

pooling and redistribution of blood from the upper and to the lower part of the body (central hypovolemia) resulting in a reflex tachycardia and vasoconstriction to maintain a normal BP.[17-19] When a normal individual is placed in an upright tilt, these cardiovascular adjustments occur very quickly, and there is no significant drop in the BP.

The study also showed that MBP was more in males and HR was more in females during head-up tilt to 60° though the differences were not significant among genders as evident from ($P > 0.05$).

In a study by Yesar *et al.* BP, CO, HR, and ECG vascular resistance were measured. All measurements were 1st done in supine position and then at 60° head up tilt table. Result showed a significant difference between the two sexes in both age groups.[20]

Under condition of stress of either physical or psychological origin, there is activation of sympathetic NS. The cold pressor response, which consists of placing the hand in cold water as painful stimulus, is used to study the autonomic response of different individuals.

In this study, it was found that SBP arose both in case of males and females and DBP arose in case of males only while there was fall in DBP in the case of females during cold exposure test from basal state. The comparison of SBP rise in between genders was statistically significant ($P = 0.016$). Comparison of DBP change from basal value between genders was also of significant difference ($P < 0.05$).

The fall in DBP in the case of females during cold exposure test can't be explained, and a more number of studies are required to corroborate the findings.

A more number of studies with more sophisticated approach are required to corroborate our findings.

CONCLUSION

We have prepared through our study standardized normal values of various data related to autonomic functions among healthy young adults in eastern India. It is seen from this study that:

- Parasympathetic responses showed that maximum responses were more in case of males
- Sympathetic responses showed that maximum responses were more in males and in some cases more in females.

Studies involving larger population should be employed with sophisticated methods of analysis of HRV and with more specific tests to validate our observations.

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