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A Comparative Study on Cardiovascular Autonomic Function Tests Indices between Young Healthy Males and Females

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Abstract: Several earlier tudies have reported that gender influences cardiovascular autonomic reactivity among adult. So present study was initiated and an attempt was made to bring out the association of autonomic functions with gender. This study was carried out in 50 male and 50 female subjects of western Rajasthan, between the age group of 18 and 30 year at Department of Physiology, Dr. S. N. Medical College, Jodhpur, Rajasthan using CAN*Win*, a window based cardiac autonomic neuropathy analysis system with interpretation. Each of the participants performed 4 parasympathetic function test and 2 sympathetic test total six noninvasive cardiovascular autonomic function tests in series after excluding the systemic diseases by clinical evaluation. The parasympathetic activity of ANS was compared by resting heart rate, 30:15 ratio, E:I ratio and valsalva maneuver. Sympathetic activity was compared by blood pressure response to standing and blood pressure response to sustained handgrip exercise(SHG).The result on comparison of various autonomic function tests amongst males and females in same age group suggested that the parasympathetic activity is higher in females as evident from E:I ratio(statistically highly significant) and while sympathetic activity is higher in males as evident from blood pressure response to standing and blood pressure response to sustained handgrip exercise (statistically significant p-value).
Keywords: Autonomic Nervous System (ANS),CAN*Win*,Resting Heart Rate,30:15 Ratio,E:I Ratio,Valsalva Maneuver, Blood Pressure Response To Standing And Sustained Hand Grip (SHG).

INTRODUCTION

In 1920, Walter Canon said that the autonomic nervous system was essential to maintain the balance of the organism; he defined this process as “homeostasis.”.We know that that the autonomic nervous system is an important neuromodulator of the cardiovascular and metabolic systems in humans. The autonomic nervous system allows the central nervous system to maintain homeostasis in the context of both acute and chronic changes in physiological and pathological states. The ANS is divided into sympathetic and parasympathetic nervous system that operates independently, but interacts reciprocally to regulate the organ functions. The sympathetic system is referred to as “flight or fight” system while parasympathetic is considered as “feed or breed” system[1].

Cardiovascular disease is recognized to show an increasing gender specific characteristic. There is a gender difference in terms of etiology, pathogenesis, clinical manifestations and outcomes of cardiovascular diseases[2].Various studies based on gender differences have revealed that men are generally at a greater risk for cardiovascular and renal disease than are age-matched, premenopausal women. Gender differences in the autonomic nervous system may be present because of developmental differences or due to the effects of prevailing levels of male and/ or female sex hormones [3,4]. The cardiovascular responses of blood pressure, cardiac output, heart rate and other variables to change in posture differ between the sexes. The reason of difference is due to greater decrease of thoracic blood volume with standing in female than the male. The overall complexity of heart rate dynamics is higher in women than men.

To our knowledge, only a few publications reports on gender-related differences in cardiac autonomic tone; also. women have a lower cardiovascular risk. The data on this aspect was lacking in this part of the country, so the present study was conducted to compare the autonomic nervous system activity in adult males and females.

MATERIALS AND METHODS

A total of 100 healthy young adults (50 males and 50 females) were included in this study with age range from 18 to 30 years. The study was conducted in the Department of Physiology at Dr.S.N.Medical College, Jodhpur. The approval of the Ethical Committee was obtained. The nonsmoker, nonalcoholic, non-diabetic, having normal pulse rate, blood pressure, and normal heart sounds and having no evidence of illness and having perfect physical, mental and psychological wellbeing were included in the study. A brief history was taken and general physical examination of all the volunteers was done with main emphasis on cardiovascular diseases, renal diseases. None of the subjects took any medication at the time of study. All the tests were carried out between 11 am to 4 pm. The procedure was explained and informed consent was obtained after the subjects had read a description of the experimental protocol.

Autonomic function tests by can win method

Tests of predominantly parasympathetic function

- Resting Heart Rate
- Heart Rate variation during deep breathing (Expiration /Inspiration ratio) :

Complex reflexes are responsible for normal beat -to- beat variation. Respiration is most important stimulus and change in depth and rate of respiration alters normal beat -to-beat variation .During period of deep breathing, there is characteristic heart rate variability seen as an increase in heart rate with inspiration due to inhibition of cardiac vagal motor discharge.

Stimulus - Deep & regular breathing at the rate of 6 breaths per minute
Afferents – Central
Efferents - Parasympathetic (Cardiovagal, Cholinergic)
Normal response - Initially increase in heart rate with inspiration & decrease in heart rate with expiration

While recording ECG, the subjects were asked to inhale deeply for 5 seconds followed by exhalation for 5 seconds at a rate of 6 breaths per minute. The ratio between longest R-R interval during expiration and shortest R-R interval during inspiration (E/I ratio) in each respiratory cycle is calculated for evaluation[5].

Values of E: I Ratio [6]:-

- Normal ≥ 1.21
- Borderline 1.20-1.110
- Abnormal ≤ 1.10
- Heart rate response to standing (30 :15 ratio)

Stimulus - Change of posture from lying to standing
Afferents - Baroreceptors & Cranial nerve ninth and tenth
Efferents - Sympathetic (adrenergic), Parasympathetic (Cardiovagal, Cholinergic)
Normal response - Initially increase in heart rate followed by decrease in heart rate

The subject was instructed to lie down comfortably and ECG was recorded to calculate the heart rate .Then the subject was instructed to stand up within 3-4 seconds and remained motionless thereafter. The 30:15 is the ratio of longest R-R interval at beat 30 during inspiration/expiration cycle and the shortest R-R interval at beat 15 after standing. It examines the integrity of the efferent parasympathetic branch.

Value of 30:15 ratio [6]:-

- Normal ≥ 1.04
- Borderline 1.03-1.01
- Abnormal ≤ 1.00

- **Heart rate response to Valsalva maneuver (VM ratio)**

The test is used most frequently because it allows evaluation of the entire reflex arc. The subject is asked to blow out or to expire forcefully through a mouthpiece attached to the sphygmomanometer to maintain the pressure at about 40 mm of Hg for 15 seconds. The ECG is recorded simultaneously during this maneuver and 15 seconds afterwards to see the RR interval changes.

The valsalva ratio = Longest R-R interval after maneuver (after the strain)/ shortest R-R interval during maneuver (during the strain).

Stimulus - Forced expiration through open glottis
Afferents - Baroreceptors & Cranial nerve ninth and tenth
Efferents - Sympathetic (adrenergic),Parasympathetic (Cardiovagal, Cholinergic)
Normal response- When forced respiration started there is increase in BP and decrease in HR, later with continuous strain there is decrease in BP and increase in HR, On releasing of respiratory strain there is decrease in BP. after that there is increase in BP and decrease in HR.

The normal valsalva ratio is [6,7,8]:-

- Normal ≥1.21
- Abnormal ≤1.21

Table - Normal, borderline, and abnormal values of cardiovascular autonomic tests

B. Test of predominantly sympathetic function

- **Blood - pressure response to standing**

The BP of the subject was recorded at lying down and again when the subject stands up from supine position.

Stimulus - Change of posture from lying to standing
Afferents - Baroreceptors & Cranial nerve ninth and tenth
Efferents - Sympathetic (adrenergic),Parasympathetic (Cardiovagal, Cholinergic)
Normal response - Initially increase in heart rate followed by decrease in heart rate and fall in blood-pressure.

In normal subjects systolic BP does not fall by more than 10 mm Hg and in autonomic dysfunction it falls by >20-30 mm Hg. Orthostatic hypotension was defined as a fall of ≥20 mm Hg in systolic and /or ≥ 10 mm Hg in diastolic BP from lying to standing position[9].

Values of orthostatic fall in systolic BP:-

- Normal ≤10 mmHg
- Borderline 11-29 mmHg
- Abnormal ≥30 mmHg

- **Blood –pressure response to Sustained Handgrip (SHG)**

This test studies the blood pressure response to an isometric handgrip exercise. Initially the subject was asked to exert maximal hand grip strength on hand grip dynamometer with dominant hand. First the maximum voluntary contraction (MVC) (MAXIMAL ISOMETRIC TENSION i.e. T_{max}) is determined and then the subjects were asked to press the handgrip dynamometer for at 30% of maximal voluntary effort. The BP was recorded in contralateral arm and rise in diastolic BP was measured.

Stimulus - Isometric exercise
Afferents-Myelinated Mechanosensitive & unmyelinated chemosensitive afferent from muscles
Efferents - Sympathetic (adrenergic)
Normal response - Increase in systolic & diastolic BP, increase in heart rate

Value of Rise in Diastolic BP after sustained handgrip exercise [Ewing and Clarke grading][10]:-

- Normal ≥16 mmHg
- Borderline 11-15 mmHg
- Abnormal <10 mmHg

Analysis of data

Collected data were entered in computer based Microsoft Excel sheet. Comparisons were done by applying Student's't' test.

RESULTS

Table-1: Comparative study of parasympathetic function tests between males and females

PARAMETER	MALE		FEMALE		P -VALUE
	MEAN	S.D.	MEAN	S.D.	
RHR	76.58	9.06	78.84	10.34	0.35 (S)
E:I RATIO	1.27	0.23	1.35	0.43	0.00002(HS)
30:15 RATIO	1.14	0.24	1.02	0.26	0.57 (S)
VALSALVA	2.27	1.15	2.01	1.37	0.22 (S)

Table-2: Comparative study of Sympathetic function tests between males and females

PARAMETER	MALE		FEMALE		P- VALUE
	MEAN	S.D.	MEAN	S.D.	
FALL IN SBP	3.6	7.47	2.06	10.14	0.034 (S)
RISE IN DBP	12.9	7.92	9.9	13.1	0.00059(HS)

DISCUSSION

The present comparative study was carried out in 50 healthy males and 50 healthy females between age group of 18-30 years. Evaluation of status of autonomic nervous system was done with the help of five non-invasive cardiovascular reflex test : 4 parasympathetic tests including resting heart rate , heart rate response to deep breathing, heart rate response to standing and valsalva maneuver; and 2 sympathetic tests consisting of blood pressure response to standing and sustained hand grip (SHG). Work done over the past few years gives us an indication of effect of gender on the

autonomic nervous system activity. The data on this aspect was lacking in this part of the country, so the present study was conducted to measure the autonomic nervous system activity in adult males and females.

In our study, parasympathetic function tests(Table no. 1) showed mean value for the resting heart rate and E:I ratio is higher in females than males and mean value of 30:15 ratio and valsalva ratio is higher in males as compared to females subjects. But statically data of only E:I ratio is significant , thus indicating more parasympathetic activity present in females.

So our results of females having more parasympathetic activity than males as evident in' our study was consistent with the studies carried out by Evan JM *et al*. [11], Antelmi *et al*. [12] and Piha SJ *et al*. [13] *et al*. Evan JM *et al*. [11] suggested that men had greater sympathetic activity whereas women had parasympathetic dominance. In a study in 1993 in Finland on males and females by Piha S J *et al.* [13], it was observed that the heart rate response to the Valsalva maneuver was greater in females of more than 50 years age than males of same age. The above results of high parasympathetic activity in females are not consistent with the studies carried out in this field by Cowan *et al*. Ramaekers *et al.* [15] and Sinnreich *et al*. [16].

In our study ,sympathetic function test- blood pressure to standing and blood pressure response to sustained handgrip exercise are more in male as compared to female subjects and on statical analysis both sympathetic tests shows significant p value 0.034 and 0.00059 respectively.

Our results of males having more sympathetic activity than females as evident in' our study was consistent with the studies carried out by Cowan *et al*. [14], Ramaekers *et al*. [15], Sinnreich *et al*. [16]. Various other studies by Larsen JA *et al*. [17], Thom T *et al*. [18], Benjamin *et al*. [19], Minson *et al*. [20] have also observed that females display lower sympathetic activity and increased cardiac vagal modulation which could reflect the lower incidence of arrhythmias, high blood pressure and sudden cardiac death compared to males. Ewing DJ *et al*. [10] described a smaller rise in diastolic blood pressure (DBP) following isometric exercise in women when compared with their men counterpart and Piha SJ *et al*. [13] in his study observed that diastolic blood pressure (DBP) response to isometric handgrip was higher in males of <50 years age than females of same age suggesting of more sympathetic activity in males. In another study, it has been observed that the difference between men and women in response to sustained handgrip was due to higher level of vasoconstrictive reserve and sympathetic flow in men during isometric exercises [21]. Our results are not in agreement with Hari Prasad *et al*. [22], in his study he observed more parasympathetic activity in male and more sympathetic activity in female subject.

CONCLUSION

So from the above discussion it is concluded that on comparison of various autonomic function tests among males and females in same age group it was found that the parasympathetic activity is higher in females as evident from E:I ratio , while sympathetic activity is higher in males as evident from blood pressure response to sustained handgrip and blood pressure response to standing. Since high sympathetic activity and low parasympathetic activity, are associated with cardiovascular disease morbidity and mortality, the favorable autonomic profile seen in women may be related to their delayed onset of cardiovascular disease and increased longevity compared with men. The exact mechanisms that are responsible for these findings have to be elucidated by further research because of the limited sample size.

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