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### Original Article

#### Influence of age on female cardiovascular autonomic sympathetic function tests

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#### ABSTRACT:

Assessment of sympathetic function is an important non-invasive investigation in medical practice. This study aimed at assessing the effects of age and on sympathetic function test indices. Two non-invasive cardiovascular autonomic function tests were carried out by CANWin Analysis System in 75 healthy female subjects between the age group of 20 to 70 years and divided into five groups, each comprises of 15 subjects. Assessment of sympathetic activity is done by systolic blood pressure (SBP) response to standing test and diastolic blood pressure (DBP) response to sustained handgrip exercise. In our study only blood pressure response to sustained handgrip test shows statically significant result and shows that with increase in age there is decline in sympathetic functions. From this study it may concluded that ageing process substantially impaired cardiovascular sympathetic activity. So evaluation of autonomic status in elderly is important factor for determining the treatment planning and drug action in the elderly in whom there may be impaired responsiveness to autonomic reflexes and receptor sensitivity.

**Key words:** Sympathetic function, CANWin analysis system, cardiovascular autonomic function tests, Systolic blood pressure (SBP), Diastolic blood pressure (DBP).

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#### INTRODUCTION

Sympathetic nervous system activity is related to situations where metabolic exertion is needed, for example physical activity or mental / physical exertion at work. Sympathetic activity also increases due to some external stimuli or fear. On activation sympathetic system shows "fight or flight" – reaction (a situation where life is threatened by some external disturbance): heart rate, blood pressure and adrenal gland hormone excretion are increased, blood flow is directed away from internal organs to the skeletal muscle, and pupils are dilated. All these changes aim for the individual to be able to cope with the physical stress situation in the best way possible.

Aging is known to alter the neurohormonal mechanisms that control the cardiovascular system. Ageing is a natural process, everyone in the world has to face problems associated with increasing age. As with advancing age the capacity of every system of human body declines.[1] The

capacity of sympathetic nervous system i.e. capacity of fight or flight response also decline. In other words with increasing age capability of a person to face stress decreases, which leads to increased susceptibility for cardiovascular events like MI, stroke etc. Published reports have an increase in sympathetic activity in the heart and vascular system with aging.[2]

Work done over the past few years gives us an indication of effect of ageing on the sympathetic nervous system activity so a formal study was planned to be carried out which involved a battery of autonomic tests to be done on females of different age groups. The changes were noticed in some parameter of sympathetic function tests during comparison between different age group.

#### MATERIAL AND METHODS

Present study was conducted on 75 healthy females with in age range from 20 to 70 years at the Department of

Physiology , Dr.S.N.Medical College, Jodhpur. Females were divided into 5 groups, each one of them included 15 female subjects.

- Group A : Subject with 20-30 yrs
- Group B : Subject with 31-40 yrs
- Group C : Subject with 41-50 yrs
- Group D : Subject with 51-60 yrs
- Group E : Subject with 61-70 yrs age range.

The approval of the Ethical Committee was obtained. The non smoker, non alcoholic, non diabetic, having normal pulse rate, blood pressure, normal heart sounds and having no evidence of illness and having perfect physical, mental and psychological well being were included in the study. The procedure was explained and informed consent was obtained after the subjects had read a description of the experimental protocol.

**Inclusion criteria**

Only healthy female subjects of age group of 20 to 60 years and average body mass index of Indian origin were included in the study.

**Exclusion criteria**

1. Haemoglobin < 10 gm %
2. Pregnancy
3. Disease interfering with the autonomic functions including diabetes mellitus, renal and liver disease.
4. Cardiovascular diseases including hypertension, ischemic heart disease and congestive heart failure.
5. Neurological diseases including multiple sclerosis, polyneuropathy or Guillain Barre syndrome.
6. Drugs that interfere with the autonomic functions including anti-hypertensives, diuretics, adrenergic drugs, anti-arrhythmics, sedatives, hypnotics and anti-epileptic drugs.

**Test of predominantly sympathetic function:-**

**1. 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. 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  $\geq 20$  mm Hg in systolic and /or  $\geq 10$  mm Hg in diastolic BP from lying to standing position.[3]

Values of orthostatic fall in systolic BP:-

- a) Normal  $\leq 10$  mmHg
- b) Borderline 11-29 mmHg
- c) Abnormal  $\geq 30$  mmHg

|   |
|---|
| 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. |

**2. 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][4]:-

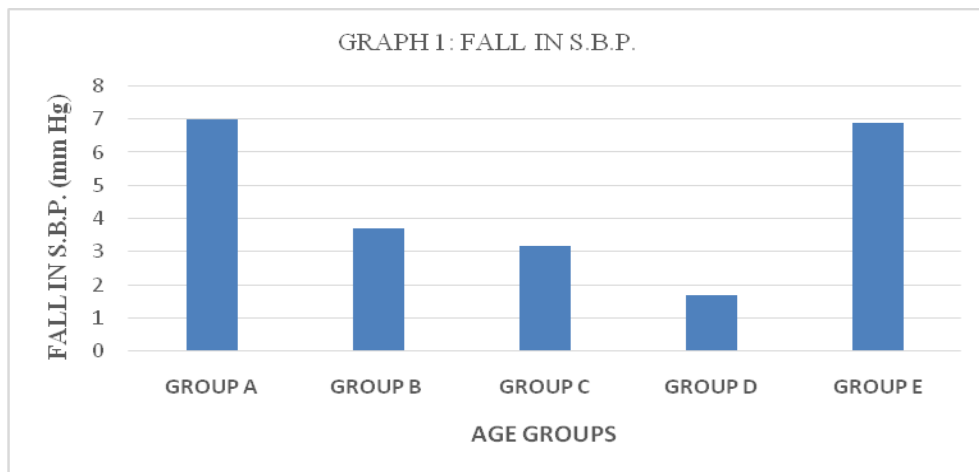
- a) Normal  $\geq 16$  mmHg
- b) Borderline 11-15 mmHg
- c) Abnormal <10 mmHg

**RESULTS**

**Table 1: COMPARISON OF ORTHOSTATIC FALL IN SYSTOLIC BLOOD PRESSURE IN RESPONSE TO STANDING AMONG DIFFERENT GROUPS**

| Age (in years) | Mean (SBP mmHg) | SD    | P value |
|----------------|-----------------|-------|---------|
| 20-30          | 7.00            | 5.68  | 0.27    |
| 31-40          | 3.70            | 4.32  |         |
| 41-50          | 3.20            | 3.85  |         |
| 51-60          | 1.7             | 7.32  |         |
| 61-70          | 6.9             | 14.09 |         |

All values expressed as mean & SD; with non significant p value(>0.05 ).

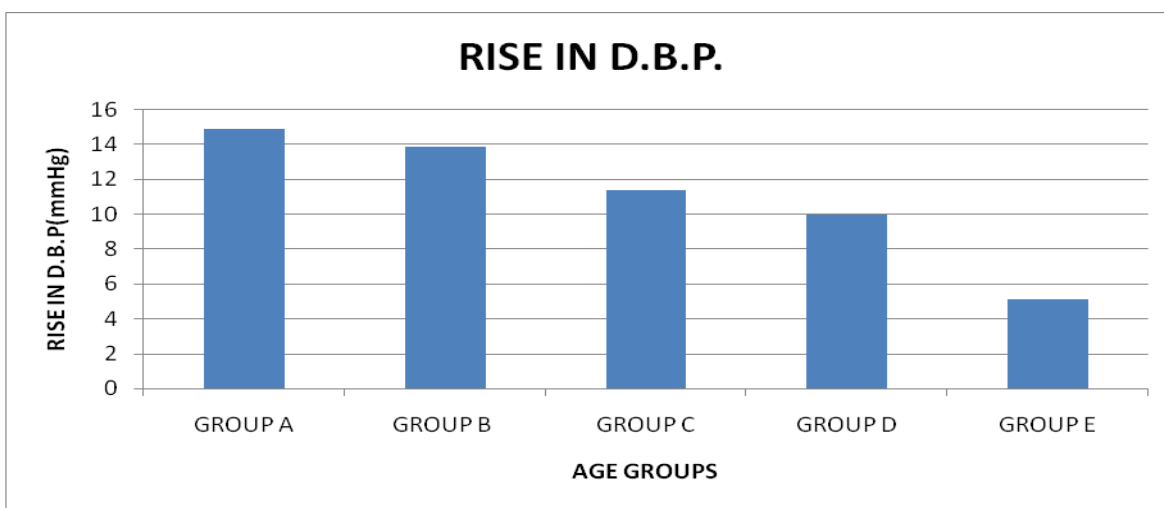


Graph no 1 shows comparison of orthostatic fall in systolic blood pressure among different groups.

TABLE 2: COMPARISON OF RISE IN DIASTOLIC BLOOD PRESSURE IN RESPONSE TO SUSTAINED HANDGRIP EXERCISE TEST AMONG DIFFERENT GROUPS

| Age (in years) | Mean (SBP mmHg) | SD    | P value |
|----------------|-----------------|-------|---------|
| 20-30          | 14.9            | 6.79  | 0.0069  |
| 31-40          | 13.90           | 6.38  |         |
| 41-50          | 11.40           | 10.31 |         |
| 51-60          | 10              | 6.55  |         |
| 61-70          | 5.1             | 7.37  |         |

All values expressed as mean & SD; with significant p value (<0.05).



Graph no. 2 shows comparison of rise in DBP after sustained hand grip (SHG) among different groups.

**DISCUSSION**

The present study was carried out in 75 healthy female subjects in the age range of 20-70 years, to assess the influence of age on sympathetic nervous function. The subjects were distributed into five age groups. Total 15 subjects (20%) were included in each group. Evaluation of status of sympathetic nervous system was done with the help of a non-invasive device, Cardiac Autonomic Neuropathy Analysis System, 'CAN Win'.

With change of posture from supine to standing the autonomic nervous system acts to produce a rise in heart rate and vasoconstriction in order to maintain blood pressure. Vasoconstriction is mediated through sympathetic innervations to blood vessels during standing.[3,5]. Blood pressure response to standing was evaluated in all the subjects. The values in various age groups for fall in systolic blood pressure on orthostatic test are shown in table no.1 and represented by graph no.1. Our study shows that there is

decrease in blood pressure response to standing with increase in age as value from age group of Group A ( $7.0 \pm 5.68$ ) years to Group D ( $1.7 \pm 7.32$ ) years age group and rise in SBP value from Group D ( $1.7 \pm 7.32$ ) to Group E ( $6.9 \pm 14.2$ ) is evident from table no.1. But result of blood pressure response to standing with ageing shows statically non significant result ( $p$  value  $> 0.05$ ). Chu TS et al [6] observed that age is correlated positively with fall in systolic blood pressure in women not in men. Sheila R et al [7] observed greater fall in systolic blood pressure on orthostatic stress in women. They attributed this to low sympathetic activity and low plasma norepinephrine concentration in women at rest and on orthostatic stress. Increase in systolic blood pressure is common in elderly postmenopausal women and is due to increased arterial stiffness resulting in decreased vascular compliance [8]. In blood pressure response to sustained hand grip test there is an increase in both heart rate and blood pressure. The cardio vascular responses to isometric exercise are mediated partially by the influence of cardio vascular centers and partially by metabolic or mechanical changes or both, in response to contraction of muscle that activates small fibers in the afferent limb of the reflex arc. The response is a rise in diastolic pressure,  $> 15$  mm of Hg and rise in the heart rate by about 30%. The blood pressure rise is due to increased sympathetic activity, heart rate rise is due to decreased parasympathetic activity [9]. Our study shows that DBP response to sustained handgrip exercise ratio decreases with age as mean of DBP response to sustained handgrip exercise in 20-30 yrs age group was  $14.9 \pm 6.79$  which decreases up to  $5.1 \pm 7.37$  in 60-70 yrs age group. But greater fall in DBP response to sustained handgrip exercise was evident between Group D (mean  $10.00 \pm 6.55$ ) & Group E (mean  $5.1 \pm 7.37$ ). Thus, sympathetic function as assessed by sustained handgrip exercise, was reduced significantly in subjects above 60 years indicating, late onset of decline in sympathetic efficiency in normal subjects, with advancing age. The results of our study are significant, ( $p$ -value  $< 0.05$ ). In our study the diastolic blood pressure response to sustained hand grip was significantly lower in postmenopausal elderly females. This is due to lower absolute muscle tension, desensitization of  $\alpha$  adrenoreceptors and decreased  $\beta$ adrenergic responsiveness in cardiovascular system [10].

Some Previous studies on sympathetic function test are- Gauschy et al [11] and Vaz M, et al [12] concluded that sympathetic function remains unchanged with increasing age but some others (Romero- Vecchione E, et al [13]) found bimodal pattern in change in sympathetic status with age i.e. increase from young to middle age and then decline towards older age group. On the other hand in a recent study by Dogru MT et al [14]) ,concluded that there is varied response in change in sympathetic parameters with age (Increase, decrease or unchanged. Weitz et al [15] have shown that the activity of sympathetic nervous system

shows gender specific differences with lower sympathoneural activity to the muscle vascular bed in women, as compared with men, with this difference vanishing after menopause

Matsukawa et al [16] have studied sympathetic nerve activity in males and females in relation to static exercise and in relation to age respectively and observed that sympathetic neural outflow is less in women as compared with men and that muscle sympathetic nerve activity increases with age in women and men that the activity is markedly lower in young women than in men, but is markedly accelerated with age. Our study also shows increased sympathetic activity in postmenopausal women. Chu TS et al [6] and Age Link NW [17] also found reduced sympathetic response in females as compared to males. While they did not find any sex related variation with respect to parasympathetic function. Kaijser & Sachs et al [18] found greater decrease in DBP above 60 yrs subjects. Our results differ with earlier studies done by Vita G et al ([19], J Gert Van Dijk [20], S J Piha et al [21], Zeigler D et al [22] and Neumann & Schmid et al [23] in that they did not observe any significant decline in blood pressure response to sustained handgrip with advancing age.

## CONCLUSION

In conclusion, among females population, age significantly affected diastolic blood pressure to sustained hand grip and increasing age has an important role in declining sympathetic autonomic functions. So in multiple of chronic diseases and in managing geriatric problems, the autonomic status of the subject and rate of its decline should be considered.

## LIMITATIONS OF STUDY

1. As we were not using facilities of Heart Rate Variability (HRV) analysis in our autonomic function lab, which could be a better choice to measure sympathetic status.
2. The effect of gender on the sympathetic status can also be included.

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