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Original Article

Physiology Section

Age Related Changes in Autonomic Functions

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ABSTRACT

Introduction: Autonomic Nervous System (ANS) imbalance may trigger or enhance pathology in different organ systems that varies in different age groups hence objective of present study was to evaluate association of different Age-groups with autonomic functions.

Materials and Methods: A cross-sectional study was conducted in 62 healthy volunteers in Department of Physiology LLRM Medical College Meerut, India. Volunteers were divided into three groups as younger (15-45 years), middle (45-60) and elder age (above 60), Autonomic functions were tested in three domains viz. Cardio-vagal, adrenergic and sudomotor functions. Numerical data was summarized as mean and standard deviation and categorical data as count and percentage. ANOVA and Chi-square test were used to find difference among groups, p<0.05 was considered statistically significant.

Results: Mean ± standard deviation OHT(Orthostatic Hypotension Test) among of younger, middle and elder age groups were 8.80±2.28, 13.40±4.64 and 21.82±6.04 respectively which represent decrease in sympathetic functions with age (p<0.001). Cardio-vagal or parasympathetic responses indicated by DBT (Deep Breathing Test) Valsalva and 30:15 ratio of HR response to standing tests has shown statistically significant (p<0.001) decrease in mean response with increasing age. Sudomotor response appeared normal in younger and middle group but was interrupted in more than half of elderly people (p<0.001).

Conclusion: Sympathetic responses & para-sympathetic responses have shown the significant decline with increasing age group. Sudomotor responses were partially interrupted in elderly age group.

Keywords: Adrenergic and sudomotor functions, Ageing, Autonomic functions, Cardio-vagal, Different age groups

INTRODUCTION

The Autonomic Nervous System (ANS) is the part of the nervous system that is responsible for maintaining homeostasis along with Endocrine and Immunological systems [1]. The ANS is of vital importance in daily life. Its regulatory action occurs without involvement of one's conscious i.e. autonomously. The central autonomic network like insular cortex, hypothalamus, Amygdala, periaqueductal grey matter, Nucleus tractus- solitarius and Ventro-lateral medulla regulates different body functions like respiratory, cardiovascular, digestive, endocrine with many other functions through brain structures [2,3].

Disorders of ANS were described in multiple and diverse diseases [4,5] that may be primary or secondary to other disorders, originates from peripheral and central nervous system which means it can directly afflict the nervous system as well as other organs where they can trigger or enhance pathological symptoms.

Chronic diseases like diabetes mellitus, hypertension and arthritis are on increase worldwide and their association has been seen with ANS. Normal human ageing is also associated with changes in the autonomic functions. The two limbs sympathetic and parasympathetic and sudomotor functions of autonomic nervous system mature with time but degree of the changes due to ageing are different because of their divergent neural pathways. Age has been considered as one of the important confounding variable for cardiac autonomic function [6,7].

American association of neurology says autonomic testing is incomplete without the assessment of all three functional domains: Sudomotor, Cardio-vagal and adrenergic [8,9]. There have been many studies on the association of ageing with ANS assessed by conventional cardiac autonomic functions method but literature is quite scarce when we tried to find out the studies in which all the three domains of autonomic assessment got evaluated in different age groups of both sexes [10]. The present study evaluated all the three domains i.e. cardio-vagal, adrenergic and sudomotor of ANS to find out the association of ageing with ANS that may help to understand pattern of autonomic dysfunction in chronic diseases with ageing.

MATERIALS AND METHODS

Study Design and Setting: A cross-sectional study was conducted in Physiology department of LLRM Medical College Meerut. The study protocol was approved by Ethics Committee of the Institute.

Sample size calculation: Sample size was calculated to compute mean difference in three groups by using one-way ANOVA with power of 80%, significance level alpha at 0.05 and effect size of 0.40. Calculated sample size was 22 in each group, thus total sample size is required 66.

Participants: The healthy care takers of Medicine OPD patients were invited to participate in the study. 100 healthy volunteers of both sexes falling between age group of 25-80 consented and they were invited to Physiology department for further screening.

Inclusion and Exclusion Criteria: Subjects with history of hypertension, diabetes mellitus, arthritis and other chronic diseases like tuberculosis were excluded out. Subjects identified with symptoms of cardiac Autonomic.

Neuropathy (CAN) that include: exercise intolerance, postural weakness, faintness, palpiation and symptoms suggestive of orthostatic hypotension e.g. dizziness, visual impairment, and syncope) were excluded.

History of current medications used by the subjects was taken, Steroids intake or any other drugs that can affect ANS were excluded.

Female subjects: The Menstruating female subjects participated were recruited during mid- follicular phase of their menstrual cycle.

Out of 100 volunteers, 12 did not turn up and 26 were excluded because of their high body mass index (BMI> 25). Hence finally 62 healthy volunteers were recruited in this study. Procedure- The participants were screened out after taking detailed medical history, clinical examination and were segregated into three age groups. Group A: Younger group (25-45 years)-20 participants, Group B: Middle (46-60 years.)-20participants, and Group C: Older (60-80 years.)-22 participants. Recruited participants were explained about the nature of study and written informed consent was obtained. All the tests were conducted in the morning after overnight fasting. A standardized protocol was applied to all tests i.e. the study was performed when the participant had no acute illness for the previous two days, unaccustomed vigorous exercise for previous 24 hour, no intake of food, tobacco and caffeine for 8 hour [11]. Each test was performed under thermo-neutral conditions except Sudomotor domain. The study subjects were asked to laid down for about 30 min in a quiet room and subjects were seemed to be emotionally stable & relax before autonomic testing.

Autonomic testing was divided into the assessment of three functional domains: Sudomotor (assessed by spoon test clinically), An Ewing's battery [12] of non-invasive Sympathetic and parasympathetic tests were performed to cover cardio vagal and adrenergic responses.

Cardio vagal (assessed by the Valsalva ratio and heart rate response to deep breathing or standing up), and adrenergic (assessed by the blood pressure response to the Valsalva maneuver) [12-14].

Resting HR (RHR) - Was determined making the subject laid down for 10 min & recorded with help of an automatic ECG recording machine (ASPEN) for one minute. Rate in excess of 100 and below 60 beats /min was considered abnormal.

HR variation (HRV) with deep breathing: subjects were asked to breathe deeply and evenly at 6 breaths/min in supine position. The ECG was recorded during the procedure. The mean difference of the maximum-minimum HR was calculated.

HR response to Valsalva manoeuvre: Subjects were asked to strain for at least 15 s. The ECG was continuously recorded during the procedure and for the following 60s. The Valsalva ratio was calculated during straining as the ratio between longest mean RR intervals to the shortest mean RR interval.

The 30:15 ratio of HR response to standing: The subjects were made to stand up as immediately as possible after lying down for 5-7 minutes. ECG was recorded immediately and continued over a period of 60 s. The 30:15 ratios (the mean ratio between the RR interval of 30th beat and the l5th beat) were estimated.

Blood pressure response to standing: Blood pressure was measured using an automatic B.P machine which was calibrated against a standard mercury sphygmomanometer. Subjects were made to stand from lying position after relaxation of 5 minutes. B.P was measured immediately after the patient stood up and at 1, 2 and 3 min intervals there after the average of the three readings was taken the difference between the average of systolic & diastolic reading at rest and after standing was measured.

Isometric Handgrip Test (HGT): Before starting manoeuvre the baseline BP was recorded. The subjects were asked to perform isometric exercise by pressing the handgrip dynamometer (Inco) at 30% of maximum voluntary contraction for 2 minutes. The blood pressure was recorded simultaneously from non-exercising arm at 1st and 2nd minute and measured after releasing of grip and recording was continued till 4th minute. Highest increase in diastolic blood pressure was taken as test response.

Sudomotor functions [15] were assessed clinically by Bed side spoon Test at normal room temperature and humidity because of unavailability and cumbersome of considered ideal Thermoregulatory and QSART method.

Kitchen soup spoon was placed on skin with its curved portion and was drawn slowly without lifting up and measured its flow whether interrupted, smooth or slightly un interrupted that measures degree of moistness of skin.

STATISTICAL ANALYSIS

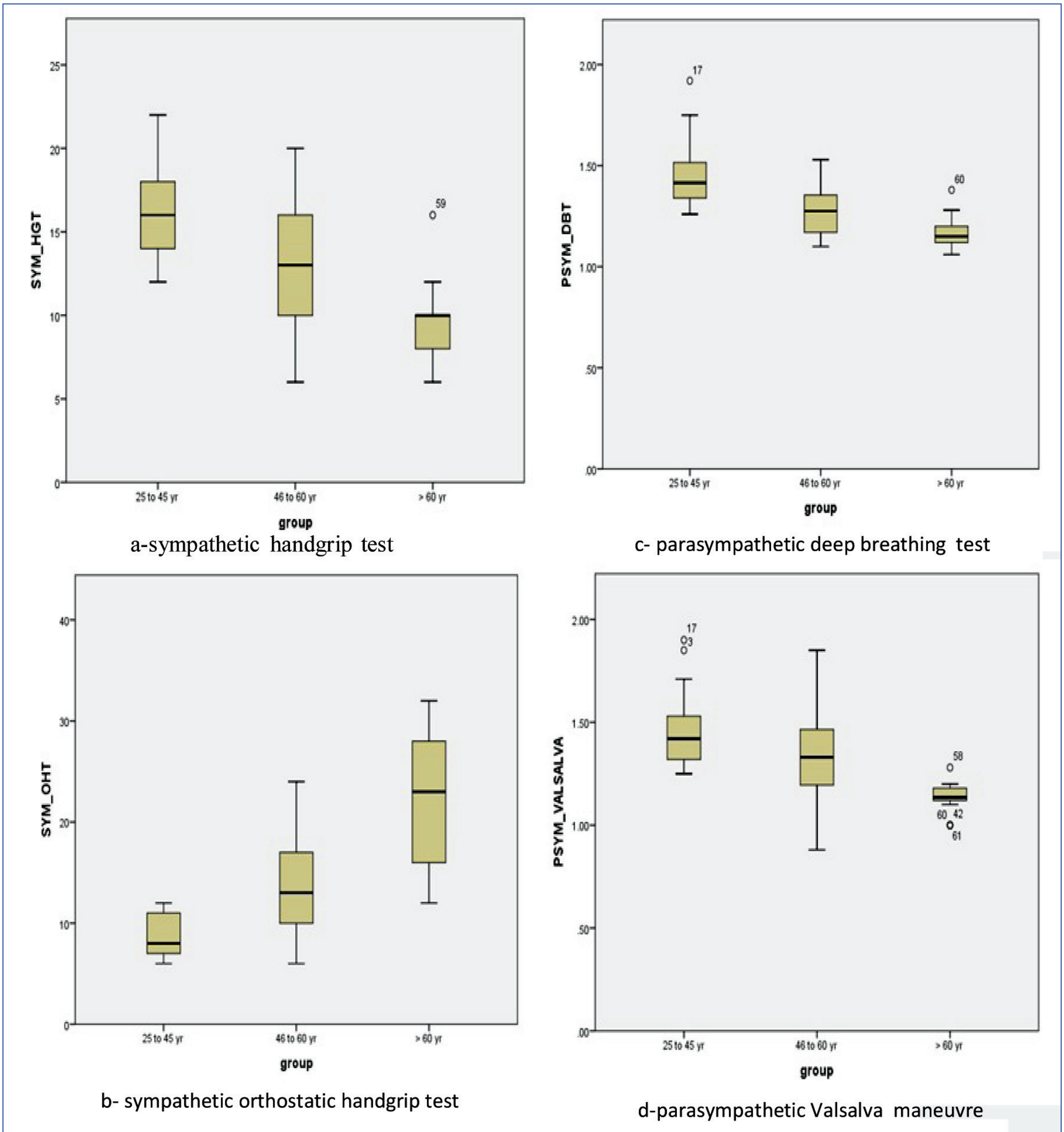
All analyses were conducted by using IBM-SPSS 21 software. Numerical data was summarized as mean and standard deviation and categorical data as count and percentage. ANOVA with Post-hoc Bonferroni test was used for pair wise comparisons and Chi-square test were used to find difference among groups, p<0.05 was considered statistically significant.

RESULTS

[Table/Fig-1] is revealing the mean values of BMI, Pulse rate, and Systolic and Diastolic Blood Pressure and shows comparison of parasympathetic and sympathetic response among three groups. Distribution of BMI was similar in all the three groups. Mean pulse rate was higher in elderly i.e. Group C than that of Group A & B. SBP was significantly lower in younger age group i.e. Group A than other groups. Similarly DBP was significantly lower in younger age group i.e. Group A than other groups It can be observed that mean levels of blood pressure response in terms of HGT (Hand Grip Test) and OHT (Orthostatic Hypotension Test) increases as age advances and this change reflects decline in sympathetic response which was statistically significant. Similarly

	25 to 45 years		46 to 60 years		> 60 years		ANOVA	Post-hoc (Bonferroni Test)		
	(A)		(B)		(C)		p-value			
Variable	Mean	SD	Mean	SD	Mean	SD		A*B	A*C	B*C
Height	1.62	0.12	1.64	0.09	1.61	0.12	0.705	1.000	1.000	1.000
Weight	57.15	8.88	56.30	10.18	54.05	7.17	0.497	1.000	0.771	1.000
BMI	21.85	3.62	21.04	2.88	21.26	2.77	0.696	1.000	1.000	1.000
Pulse(/min)	79.50	7.70	79.85	8.92	87.14	9.76	0.010	1.000	0.021	0.030
SBP(mmHg)	118.70	8.71	127.50	7.65	131.27	8.15	<0.001	0.004	<0.001	0.425
DBP 9mmHg)	77.20	5.04	81.30	6.33	82.00	5.27	0.016	0.070	0.210	1.000
SYM_HGT	16.50	2.82	13.40	3.90	9.36	2.34	<0.001	0.007	<0.001	<0.001
SYM_OHT	8.80	2.28	13.40	4.64	21.82	6.04	<0.001	0.080	<0.001	<0.001
PSYM_DBT	1.46	0.17	1.28	0.12	1.16	0.08	<0.001	<0.001	<0.001	0.009
PSYM3015RATIO	1.29	0.23	1.06	0.06	1.00	0.03	<0.001	<0.001	<0.001	0.463
PSYM_VALSALVA	1.47	0.19	1.35	0.22	1.14	0.07	<0.001	0.087	<0.001	<0.001

[Table/Fig-1]: Age wise distribution of study variables among three groups.
Sympathetic and Parasympathetic tests and baseline parameters with Anova suggesting significant decline with increasing age
P≤0.05 considered as significant



[Table/Fig-2a-d]: Box plot showing decline in different sympathetic and parasympathetic functions with increasing age group

mean levels of parasympathetic response in terms of DBT, Valsalva and 30:15 ratio decreases as age advances and this change was also statistically significant [Table/Fig-1,2].

Sudomotor function was slightly interrupted in more than one third of elderly patients. This was statistically significant, however test needs to be interpreted with caution as 4 cells contained zero value [Table/Fig-3].

Sudomotor function	25 to 45 years N (%)	46 to 60 years N (%)	>60 years N (%)	Chi-square Test (p-value)
Slightly Interrupted	0 (0.0)	0 (0.0)	14 (63.6)	<0.001
Normal i.e. interrupted	20 (100.0)	20 (100.0)	0 (0.0)	
Un interrupted	0 (0.0)	0 (0.0)	8 (36.4)	

[Table/Fig-3]: Age group wise distribution of sudomotor function assessed by clinical spoon test.
Interruption is decreasing in elder age group suggesting significant decline among sudomotor functions as age increases.

DISCUSSION

The Autonomic Nervous System (ANS) is involved in virtually every aspect of our daily life. It is a known fact that proper balance between sympathetic and parasympathetic status is necessary for proper functioning of most of the visceral organs especially cardiovascular system [1-3]. Not only that Thayer and Lane et al., & Critchley stated that ANS signals modulates homeostatic reactions to meet the metabolic demands of motor, emotional, and cognitive challenges [2,16]. A chronic disease usually begins with changes in autonomic functions or vice versa and its dysfunction can lead to morbidity and mortality in chronic diseases which may get worsened with age. Vita G et al., suggested the age related decrease response in autonomic functions in 1986 [17] that is proved as well by newer studies done with help of heart rate variability method but Non-invasive cardiac autonomic functions tests i.e. 'Ewing's battery, tests revealed varied responses for e.g. Chu TS et al., revealed varied response during evaluation of cardiovascular autonomic function tests in normal subjects [12] while dr. Phillip A et al., stated that Cardio-vagal function gets impaired but postganglionic sympathetic function is little affected by age, suggesting selectivity of effects of ageing on autonomic function [18]. Similarly some research workers (Snyder dl et al., and Vaz M et al., concluded that sympathetic function remains unchanged with increasing age [19,20] but on other side (Romero-Vecchione et al.,) found atypical pattern among changes in sympathetic functions with age i.e. increase from young to middle age and then decline towards group older age [21]. On the other hand in a recent studies in world-wide science organisations among sympathetic neural responses, such as studies of Qi Fu et al., [22].

It was concluded that there is varied response among change in sympathetic parameters with age (Increase, decrease or unchanged). That needs further exploration of age related changes in cardiac autonomic functions tests.

According to American neurology academy and study suggested by Jaradeh SS et al., that autonomic functions should be evaluated in all the three domains cardio vagal, adrenergic and sudomotor functions [9]. However, very few age related data on autonomic functions is available with controversial findings or with use of technique touching one domain alone such as HRV [18-21].

Findings in our study suggested that there is significant reduction in cardio vagal (best assessed by heart response to standing, deep breathing & Valsalva manoeuvre), $p<0.001$, adrenergic (best assessed by Blood pressure response to isometric hand grip test, immediate standing & blood pressure response to valsalva maneuvere) $p<0.001$ among all the three groups. Variation in heart rate response to deep breathing and valsalva manoeuvre proves impaired vagal control of heart rate with increasing age.

Sudo-motor functions said to be best assessed by. Thermore-gulatory & QSART that evaluates sympathetic cholinergic responses reflect about the status of distal small fibres, instead of using lengthy, cumbersome costly method in a developing country sudomotor functions were assessed in our study by simple bedside clinical method i.e. spoon test (Tsementzis SA & Hitchcock ER et al.,) [15]. Results in our study suggested normal sudomotor functions in all groups except mild derangement was found in some individuals of older age group which were statistically significant. Similar pattern was seen in studies of Age-related reductions by Yukishita et al., suggested that changing position from supine to standing may trigger dizziness more frequently with ageing reflect the diminished cardiovascular sympathetic modulations and significant decline in overall autonomic functions of men in their thirties more than women as a result of their decrease in physical strength [23].

Similarly the recovery of heart rate after exercise becomes blunted with age as a result of sluggish cardiac vagal response to adjust the cardiac activity, Thus with the findings of our study it may be suggested that by slowing down the decline in sympathetic status we can delay the appearance of many geriatric complaints. Regular meditation [24,25] or aerobic exercise may be a tool to arrest the persistent decrease in sympathetic status with age. Common following observations may prove it peoples doing regular meditation like different types of yoga asana or any other type of meditation show delayed appearance of geriatric symptoms like orthostatic hypotension, constipation etc. i In older humans, aerobic exercises lowers heart rate at rest and plasma catecholamines and found to improves left ventricular performance during peak exercise [26].

Thus it may be suggested that subjects having better autonomic control may have decreased incidence of cardiovascular chronic diseases like hypertension, angina etc. and also emergencies like stroke, myocardial infarction etc. So in multiple of chronic diseases & in managing geriatric problems, the autonomic status of the subject and rate of its decline may be useful.

LIMITATIONS

However, the influence of gender on age-related autonomic changes and its modulation by regular exercises or yoga can be studied further.

CONCLUSION

Hence based on the results of above study it is concluded that increasing age has an important role in declining 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.

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