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Age Related Changes in Autonomic Functions

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KEYWORDS :

1.INTRODUCTION:

The population in the age group of 60 years and above is increasing more rapidly than the population as a whole. Greying population is one of the most significant characteristics of twentieth century. WHO in 1972 reported that number one priority should be the 'care of aging' and declared 1999 as the international year of the elderly with the slogan – "Active aging makes the difference"[1].

As age increases, degenerative changes occur in the tissues leading to decline in their function. The decline in various functions continues slowly and eventually becomes considerable & functionally significant as age advances. Thus physiologically aging refers to impaired ability to maintain homeostasis in the face of external or internal challenges or stresses [2]. As a result, the individual becomes more vulnerable to these challenges & stresses and may finally succumb to one of these.

Since the exact reason of aging is not known different theories have come forward. These different theories can be combined in two groups. According to the first group, aging is the cumulative result of random cell damage which goes throughout life. While the other group considers aging to be inevitable result of genetic programming.

Different theories of aging include (1) the error catastrophe theory, (2) the somatic mutation theory, (3) free radical theory, (4) changes in telomere with aging and (5) genetic theory [3,4]. Major age related changes in various systems include: hemopoietic marrow is gradually replaced by fatty marrow, which is first seen in long bones; cell mediated and antibody responses are diminished resulting in susceptibility to infection [2]. There is increase in T-cell auto-reactivity & autoantibody titre making person susceptible to autoimmune diseases; with advancing age, alveoli become shallower & flatter, the alveolar wall gets thinner whereas capillary blood vessels show increase in wall thickness. The total lung compliance is reduced by the age of 60 years; the myocardium of the elderly shows atrophy accompanied by deposition of brown pigment lipofusin. It shows fibrotic & amyloid deposits. Structural changes also occur in valves; dysphagia occurs due to weakness of pharyngeal musculature and abnormal relaxation of cricopharyngeal muscle. In stomach there is age related mucosal atrophy. In small intestine there is reduced villus height leading to reduced absorption. Liver and pancreas also show degenerative changes; weight of kidneys decreases due to reduction in number and size of nephrons and increased interstitial connective tissues; the functional activity of thyroid gland decreases with age. Also there is decrease in glucose tolerance with aging due to diminished sensitivity of tissues to insulin. The effect of age on reproductive hormones is most consistent; with aging there is neuronal loss and varying degrees of atrophy of brain cells. Also there is accumulation of lipofucin, degenerative changes in vasanervorum, loss of synapses and dendrites. The neurotransmitter system is impaired.

The aim of the present study is to therefore planned to study sympathetic and parasympathetic function tests in normal subjects, to compare the results of autonomic function tests in different age groups and to find out the relationship of autonomic function tests if any with advancing age and to compare the results of autonomic function tests in males and females.

2. MATERIALS AND METHODS

This study was carried out in 220 subjects. The subjects selected were in the age range of 21 to 80 years. The distribution of males and females in different age groups is shown in Table No.1.

The subjects were randomly selected from the general population of Kurnool city. Informed consent was obtained from each subject. The study was approved by the ethical committee of Viswabharathi Medical College, Kurnool.

Age groups	Group-I	Group-II	Group-III	Group-IV	Group-V	Group-VI	Total
Age range	21-30	31-40	41-50	51-60	61-70	71-80	
Males	24	24	22	21	18	21	130
Females	18	16	18	17	12	09	90
Total	42	40	40	38	30	30	220

All the subjects underwent a thorough clinical examination. The subjects without signs of cardiovascular, endocrinological, neurological, hematological and inflammatory diseases were selected for the study. The subjects with any of the following findings were excluded from the study.

- Evidence of hypertension,
- Clinical signs of cardiac failure or ECG changes suggestive of arrhythmia , ischemia
- Subjects receiving drugs that are known to interfere with cardiac or respiratory functions such as beta blockers, sympathomimetic drugs, antihypertensive drugs, vasodilators and diuretics.
- Associated diseases or conditions known to affect autonomic functions e.g. anemia, gullen barrie syndrome, polio, diphtheria , tuberculosis, syphilis, CRF, Diabetes
- Subjects having history of chronicalcohol consumption, chronic tobacco consumption in any form.
- Pregnant women.

All the selected subjects were asked to come to the neurophysiology laboratory of Physiology Department at 8am. The subjects were instructed to come on empty stomach. They were also told not to take any self-prescribed medication twelve hours before the study. All the tests were conducted between 8 to 10am in cool and calm atmosphere at room temperature varying from 27 to 30ºC.The subjects were asked to relax in supine position for 30minutesin the lab; tests were performed only after confirming complete relaxed physical and mental state of the subject. Also a sufficient time of 10mnts rest was given to the subject in between each test to achieve relaxation.

The ECG recording for these tests was done on 'Polyrite Recording Machine' (Medicare Inco. Recorder and Medicare system Chandigarh). ECG was recorded in Lead-II, at a paper speed of 25mm/sec. the machine provides facility to record ECG simultaneously with time tracing & event marking. Blood pressure was measured with the help of sphygmomanometer. All procedures were explained to the subjects and trials were done before final measurements.

The autonomic nervous function tests were selected as recommended by American Diabetic Association and performed as per methods described by Sir Roger Bannister.

The sympathetic activity was assessed by

- Heart rate response to deep breathing,
- Heart rate response to Valsalvamanoeuvre,
- Immediate heart rate response to orthostatic test.

For Heart rate response to deep breathing, the subject Laid quietly for 1 minute and after a verbal command started to breathe deeply & continuously at a rate of 6 breaths/min (5sec inspiration and 5 sec expiration) as trained before. ECG was continuously recorded. The inspiration was marked with event marker. The heart rate ratio during deep breathing was expressed as:

Mean of longest R-R intervals during each expiration
E/I ratio = ---
Mean of shortest R-R intervals during each inspiration

For heart rate response to Valsalva manoeuvre, the subject laid comfortably in supine position. A nose clip was applied and the subject was asked to blow through the mouth piece attached to the mercury manometer for 15 seconds mai9natining a pressure of 40mm of Hg. A small air leakage in the mouth piece was done to ensure that the subject does not blow with his cheeks. Throughout the manoeuvre ECG was recorded continuously and for 30 seconds after release of strain. The heart rate response to Valsalva manoeuvre was expressed as:

Longest R-R intervals after the manoeuvre
Valsalva ratio = --
Shortest R-R interval during the manoeuvre

For immediate heart rate response to orthostatic test, the subject rested in supine position for 5 minutes after which he was asked to stand up unaided within 5 seconds and to remain standing for 1 minute. Continuous ECG recording was done starting from 1st beat after standing up to the 60th beat. The normal response to orthostatic test is immediate tachycardia followed by relative bradycardia. The shortest R-R interval during tachycardia and the longest R-R interval during bradycardia was selected. The result was expressed as:

Maximum R-R interval during bradycardia
Max/Min ratio = --
Minimum R-R interval during tachycardia

The sympathetic activity was assessed by:
Blood pressure response to orthostatic rest,

Blood pressure response to sustained hand grip exercise.

For Blood pressure response to orthostatic rest, the subject rested comfortably in supine position for 15minutes, and then the subject was asked to stand up unaided & remain standing for 2 minutes. Systolic blood pressure was recorded in resting supine position & 2 minutes after standing up and the difference in systolic blood pressure was noted.

For Blood pressure response to sustained hand grip exercise, the subject was asked to sit comfortably in chair. Initially the subject was asked to exert maximal hand grip strength on hand grip dynamometer with dominant hand to determine the maximum voluntary contraction (MVC). The subject was then asked to exert 30% of MVC for 5 minutes (at least for 3 minutes) with dominant hand. Diastolic blood pressure was measured in the non-dominant hand at rest and at a 1 minute intervals during hand grip. The maximum rise in diastolic BP during 30% of MVC over the resting diastolic blood pressure was noted.

The data was suitably arranged and was subjected to statistical analysis with the help of student t-test. The results were expressed as non-significant if p>0.05, significant if p<0.05 or 0.01 and highly significant if p<0.001.

3. RESULTS

Age groups	**Group 1**	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**
Age	**21-30 years**	**31-40 years**	**41-50 years**	**51-60 years**	**61-70 years**	**71-80 years**
	Mean ±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)
Males	1.47±0.1	1.32±0.12	1.26±0.12	1.26±0.12	1.195±0.06	1.175±0.08
Females	1.45±0.16	1.27±0.09	1.28±0.13	1.22±0.08	1.20±0.06	1.46±0.05
Significance	p>o.o5	p>o.o5	p>o.o5	p>o.o5	p>o.o5	p>o.o5

Table No.2.Comparision of E/I ratio between males & females

Age groups	**Age range**	**Mean in mm Hg**	**S.D.**
Group 1	21-30 years	1.46	±0.13
Group 2	31-40 years	1.30	±0.11
Group 3	41-50 years	1.27	±0.13
Group 4	51-60 years	1.24	±0.11
Group 5	61-70 years	1.20	±0.06
Group 6	71-80 years	1.16	±0.08

Table No.3. E/I ratio in different age groups

Age groups	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**
Age range	**31-40 years**	**41-50 years**	**51-60 years**	**61-70 years**	**71-80 years**
Group 1 21-30 years	p<0.01	p<0.01	p<0.001	p<0.001	p<0.001
Group 231-40 years		p>0.05	p<0.05	p<0.001	p<0.001
Group 341-50 years			p>0.05	p<0.01	p<0.001
Group 451-60 years				p<0.05	p<0.01
Group 561-70 years					p>0.05

Table No.4.Comparision of E/I ration in different age groups

Age groups	**Group 1**	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**
Age range	**21-30 years**	**31-40 years**	**41-50 years**	**51-60 years**	**61-70 years**	**71-80 years**
	Mean ±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)
Males	1.68±0.28	1.46±0.23	1.40±0.17	1.29±0.16	1.24±0.107	1.180±0.079
Females	1.65±0.35	1.53±0.22	1.41±0.20	1.28±0.10	1.15±0.045	1.158±0.070
Significance	p>o.o5	p>o.o5	p>o.o5	p>o.o5	P<o.o5	p>o.o5

Table No.5.Comparision of Valsalva ratio(VR) in males & females

Age groups	Age range	Mean in mm Hg	S.D.
Group 1	21-30 years	1.67	±0.30
Group 2	31-40 years	1.51	±0.23
Group 3	41-50 years	1.40	±0.18
Group 4	51-60 years	1.29	±0.13
Group 5	61-70 years	1.20	±0.097
Group 6	71-80 years	1.17	±0.07

Table No.6. Valsalva ratio in different age groups

Age groups	Group 2	Group 3	Group 4	Group 5	Group 6
Age range	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years
Group 1 21-30 years	p<0.05	p<0.01	p<0.001	p<0.001	p<0.001
Group 231-40 years		p<0.05	p<0.001	p<0.001	p<0.001
Group 341-50 years			p<0.01	p>0.001	p<0.001
Group 451-60 years				p<0.01	p<0.001
Group 561-70 years					p>0.05

Table No.7.comparision of Valsalva ratio in different age groups

Age groups	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Age range	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years
	Mean ±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)
Males	1.611±0.67	1.36±0.18	1.27±0.13	1.247±0.12	1.11±0.03	1.120±0.08
Females	1.51±0.23	1.32±0.17	1.27±0.11	1.23±0.08	1.143±0.06	1.091±0.07
Significance	p>o.o5	p>o.o5	p>o.o5	p>o.o5	p>o.o5	p>o.o5

Table No.8.comparision of max/min ratio between males & females

Age groups	Age range	Mean in mm Hg	S.D.
Group 1	21-30 years	1.57	±0.53
Group 2	31-40 years	1.34	±0.17
Group 3	41-50 years	1.28	±0.12
Group 4	51-60 years	1.24	±0.10
Group 5	61-70 years	1.13	±0.057
Group 6	71-80 years	1.11	±0.08

Table No.9. Max/Min ratio in different age groups

Age groups	Group 2	Group 3	Group 4	Group 5	Group 6
Age range	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years
Group 1 21-30 years	p<0.05	p<0.05	p<0.001	p<0.001	p<0.001
Group 231-40 years		p>0.05	p<0.01	p<0.001	p<0.001
Group 341-50 years			p>0.05	p>0.001	p<0.001
Group 451-60 years				p<0.001	p<0.001
Group 561-70 years					p>0.05

Table No.10.comparision of max/min ratio in different age groups

Age groups	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Age range	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years
	Mean ±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)
Males	6.78±4.17	8.08±5.50	6.27±4.79	8.47±4.08	9.33±4.66	13.02±4.69
Females	8.22±4.30	7.75±4.61	7.87±5.78	8.82±5.00	10.66±4.04	15.75±4.49
Significance	p>o.o5	p>o.o5	p>o.o5	p>o.o5	p>o.o5	p>o.o5

Table No.11 comparision of SBP response to orthostatic test in males & females

Age groups	Age range	Mean in mm Hg	S.D.
Group 1	21-30 years	7.50	±4.21
Group 2	31-40 years	7.91	±5.02
Group 3	41-50 years	7.07	±4.92
Group 4	51-60 years	8.64	±4.28
Group 5	61-70 years	10.00	±4.23
Group 6	71-80 years	14.38	±4.50

Table No.12.SBP response to orthostatic test in different age groups.

Age groups	Group 2	Group 3	Group 4	Group 5	Group 6
Age range	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years
Group 1 21-30 years	p>0.05	p>0.05	p>0.05	p>0.05	P<0.01
Group 231-40 years		p>0.05	p>0.05	p>0.05	P<0.01
Group 341-50 years			p>0.05	p>0.05	P<0.01
Group 451-60 years				p>0.05	P<0.01
Group 561-70 years					p<0.05

Table No.13.Comparison of SBP response to orthostatic test in different age groups

Age groups	**Group 1**	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**
Age range	**21-30 years**	**31-40 years**	**41-50 years**	**51-60 years**	**61-70 years**	**71-80 years**
	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)	Mean±SD (mmHg)
Males	20.17±4.12	18.16±4.21	20.54±5.28	19.86±4.92	15.57±5.13	13.52±3.77
Females	19.33±3.82	19.00±5.16	16.44±4.57	17.41±6.03	14.00±3.39	12.00±4.14
Significance	p>o.o5	p>o.o5	p<o.o5	p>o.o5	p>o.o5	p>o.o5

Table No. 14. Comparision of DBP response to sustained hand grip in males & females

Age groups	**Age range**	**Mean in mm Hg**	**S.D.**
Group 1	21-30 years	19.8	±3.97
Group 2	31-40 years	18.59	±4.57
Group 3	41-50 years	18.49	±5.33
Group 4	51-60 years	18.64	±5.64
Group 5	61-70 years	14.79	±4.94
Group 6	71-80 years	12.76	±3.98

Table No.15.Comparision of DBP response to sustained hand grip in different age groups

Age groups	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**
Age range	**31-40 years**	**41-50 years**	**51-60 years**	**61-70 years**	**71-80 years**
Group 1 21-30 years	p>0.05	p>0.05	p>0.05	P<0.05	P<0.01
Group 2 31-40 years		p>0.05	p>0.05	P<0.05	P<0.01
Group 3 41-50 years			p>0.05	P<0.05	P<0.01
Group 4 51-60 years				P<0.05	P<0.01
Group 5 61-70 years					P>0.05

Table No.16.Comparision of DBP response to sustained hand grip in different age groups

4. DISCUSSION

The present study was carried out in 220 healthy subjects in the age range of 21-80 years, to assess the influence of age and sex on autonomic nervous function. The subjects were distributed into six age groups as shown in Table No.1. Evaluation of status of autonomic nervous system was done with the help of five simple, noninvasive tests. Parasympathetic function was assessed by heart rate response to deep breathing, heart rate response to Valsalva manoeuvre and heart rate response to orthostatic test. The sympathetic function was assessed by blood pressure response to orthostatic test and blood pressure response to sustained handgrip exercise.

4.1 Heart rate response to deep breathing: is a normal phenomenon and is primarily due to fluctuation of parasympathetic output to the heart. Heart rate response to deep breathing was evaluated in all the subjects, the values of E/I ratio in different age groups are shown in Table No.3.It is evident from Table No.4 that various age groups differ significantly with respect to E/I ratio. When E/I ratio of age group 1 was compared with age groups 2 to 6. A significant decline in E/I ratio observed in age groups 2 & 3. But the decline in E/I ratio was highly significant in age groups 4,5 and 6.

When E/I ratio of age group 2 was compared with other groups, decreased values were observed in age group 3 but the decrease was not statistically significant. Further comparison with other groups revealed a significant decline in age group 4 with highly significant decline in age groups 5 & 6. Similarly comparison of E/I ratio of age group 3 with that of age groups 4 to 6 showed a insignificant decline in E/I ratio in age group 4 with signifi9cant decline in age group 5 and highly significant decline in age group6. While comparison of E/I ratio of age group 4 with that of age groups 5 and 6 showed a significant decline in group 5 and 6. But the difference was insignificant when E/I ratio of age groups 5 & 6 was compared with each other. Thus heart rate response to deep breathing which is an indicator of parasympathetic function was reduced linearly with advancing age in our study. Our findings are in accordance with earlier studies done by Wieling W et al(1982), Kaijser and Sachs (1985), Jain A.D O' Brien et al (1985), Bengt Bergstrom et al (1986), Vita G et a (1986), Chu T.S. et al (1989), Philip A low et al (1990), J Gert Van Dijk et al (1991), S.J. Piha (1991), Zeigler D et al (1992), Neumann &Schmid (1997) and Agelink N.W et al (2001). Vita G et al (1986), Bengt Bergstrom et al (1986), Philip A low et al (1990) and Neumann and Schmid (1997) observed a linear decline in heart rate response to deep breathing with advancing age as observed in our study. Vita G et al (1986) attributed this decline to reduction in number of fibers in the vagus nerve, increase in empty Schwann cell bands and accumulation of pigments in neurons as the age advances. Lain A D O' Brien et al (1985) observed a nonlinear decline in heart rate response to deep breathing with advancing age. They attributed this age related decline to altered vagal activity, since ahronotropic response to atropine was also reduced in older subjects.Kaijser& Sachs (1985) found no significant decline in heart rate response to deep breathing in subjectsupto 60 years of age but they observed an accelerated decline in those above 60 years of age. They attributed this decline to decreased nerve function and decreased end organ sensitivity or function in older subjects.

4.2 Heart rate response to Valsalva manoeuvre: is characterized by a decrease in the pulse pressure and tachycardia during the strain and blood pressure overshoot and bradycardia following the strain. The Valsalva manoeuvre tests the integrity of both sympathetic & parasympathetic divisions of the autonomic nervous system. The hemodynamic changes during the manoeuvre are mediated via baroreceptors. With parasympathetic affection, the baroreceptor mediated reflex bradycardia response to elevated blood pressure will be reduced. Heart rate response to Valsalva manoeuvre was evaluated in all the subjects. The observed values for Valsalva Ratio in various age groups are shown in Table No.6. It is evident from Table No.7 that the various age groups differ significantly with respect to Valsalva ratio. Comparison of VR of age group 1 with that of age groups 2 to 6 revealed a significant decline in VR in age groups 2 and 3. But the decline was highly significant in age groups 4,5 and 6. A significant decline in VR was observed in age group 3 with highly significant decline in age groups 4,5& 5 when VR of above age groups was compared with that of age group 2. Similarly when, VR of age group 3 was compared with that of age groups 4 to 6, a significant decline was observed in VR of age group 4 but the decline was highly significant in age groups 5 & 6.while comparison of VR of age group4 with that of age groups 5 & 6 showed a significant decline in age group 5 but a highly significant decline in age group 6. No significant decline in VR was observed when values of age groups 5 & 6 were compared with each other. Thus heart rate response to Valsalva manoeuvre which is a sensitive test of parasympathetic function reduced linearly with advancing age in our study. Our findings are in accordance with earlier studies done by Jain A D O'Brien et al (1985), Chu T S et al (1989), Philip A low et al (1990), S J Piha (1991), Zeigler D et al (1992), Romero Vecchione et al (1993). Jain A D O'Brein et al (1985) observed a nonlinear decline in heart rate response to Valsalva manoeuvre with advancing age, but we observed a linear decline in our study. Our results were not in agreement with Kaijser& Sachs (1985), Vita G et al (1986), Neumann&Schmid (1997). They did not observe a decline in heart rate response to Valsalva manoeuvre with advancing age.Kaijser& Sachs (1985) observed a decline in response with advancing age for deep breathing test but not forValsalvamanoeuvre. Thedisparityin the results of deep breathing test & VR which aremediatedby sameef-ferentvagalpathwaywasattributedtoearlieraffection ofafferent nerves-fromlowpressureareasofcirculationthanafferentfibersfrombarore-ceptors.Because afferent signals during deep breathing are carried by afferents from low pressure areas of circulation while that for Valsalva manoeuvre by baroreceptor afferents.

4.3 Heart rate response to orthostatic test: in normal subjects consists of tachycardia maximum around 15th beat followed by relative bradycardia around 30th beat after standing. These hemodynamic responses are mediated by baroreceptors. The relative bradycardia is abolished byatropine,confirmingthatitismediatedthroughvagus. Heart rate response to orthostatic test was evaluated in all the subjects. The values for max/min ratio in various age groups are shown in Table No.9. It is evident from Table No.10 that various age groups differ significantly with respect to max/min ratio. When max/min ratio of age group 1 was compared with that of age groups 2 to 6, a significant decline in max/min ratio was found in age groups 2 &3. But the decline in max/min ratio was highly significant in age groups 4,5& 6. Comparison of max/min ratio of age group 2 with that of age groups 3 to 6 showed a significant decline in max/min ratio in age group 4 with highly significant decline in age groups 5 & 6. But the decline in age group 3 was insignificant.Similar comparison of max/min ratio of age group 3 with other groups showed a insignificant decline in age group 4 with a highly significant decline age groups 5 & 6.While comparison of max/min ratio of age group 4 with that age groups 5 & 6 showed a highly significant decline in age groups 5 & 6. No significant decline was observed when age groups 5 & 6 were compared with each other. Thus heart rate response to orthostatic test which is a sensitive test to assess parasympathetic integrity was found to reduce linearly with advancing age in our study. Our findings are in conformity with earlier studies done by Weiling W et al (1982), Lain A D O'Brien et al (1985), Bengt Bergstrom et al (1986), Vita et al (1986), Chu T S et al (1989), J Gert Van Dijk et al (1991), Piha S J (1991), Romero Vecchione (1993), Gianfranco Piccirillo et al(1995), Neumann & H Schmid (1997), Agelink N W et al(2001).BengtBerstrom et al (1986), Vita G et al (1986), J Gert Van Dijk et al(1991), Neumann &Schmid(1997) observed a linear decline in heart rate response to standing which was similar to our finding. Lain A D O'Brien et al (1985) found a non-linear decline in heart rate response to orthostatic test with advancing age.Piccrillo et al (1995) observed an accelerated decline in heart rate response to orthostatic test in subjects beyond 60 years of age. While in subjects below 60 years of age they did not observe a significant decline.

4.4 Blood pressure response to orthostatic test: 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. 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.12. significant fall in systolic blood pressure on standing was observed only in group 6, but no such significant fall was observed in group 2 to 5(Table No.13).Thus increased fall in systolic blood pressure on standing was found only in subjects beyond 70 years of age indicating late onset of decline in sympathetic efficiency in normal subjects as age advances. Our results are in accordance with results of Sheila R Barnett et al (1999). They observed a greater fall in systolic blood pressure on standing in subjects above 60 years of age. They attributed this age related decline in blood pressure response to reduced sympathetic vasomotor responsiveness in elderly subjects. Our findings were not in aggrement with Kaijser& Sachs (1985), Lain AD O'Brein(1985), Bengt Bergstrom et al(1986), Chu TS et al(1989), J gert Van Dijk et al (1991), S J Piha (1991) and Neumann &Schmid (1997). They did not observe any significant fall in systolic blood pressure with advancing age.

4.5 Blood pressure response to sustained handgrip exercise: It was DJ Ewing et al(1973) who first showed that during sustained handgrip, there was a sharp rise in diastolic blood pressure due to increase in peripheral vascular resistance. Blood pressure response to sustained handgrip was evaluated in all the subjects. The observed values in various age groups for rise in diastolic blood pressure over normal diastolic blood pressure after sustainedhandgrip exercise are shown in table No.15. Age groups 1 to 4 did not show any significant variation in diastolic blood pressure response. The diastolic blood pressure response to sustain handgrip was significantly lower in age groups 5 and 6 while difference between age groups 5 and 6 was insignificant(table No.16). thus sympathetic function as assessed by sustained handgrip exercises was reduced significantly in subjects above 60 years of age indicating late onset of decline in sympathetic efficiency in normal subjects with advancing age. Our findings are in conformity with findings of Kaijser Sachs (1985) and Sachs et al(1985).Kaijser&Sachs(1985) observed a decreased blood pressure response to handgrip test in older subjects, above 60 years of age. They attributed this decline in older subjects, to reduced effecter organ sensitivity. Sachs et al(1985) studied sustained handgrip response in 10 healthy old subjects (mean age 71) and in healthy younger subjects (mean age 26 years). They observed a lowered blood pressure response in older subjects than younger subjects on sustained handgrip exercise. They attributed this to reduced maximal capacity of older subjects to release noradrenaline and adrenaline upon exercise provocation. Our results differ with earlier studies done by Vita G et al(1986), J Gert Van Dijk(1991), Zeigler D et al (1992), S J Piha(1991) and Neumann &Schmid(1997) in that they did not observe any significant decline in blood pressure response to sustained handgrip with advancing age.

4.6 Gender related variations in autonomic nervous functions were done in 130 males and 90 females. Except a significant low response to Valsalva manoeuvre in females of age group 51-60 years and a significant decreased diastolic blood pressure response in females in age groups 41-50 years, no significant variation in values of different tests for sympathetic and parasympathetic function was observed in females as compared to males (Table Nos. 2,5,8,11& 14). Thus no significant sex variation was observed in autonomic nervous function in our study. Our results are in accordance with the results of earlier studies done by Lain AD O'Brien et al (1985), Kaijser& Sachs et al(1985), Bengt Bergstrom et al (1986), Philip A et al (1990), Zeigler D et al(1992) & Neumann & H Schmid(1977). Our findings were not in agreement with Chu T S et al(1989), Sheila R Barnett et al(1999), Age link N W et al(2001). Chu TS et al and Age Link NW found reduced sympathetic response in females as compared to males. While they did not find any sex related variation with respect to parasympathetic function. Sheila R et al observed greater fall in systolic blood pressure on orthostatic stress in women. They attributedthis to low sympathetic activity and lowplasma norepinephrine concentration in women at rest and on orthostatic stress. We assessed parasympathetic activity by heart rate response to deep breathing, heart rate response to Valsalva manoeuvre and heart rate response to orthostatic test. The results of these tests, revealed a significant linear decline in values with advancing age. Assessment of sympathetic activity by blood pressure response to orthostatic test and blood pressure response to sustained handgrip exercise revealed a significant lower response in subjects above 60 years of age. No significant variation in the values of males & females was found in the tests used to study sympathetic & parasympathetic activity. Thus in our study we found a linear decline in parasympathetic activity with advancing age while reduced efficiency of sympathetic activity was found only in subjects above 60 years of age. No sex variation was found in the results of autonomic function tests. With advancing age, changes in neurons such as pigment accumulation, Schwann cell demyelination, neuronal loss and axonal degeneration has been reported. Decline in parasympathetic activity observed in our study may be attributed to reduction in number of vagal fibreswith advancing age as reported by Vita G et al. and decreased in biosynthesis and hydrolysis of acetylcholine with advancing age as reported of Frolkies V V et al. the decline in sympathetic efficiency in subjects above 60 years of age as observed in our study may be due to progressive reduction in preganglionic sympathetic neurons of intermediolateral column of spinal cord beginning in the adult life as reported by Philip A Low. Thus aging is complicated, multifactorial process that clearly affects the autonomic nervous system. The impact on the autonomic nervous system appears to be multiple levels of autonomic neuraxis. The knowledge about the status of autonomic nervous system with advancing age will be useful in the management of cardiovascular, respiratory, urinary, gastrointestinal disturbances, the frequency of wjich increases with advancing age. The alteration of autonomic balance with advancing age will also have a bearing on drug action and in determining therapeutic strategy in the elderly.

The present study was carried out in 220 healthy subjects to assess the influence of age and sex on autonomic nervous function. We found a nonlinear decline in parasympathetic function with advancing age; a nonlinear decline I sympathetic function with advancing age. There was no significant variation in sympathetic function in subjects from 21-60 years age group. Significant reduction in sympathetic function was found only in subjects aging above 60 years of age; no sex variation in either parasympathetic or sympathetic function was found in our study. These tests are simple, inexpensive and noninvasive. The population of elderly individuals above 60 years of age is rapidly increasing than the population as a whole. Thus the knowledge of autonomic status will have an important bearing on determining the therapeutic strategy and drug action in the elderly in whom there may be altered responsiveness to autonomic reflexes and receptor sensitivity.

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