Original Article

Study of Autonomic Function Tests in Geriatric Population

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ABSTRACT

Autonomic dysfunction worsens with old age. It results from an imbalance between the sympathetic and parasympathetic divisions. Autonomic function tests were carried out in 50 healthy subjects in the age group of 65 to 90 years and compared with 50 controls in the age group of 25 to 65 years. The Parasympathetic activity was assessed by heart rate response to deep breathing, valsalva maneuver and orthostatic tests. Sympathetic function was assessed by blood pressure response to cold pressor test and sustained hand grip exercise. We found a decline in sympathetic and parasympathetic function with advancing age. No gender variation in both sympathetic and parasympathetic function was observed in this study. The E: I ratio values were significantly decreased in geriatric population. (p-value 0.037). In cold pressor test, the SBP and DBP difference values were significantly reduced in geriatric population. (p-value-0.000). Heart rate response to hand grip test was reduced significantly (p-value-0.035). 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.

KEY WORDS: Autonomic function, sympathetic, parasympathetic, blood pressure, cold pressor test and hand grip exercise.

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INTRODUCTION

Ageing is a natural process of merely growing order in a temporal sense and should be welcomed. The different theories can be combined into two groups, according to the first group, ageing is the cumulative result of random cell damage which goes throughout life, while the other group considers ageing is an inevitable result of our genetic programming [1]. In India 7.1% of the people are over 65 years as against 12% in U.S.A and Britain (as per 2001 census). Also in India although the percentage of aged persons to total population is low in comparison to developed countries, nevertheless, the absolute size of aged population is considerable. Thus number of aged persons is continually on the increase in India and worldwide. Most organs of the body receive dual innervations from the ANS. Eg.: Heart, Endocrine glands, and smooth muscles in the walls of hollow viscera. Some of the organs are innervated by only one division of the ANS. Eg.: Uterus, Adrenal medulla and most arterioles are innervated by sympathetic division. Glands of the stomach and pancreas are innervated by parasympathetic division only. The effects of Parasympathetic stimulation are usually short lived as Acetyl choline is degraded rapidly, whereas the effects of sympathetic stimulation are wide spread and long lasting. The Autonomic reflexes are based on reflex arc which consists of receptors, sensory neurons, center of integration, autonomic motor neurons and visceral effectors. The Autonomic reflexes regulate activities of smooth muscles, cardiac muscles and glands. The Hypothalamus controls and integrates the functions of both the divisions of Autonomic nervous system. During emotional states, limbic cortex controls the Autonomic nervous system [2]. The decline in various functions continues slowly and eventually become considerable and functionally significant as age advances. Thus physiologically, ageing refers to an impaired ability to maintain homeostasis in the face of external and/or internal challenges or stresses. As a result an individual becomes more vulnerable to these challenges and stresses and may finally succumb to one of these [3]. Both parasympathetic and sympathetic nervous system which constitute the autonomic nervous system (ANS) are affected by ageing. A number of tests to assess the functional status of ANS. The parasympathetic nervous system tests include beat to beat variation [4], Valsalva ratio [5] and the baro reflex sensitivity [6] and sympathetic nervous system tests include the hand grip test [7], the galvanic skin resistance [8, 9] and the cold pressor response [10]. In earlier also suggested an indication of affect of ageing on the autonomic nervous system activity so a formal study was planned to be carried out which involved a battery of autonomic tests to be done on 25-65 years age and >65years groups. The changes were noticed in some parameter of both sympathetic and parasympathetic function tests during comparison between 2 groups and amongst males and females of same age group.

SUBJECTS AND METHODS

This is a cross-sectional study undertaken by me in the Department of Physiology, Narayana Medical College, and Nellore, Andhra Pradesh, India, for a period of 10 months beginning from August 2009. After Informed consent was taken, 50 were healthy elderly individuals ageds above 65 years with 50 were teaching and non-teaching staff of Narayana Medical College aged 25 to 65 years. Systolic blood pressure 100-140 mm of Hg, Diastolic blood pressure 60-90 mm of Hg and Random Blood Sugar 100-140 mg / dL from general population. <65 years, H/o Hypertension and H/o Diabetes mellitus were excluded from the study.

All subjects underwent autonomic function tests which included Deep Breathing Test assess the parasympathetic activity, by using Cardiowin system; PC based 12 channel simultaneous digital ECG, Genesis Media System Pvt Ltd. and ECG Jelly. Subject was instructed by made to lie down comfortably in supine position with head elevated to 30^0 and ECG electrodes were connected for recording Lead II ECG, to maintain deep breathing at a rate of six breaths per minute (allowing 5 seconds each for inspiration and expiration) maximum and minimum heart rates were recorded with each respiratory cycle. Expiration (E) to inspiration (I) ratio was determined by using the formula:

$$\text{E : I ratio} = \frac{\text{Maximum R-R interval during deep expiration}}{\text{Minimum R-R interval during deep inspiration}}$$

Normal Values of E: I ratio in different age groups [11]

Valsalva Manoeuver is a measure of parasympathetic and sympathetic functions [11, 12]. For the response to occur in valsalva manoeuver parasympathetic acts as afferent and efferent and sympathetic acts as a part of the efferent pathway. Therefore the valsalva ratio assesses more of parasympathetic function. By using Cardiowin system; PC based 12 channel simultaneous digital ECG, Genesis Media System Pvt Ltd., ECG Jelly, Sphygmomanometer (Diamond) and Mouth Piece. Subject was made to lie down in a semi recumbent or sitting position, Nostrils were closed manually, Mouth piece was put into the mouth of the subject and the Mercury manometer was connected to the mouth piece. ECG machine was switched on for continuous recording. Subject was asked to exhale forcefully into the mercury manometer and asked to maintain the expiratory pressure at 40 mm of Hg for 10 – 15 seconds. ECG changes were recorded throughout the procedure, 30 seconds before and after the procedure. Valsalva ratio was calculated by using the formula:

$$\text{Valsalva ratio} = \frac{\text{Longest R-R interval after the manoeuver (Phase-IV)}}{\text{Shortest R-R interval during the manoeuver (Phase-II)}}$$

Normal values of valsalva ratio in different age groups. Valsalva ratio more than 1.45 is considered to be normal. When it is 1.2 – 1.45, it is border line and if it is less than 1.2, it is regarded as abnormal. During the valsalva manoeuver failure of heart rate to increase during strain suggests a sympathetic dysfunction and failure of heart rate to slow down after the strain suggests parasympathetic dysfunction.

Cold Pressor test (Cold pressure test) [11, 13, 14] the afferent limb of the reflex pathway in cold pressor test is somatic fibers whereas the efferent limb is sympathetic fibers. Beaker containing Ice cold water, Sphygmomanometer (Diamond), and Stethoscope (Littmann). Blood pressure was recorded under basal conditions. Cold water was taken in a container. Subject was asked to submerge one of his upper limbs in cold water up to the middle of the fore arm for 60 seconds. Blood pressure was recorded at the end of 60 seconds of submersion of the limb. Submersion of the limb in ice cold water increases systolic blood pressure by about 10-20 mm of Hg and diastolic blood pressure by about 10 mm of Hg.

Heart rate response to standing on changing the posture from supine to standing heart rate increases immediately by 10-20 beats per minute. This response is detected by recording ECG in supine and standing postures [11, 12, 13]. By using Cardiowin system; PC based 12 channel simultaneous digital ECG, Genesis Media System Pvt Ltd., and ECG Jelly. Subject was made to lie down in supine posture. ECG electrodes were connected from the subject to the cardiowin system. Subject was asked to relax completely for a minimum period of 10 minutes. Basal heart rate was recorded by using cardiowin system. Subject was asked to stand up immediately and change in heart rate was noted from the cardiowin, monitoring screen. Heart rate response to standing was determined by using the formula:

Heart rate in standing position – Heart rate in supine position.

Hand grip test in the hand grip test, there is a rise in heart rate and blood pressure. The blood pressure rise is due to increased sympathetic activity and heart rate rise is due to decreased parasympathetic activity [11, 13]. By using Cardiowin system; PC based 12 channel simultaneous digital ECG, Genesis Media System Pvt Ltd., and ECG Jelly Sphygmomanometer (Diamond), Stethoscope (Littmann), and Hand Grip Dynamometer. Subject was made to lie down in semi recumbent position. ECG electrodes were connected for lead II recording of ECG and sphygmomanometer for blood pressure measurement. Basal heart rate and blood pressure were recorded by instructed to maintain a pressure of 30% of the maximum activity in the hand grip dynamometer for about 5 minutes. Heart rate and change in SBP, DBP were recorded. The normal response is rise in DBP by > 10-15 mm of Hg and rise in heart rate by about 30% of the pretest value.

RESULTS

Table 1: Showing the E : I ratio values of means, Std. deviation, and p-values in controls and cases.

Age in years	Mean	Std. Deviation	P Value
Controls 25-65 years	1.1878	0.14399	0.037*
Cases 65-90 Years	1.1324	0.11729	0.037*

*statistically significance. <0.05 is statistically significant.

Graph 1: showing the means of E : I ratio values in controls and cases.

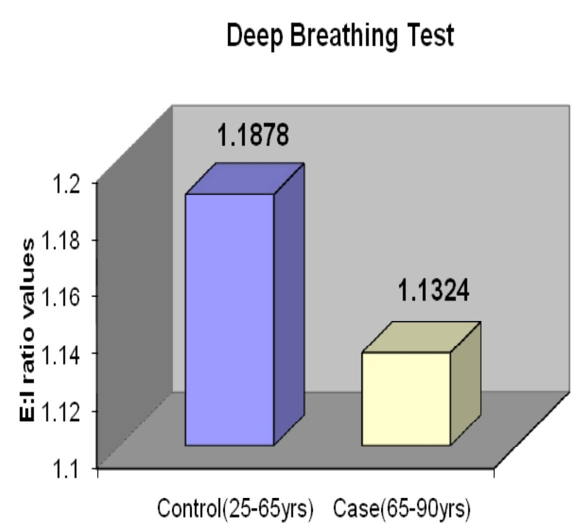


Table 2: showing the Valsalva ratio values of means, Std. deviation, and p-values in controls and cases.

Age in years	Mean	Std. Deviation	P Value
Controls 25-65 Years	1.2108	0.18359	0.387
Cases 65-90 years	1.1828	0.13513	0.387

Graph 2: showing the means of Valsalva ratio values in controls and cases.

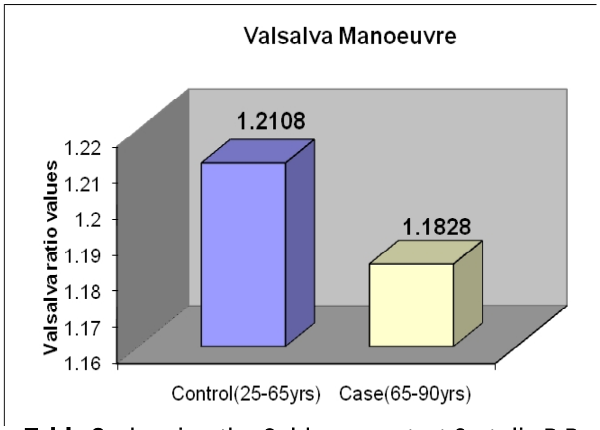


Table 3: showing the Cold pressor test Systolic B P values of means, Std. deviation, and p-values in controls and cases.

Age in years	Mean	Std. Deviation	P Value
Controls 25-65 years	11.52	7.189	0.000**
Cases 65-90 years	7.08	4.28	0.000**

**statistically more significance. <0.05 is statistically significant.

Graph 3: showing the means of Cold pressor test Systolic B P values in controls and cases.

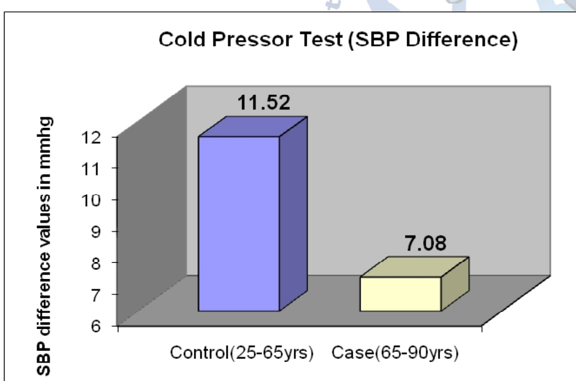


Table 4: Showing the Cold pressor test Diastolic B.P values of means, Std. deviation, and p-values in controls and cases.

Age in years	Mean	Std. deviation	P Value
Control 25-65 years	11.44	8.917	0.000**
Cases 65-90 Years	6.12	5.021	0.000**

**statistically more significance. <0.05 is statistically significant.

Graph 4: showing the means of Cold pressor test Diastolic B.P values in controls and cases.

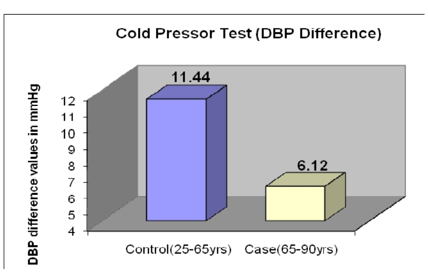


Table 5: showing the Heart rate response to standing values of means, Std. deviation, and p-values in controls and cases.

Age in years	Mean	Std. Deviation	P Value
Controls 25-65 Years	12.52	7.83	0.081
Cases 65-90 Years	9.24	10.58	0.081

Graph 5: Showing the means of Heart rate response to standing values in controls and cases.

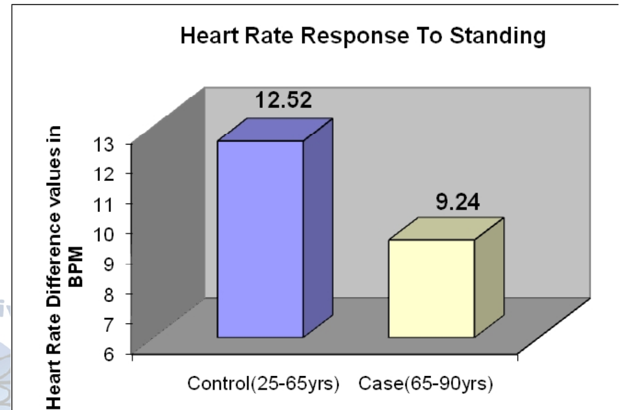


Table 6: showing the Heart rate response – before & after hand grip values of means, Std. deviation, and p-values in controls and cases.

Age in years	Mean	Std. deviation	P Value
Controls 25-65 years	15.4	8.947	0.035*
Cases 65-90 years	11.6	8.869	0.035*

*statistically significance. <0.05 is statistically sign ificant.

Graph 6: showing the means of Heart rate response – before & after hand grip values in controls and cases.

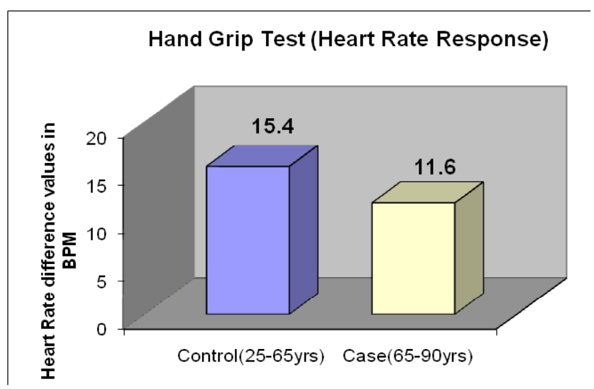


Table 7: showing the Systolic blood pressure – before & after hand grip values of means, Std. deviation, and p-values in controls and cases.

Age in years	Mean	Std. Deviation	P Value
Controls 25-65 years	8.84	6.3	0.71
Cases 65-90 years	9.32	6.585	0.71

Graph 7: showing the means of Systolic blood pressure – before & after hand grip values in controls and cases.

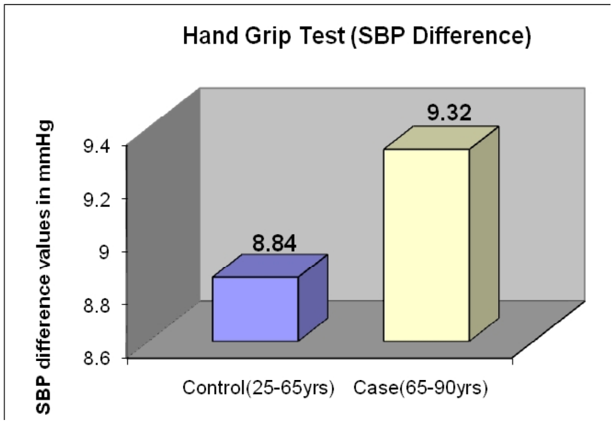
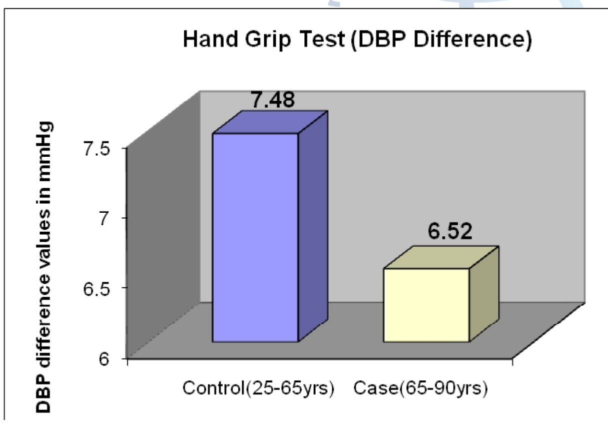


Table 8: showing the Diastolic blood pressure – before & after hand grip values of means, Std. deviation, and p-values in controls and cases.

Age in years	Mean	Std. Deviation	P Value
Controls 25-65 years	7.48	4.156	0.212
Cases 65-90 years	6.52	3.448	0.212

Graph 8: showing the means of Diastolic blood pressure – before & after hand grip values in controls and cases.



DISCUSSION

In healthy young individuals breathing at a normal rate, the HR varies with the phases of respiration i.e., HR accelerates during inspiration and decelerates during expiration, this is known as sinus arrhythmia. Sinus arrhythmia is a normal phenomenon and is due to fluctuations in parasympathetic output to the heart. Baroreceptors are solely responsible for resting vagal tone in the normally breathing individuals. During inspiration, neuronal activity of inspiratory neurons in the medulla besides initiating inspiration also discharge to Nucleus of tractus solitarius (NTS), Nucleus ambiguus(NA), and inhibit both the relay centers of the Baroreceptors, NTS-NA pathway. This leads to inhibition of cardiac vagal motor discharge which in turn leads to an increase in HR during inspiration and decrease in HR during expiration [2]. Heart rate response to deep breathing was evaluated in all the subjects. There was a significant decline in E/I ratio with advancing age (p value=0.037). Our results are supporting the earlier studies done by , Iain A D O'Brien, Paul O' Hare , et al [15], Vita G et al [16], Sampo J piha et al [17] and Agelink N W et al [18]. There are two explanations put forward to explain the decreased E/I ratio with age greater than 60 years. First is decreased autonomic nerve function and decreased organ sensitivity or function [19]. Second is an age related decline in vagal activity as evidenced by decreased chronotropic response to atropine in older subjects [20].

Under conditions of either physical or psychological stress there is activation of Sympathetic nerve fibers. In cold pressor test submerging the limb in cold water, increases systolic pressure by about 20 mm of Hg and diastolic blood pressure by about 10 mm of Hg. The afferent limb of the reflex pathway is somatic fibbers, whereas the efferent pathway is the sympathetic fibbers [11, 12]. In our study, both systolic and diastolic blood pressure differences, before and after cold pressor test, are decreased. The results of the above mentioned tests are statistically significant (p value=0.000), for both systolic and diastolic blood pressure. Our findings are correlating with the studies of Marcella Pascualyaab et al [21] and R.G. Victor et al [20]. Findings can be explained as follows, plasma norepinephrine and epinephrine levels at rest and after cold pressor test are increased significantly with advancing age [21]. Increased muscle sympathetic nerve activity during cold pressor test leads to an increase in both mean arterial pressure and peripheral venous norepinephrine levels [20].

In the hand grip test, there is an increase in both heart rate and blood pressure. The cardiovascular responses to isometric exercise are mediated partly by the influence of cardiovascular centers and partly by metabolic or mechanical changes, or both, in response to contraction of the muscle that activate small fibbers in the afferent limb of the reflex arc .The response is a rise in diastolic pressure, more than 15 mm of hg and rise in the heart rate by about 30 per cent. The blood pressure rise is due to increased sympathetic activity, heart rate rise is due to decreased parasympathetic activity [11]. In our study a gradual decrease in heart rate response was observed. The results of our study are significant (p-value-=0.035.) Our findings are corroborating with S Suchiritha, A V Bharathi et al [22] and J .Gert Van Dijic at al. [23]. Heart rate response to handgrip test measures cardiac vagal tone. Decreased baroreceptor sensitivity with advancing age and parasympathetic withdrawal may explain the diminished heart rate response.

Blood pressure response to sustained hand grip was evaluated in all age groups, a rise in systolic blood pressure was observed in all subjects. These results are not statistically significant, (p value= 0.710). In our study the diastolic blood pressure response to sustained hand grip was significantly lower in all age groups. Thus, sympathetic function as assessed by sustained handgrip exercise, was reduced significantly in subjects above 60years indicating, late onset of decline in sympathetic efficiency in normal subjects, with advancing age. The results of our study are not significant, (p-value=o.212). Our findings are matching with the findings of Kaijser and Sachs [19], who observed a decreased blood pressure response to sustained handgrip test in older subjects, due to reduced effector organ sensitivity. However our results differ with earlier studies done by Vita G et al [16] S J Piha [24] and J Gert Van Dijik et al [23], who did not observe any significant decline in blood pressure response to sustained handgrip test, with advancing age.

The Valsalva maneuver has four phases; Phase 1 consists of the onset of strain. In this phase there occurs transient increase in B.P that lasts for a few seconds. This is due to increased intra thoracic pressure and mechanical compression of great vessels. However the H.R does not change much. Phase-2 is a phase of straining. In the early part of this phase venous return decreases, due to sustained rise in intrathoracic pressure. This change persists for four seconds. In the later part of this phase, B.P returns towards normal due to increased peripheral resistance as a result of sympathetic vaso constriction. However H.R increases steadily throughout this phase due to vagal withdrawal in early phase and sympathetic activation in the latter phase. Phase-3 occurs following the release of strain in which there occurs transient decrease in BP lasting for a few seconds. This is caused by mechanical displacement of blood to pulmonary vascular bed, which was under increased intrathoracic pressure. There is little change in heart rate during the phase. Phase-4 occurs with further release of strain. The BP slowly increases due to persistent sympathetic mediated increase in peripheral resistance. This decreases HR proportionately through Baroreceptor stimulation [11]. Valsalva ratio is the ratio of the maximal tachycardia to the maximum bradycardia, induced by a standard valsalva maneuver.

The valsalva maneuver tests the integrity of both sympathetic and parasympathetic divisions of the Autonomic nervous system; However it is more of a parasympathetic test. The valsalva ratio has been widely used as a test of cardio vagal and baroreceptor function. In our study valsalva ratio showed a decline in the geriatric population. However, this was not statistically significant (p-value= 0.081), but the decreasing trend was similar to the study conducted by I A O'Brien et al (15), Dan Ziegler et al [25] and Jain A D O'Brien [15].

When subject assumes an erect posture, from supine posture, gravity causes pooling of blood in the lower limbs. As a result venous return, cardiac output and arterial BP decreases. This leads to decreased stretch of baroreceptors, activation of vasomotor center, which leads to increased sympathetic discharge, decreased vagal tone and an instantaneous increase in HR. On standing the heart rate increases until it reaches a maximum at about the 15th beat, after which it slows down to a stable state at about 30th beat. The ratio of R-R intervals corresponding to the 30th and 15th heart beat is called the 30:15 ratio. The 30:15 ratio is a measure of parasympathetic function. The ratio decreases with age [11]. In our study heart rate response to standing is decreased, However these results are statistically not significant, (p-value-0.081). A, I. O Brien, et all [15], Vita G. et al [16] and Gret Van Dijik et al, [23] Agelink N W et all [18] observed a linear decline in heart rate response to standing, which was not similar to our findings.

In order to see any significant variation in the autonomic response in males versus females, we compared the results of autonomic function tests in 30 males and 20 females. No significant variation was observed in autonomic function in our study. Our results are in accordance with the results of earlier studies done by Ken Umetani, M D et al [27]. Agelink M .W. et al [18], Sampo j piha et al [17] and Gautschy B et al. [28] Gender differences are most pronounced in subjects less than 30 years, heart rate variability of young male subjects being significantly greater than that of age matched female subjects. Differences disappear by the age of 50 years. The knowledge about the status of autonomic nervous system with advancing age will be useful in the management of cardiovascular, respiratory, urinary and gastro intestinal disturbances, the frequency of which 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.

CONCLUSION

The autonomic function tests can be used to assess the status of autonomic nervous system in the elderly, as these tests are simple, non-invasive and inexpensive. The population of elderly individuals above 60 years of age is rapidly increasing. It has been proved by many studies in our review that, regular physical exercise can attenuate the age related changes in the cardiovascular autonomic functions by increasing parasympathetic outflow. 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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