INTERNATIONAL JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

ISSN 2249 – 6467

MODIFICATIONS IN AUTONOMIC FUNCTIONS AFTER PHYSICAL EXERCISE.

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ABSTRACT

The present study was conducted on 70 medical students (35 males and females each), in the age group of 18 to 21 years, to assess the effect of fifteen days moderate physical training on the autonomic nervous system functions. . The age, sex, height, weight, body surface area of the subjects were recorded. The subjects were made to undergo supervised physical training in form of bicycling on a stationary bicycle ergometer for a period of fifteen days various tests and parameters were assessed for sympathetic and parasympathetic activity before the training and after the training.

The pulse rate , systolic and diastolic blood pressure, changes in blood pressure with change in posture (orthostasis), cold and mental stress (mental arithmetic test), revealed significant decrease after the training . Whereas Valsalva ratio , expiratory inspiratory ratio, variations in heart rate in the form of heart rate response, corrected QT interval, heart rate variability, standing lying ratio and 30 : 15 ratio indicated a significant increase after the training .These results suggest a decreased sympathetic activity and increased parasympathetic activity .

The conclusions -Short duration of physical training leads to significant improvement in the cardiovascular status due to favorable alterations in the autonomic nervous system as a result of decrease in sympathetic activity with a simultaneous increase in parasympathetic activity.

Key Words-autonomic functions ,effect of moderate exercise, cardiovascular parameters,

Introduction

The autonomic nervous system helps to control arterial pressure, gastrointestinal motility and secretion, urinary bladder emptying, sweating, body temperature and many other activities, some are controlled almost entirely and some only partially . It is well known that physical training results in favorable cardiovascular changes on variables such as heart rate and blood pressure as both sympathetic and parasympathetic nervous systems undergo changes with regular physical training**. (1)**

Exercise improves the oxygen transport capacity of the circulatory system and the oxidative capacity of skeletal muscle cells **(2)** thereby enhancing oxygen consumption. The ANS regulates the sympathetic and parasympathetic functions of the body. The predominance of sympathetic or parasympathetic is an essential feature of diurnal variation as it allows both alternatively increased activity of organism followed by restful recuperating lapses. Under conditions of stress of either physical or psychological origin there is activation of sympathetic nervous system.

ISSN 2249 – 6467

Effect of physical training on autonomic functions has been studied mostly in well-trained athletes but there is hardly any meaningful data elucidating effects of short-term exercise training in sedentary subjects . Moreover review of literature reveals that there

is a paucity of research work that evaluates the effects of physical training on both limbs of autonomic system in a comprehensive manner .Therefore the present study was undertaken to evaluate effect of fifteen days of moderate exercise training on the autonomic nervous system functions using wide range of battery of tests to obtain broad coverage of both sympathetic and parasympathetic divisions

Materials and methods –The study was conducted in healthy medical students of Government Medical College Jammu . Hundred students were screened and detailed medical history and general physical examination was done .

The volunteers using medications or any hormonal preparations and those already undergoing any physical training were excluded from the study. 70 students were enrolled after screening which comprised of 35 males and females each , in the age group of 18 to 21 years of. The effects of 15 days moderate physical training on autonomic functions was evaluated . Initial values of all parameters used to assess sympathetic and parasympathetic activity were recorded. Then, the volunteers were made to undergo supervised physical exercise consisted of bicycling 15 minutes per day, 6 days a week for 15 days on stationary bicycle ergometer.

For assessing sympathetic system activity, the parameters recorded were: -

Pulse rate: It was recorded by palpatory method using three fingers. **(3)** .

Blood pressure: It was measured under casual conditions using a sphygmomanometer, by auscultatory method . **Orthostasis**: The change in systolic and diastolic blood pressure in response to change in posture from supine to standing position was determined **(4)** **Cold Pressor Test**: The volunteers were asked to place their hands in cold water at a temperature of 4^0C for one minute or until the pain threshold was reached. Blood pressure was recorded at the end of thirty seconds and sixty seconds of immersion in cold water and thereafter in the opposite arm. The maximal reading was recorded as the index of response. **(5)** **Mental Arithmetic Test(MAT**): Blood pressure was recorded when the subject was made to solve mathematical problems like multiplication problem. **Corrected QT interval (QT_C)**- QT interval was measured from the electrocardiogram and then standardized by converting it to QT_C **(6).**For this Bazetts formula was used **(7)** . $QT_C = \frac{\text{QT interval}}{\sqrt{\text{R-R}' \text{ interval}}}$ QT interval and R-R´ interval were measured in seconds. QT_C was expressed in seconds.ECG was recorded were carried out with lead II.

Parasympathetic activity was assessed by parameters recorded by **Pulse Rate, Valsalva Ratio:** This was performed by asking the subjects to expire into a mouth piece connected to a mercury manometer, with the expiratory pressure being maintained at 40 mm Hg for 15 seconds **(8).** During and subsequent to this maneuver, ECG was recorded. Valsalva ratio was calculated as the ratio between the longest R- R´ interval after the release of strain and the shortest R-R´ interval during the strain,

Heart Rate Response(HRR): Subjects were made to change their position from the supine to erect position, and ECG recording was taken in both positions. The difference in heart rate in the two positions was recorded.

Expiratory Inspiratory Ratio(EI Ratio): This was taken as the ratio of the longest R-R interval during expiration to the shortest R-R interval during inspiration. The subjects were asked to breathe deeply and steadily at six breaths per minute, while ECG was recorded. **(9, 10). Heart Rate Variability(HRV):** It was taken as the maximum and minimum heart rate during quiet breathing. **Standing Lying Ratio(SL Ratio):** The subjects were asked to lie down after standing quietly for 2 minutes. The ECG was recorded in both positions and the Standing Lying ratio was calculated as the ratio of the longest R-R interval during the 5 beats before lying down to the shortest interval during the 10 beats after lying down **(11) 30 : 15 Ratio**: The subjects were made to stand up from a lying down position and ECG was recorded. The 30: 15 ratio was calculated as the ratio between the R-R interval at beat 15 and R-R interval at beat 30 of the ECG recorded immediately upon standing **(12)**

Physical Parameters recorded were: **Height**. The height was recorded to the nearest centimeter (Cm) **(13) Weight**: was recorded to the nearest kilogram (Kg). Body surface Area (BSA): **Body surface** area was calculated from the Dubois Nomogram in square meters (m^2) **(14).**

Statistical Analysis:

Statistical analysis was performed using computer software and Paired t test was applied .Comparison was done between the variables before and after the training and p value of < 0.05 was considered significant.

Results

Age: Mean age of volunteers was 19.2 ± 0.66 years **Height**: Mean height was 161.1 ± 4.777 cms **Weight**: Mean weight was 54.6 ± 4.09 Kgs, **Body Surface Area**: The mean body surface area was 1.69 ± 0.06 sq mts

There was significant decline in post exercise values from pre training values of mean pulse rate (P < 0.05) , systolic and diastolic blood pressure, blood pressure with postural change (Orthostasis) . blood pressure at 30 Seconds and 60 seconds after immersion in cold water (Cold Pressor Test); blood pressure during mathematical problems (MAT)

(P < 0.001). There was a significant increase in Valsalva Ratio ,Heart Rate Response (HRR) Expiratory Inspiratory Ratio (EI RATIO) , Heart Rate Variability HRV) Standing Lying Ratio (SL RATIO), 30 : 15 Ratio , Corrected QT Interval (QTc) in post physical exercise values from pre exercise values (P < 0.001). **(TABLE 1)**

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Table1 showing changes in autonomic parameters after moderate exercise

Test	Male Before exercise	Male after exercise	Female before exercise	Female after exercise	Combined before exercise	Combined after exercise	P
Mean pulse rate	71.83± 2.3	71.17± 2.2	72.40± 2.5	71.69± 2.4	72.11± 2.4	71.40± 2.36	*
SBP	116.8± 8.9	114.6± 6.2	118.7± 8.1	114 .5± 5.8	117.8± 8.5	114.5± 3.89	**
DBP	77.9± 3.86	76.2 ± 3.24	77.8 ± 3.98	74.7 ± 3.25	77.9 ± 3.89	75.5 ± 3.31	**
ORTHOSTASIS							
SBP	7.83 ± 4.45	6.74 ± 1.54	6.54 ± 3.1	6.4 ± 1.7	6.69 ± 4.00	6.571 ± 1.63	**
DBP	7.83 ± 4.86	5.89 ± 1.93	7.54 ± 3.6	4.51 ± 3.4	7.69 ± 4.26	5.2 ± 2.86	**
COLD PRESSOR							
30 SEC SBP	122.6 ± 9.8	119.4 ± 5.1	124.5± 5.3	118.6± 5.2	123.5± 9.4	119.0 ± 5.260	**
DBP	84.6 ± 3.86	81.3 ± 3.85	85.1 ± 5.32	79.8±4.222	84.9± 5.87	80.5 ± 4.08	**
60 SEC SBP	126.7± 9.1	122.8± 5.7	125.9± 9.2	120.9± 5.5	127.5±9.02	121.9 ± 5.68	**
DBP	87.1± 5.38	87.1 ± 5.38	88.2 ± 4.15	81.7± 3.92	87.6± 4.81	82.3 ± 3.970	**
MAT SBP	125.1±12.1	119.9± 7.6	128.5±12.1	119.9± 7.6	126.8±12.1	119.9 ± 7.96	**
DBP	86.2 ± 4.48	80.9 ± 2.13	87.1 ± 4.0	80.9 ± 1.95	86.7 ± 4.29	80.9 ± 2.03	**
Valsalva ratio	1.38±0.041	1.49 ± 0.05	1.37 ± 0.03	1.47 ± 0.05	1.37 ± 0.03	1.48 ± 0.05	**
HRR	15.97± 6.8	17.06 ± 7.1	13.71 ± 6.7	15.20 ± 6.6	14.84 ± 6.8	16.13 ± 6.91	**
HRV	7.60 ± 03.2	6.89 ± 3.1	7.80 ± 2.72	6.86 ± 2.89	7.70 ± 2.95	6.87 ± 2.97	**
EI RATIO	1.33 ± 0.049	1.44 ± 0.061	1.32 ± 0.056	1.42 ± 0.071	1.33 ±0.053	1.43 ± 0.067	**
SL RATIO	1.00 ± 0.107	1.03 ± 0.107	1.02 ± 0.102	1.04 ± 0.108	1.01 ± 0.104	1.04 ± 0.106	**
30:15 RATIO	0.97 ± 0.053	1.04 ± 0.053	0.97 ± 0.049	1.03 ± 0.054	0.97 ± 0.051	1.04 ± 0.053	**
QTc	0.37 ± 0.006	0.38 ± 0.007	0.37 ± 0.008	0.38 ± 0.007	0.37 ± 0.007	0.38 ± 0.007	**

* P VALUE > 0.05, ** P VALUE > 0.001.

ISSN 2249 – 6467

Discussion

The role of Physical activity in cardiovascular health has received attention in recent years. Number of reports have indicated that with high levels of physical activity tend to have a lower prevalence of symptomatic coronary artery disease and lesser death rates from cardiovascular diseases. **(15 ,16)**

Although no single report provides complete proof that physical activity has a protective effect, the evidences heavily favors this conclusion. Thus, an understanding of the adaptations that the cardiovascular system undergoes during exercise is of utmost importance for physiologists , clinicians, public health workers and sports professionals. The regularly performed endurance (aerobic) exercise induces adaptations in the autonomic nervous system leading to changes in cardiovascular variables at rest and alteration in the reflex control of the circulation. **(17).**

Interaction of sympathetic and parasympathetic nervous system is important in cardiovascular regulations in both novice and trained individuals**, (18).** There is a strong influence of sympathetic nervous system on myocardial contractility and some effect on heart rate control, whereas vagal effect is essentially on heart rate control and the extent of control of Cardiovascular system by the two limbs of autonomic nervous system varies from individual to individual and is also affected by many diseases (**19**). By and large a tilt towards vagal dominance is beneficial for cardiovascular system in health as well as for the outcome of some diseases especially after myocardial infarction

Exercise improves first and foremost the oxygen transport capacity of circulatory system and the oxidative metabolic capacity of the skeletal muscle cells. Regular indulgence in physical exercise affects the cardiovascular status autonomic nervous system is the prime mediator of the response leading to decrease in sympathetic and increase in parasympathetic tone. The autonomic profile of individual changes during exercise as well as recovery, phase is dependent on intensity of exercise **(17 ,20, 21).**

As there are few studies involving short duration of endurance exercise training effects on autonomic profile **(19,22) ,** therefore the present study was conducted on 70 normal subjects to study the effects of fifteen days of moderate exercise training on the autonomic nervous system functions. No adverse effect was observed during study.

In the present study there was a significant decrease in the pulse rate ($P < 0.05$) similar to other reports **(17,23,24).** Training changes the balance between the sympathetic and parasympathetic activity in the heart toward greater dominance of the parasympathetic component. The reduction in heart rate induced by training is accompanied by a proportional increase in splanchnic hepatic blood flow. **(2) .**

It has been seen that training causes a decrease in resting sympathetic tone **(17)** and decrease in catecholamine responses to heart rate in acute exercise after three weeks of physical training**.(25)**

It was observed that there was significant decrease in systolic and diastolic blood pressure after training(

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P< 0.001). Earlier studies have also observed a significant (P<0.05) fall in systolic blood pressure**(26)** , and fall in diastolic blood pressure of 11.8 mm Hg in a hypertensive and of 6 mm Hg in normotensive subjects after training **(27)**

Central command arising from mesencephalic locomotor region (MLR) as well as the exercise pressor reflex are capable of resetting the carotid baroreflex response during exercise **(28,29)** and pressor reflex is a important contributor in changes in blood pressure response seen after regular physical training and autonomic nervous system is one of the most important mediator of this response **(19).**

Orthostatic hypotension refers to systolic blood pressure fall greater than 30 mm Hg upon standing caused mainly by gravity and lack of increase in peripheral vascular resistance upon standing up due to dysfunction of sympathetic vasoconstrictor nerves **(9).** In the current study there was decrease in mean value of systolic and diastolic blood pressure after the training during orthostatsis (P < 0.001) . However, study of literature failed to reveal any comparative study on effect of moderate exercise on autonomic nervous system using orthostasis as a measure of sympathetic activity.

The cold is a painful stimulus which leads to activation of the sympathetic nervous system and it has been used to test the autonomic response of different individuals **(30).** The reactivity of blood pressure in cold pressor test is due to widespread vasopressor reaction initiated through a neurogenic reflex arc . The increase in blood pressure in cold pressor test is attributed to an activation of the sympathetic nervous system **(31)**

In the present study maximal responses in cold pressor test were taken and evaluated at the end of the 30 second and at end of 60seconds. There was decrease in systolic and diastolic blood pressure after training at end of 30 and at end of 60seconds and change were significant in all groups (P <0.001). Similarly blood pressure recording during exposure to mathematical problems also revealed that there was a decrease in systolic and diastolic blood pressure after training (P<0.001) An exhaustive study of the available literature has revealed no comparative study except one study wherein similar results are reported on effects of short term physical training **(19) .**

The QT interval includes both ventricular depolarization and repolarisation times and it varies inversely with the heart rate. The rate related corrected QT internal (QTc) calculated by Bazett's formula is also used as a measure of sympathetic activity **(6,32)** In the current study there was an increase in mean value QTc interval after training and change (P<0.001) and scan of literature showed no report of comparative evaluation using QTc as a measure of sympathetic activity during the effects of short term physical training on ANS.

Valsalva Ratio is employed to assess both low and high pressure barroreceptors integrity during and after valsalva maneuver. Changes occur in the cardiac vagal efferent and sympathetic vasomotor activity, that are due to stimulation of afferents from baroreceptors stretch receptors in the heart, the lungs, aorta, carotid sinuses

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and muscles of chest wall . Valsalva maneuver involves passive changes in the blood pressure leading to reflex heart rate changes. The valsalva maneuver has the advantage of being simple, easy to perform, non-invasive and reproducible **(33).**

Thus Valsalva maneuver elicits a complex series of hemodynamic events that result in activation of sympathetic and parasympathetic neurons and is independent of heart rate . Valsava maneuver may be used as an effective measure of parasympathetic integrity but it may not be a reliable index of sympathetic integrity . In the present study the mean value of valsalva ratio increased significantly after training ($P<0.001$) . In a similar study to ours a numerical increase in valsalva ratio in 25 adult males has been reported who were trained for 15 days**(19).**

Heart Rate Response is taken as the difference in heart rate from electrocardiogram recording in supine and standing position is determined predominantly by vagal background and autonomic activity. Changing from supine to erect position causes an increase in heart rate . In the present study there was significant increase in mean value of heart rate response after training ($P < 0.001$) and no study is found to have used heart rate response as a measure of parasympathetic activity to see the effect of short term training on autonomy nervous system.

The expiratory inspiratory ratio is a good index of cardiac efferent parasympathetic function **(34).**.In the case of expiratory inspiratory ratio the increase in heart rate during inspiration results from decreased cardiac vagal activity We have found an increase in ratio after training and change was significant ($P<0.001$) .However a previous study has reported no significant change in expiratory inspiratory ratio after training **(19)** . Some variations in results is possible as expiratory inspiratory ratio though a simple procedure is effort dependant and varies from individual to individual .

Heart rate variability is mediated by the combined effects of cardiac vagal and sympathetic nerves acting upon the sinoatrial node . Heart rate variability is now considered as an important tool to assess the influence of resting autonomic tone on cardiovascular system **(19).** The heart rate variability is more considered to be due to parasympathetic activity , since in normal man the sinus arrhythmia is abolished with atropine, but not with propranolol **(9)**

In the present study the mean value of heart rate variability showed a decrease($P<0.001$). A trend towards an increase of parasympathetic nervous system activity as measured by LF:HF ratio, absolute HF and HF_{nu}. has also been reported **(19)**

Standing lying ratio and 30 : 15 ratio is considered as a measure of cardiac vagal function The ratio between R-R interval at beat 15 and R-R interval at beat 30 is the 30:15 ratio **(9,11,12).** There was increase in standing lying ratio increased in a significant manner ($P<0.001$).A single study done earlier has also found numerical increase in 30:15 ratio from 1.43 ± 0.20 to 1.49 ± 0.27 after the training **(19)**. No other study has used 30:15 ratio and standing lying ratio as a test for parasympathetic function in relation to effect of short duration of exercise on autonomic nervous system .

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The goal of the present study was to find out the effect of short duration of physical training on autonomic nervous system .Our results show decrease in heart rate , blood pressure both systolic and diastolic and increase in corrected QT interval suggesting decrease in sympathetic activity with physical training.

Even in certain disease states short duration of physical training affects the cardio respiratory parameters in favorable way .It has also been observed that physical training results in a decrease in plasma norepinephrine levels and catecholamine response to heart rate after exercise **(25,26,35, 36).**

In the present study, the results of orthostasis, cold pressor test, mental arithmetic test also showed a decrease in response after training. The results of valsalva maneuver, expiratory inspiratory ratio, standing lying ratio, heart rate variability, heart rate response, and 30:15 ratio all showed an increase in response after exercise indicating an increased parasympathetic reactivity.

Outcome of our study is that the short duration of training leads to significant favorable changes in parameters of autonomic nervous system comprised of increase in parasympathetic (vagal) and decrease in sympathetic tone. Thus clinical impact of the present study is that short term physical training can be used for promotion of health and to have a lower prevalence of symptomatic coronary artery disease and lesser death rates from cardiovascular diseases.

References

1. Malfatto G, Facchini M, Bragato R, Branzi G, Sala L and Leonetti G. Short and long term effects of exercise training on the tonic autonomic modulation of heart rate variability after myocardial infarction. Eur. Heart J. 1996; 17: 532 – 538,
2. Clausen J. P. Effect of Physical training on cardiovascular adjustments to exercise in man. Pysiological Review 1977; 57: 779-815.
3. Hutchison's Clinical Methods Editor M. Swash Physical Examination – pulse 2002, page 17 W.B.Saunders, London.
4. Heidbreder E, Schafferhans K and Heidland A. Autonomic neuropathy in chronic renal insufficiency. Nephron 1985; 41: 50-56.
5. Hines E.A and Brown G.E The cold pressor test for measuring the reactivity of blood pressure .Am Heart J. 1936; 11 (1): 1 – 9.
6. Kumar R and Ahuja V. MGlaucoma and concomitant status of autonomic nervous system. Indian J. Physiol. Pharmacol. 1998; 42(1): 90-94.
7. Schamroth L. An introduction to electrocardiography. 1994 ; 7th edition revised by Schamroth C :5–33. Oxford University Press, New Delhi.
8. Levin A.B A simple test of cardiac function based upon the heart rate changes induced by the valsalva maneuver. The Am. J. Cardiol. 1966; 18: 90-99.

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9. Hilsted J. Autonomic neuropathy : the diagnosis. Acta. Neurol.Scand .1983; 67: 193 – 201.

10. Mcleod J.G, Phill D and Tuck R.R Disorders of the autonomic nervous system. Part 2: Investigation and treatment Ann. Neurol. 1987; 21: 519-529.

11. Rodrigues E. A and Ewing D.J Immediate heart rate response to lying down simple test for cardiac parasympathetic damage in diabetics. Br. Med. J. 1983; 287: 800.

12. Ewing D.J, Campbell I.W, Murray A, Neilson J.M.M and Clarke B.F Immediate heart rate response to standing, simple test for autonomic neuropathy in diabetes. Br. Med. J. 1978; 1:145 -47.

13. Jellife D.B WHO Monograph series No 53. 1966.

14. Jain A.K Manual of practical physiology,1st edition 2000 Pg 1198. Vishal Printers, Delhi.

15. Fox SM, Naughton JP and Haskell WL .Physical activity and prevention of coronary heart disease . Ann. Clin. Res. 1971; 3:404-432.

16. Paffenbarger R.S. J and Hale W.E Work activity and coronary heart mortality. New Engl. J. Med 1975; 292: 545-550.

17. Scheuer J and Tipton C.M Cardiovascular adaptations to physical training Ann. Rev. Physiol. 1997; 39: 221-225

18. Rosenbleuth A and Simeone F.A The interactions of vagal and accelerator effects on cardiac rate. Am J Physiol 1934; 110: 400-411

19. Sharma R.K , Deepak K.K, Bijlani R.L and Rao P.S. Short term physical training alters cardiovascular autonomic response amplitude and latencies. Indian J. Physiol. Pharmacol. 2004; 48 (2): 165 – 173.

20. Robinson R.A , Epstein S .E , Beiser G.D and Braunwold E. Control of heart rate by autonomic nervous system. Studies in man in interrelationship between baroreceptor mechanisms and exercise. Circ. Res. 1966; 19: 400-411.

21. Kavalen and Moder Paradoxical effects of epinephrine on excitation – contraction coupling in cardiac muscle. Circ. Res. 1974; 34 : 599-603.

22. Nagai N , Hamada T , Kimura T and Moritani T . Moderate physical exerciseincreases cardiac autonomic nervous system activity in children with low heart rate variability. Childs Nrv Syst. 2004; 20 (4): 209 – 214.

23. Seals D.R and Chase P.B. Influence of physical training on heart rate variability and baroreflex circulatory control. J. Appl. Physiol. 1989; 66 (4): 1886 – 1895.

24. Yama moto K, Miyachi M, Saltoh T, Yoshioka A and Onodera S. Effects of endurance training on resting and post exercise cardiac autonomic control. Med. Sci. Sports Exerc. Sept, 2001; 33 (9): 1496-1502.

25. Winder W.W, Hagberg J.M, Hickson R.C, Ehsani A.A and Mclone J.A. Time course of sympatho adrenal adaptation to endurance exercise training in man. J. Appl. Physiol 1978; 45 (3): 370 – 374.

26. Sharma R.K and Deepak K.K. A short duration of physical training benefits cardiovascular performance. Indian J. Physiol. Pharmacol. 2004; 48(4) : 481-485.

27. Boyer John L and Kasch Fred W. Exercise therapy in hypertensive men. JAMA.1970; 211: 1668-1671.

28. Mciiveen S.A, Hayes S.F and Kaufman M.P Both Central Command and exercise pressor reflex reset carotid sinus baroreflex. Am. J.Physiol, Heart Circ. Physiol. 2001; 280 : 1454-1463.

29. Somers V.K, James C, Jim J and Peter S. Effects of endurance training on baroreflex sensitivity and blood pressure in border line hypertension. The lancet 1991; 337: 1363 – 68.

30. Le Blanc J ,Dulac S ,Cote J and Girard B. Autonomic nervous system and adaptation to cold in man. J. Appl. Physiol. 1975; 39(2) : 181-186.

31. Bedi M, Babbar R and chakrabarty A.S Cold pressor response in normal and malnourished children. Indian J.Physiol. Pharmacol. 1998; 42(4) : 569-571

32. Gold berger A.L Electrocardiography. Harrison’s principle of internal medicine Vol.1 1998; 14th edition : 1237-1253. Mc Graw Hill-International edition.

33. Ewing D.J, Campbell I.W and Clarke B.F Assessment of cardiovascular effects in diabetic autonomic neuropathy and prognostic implications. Annals, of Internal Medicine 1980; 92(2): 308-311.

34. Agarwal A , Anand I.S, Skhuja V and Chugh K.S.Effect of dialysis and renal transplantation on autonomic dysfunction in chronic renal failure Kidney International 1991; 40; 489-495.

35. Martinsen E.W , Medhus A.S and Sandvik L Effect of aerobic exercise on depression : a control study. Br. Med. J. 1985; 291:109.

36. Hartley L.H , Mason J.W, Hogan R.P, Mougey E.H, Wherry F.E, Pennigton L.L, and Ricketts P.T. Multiple hormonal responses to graded exercise in relation to physical training. J. Appl. Physiol 1972; 33 (5): 602 – 606.