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"A Longitudinal study of heart rate and blood pressure responses to Tread-Mill exercise and recovery in Katihar district, Bihar. India".

Physiology

KEYWORDS: Blood Pressure; Heart Rate; Heart Rate Variability; Tread mill exercise.

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ABSTRACT

BACKGROUND: The clinical relevance of heart rate variability was first appreciated in 1965 when Hon and Lee noted that fetal distress was preceded by alterations in inter beat intervals before any appreciable change occurred in heartbeat. **AIMS AND OBJECTIVE:** This study was undertaken to identify abnormal heart rate and blood pressure responses to tread-mill exercise among young adult normotensive males with and without a parental history of hypertension. The second objective was to elaborate possible correlation (if any), between heart rate responses and heart rate variability parameters during post exercise recovery period. **METHODS AND MATERIAL:** A total of 98healthy normotensive males with normal BMI (18.5 – 24.9 kg/m^2) and average physical fitness index were chosen for the study. They were classified into two groups based on their parental history of hypertension. All subjects underwent a sub maximal tread-mill exercise test as per Bruce protocol. The exercise was continued at the same Bruce stage for three minutes at the target heart rate. ECG and heart rate were recorded at baseline, during exercise and during recovery period of ten minutes while blood pressure was recorded at baseline and recovery. **RESULT:** The basal systolic blood pressure and the recovery systolic blood pressures at the 1st, 3rd, 5th, 7th, and 9th minute of recovery were significantly higher in the group with parental history of hypertension than in the other group .The baseline LF normalized units and LF/HF ratio were significantly higher in the group with parental history of hypertension than the other group. The baseline HF normalized unit was significantly lower in the group with parental history of hypertension than the other group. **CONCLUSION:** A difference in baseline systolic blood pressure, a higher LF normalized units and a lower HF normalized units found in offspring of hypertensive parents may be an early marker of cardiovascular change in subjects with a genetic predisposition to hypertension.

INTRODUCTION:

Hypertension is an important Worldwide public health challenge because of its high frequency and concomitant risk of cardiovascular and kidney disease.[1,2]It has been identified as the leading risk factor for mortality and is ranked third as a cause of disability- adjusted life-years.[3] It is commonly asymptomatic, readily detectable and usually easily treatable and often leads to lethal complications if left untreated.The number of unidentified cases of hypertension is phenomenally high. Early detection and appropriate treatment is the solution.[4]Measurements of blood pressure, such as pressure reading during basal conditions[5] ambulation[6,7] or exercise[8] may be better indicators of mortality and morbidity risk. Given the health costs and potential importance of early detection of hypertension, several studies have examined the blood pressure response to exercise as a risk factor for the development of hypertension.[9,10]Researchers have found that normotensive people who are at high risk of developing systemic hypertension have greater cardiovascular reactivity to physical stress. A high cardiovascular reactivity to exercise is also postulated to be inversely proportional to myocardial coronary blood flow. These normotensive show an exaggerated blood pressure response as well as higher Chronotropic response to exercise tests.[9] Exercise tests bring about changes in all the hemodynamics of the cardiovascular system including blood pressure and heart rate.[11] In humans, anticipation of physical activity inhibits the vagal nerve impulses to the heart and increases sympathetic discharge. The tachycardia and enhanced contractility increases cardiac output. As a result, there is an increase in heart rate and blood pressure.[12]A rise in the systolic blood pressure and a normal or low diastolic blood pressure is a normal response to isotonic exercise.[13] Studies have shown that persons with high-normal resting blood pressure or unusually high blood pressure response to exercise are prone to develop hypertension.[14] An elevated systolic blood pressure at the third minute of recovery and elevated exercise systolic blood pressure response were also predictors of new onset hypertension.[15]The heart rate response to exercise is another determinant of the healthy cardiovascular system. An attenuated heart rate response to exercise has been shown to be predictive of mortality and coronary heart disease risk.[15]It may be sub-clinical manifestations of cardiovascular disease, E.g. Chronotropic incompetence. It is defined as failure to reach 85% of age predicted heart rate.[15]Recovery of the heart rate immediately after cessation of exercise is a function of vagal reactivation. A delayed decrease in the heart rate during the first minute of rest, following cessation of graded exercise may be a powerful predictor of overall mortality. Studies have shown that there is an inverse association between heart rate recovery and exercise capacity.[16]During the last three decades, researchershave recognized the significance of the relationship between autonomic system and cardiovascular mortality. This has encouraged the development of quantitative markers functions of autonomic nervous system like heart rate variability.[17]Heart rate variability is the amount of heart rate fluctuations around the mean heart rate. It is a valuable tool to investigate sympathetic and parasympathetic function of the autonomic nervous system.[18]

Studies have shown thatcardio-decelerationis independent of heart rate variability measures during the resting period but is related to the early post exercise heart rate variability measurements.[19]

Exercise hypertension is defined as a rise in systolic blood pressure during exercise above a threshold usually between 190 and 220 mm Hg.[20] Some studies suggest that exercise hypertension predicts future arterial hypertension in people with normal resting blood pressure.[21,22]

MATERIAL AND METHODS.

A total of 98healthy normotensive males (non-smokers) in the age group of 18-30 years with normal BMI (18.5-24.9 kg/m^2) were chosen for the study. They were classified in to two groups, group-A based on their parental history of hypertension. 36 of them had a parental history of hypertension while 62 of them did not have.

Study design:	Longitudinal study.
Study setting:	Katihar Medical College, Katihar, Bihar, India.
Study period:	Sep.2009- Dec.2011.

Inclusion criteria: Males in the age group of 18-30 years, Non-smokers, Normal BMI (18.5-24.9 kg/m^2), Fasting overnight, and Physical fitness index above 55 using Harvard Step Test, are included in this study.

Exclusion criteria: Subject having any acute illness, Diabetes Mellitus, Anti-hypertensive medication, History of chest pain,

breathlessness, Orthopnea was excluded from the study. Also person having Physical disability like arthritis of the knee which may impair cycling, Any recent illness during the past two weeks, Physical fitness index below 55 using Harvard Step Test and BMI >/= 25 kg/m^2

All subjects were made to undergo a treadmill exercise test as per Bruce protocol.The exercise was set at a workload so that they reached a maximum target heart rate (basal heart rate +60% heart rate reserves). The exercise was continuedat the same intensity for three minutes at the maximum target heart rate. Continuous ECG and heart were recorded at base line, during exercise and during the recovery period of first ten minutes, while blood pressure was recorded at baseline and recovery during 1to3 minutes (early recovery), 4 to 7 minutes (mid-recovery) and 8 to 10 minutes (late recovery).

Formulae used for calculations are as:

1. MPHR (Maximum Predicted Heart Rate) = 220- Age.
2. HRR (Heart Rate Reserve) = MPHR – Heart Rate at rest = [(220-Age) – Heart Rate at rest].
3. Chronotropic incompetence = Failure to achieve 80% of HRR.
4. MTHR (Maximum Target Heart Rate) = Heart Rate at rest + 60% of HRR (Heart Rate Reserve).[23,24]

PROTOCOLS:

1. The Harvard Step Test protocols for estimating physical fitness index.
2. The Bruce Protocol for exercise testing on automated treadmill.

The Bruce Tread Mill Test Protocol:

The Bruce Treadmill Test Protocol was designed in 1963 by Robert. A .Bruce, MD, as non-invasive test to assess patients with suspected heart disease. In a clinical sitting the Bruce treadmill Test is sometimes called a stress test or exercise tolerance test. Today the Bruce Protocol is also one common method for estimating VO_2 max in athletes. VO_2 max or maximal oxygen uptake is one factor that can determine a subject's capacity to perform sustained exercise and is linked to aerobic endurance. VO_2 max refers to the maximum amount of oxygen that an individual can utilize during intense or maximal exercise. It is measured as millimeters of oxygen used in one minute per kilogram of body weight. (ml/ kg/min.)

The Bruce Protocol is a maximal exercise test where the subject works to complete exhaustion as the treadmill speed and incline is increased every three minutes (See chart). The length of time on the treadmill is the test score and can be used to estimate the VO2 max value. During the test, heart rate, blood pressure and ECG are continuously monitored.

Bruce Treadmill stages: Duration of each stage is 3 minutes, e.g. After 3 minutes of stage 1, stage 2 starts automatically with increase in speed to 2.5m/hr. and an increase in gradient to 12%.

Instrumentation:

Metronome:

For timing during physical fitness assessment.

Height and Weight measurement.

Weight was measured to the nearest 100 grams using an electronic weighing scale (Ling Xuang Model EB-882, Made in PRC) and height was measured to the nearest 0.1 cm using a stadiometer (Holtain, CRYMYCH, DYFED, Made in UK).

Automated Treadmill.

All exercises were performed electrically operated computerized treadmill (Nasan Medical Electronics, India. Model-T6532).

Automated Sphygmometer.

Blood pressure was measured with an electronic Sphygmometer (Omron Inteilisense HEM 7203, Omron Medical Inc. Made in Germany) and has been clinically tested.

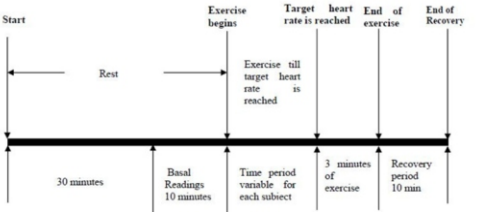
Experiment Protocol:

Subjects were recruited based on the inclusion and exclusion criteria. A brief history, general and systemic examination was performed. Subjects were interviewed the previous day and a detailed description of the protocol was explained to them. Then they underwent a warm up exercise session on a Harvard step. It was simultaneously used for estimating the physical fitness index of the subject. Experiment was conducted in the morning in the fasting state with the instruction last meal by 10:00 hrs. Refrain from caffeinated beverages 24 hrs. Prior to the experiment and to avoid strenuous physical activity from previous evening.

A written informed consent was also obtained in presence of witness on the day of experiment. Subjects were explained in detail about the experimental procedure and then they underwent instrumentation as follows:

Blood pressure measurement with automated blood pressure monitoring device was secured on the right upper limb, pulse oxymeter plethysmographic was placed on the left middle finger. They were asked to take a mandatory 30minutes of rest. At the end of 30 minutes rest period, the ECG (II lead) and pulse plethysmographic recordings were started along with blood pressure recording every 5 minute s for the next 10 minutes. Three blood pressure recordings were obtained during this period. Basal heart rate and Blood pressure was determined. From the value of basal heart rate following parameters (Heart rate reserve and target heart rate) were calculated.Now, the subject was instructed to walk on the electrically operated automated treadmill from stage I with each stage increments at every three minutes till Target Heart Rate achieved. Subject was instructed to continue at the same intensity of work for the next three minutes at the same Bruce protocol stage. The ECG and the pulse plethysmographic readings are continuously recorded during this period. Treadmill was stopped on reaching maximum heart rate and the subject was made to relax. Recovery period began from the cessation of exercise and lasted for 10 minutes. Blood pressure was recorded every alternate minute during the recovery period. The ECG, Blood pressure and the pulse plethysmographic recordings were continuously recorded during the recovery period and stopped after ten minutes.

Flow chartof experiment is as follows:



GUIDELINES:

The experiment was set up along the recommendations of "American Heart Association guidelines for exercise testing."

The metronome is set at one ring per second. The subject is then told to practice stepping up in the following manner against the rings of the metronome.

Initial position, both feet on the ground. First ring, right foot on the first step. Second ring, left foot on the second step. Third ring, both feet on the second step. Fourth ring, left feet on the first step. Fifth ring, right foot on the ground.Finally, on the sixth ring,both feet on the ground. This completes one cycle of steps in 6 rings or 10 cycles in one minute. When the subject has mastered this rhythm, he rests till his pulse rate comes to normal and then exercises for five minutes, the ECG and pulse plethysmograph are recorded withthe subject seated. The number of heart beats between 1-1.5, 2-2.5 and 3-3.5 minutes is noted.

Physical Fitness Index = 100 x Test duration in seconds.

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2X total heart beat in the recovery period.

Grading of Physical Fitness Index using Harvard Step Test:

Excellent	>90
Good	80-89
High average	65-79
Low average	55-64
Poor	<55

Statistical Analysis:

All collected data were analyzed statistically and significance if any was noted to test the hypothesis. The data was examined for normality. Wherever the data wasnot distributed normally, non-parametric testing methods were used. Mean +/- SD has been used to describe normally distributed data while median and interquartile ranges have been used to describe the non-normally distributed data. The student independent t test has also been used to find significance between subjects with and without parental history of hypertension.

The Mann Whitney U test has been used to assess difference in heart rate variability parameters between the two groups if data was not normally distributed.Friedman test – non-parametric test for repeated measurements has been used to find the significance of recovery changes within each group. The corrected data was then submitted to the null hypothesis (at P<0.05).SPSS version 11.0 and Systat 8.0 software packages were used for analysis of data.

Result:

Table –I: Subject characteristics of the 98 normotensive males.

Basic characteristics.	Without parental history of hypertension. n=62	With parental history of hypertension. n=36	P value.
Age in years	19.45± 1.71	20.94± 2.94	0.061
BMI in kg/m^2	21.17 ± 2.15	22.13 ± 1.91	0.127
Physical fitness index	108.59 ± 12.69	105.36 ± 13.46	0.406
Mean Basal Heart Rate	63.1 ± 8.73	65.43± 9.46	0.387
Mean Basal Systolic Blood pressure	106.87 ± 6.98	113.67 ± 7.21	0.002
Mean Basal Diastolic Blood pressure	65.68 ± 4.91	68.44± 6.16	0.09

Table –I summarize the subject characteristics. There was no significant difference in age, BMI, Physical fitness index, Mean basal diastolic blood pressure and mean basal heart rate between the two groups. Although Mean basal systolic blood pressure was significantly higher in the group with parental history of hypertension.

Table: II Heart rate changes during exercise.

Exercise H.R (beats/min)	Overall n=98	Without parental history of hypertension. n=62	With parental history of hypertension. n=36	P value.
At 1 minute	147.45	147.23	147.83	0.742
At 2 minute	150.14	149.87	150.61	0.751
At 3 minute `	152.29	151.68	153.33	0.511

Table-II shows that exercise heart rate has increased gradually over three minutes of exercise. There is no significant difference in the exercise heart rate during the first, second and third minutes of exercise between two groups. This is expected as the study design required the subjects to achieve their target heart rate. (Basal Heart Rate + 60% of heart rate reserve), and all included subjects were physically fit.

Table –III : Recovery Heart Rate in response to exercise.

Recovery Heart Rate	Without parental history of hypertension. n=62		With parental history of hypertension. n=36		**P value**
	Mean	S.D	Mean	S.D	
At 1 minute.	116.39	12.27	119.22	16.24	**0.493**
At 2 minute	103.16	11.27	106.06	17.98	**0.491**
At 3 minute	102.58	11.19	104.33	16.01	**0.656**
At 4 minute	98.13	11.35	99.83	13.38	**0.637**
At 5 minute	100.71	11.50	104.50	12.92	**0.293**
At 6 minute	94.19	13.80	97.11	13.09	**0.471**
At 7 minute	97.32	14.13	101.33	12.10	**0.319**
At 8 minute	95.32	12.77	96.11	12.35	**0.634**
At 9 minute	96.29	13.62	99.44	11.60	**0.414**
At 10 minute	95.42	11.61	95.83	11.69	**0.905**

Table III shows that during the 10 minutes recovery period there was no significant difference between the two groups in the heart rate.

Table IV: Recovery systolic blood pressure.

Recovery SBP	Without parental history of hypertension. n=62		With parental history of hypertension. n=36		P value
	Mean	S.D	Mean	S.D	
At 1 minute.	134.94	12.73	146.44	14.58	0.006
At 3 minute	118.90	8.54	128.61	10.01	0.001
At 5 minute	113.81	10.27	121.11	11.31	0.025
At 7 minute	108.81	21.56	121.06	9.47	0.027
At 9 minute	111.00	9.02	117.67	8.89	0.016

Table IV shows that recovery systolic blood pressure has been significantly higher in the group with parental history of hypertension than in the group without parental history.

Table V: Recovery Diastolic blood pressure.

Recovery DBP	Without parental history of hypertension. n=62		With parental history of hypertension. n=36		P value
	Mean	S.D	Mean	S.D	
At 1 minute.	78.32	7.04	81.72	5.83	0.090
At 3 minute	75.52	6.52	78.61	6.59	0.117
At 5 minute	74.77	7.68	76.28	6.10	0.481
At 7 minute	73.35	9.34	75.78	6.98	0.345
At 9 minute	74.55	7.89	75.67	7.64	0.631

Table V shows that recovery diastolic blood pressure is higher in the group that has parental history of hypertension than in the control group even though not statistically significant.

Table VI: Results of analysis of Heart rate variability parameters using Friedman (non parametric) test.

Heart rate variability parameters		Basal	Early recovery	Mid recovery	Late recovery	Recovery changes. P value
LF in ms^2	Control	419	28	33	68	<0.001
	Experimental	746	29	35	58	<0.001
HF in ms^2	Control	564	09	08	19	0.003
	Experimental	526	10	05	08	0.559
LF/HF	Control	0.927	2.91	6.15	4.313	0.023
	Experimental	1.38	2.648	4.327	4.708	0.113
LF normalized units.	Control	48.1	74.4	86	81.2	<0.001
	Experimental	58	72.6	81.2	82.5	<0.001
HF normalized units.	Control	51.9	25.6	14	18.8	0.023
	Experimental	42	27.4	18.3	17.5	0.113

Heart Rate variability parameters are expressed as Median and inter quartile range. The group with parental history of hypertension showed an overall significant increase LF and LF normalized units. There was no significant change during recovery in HF, LF/HF ratio and HF normalized units. The group without parental history of

hypertension showed an overall significant increase during recovery in the LF, HF, LF/HF ratio and LF normalized units and a overall significant decrease in HF normalized units.

Discussion.

The treadmill remains the most commonly used dynamic exercise testing device. American Heart AssociationExercise Standards were maintained in the study- includes proper equipped exercise laboratory, under the supervision of a physician, patient's medical history, 12 lead resting ECG, provision for advanced CPR if necessary and a defibrillator with appropriate emergency medication.

Some subjects are forced to stop prematurely becauseof musculoskeletal difficulties or inability to tolerate the high workload increments.Regardless of technique used, the optimum exercise testing protocol should last 6-12 minutes and should be adjusted to the type of patient being tested.Of the 36 normotensive subjects with parental history of hypertension, the ECG of two subjects could not be analyzed as there were too many artifacts which could not be manually edited. The intra and inter individual variability was assessed for heart rate, systolic as well as diastolic blood pressure during baseline recording, exercise and recovery. The range of intra individual coefficient of variation was 4-11% while the inter-individual was 5-12%. Since the coefficient of variation <20% in all the parameters, the repeatability and methodology is statistically accepted. Further the intra individual and inter individual coefficient of variationduring exercise of 1.5-2.5% and of 3-5% respectively shows, that there is not much difference in the heart rates achieved during exercise in our subjects. As the study design requires that the level of heart rate achieved during exercise is same in all subjects, the low intra and inter individual variation proves that the level of heart rate achieved was maximum in all our subjects.

Julius et al suggested that those who have a positive family history of hypertension frequently exhibithyperactive sympathetic nervous system. The consequences of sympathetic stimulation are peripheral vasoconstriction, an increase in heart rate, resulting in increase in peripheral vascular resistance with rise in systemic blood pressure.[23] Studies have shown that normotensive with a family history of hypertensionexhibit alteredsympathovagal balance with decreased parasympathetic activity at the cardiac level.[24]In accordance with these studies, basal high frequency power is lesser in the group with parental history of hypertension than the group without. The LF/HF ratio is considered by some to mirror sympathovagal balance.**During the treadmill exercise, one subject developed hypotension and he was excluded from the study.**The sample was of modest size because of difficulty in recruiting subjects due to restrictions like, including only males and subjects with normal body mass index. A large sample size would have resulted in better result. Simultaneous recording of beat to beat heart rate and blood pressure would have given valuable information about baroreceptor sensitivity. Additional use of tilt-table screening test to rule out autonomic dysfunction in our subjects would have been an added advantage.

Conclusion.

There was no difference in the heart rates at rest and during recovery between the two groups. There was a significant difference in systolic blood pressurebetween the two groups at base line and during recovery. There was no significant difference in diastolic blood pressure during baseline and during recovery. A difference in baseline systolic blood pressure found in those with parental history of hypertension which may be an early marker of cardiovascular change in subjects with a genetic predisposition to hypertension. The area under the curve for systolic blood pressure during recovery was significantly greaterin the group with parental history of hypertension than the other group.

There was no significant difference in low frequency (LF) and high frequency (HF) at baseline between the two groups. However low frequency normalized units and LF/HF ratios are significantly higher in the group with parental history of hypertension and HF normalized units is significantly lower in the groups with parental history of hypertension than the other group. This indicates a higher sympathetic and lower parasympathetic activity in those with parental history of hypertension.

There was no difference in the heart rate variability parameters between the two groups during the recovery period. Both the groups showed a significant change during recovery in all the heart rate variability parameters except HF, LF/HF ratio and HF normalized units in the group with parental history of hypertension.This is because of poor parasympathetic reactivation following cessation of the exercise during the recovery period.

The correlation between the delta heart rate (difference between the 3rd minute of exercise heart rate and 1st minute of recovery heart rate / 3rd minute exercise heart rate x 100) and heart rate variability parameters during the recovery period in the group with parental history of hypertension and not in the group without parental history of hypertension cannot be explained physiologicallyand requires further research in the same.

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