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Effect of Supervised Integrated Exercise on Deep Breathing-Heart Rate Variability in Male Hypertensive Patients

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The aim of the study was to evaluate if prolonged supervised integrated exercise in male hypertensive patients reverses the deterioration of heart rate variability. Sixty six male hypertensive patients were divided into exercise (n = 30) and non-exercise groups (n = 36). Exercise group patients underwent a supervised integrated exercise program for one-year. Time domain analysis of heart rate variability was performed from electrocardiogram during deep breathing. Heart rate variability decreased significantly ($p < 0.001$) in hypertensive patients. HRV increased significantly after six months ($p < 0.001$) and 12 months ($p < 0.01$) of integrated exercise training. There was a significant decrease in blood pressure ($p < 0.001$) in exercised hypertensive patients after 12 months compared to non-exercised group. Heart rate variability was significantly decreased ($p < 0.001$) than normotensives after one-year in the non-exercised hypertensive patients. Long term supervised integrated exercise increased deep breathing heart rate variability and decreased blood pressure in the hypertensive patients. This suggested that integrated exercise program was able to reverse the autonomic dysregulation seen in hypertensive patients.

Key words: Blood pressure, hypertension, deep breathing, heart rate variability, exercise

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INTRODUCTION

An elevated arterial pressure is probably the most important public health problem. Although our understanding of the pathophysiology of elevated arterial pressure is increased, in 90-95% of the cases the etiology is unknown (Wolf-Maier *et al.*, 2001). The positive relationship between systolic and diastolic blood pressure and cardiovascular risk has long been recognized. This relationship is strong, continuous, consistent and etiologically significant (Fagard *et al.*, 2001). The risk for cardiovascular disease in patients with hypertension is determined not only by the level of blood pressure, but also by the presence or absence of target organ damage or other risk factors such as smoking, diabetes, dyslipidemia. Obesity and physical inactivity are also predictors of cardiovascular risk and interact with other risk factors (Fagard *et al.*, 2001; Chobanian *et al.*, 2003).

Heart rate variability (HRV) is a non-invasive electrocardiographic marker, reflecting the activity of the sympathetic and vagal components of the autonomic nervous system on the sinus node (Malik, 1998; Sztajzel, 2004). It expresses the total amount of variations, both instantaneous heart rate and R-R intervals (Benett *et al.*, 1978). Heart rate variability during deep breathing is approximately doubled than during quiet breathing. So, HRV during deep breathing is a more precise measure of autonomic function and it is a much simpler and easier method of determining R-R variability (Diehl *et al.*, 1997; Katz *et al.*, 1999; Prakash *et al.*, 2006).

Regular exercise is a key component of cardiovascular risk prevention strategies; because it is associated with variety of beneficial metabolic and neurovegetative affects that reduce mortality and the incidence of adverse events due to coronary heart disease (Malfatto *et al.*, 1998; Shephard and Balady, 1999). Data on the effects of physical training on the autonomic control in healthy subjects remain controversial (Carter *et al.*, 2003). The mortality reduction observed in physically active subjects compared with sedentary person strongly suggests that exercise is beneficial. Activities of moderate intensity are commonly accepted to improve health and lower cardiovascular risks, some studies have argued that high intensity training may have proportionately greater cardio protective effects (Carunchio *et al.*, 2000). Other studies have reported that both moderate and vigorous exercise induce similar health benefits (Lazoglu *et al.*, 1996; Verheyden *et al.*, 2006).

Reduced HRV is associated with increased mortality (Bigger *et al.*, 1992). Researchers found that many of the interventions associated with decreased mortality were also associated with increased HRV. These can be

combination of pharmacological interventions, exercise, relaxation technique etc. (Stein and Kleiger, 1999). HRV has been shown to be related to cardio respiratory fitness (Shephard and Balady, 1999), although some studies do not agree with this (Verheyden *et al.*, 2006). In some longitudinal exercise training studies with old healthy subjects, HRV has been reported to increase (Leitch *et al.*, 1997). However, some studies have not found any significant effect of exercise training on heart rate variability (Lazoglu *et al.*, 1996; Mikko *et al.*, 1998; Verheyden *et al.*, 2006).

One minute deep breathing heart rate variability (DB-HRV) test was chosen as a short and simple bedside test in testing autonomic nervous control of the heart (Bennett, 1978; Tamosiunaite *et al.*, 2005). This method has been validated as an independent predictor in a few cardiac diseases including myocardial infarction. During deep breathing, changes in heart rate occur primarily because of alterations of vagal-cardiac activity. An impairment of this system can lead to depressed HRV (Katona and Jih, 1975; Tamosiunaite *et al.*, 2005). The changes in heart rate associated with respiratory activity are mediated primarily by changing levels of cardiac vagal and sympathetic activity and mechanically induced sinus node stretch with each respiration (Hirsch and Bishop, 1981). The degree of the contribution from each of these components is related to the frequency and amplitude of the respiratory signal, the mean level of vagal and sympathetic activity and the mechanical state of the airways.

Controlled, randomized long-term studies on the effect of regular physical exercise on 1 min deep breathing HRV and blood pressure are missing. The present research work was designed to investigate the effects of 12 months of supervised, integrated exercise on deep breathing heart rate variability in hypertensive patients, with the hypothesis that integrated exercise will increase the deep breathing heart rate variability and has beneficial effect on cardiac autonomic regulation.

MATERIALS AND METHODS

Patients: Sixty-six randomly chosen male hypertensive patients from Kasturba Medical College Hospital, Mangalore, India, who volunteered to take part in the study, were recruited for the project. To prevent for possible confounding neuro-humoral effects on HRV, only men were included in this study. The study was conducted from November 2003 to October 2005. All the subjects gave informed consent for the study and the study protocol was approved by the University Ethics Committee. Patients were interviewed and invited for the

baseline clinical examination. Patients height, weight, waist-hip ratio, blood pressure, pulse rate, respiratory rate, medications were recorded. All measurements were carried out between 9 to 10 AM. Subjects were asked to refrain from tea, coffee and alcohol or heavy meal within 4 h before physiological assessment. A 12 lead resting electrocardiogram was recorded and findings were noted down.

Subjects were excluded if they met any of the following criteria; clinical evidence of myocardial infarction, congestive heart failure, atrial fibrillation, diabetes mellitus, frequent ectopic beats, abnormal plasma creatinine concentrations, unable to perform integrated exercise test.

Blood pressure recordings: Blood pressure was measured in the left arm twice with the subject in the seated position, using mercury column sphygmomanometer. The average values were then used to derive the respective examination systolic and diastolic blood pressures. Patients with systolic blood pressure >140 mmHg and diastolic blood pressure >90 mmHg, regardless of duration of hypertension were included in the study.

Thirty-one age matched control subjects were also included for the study. The criteria for the control subjects were; no history of diabetes, hypertension, no systemic illness, no history of drug treatment and no sign of cardiologic or neurologic involvement.

Exercise program: Of the 66 hypertensive patients, randomly chosen 30 patients were enrolled for the exercise program which was conducted under the supervision of hospital physiotherapist. These patients were requested to visit the physiotherapy ward of the hospital regularly for 5 days per week for exercise program. Remaining 36 hypertensive patients were not included in the exercise intervention program were taken as non-exercised hypertensive group.

The type of exercise taught to the patients under the guidance of physiotherapist was as follows:

- Warming up exercise for 5 min
- Cycling or treadmill exercises for 30 min
- Cooling down exercises for 10 min

Total duration of the exercise in each session was not more than 45 min.

Heart rate variability measurement: Deep breathing HRV test was done (Katz *et al.*, 1999; Prakash *et al.*, 2006) in all patients and control subjects. The subjects were in supine

position and were taught to breathe at a rate of six respiratory cycles per minute; 5 sec each for inspiration and expiration. Electrocardiogram was recorded in limb lead II for one minute with patient breathing deeply as instructed. The R-R intervals between adjacent QRS complexes resulting from sinus node depolarization were measured manually. The variability in the heart rate was calculated as the difference between the shortest and longest R-R intervals. Each patient and the control subjects in the study group were examined on a regular basis.

The study was continued for a period of 12 months. During the follow up, blood pressure, pulse rate and body weight were measured. Follow up HRV was measured after 6 months and at the end of 12 months. To avoid possible influences of previous training sessions on HRV the participants were not allowed performing strenuous physical exercise the day before examination. No changes were made in the medication used and lifestyle reported by the patients at baseline.

Statistical analysis: The results are expressed as Mean±SEM. SPSS statistical package was used for the data analysis. Mann-Whitney U-test was employed to compare the parameters in exercised and non-exercised groups. Wilcoxon signed rank test was employed for comparison between baseline and follow-up measurements. A stepwise multiple regression analysis was used for assessing the relationship between variables. p-value less than 0.05 was considered for statistical significance.

RESULTS

Statistical analysis revealed that the study groups were well balanced and there was no significant difference in age, body mass index, smoking, duration of hypertension and the medication among the exercised and non-exercised groups (Table 1). Table 2 shows the heart

Table 1: Demographic and clinical characteristics

Parameters	Normal control (n = 31)	Non-exercised hypertensives (n = 36)	Exercised hypertensives (n = 30)
Age (years)	47.39±3.13	49.18±2.08	52.71±3.61
BMI (kg m ⁻²)	25.08±0.44	27.41±0.31	27.62±0.18
Smoking	8.0	14.0*	16.0*
Coffee (cups day ⁻¹)	2.5±0.120	2.70±0.08	2.80±0.18
Duration of hypertension (months)	-	38.60±2.80	40.21±1.26
Drugs			
ACE inhibitors		8	6
Beta blockers		10	12
Calcium channel blockers		4	3
Diuretics		6	4

Results are expressed as Mean±SEM; *p<0.05-control with other groups

Table 2: Effect of exercise on deep breathing heart rate variability (beats min⁻¹) during various duration of training

Duration of training	Normal control (n = 31)	Non-exercised hypertensives (n = 36)	Exercised hypertensives (n = 30)
Baseline	18.74±2.06	13.68±1.59 ⁺⁺	12.29±1.79 ^{+++NS}
After 6 months	18.20±1.22	12.17±1.46 ⁺⁺⁺	14.17±1.75 ^{***†}
After 12 months	17.87±2.18	11.08±0.84 ^{*****}	16.41±1.06 ^{***†††}

Values are Mean±SEM, Baseline vs. 6 months vs. 12 Months; *p<0.05; **p<0.01; ***p<0.001, Control vs. Non-exercised and Exercised; †p<0.01; ††p<0.001, Non-exercised vs. Exercised; NS: Not Significant, †p<0.05, ††p<0.01, †††p<0.001

rate variability recorded at the baseline level. There was a significant difference in the HRV between control and hypertensive groups. Baseline HRV was significantly lower (p<0.001) in both exercised and non-exercised hypertensive patients compared to control subjects. Even after six months, HRV showed a significant decrease in both hypertensive groups (p<0.001; non-exercised group; p<0.01; exercised group) than control. Non-exercised hypertensive patients had significantly lower HRV compared to controls after 12 months follow up study.

When HRV at baseline, 6 months and after 12 months were compared in the hypertensive patients, a significant decrease was noted (p<0.01) after one-year in the non-exercised group, where as HRV increased significantly after six months (p<0.05) and 12 months (p<0.001) in the exercised hypertensive patients (Table 2). Integrated exercise program significantly increased (p<0.05) HRV after six months follow-up. More significant increase (p<0.001) in heart rate variability was recorded after 12 months follow-up in the exercised hypertensive patients than non-exercised hypertensives (Table 2).

Systolic and diastolic blood pressure decreased significantly after six months follow up in the exercised group (p<0.05-SBP; p<0.01-DBP) compared to baseline (Table 3). More significant fall in blood pressure was recorded (p<0.001-SBP; p<0.001-DBP) after 12 months exercise program and the blood pressure was significantly lower than 6 months recording. The blood pressure returned to the near normal control levels after 12 months integrated exercise program in hypertensive patients (Table 3). Blood pressure recordings from the exercised hypertensive patients were significantly lower after 6 months and one-year follow up when compared to the recordings from the non-exercised hypertensives (Table 3).

When stepwise regression analysis were done, integrated exercise accounted for 62.5 % (R = 625) of the variation in heart rate variability after 12 months follow up. When other predictors were also included, there was a greatest t-value for exercise (t = 4.967; p<0.01) which indicated that exercise has contributed maximally for the observed changes in the heart rate variability. Greater

Table 3: Effect of exercise on blood pressure during various duration of training

Duration of training	Normal control (mmHg) (n = 31)	Non-exercised hypertensives (mmHg) (n = 36)	Exercised hypertensives (mmHg) (n = 30)
Baseline			
SBP	125.48±1.77	149.31±3.38 ⁺⁺⁺	148.94±4.31 ⁺⁺⁺
DBP	79.54±1.30	92.44±3.08 ⁺⁺⁺	91.41 3.82 ⁺⁺⁺
After 6 months			
SBP	127.23±4.11	154.73±3.18 ⁺⁺⁺	140.35±2.15 ^{***†††}
DBP	82.17±3.33	94.17±2.41 ⁺⁺⁺	84.70±2.82 ^{***††}
After 12 months			
SBP	126.34±4.17	158.89±2.37 ^{*****}	136.85±1.99 ^{***†††}
DBP	83.18±4.16	95.77±1.76 ⁺⁺⁺	83.29±2.92 ^{***†††}

Values are Mean±SEM; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure, Baseline vs. 6 months vs. 12 months; *p<0.05, **p<0.01; ***p<0.001, Control vs. Non-exercised and exercised; †p<0.001, Non-exercised vs. Exercised; †p<0.05, ††p<0.01, †††p<0.001

co-efficient value for the exercise confirmed that exercise has maximum contributions among all the predictors (age, duration of the diabetes, medications).

DISCUSSION

In the present study, supervised integrated exercise for one-year duration increased heart rate variability in hypertensive patients. A significant increase in deep breathing HRV was observed after six months of exercise program and the HRV was significantly more than the non-exercised hypertensive group. After 12 months, exercised hypertensive HRV reached near normal control HRV, indicating the significant shift in the autonomic balance. The other important findings from this study is that integrated exercise continued for 12 months duration has reduced both systolic and diastolic blood pressures in the hypertensive patients. But the blood pressure was increased in the non-exercised hypertensive groups over the duration of 12 months.

The observed decrease in heart rate variability in male hypertensive patients compared to age matched healthy controls is in agreement with previous large, population based and case control studies (Liao *et al.*, 1996). Cardiovascular autonomic regulation is known to be impaired in systemic hypertension (Mussalo *et al.*, 2001). A significantly lower baroreceptor reflex sensitivity was reported in hypertensive subjects (Huikuri *et al.*, 1996). Baroreflex sensitivity estimates the reflex vagal heart rate control in hypertensive patients. Huikuri *et al.* (1996) reported a widespread autonomic abnormality in the early phases of hypertension and an overwhelming and excessive sympathetic activity.

Exercise brings about a significant effect on the parasympathetic control on the heart. The interplay between the sympathetic and vagal regulation of heart rate is usually organized in a reciprocal fashion, i.e.,

increased activity in one system is accompanied by decreased activity in the other (Cooper *et al.*, 2000). There may be changes in the autonomic regulation caused by exercise resulting in concordant changes in the properties of heart rate dynamics (Goldsmith *et al.*, 1992). One potential mechanism for the protective effect of parasympathetic tone is related to its direct effects on the cardiac electrophysiology (Mikko *et al.*, 1998). A parasympathetic effect on cardiac electrophysiology prolongs sinus cycle length, AV conduction time and ventricular refractory period (Martinus and Zipes, 1980). Thus increase activity of the parasympathetic nervous system during exercise might have increased the heart rate variability in exercised hypertensive group after 6 and 12 months of recording. Thus, the results show the positive effects of exercise training in patients with hypertension involving an attenuation of the reduced HRV responses and that this improvement might have prognostic significance.

Several studies have reported that the cardio protective effects of physical training might be in part mediated by the anti arrhythmic effect of increased vagal control of the heart (Goldsmith *et al.*, 1992; Hull *et al.*, 1994). Activities of moderate intensities are commonly accepted to improve health and lower cardiovascular risks. Some studies have argued that increased intensity and prolonged training may have proportionately greater cardio protective effect (Singer *et al.*, 1988; Tsuji *et al.*, 1996).

Exercise also reduced both systolic and diastolic blood pressure in hypertensive patients in this study. Physical activities and fitness are inversely related to incidence of cardiovascular disease and mortality. Individual studies were usually inconclusive and often contradictory with regard to the hemodynamic mechanism of the blood pressure response in hypertensives (Cooper *et al.*, 2000). Random, controlled trials have shown that chronic dynamic endurance training is able to reduce blood pressure (Fagard, 2001). A decreased activity of the sympathetic nervous system is most likely involved in the exercise induced reduction of blood pressure (Pescatello *et al.*, 2004). Reduction in the sympathetic nervous system activity also affects the kidneys which is the most potent factor in long term blood pressure regulation. Exercise is known to reduce the insulin resistance and improve the endothelial function, which might have played an important part in the blood pressure reduction in the exercised hypertensive group (Varonique and Fagard, 2005).

Earlier research has demonstrated that exercise training increases resting stroke volume, reduces resting heart rate and total peripheral resistance (McArdle *et al.*,

1994). These changes in hemodynamic pattern also could be the cause for observed decrease in blood pressure in the present study. Antihypertensive medications strive to have a long-term beneficial effect on the hemodynamic pattern by lowering blood pressure and total peripheral resistance (Leonetti and Cuspidi, 1995). The present study supports the view that exercise can shift hemodynamic pattern towards more favorable phase and reduce the blood pressure, similar to that achieved with antihypertensive therapy (Lund-Johansen, 1994). The study further suggests that exercise may be an effective non-pharmacological treatment for increased blood pressure. The reduction in the resting blood pressure identified in this study would be important in terms of protection against cardiovascular diseases. Exercise may be recommended as a means of blood pressure reduction, to be used prior to and in conjunction with pharmacological approaches.

Since late 1970s HRV measured with a ruler on an ECG obtained during spontaneous respiration has been known to reflect the prognosis after MI (Wolf *et al.*, 1978). Due to the larger variations in R-R intervals during deep breathing, DB-HRV is probably a more precise measure and recently DB-HRV has been shown to be an independent prognostic marker after MI. HRV measures obtained during deep breathing are more informative than the ones in regular conditions. Measuring deep breathing HRV is easy and can be carried out in majority of the general population. HRV induced by deep breathing is almost exclusively mediated by the parasympathetic fibers; where as the other tests are mediated in a more complex manner (May *et al.*, 1999; Tamosiunaite *et al.*, 2005). HRV during deep breathing test has shown that vagal-cardiac activity is diminished in patients with coronary artery disease. Deep breathing HRV method has been validated as an independent predictor in a few cardiac diseases including myocardial infarction. In general this study shows that deep breathing test could be quite sensitive to heart rate variability assessment in hypertensive patients as well and better standardization needs be developed during further work on this test.

Study limitations: This study has several limitations. Absence of metabolic data, lack of accompanying cardiovascular measures, the effect of different meal compositions on HRV, measurement of exercise capacity (peak VO_2) and absence of echocardiographic data are the major limitations. One of the major difficulties we faced is the lack of frequency domain HRV analysis which is more widely accepted method of HRV analysis and which has higher sensitivity and specificity. However, the clinical usefulness of heart rate variability recordings from short

term ECG recordings is well established and the major objective of this study was to validate 'one-minute deep breathing HRV analyses in hypertensive patients. The influence of drug treatment and its discontinuation on heart rate variability should be carefully considered before drawing any conclusions.

In conclusion, long term exercise training for 6 months was sufficient in achieving a substantial change in vagal modulation of the heart evidenced by increased deep breathing heart rate variability than non-exercised hypertensives and more prolonged exercise up to one-year produced a greater enhancement of these changes and was successful in returning HRV to pre training values. Thus, the study supports the supervised integrated exercise program as an important component of lifestyle modification for changing the autonomic nervous system activity on heart and to protect against cardiovascular diseases. The present study extends the utility of the one minute deep breathing HRV in hypertensive patients. Deep breathing HRV may help to guide the selection of pharmacological intervention in hypertensive patients.

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