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Therapeutic Role of Continuous Training Program on High Density Lipoprotein Cholesterol in Men with Hypertension: A Randomized Controlled Trial

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Abstract

Objective: Some of the reported factors that increased the risk for coronary events in hypertensive individuals included elevated total cholesterol (TC) and low density lipoprotein cholesterol (LDL), reduced high density lipoprotein cholesterol (HDL) and physical inactivity. The purpose of the present study was to investigate the effect of interval training programme on blood pressure and lipid profile in subjects with hypertension.

Methods: Two hundred and seventeen male patients with mild to moderate (systolic blood pressure [SBP] between 140-180 & diastolic blood pressure [DBP] between 90-109 mmHg) essential hypertension were age matched and grouped into interval and control groups. The interval (n=112; 58.63 ± 7.22 years) group involved in an 8 weeks continuous training (60-79% HR max reserve) programme of between 45minutes to 60 minutes, while age-matched controls hypertensive (n=105; 58.27 ± 6.24 years) group remain sedentary during this period. Cardiovascular parameters (SBP & DBP), VO_2max, TC, LDL, HDL and Artrogenic Index (AI) were assessed. Students't test and Pearson correlation test were used in data analysis.

Results: Findings of the study revealed significant decreased effect of interval training programme on SBP, DBP, TC, LDL and significant increased effects on VO_2 max and HDL level at $p < 0.05$. Also there was a significant negative and positive correlation between changes VO_2 max and changes in TC and HDL respectively.

Conclusions: it was concluded that interval training programme is an effective adjunct non-pharmacological management of hypertension and a means of normal regulation of lipid profile.

Keywords: Hypertension; Blood pressure; Lipid profile; Continuous exercise

Introduction

Hypertension is a major global health problem and public-health challenge, demanding a vast proportion of health care resources directly and indirectly because of its high and increasing prevalence and the concomitant risks of cardiovascular and kidney disease, disability-adjusted life-years and mortality [1,2]. It has been reported that sedentary and unfit normotensive have 20-50% increased risk of developing hypertension during follow up when compared with their more active and fit peers [3]. Regular aerobic physical activity adequate to achieve at least a moderate level of physical fitness has been shown to be beneficial for both preventive and treatment of hypertension [4].

According to Nieman [5] about 40% of hypertensive patients also have high blood cholesterol levels. However, factors that increase risk for coronary events in hypertensive individuals included elevated low density lipoprotein cholesterol (LDL) or total cholesterol (TC), smoking, impaired glucose tolerance with or without diabetes mellitus and reduced high density lipoprotein cholesterol (HDL). Elevation in serum TC concentration confer approximately a 1.9 fold increase in the risk of CHD in men and 1.8 fold increase in women [6].

The association of BP and blood cholesterol with the risk of stroke and CHD has been investigated; and reports have show direct association of DBP, with the risk of both stroke and CHD [7-9]. Similarly, diabetes, valvular heart disease, myocardial infarction, and left ventricular hypertrophy are associated with increased risk for congestive heart failure in hypertensive individuals [10].

Several studies [11-13] have evaluated the influence of physical activity on hypertension. Others [14-18] have also investigated the effects aerobic training on other factors in hypertension.

The purpose of the present study was to determine whether an 8-week program of moderate-intensity continuous training would significantly elevate HDL and reduce the TC and atherogenic index (AI) in male subjects with hypertension.

Methodology

Research design

In the present study, age matched randomized double blind independent groups design was used to determine the influence of the continuous training program on lipid profile and cardiovascular parameters. Subjects' age were arranged in ascending order (50 to 70 years) and then assigned to, continuous and control groups in an alternating pattern (age matched). One week wash out period was established and pretest (fasting blood sample collection and stress test)

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was administered to all subjects on the last day of the wash out period. Following wash out and pretest, all subjects (interval & control) were placed on antihypertensive (methyldopa) drug, the and continuous groups involved in continuous training programs for 8 weeks, while the control group remains sedentary during this period, (all subjects were on methyldopa during the 8 weeks training and sedentary period) and at the end of the training and sedentary period. Another one week wash out period was established and posttest was administered to all subjects on the last day of the wash out period.

Subjects

Population for the study was male essential hypertensive subjects attending the hypertensive clinic of Murtala Mohammed Specialist Hospital, Kano, Nigeria. Subject were fully informed about the experimental procedures, risk and protocol, after which they gave their informed

Inclusion criteria

Only those who volunteered to participate in the study were recruited. Subjects between the age range of 50 and 70 years with chronic mild to moderate and stable (> 1 year duration) hypertension (SBP between 140-180 & DBP between 90-109 mmHg) were selected. Only those who had stopped taking antihypertensive drugs or on a single antihypertensive medication were recruited [19]. They were sedentary and have no history of psychiatry or psychological disorders or abnormalities.

Exclusion criteria

Obese or underweight (BMI below 20 & above 30 kg/m^2), smokers, alcoholic, diabetic, other cardiac, renal (particularly nephrosclerosis), respiratory disease patients were excluded. Those involved in vigorous physical activities and above averagely physically fit (VO_2max >27 & >33 ml/kg.min for over 60 & 50 years old respectively) were also excluded.

A total of 323 chronic and stable, essential mild to moderate male hypertensive patients satisfied the necessary study criteria. Subjects were aged matched and randomly grouped into experimental (162) and control (161) groups (Figure 1). They were fully informed about the experimental procedures, risk and protocol, after which they gave their informed consent in accordance with the American College of Sports Medicine (ACSM) guidelines, regarding the use of human subjects [20] as recommended by the human subject protocol. Ethical approval was granted by the Ethical Committee of Kano State Hospitals Management Board.

Pretest procedure

Wash out Period: All subjects on antihypertensive drugs were asked to stop all forms of medication and in replaced, were given placebo tablets (consisted of mainly lactose and inert substance) in a single blind method [21,22]. All subjects including those not on any antihypertensive medications were placed on placebo tablets for one week (7 days); this is known as "Wash out period". The purpose of the wash out period was to get rid of the effects of previously taken antihypertensive drugs/medications. During the wash out period all subjects were instructed to report to the hypertensive clinic for daily blood pressure monitoring and general observation. The pretest procedure was conducted at the last day of the wash out period, and in the Department of Physiotherapy of Murtala Mohammed Specialist Hospital (MMSH), Kano between 8:00 am and 10:00 am.

Physiological measurement

Subjects resting heart rate (HR), SBP, and DBP were monitored from the right arm as described by Walker et al. [23] using an automated digital electronic BP monitor (Omron digital BP monitor, Medel 11 EM 403c; Tokyo, Japan). These measurements were monitored between 8:00 am and 10:00 am each test day.

Anthropometric measurement

Subjects' physical characteristics (weight [kg] & height[m]) and body composition (body mass index [BMI] (kg.m^{-2})) assessment was done in accordance with standardized anthropometric protocol [24].

Blood sample collection (Venipuncture method)

Both pre and post treatment venous blood samples were obtained between 8:00 am and 10:00 pm after about 12 hour overnight fast (fasting blood sample). Five ml syringe was used for blood sample collection, using the procedure described by Bachorik [25]. About 5ml of blood was draw from the antecubital vein of each subject under strict antiseptic condition. Blood samples were allowed to coagulate (clot) at room temperature for one hour and centrifuged for serum. Serum samples were transferred in to plastic containers (Vials), sealed and labeled. All samples were stored in a refrigerator at -800°C until analysis [26].

Stress test

The Young Men Christian Association (YMCA) submaximal cycle ergometry test protocol was used to assess subject's aerobic power [20]. The YMCA protocol uses two to four 3-minutes stages of continuous exercise, two HR-power output data points will be needed (steady state HR) of between 110 and 150 beat/min. The two steady state HR were plotted against the respective workload on the YMCA graph sheet. A straight line was draw through the two points and extended to the subjects predicted maximum HR (220-Age). The point at which the diagonal line intersects the horizontal predicted HR max line represents the maximal working capacity for the subject. A perpendicular line was dropped from this point to the baseline where the maximal physical workload capacity was read in kg.m.min^{-1}, which was used to predict the subjects VO_2 max. This procedure was done for both pre and posttest stress test.

Test procedure

The test procedure was also conducted in the Department of Physiotherapy of MMSH, Kano between 8:00 am and 10:00 am.

Training programme

Following stress test and prior to the exercise training, all subjects in both control and interval groups were re-assessed by the physician and were prescribed with aldomet (methyl dopa) as necessary. During the training and sedentary period (8 weeks) all subjects in both continuous and control groups were placed on methyldopa according to their pre recruitment doses and responses at 250mg and 500mg daily. Aldomet was preferred because it does not alter normal hemodynamic responses to exercise [27]. It is a well-tolerated and mostly prescribed antihypertensive drug in Nigeria, particularly Northern Nigeria where the study was conducted and it is also useful in the treatment of mild to moderately severe hypertension [28]. Subjects maintain these prescriptions with regular medical consultation and observation through-out the period of training.

The continuous group (group 1)

Subjects in the continuous group exercised on a bicycle ergometer

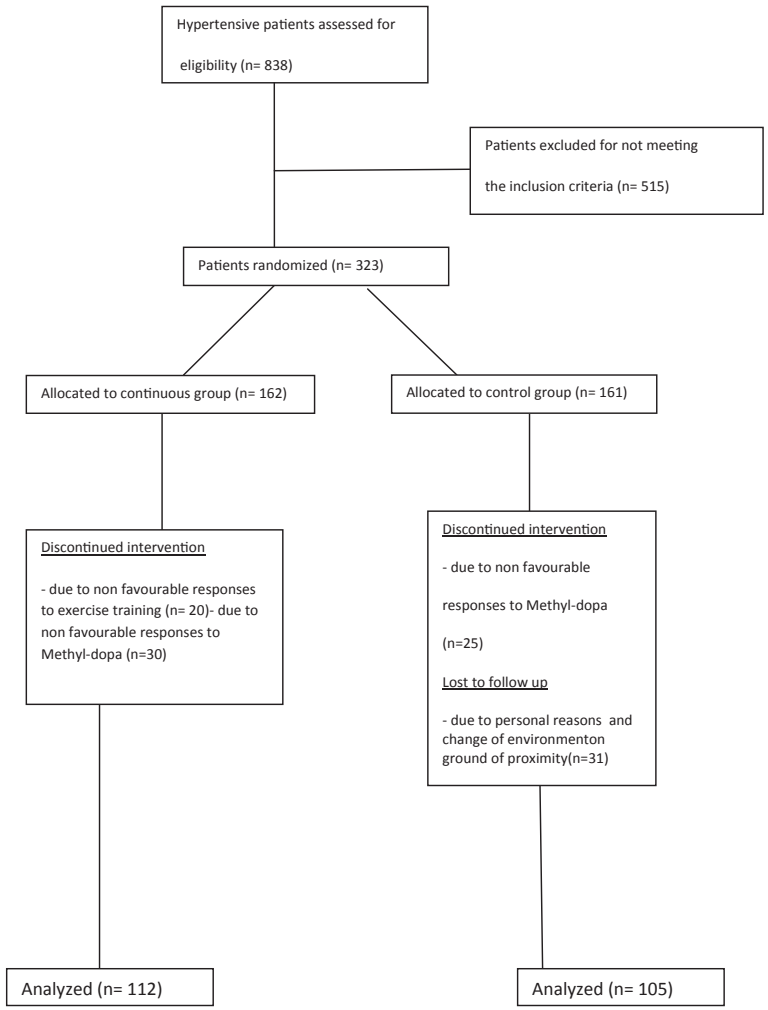


Figure 1: Study design flow chat.

at a moderate intensity of between 60-79% of their HR max reserve that was estimated from 220 minus the age of a subject as recommended by ACSM [29,30]. The starting workload was 100 kgm (17 watts) which was increased at a pedal speed of 50rpm to obtain a HR max reserve 60% was increased in the first two weeks to and level up at 79% HR max reserve throughout the remaining part of the training period. The initial of exercise session was increased from 45 minutes in the first two weeks of training to and leveled up at 60 minutes throughout the remaining part of the training. Exercise session of three times per week was maintained throughout the 8 weeks period of training for interval group.

The control group (group 2)

Subjects in the control group were instructed not to undertake any vigorous physical activity during the 8 weeks period of study.

Lipid profile analysis

Serum lipid analysis for TC and HDL were determined using commercial enzymatic method (Randox kits and manuals by Randox Laboratory, Antrim, United Kingdom). Artergenic index was estimated from the ratio of TC and HDL (TC/HDL) [31].

Posttest procedure

Wash out period: At the end of the 8 weeks training period, all subjects were asked to stop methyldopa and subjects were prescribed with placebo tablets in a single blinded method for one week in order to get rid the effect of the methyldopa taken during the training period.

Blood sample collection: Immediately after the post training wash out period, fasting blood samples were collected as earlier described.

Post training SBP, DBP, VO_2max, lipid profile analysis/assessment and stress test were conducted as earlier described in the pretest procedures using standardized protocols, techniques and methods.

All pre and post test measurements were recorded on a data sheet. Two hundred and seventeen subjects (112 from continuous, and 105 from control group) completed the eight weeks training program. One hundred and six subjects (50 from continuous, and 56 from control group) had dropped out because of non-compliance, unfavorable responses to methyldopa and exercise training or had incomplete data; therefore, the data of 217 subjects were used in the statistical analysis (Figure 1: flow chart).

Statistical analysis

Following data collection, the measured and derived variables

were statistically analyzed. The descriptive statistics (Means, standard deviations and % change) of the subjects physical characteristics, estimated VO_2max, lipid profile and cardiovascular parameters were determined. Students't test and Pearson product moment correlation tests were computed for the variables of interest. In the t and correlation tests, the difference between subjects post-training and pre-training measurements (changed score) were used as dependent measures. All statistical analysis was performed on a Toshiba compatible microcomputer using the statistical package for the social science (SPSS), (Windows Version 16.0 Chicago IL, USA). The probability level for all the above tests was set at 0.05 to indicate significance.

Results

The subject's age ranged between 50 and 70years. Mean age, height, weight and BMI: of subjects in continuous exercise group were (58.63 ± 7.22years, 1.73 ± 6.97m, 67.49 ± 10.16kg, 22.48 ± 2.89 $kg.m^{-2}$) respectively while for the Control group Mean age, height, weight and BMI were (58.27 ± 6.24years, 1.68 ± 5.31m, 68.47 ± 17.07 kg, 23.37 ± 5.31 $kg.m^{-2}$ respectively). There was no significant difference in age (t = .390, p = .697), SBP (t =.540, p=.597), DBP (t =.530, p =.597) and VO_2max (t = -.406, p = .685) between groups. The physical characteristics of the subjects are comparable.

Subject's pre and post treatment mean BP ± SD mmHg; and VO_2max ($ml.kg^{-1}.min^{-1}$) for the exercise and control groups are depicted in table 1. Students't test results (Table 2) indicated a significant reduction in the exercise groups over control in SBP (p=0.000), DBP (p=0.040), TC (p=0.000), LDL (p=0.000), AI (p=0.000) and increased VO_2 max (p=0.000) and HDL (p = 0.000) at $p < 0.05$.

There was a significant negative and positive correlation between changes in VO_2max and changes in TC (r= -0.328) and HDL (0.225) respectively at p<0.05 (Figure 2).

Discussion

Findings from the present study revealed a significant decrease in SBP, DBP and increase in VO_2 max and HDL in the continuous exercise group over control group. The favorable changes resulting from aerobic training in both SBP and DBP demonstrated in the present study is consistent with several other studies [32-34]. Also, result of the present study indicated a significant reduction in TC, AI and increased HDL in the continuous group over control. There was a significant correlation between changes in TC, HDL and VO_2max. The results of this study suggest that 8 weeks of high-intensity interval training can elicit favorable changes in HDL-C and the lipoprotein ratio in men with hypertension.

Finding of the present study is in agreement with several studies

Variable	Continuous		Control	
	n= 112		n= 105	
	pre	post	pre	post
	X± SD	**X± SD**	**X± SD**	**X± SD**
SBP (mmHg)	170.45±15.57	157.82±23.91	160.87±13.23	163.47±14.88
DBP (mmHg)	97.56±7.53	94.83±7.21	97.17±1.43	96.10±2.61
VO_2max	20.69±12.49	28.68±13.60	21.23±5.76	22.82±7.44
HDL (mg/dl)	25.75±7.44	35.00±7.18	29.53±6.55	29.54±6.57
LDL (mg/dl)	112.64±49.99	99.14±43.33	121.73±33.35	125.40±33.05
TC (mg/dl)	163.56±490.14	149.69±50.65	163.20±36.60	169.40±35.47
AI	6.80±2.29	4.37±1.98	5.62±1.10	5.84±1.06

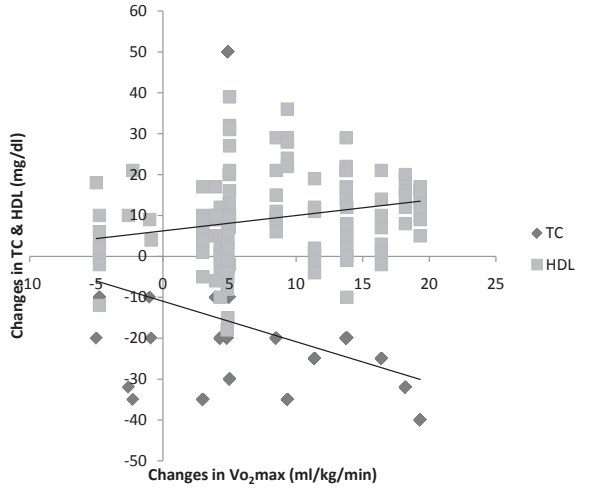
VO_2max (ml/kg/min)

Table 1: Groups pre and posttest mean(X) ± standard deviation (SD) (N = 217).

Variable	Change Score Values			
	Continuous	Control		
	X±SD	**X±SD**	**t**	**p**
SBP (mmHg)	-13.94±12.60	2.61±7.85	119.345	0.000*
DBP (mmHg)	-7.41±6.27	-1.07±1.76	53.171	0.040*
VO_2max (ml/kg/min)	7.79±6.62	1.59±3.54	285.429	0.000*
HDL (mg/dl)	9.25±11.05	0.01±0.33	8.562	0.000*
LDL (mg/dl)	-14.70±31.52	3.67±3.42	-5.937	0.000*
TC (mg/dl)	-18.88±19.97	6.20±7.95	-12.005	0.000*
AI	-2.43±3.03	0.22±0.30	-8.923	0.000*

*significant p<0.05

Table 2: Groups changed scores mean(X) ± standard deviation (SD) and t-test values (N = 217).



TC (r) = -0.328**

HDL (r) = 0.225**

Significant at 0.01**

Figure 2: Correlation between training changes in VO_2max, HDL and TC (N=245).

[35-37]. Tsai et al. [4]; in their study, a total of 42 patients (23 men and 19 women) with white coat hypertension (mean 24-h ambulatory BP 119.2 +/- 6.6/78.3 +/- 5.8 mm Hg) were divided randomly into two groups: control (n = 20) (no exercise), and moderate-intensity exercise (n = 22). The training group exercised three times per week at the prescribed exercise intensity using a treadmill exercise program. They reported significant reductions in clinic and ambulatory BP. They also reported significant reductions in plasma TC, LDL and triglyceride. Elevation of HDL was also noted.

Sasaki [38] investigated the effect exercise on lipid profile of 10 patients with essential hypertension. Subjects were on regimen of supervised mild exercise, a multi-stage exercise was done for 30 minutes three times weekly for 10 weeks. They reported significant reduction of both systolic and diastolic blood pressure. Serum concentrations of HDL_2 cholesterol increased significantly, but there were no changes in TC and HDL_3 cholesterol subtraction. They concluded that, mild exercise lowers blood pressure and improves the lipoprotein profile. However, several others have reported contrary findings [39-41]. The differences in findings could be attributed to the differences in exercise intensities, subjects' health status and pre (baseline) training lipid

profile status. The more-unfavorable baseline concentrations of HDL in our subjects may have allowed for greater increases with training and contributed to the significant improvement, which has been observed previously [31,42].

Results of the present study indicate that moderate-intensity continuous training programme is capable of reducing blood pressure and elevating HDL and reducing the TC and atherogenic index in men with hypertension. This training method should form an adjunct therapy in the maintenance of favorable lipid profile and general management of hypertension.

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