ORIGINAL ARTICLE

Randomised controlled trial: Effects of aerobic exercise training programme on indices of adiposity and metabolic markers in hypertension

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Abstract

Objective: To investigate the effects of interval training programme on blood pressure, maximal oxygen consumption, indices of adiposity and metabolic markers in black African men with essential hypertension.

Methods: The study was conducted at Murtala Muhammed Specialist Hospital, Kano, Nigeria, from October 24, 2007 to February 24, 2009. It comprised 245 male patients with mild to moderate (systolic blood pressure 140-179 and diastolic blood pressure 90-109 mmHg) essential hypertension who were age-matched and grouped into experimental and control groups. The experimental group was involved in an 8-week training programme of between 45 and 60 minutes, while the controls remained sedentary during the period. Cardiovascular parameters, maximal oxygen consumption, per cent body fat, waist-to-hip ratio, body mass index, fasting blood sugar, total cholesterol, triglyceride, high density lipoprotein, low density lipoprotein and artherogenic index were assessed. Analysis of co-variance and Pearson correlation tests were used in data analysis which was done using SPSS 16.

Results: The study had 140 (57.1%) cases with a mean age of 58.90±7.35 years, and 105 (42.9%) controls with a mean age of 58.27±6.24 years. It revealed significant increased effect of interval training programme on maximal oxygen consumption and high-density lipoprotein. There was significant reduction in on all the other controls. Changes in maximal oxygen consumption as a result of interval training significantly and negatively correlated with the other variables except high-density lipoprotein.

Conclusions: The therapeutic role of interval exercise training on blood pressure reduction may be mediated through elevation of high-density lipoprotein, reduction of other markers of metabolism, and reduction in bodyweight and fatness.

Keywords: Hypertension, Adiposity, Metabolic markers, Lipid profile, Artherogenic, Exercise. (JPMA 63: 680; 2013)

Introduction

Hypertension and Hypercholesterolaemia contribute to endothelial dysfunction accompanied by inflammation in the vessel wall, increased lipoprotein oxidation, smooth muscle cell proliferation, extracellular matrix deposition, accumulation of lipid-rich material, activation of platelets, and thrombus formation; these pathogenic features contribute to the development of atherosclerosis and coronary heart disease (CHD).[1]

Hypertension has become one of the most powerful predictors of CHD and the risk increases markedly when high blood pressure is accompanied with other risk factors. High levels of high-density lipoprotein (HDL) may have a protective role against coronary atherosclerosis.[2] About 40% of hypertensive patients also have high blood cholesterol levels and factors that increase risk for coronary events in hypertensive individuals which include; elevated low-density lipoprotein (LDL) or total cholesterol (TC), smoking, impaired glucose tolerance (IGT) and reduced HDL.[3]

Most of the previous studies investigating the effects of exercise on older hypertensive population have been conducted using white, Caucasian and other mixed black subjects. However, studies have implicated genetics, heredity, race, ethnicity, environmental factors and gene-environmental interaction in the aetiology and biomarkers of inflammation in hypertension.[4] Furthermore, Bouchard et al reported that genetics plays a major role in a person's maximal oxygen consumption (VO_2max), and that heredity can account for up to 25-50% of the variance seen between individuals.[5] This interpersonal and inter-racial difference clearly indicates the needs for study on pure black African population. It was for this very purpose that the current study was conducted.

Subjects and Methods

The age-matched randomised independent-control group (pretest-post-test) study was conducted on male essential hypertensive subjects attending the Hypertensive Clinic of Murtala Muhammed Specialist

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Hospital, Kano, Nigeria, between October 24, 2007 and February 24, 2009. Sample size was determined using the sample size calculator by Creative Research System Survey Software (CRSSS) (Petaluma, CA, USA).[6] The subjects were fully informed about the experimental procedures, risk and protocol, and informed consent was obtained from each of them in accordance with the American College of Sports Medicine (ACSM)[7] guidelines. Only those who volunteered to participate in the study were recruited. Subjects between the age range of 45 and 70 years with chronic mild to moderate and stable (> 1 year duration) hypertension (systolic blood pressure [SBP] between 140-179 and diastolic blood pressure [DBP] between 90-109 mmHg) were selected. Only those who had stopped taking anti-hypertensive drugs or were on a single anti-hypertensive medication (monotherapy) were recruited.[8] They were sedentary and had no history of psychiatry or psychological disorders or abnormalities.

Obese or underweight (body mass index [BMI] between 20 and 30 kg/m^2), smokers, alcoholics, diabetics, other cardiac, renal, respiratory disease patients were excluded. Those involved in vigorous physical activities and above-average physical fitness (VO_2max >27 and >33ml/kg.min for over 60 & 50 years old respectively) were also excluded.

A total of 324 chronic and stable, essential mild to moderate male hypertensive patients satisfied the necessary study criteria. The subjects were age-matched and randomly grouped into cases (162) and controls (162) groups. Ethical approval was granted by the Ethical Committee/Board of Kano State Hospitals Management Board.

Initially, all subjects on anti-hypertensive drugs were asked to stop all forms of medication and were given placebo tablets consisting of mainly lactose and inert substance, in a double-blind method. All subjects including those not on any anti-hypertensive medications, were placed on placebo tablets for during the 'wash out' phase which lasted 7 days. The purpose of the period was to get rid of the effects of previously taken anti-hypertensive drugs/medications. During the period all subjects were instructed to report to the hypertensive clinic for daily blood pressure monitoring and general observation. The pre-test procedure was conducted on the last day of the 'wash out' period at the Department of Physiotherapy of the hospital.

Subjects' resting SBP and DBP were monitored from the right arm as described in literature,[9] using an automated digital electronic BP monitor (Omron digital BP monitor, Medel 11 EM 403c; Tokyo Japan). These measurements were monitored between 8am and 10am on each test day.

Both pre- and post-treatment venous blood samples were obtained between 8am and 10pm after about 12-hour overnight fast (fasting blood sample). A 5ml syringe was used for blood sample collection.[9] One milliliter from the blood sample was immediately transferred to a special container containing anti-coagulant (heparin, 75U/ml) for white blood cell (WBC) count. The remaining 4ml blood samples were allowed to coagulate (clot) at room temperature for one hour and centrifuged for serum. Serum samples were transferred to plastic containers (vials), sealed, labelled and stored in a refrigerator at -80°C until analysis.

Fasting blood sugar (FBS) was determined using commercial enzymatic method (Randox kits and manuals by Randox Laboratory, Antrim, United Kingdom).

Serum lipid analysis for TC, TG and HDL were determined using commercial enzymatic method (Randox kits and manuals by Randox Laboratory, Antrim, United Kingdom). LDL was estimated indirectly using the formula: Adults LDL = TC- (TG/5)-HDL.[10]

Artherogenic index was estimated from the ratio of TC and HDL (TC/HDL).[9]

The Young Men Christian Association (YMCA) submaximal cycle ergometry test protocol was used to assess subject's aerobic power.[7] The protocol uses two to four 3-minute stages of continuous exercise, needing two heart rate (HR) output data points (steady state HR) of between 110 and 150 beats/min. The two steady-state HR were plotted against the respective workload on the YMCA graph sheet. A straight line was drawn 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_2max. This procedure was done for both pre- and post-test stress test.

Following the stress test and prior to the exercise training, all subjects in both the groups were re-assessed by physicians and were prescribed with methyldopa (500mg-1g daily 2-4 in divided doses) based on the subjects' responses and tolerance to

therapy. Methyldopa was preferred because it does not alter normal haemodynamic responses to exercise,[10] and it is a well-tolerated antihypertensive drug in Africa.[11,12] In addition, it is the drug prescribed the most in Kano, where the study was conducted and had proved useful in the treatment of mild to moderately severe hypertension either as monontherapy or combination therapy.[12] Subjects maintained these prescriptions with regular medical consultation and observation throughout the 8-week period of exercise training.

The cases exercised on a bicycle ergometer at a low intensity of between 60-79% of their HR max reserve that was estimated from 220 minus the age of a subject. The starting workload was 100kgm (17 watts) which was increased at a pedal speed of 50rpm. The HR max reserve of 60% increased in the first two weeks to level up at 79% HR max reserve throughout the remaining part of the training period at a work/rest ratio of 1:1 of 6 minutes each. The initial duration of exercise session was increased from 45 minutes up at 60 minutes throughout the remaining part of the training. Exercise sessions three times per week was maintained throughout the study period of training for the cases.

The controls were instructed not to undertake any vigorous physical activity during the study period.

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

Immediately after the post-training 'wash out' period, fasting blood samples were collected.

Post-training SBP, DBP, C-reactive protein (CRP), WBC, FBS, TC, TG, HDL, LDL, and artherogenic index (AI) assessment and stress test were conducted as earlier described in the pre-test procedures. All pre and post test measurements were recorded on a data sheet.

Following data collection, the measured and derived variables were statistically analysed. The descriptive statistics (Means ± standard deviations) of the subjects' physical characteristics, estimated VO2max, BP, per cent body fat (%BF), BMI, waist-to-hip ratio (WHR), FBS and lipid profile were determined. Analysis of co-variance (ANCOVA) was used to assess the outcome variables. In ANCOVA, the post-test values were the outcome variables and the co-variates were the age and pre-test (baseline) values. Pearson product moment correlation tests were computed for the variables of interest. In the correlation tests, the difference between subjects post-training and pre-training measurements (changed score) were used as dependent measures. The score changed was the difference between the post-test and pre-test values. All statistical analysis was performed on a Toshiba compatible microcomputer using SPSS 16.0. The probability level for all the above tests was set at 0.05 to indicate significance.

Results

Of the total, 245 (75.61%) subjects (140 [57.1%] from the

Table-1: Groups mean (x) and standard deviation (SD) for pre- and post-test values (n= 245).

Variables	Interval group x±SD		Control group x±SD	
	Pre-test	Post-test	Pre-test	Post-test
SBP (mmHg)	166.05±14.10	150.00±16.67	160.87±13.23	163.47±14.88
DBP (mmHg)	96.80±3.38	94.98±5.04	97.17±1.43	96.10±2.67
VO2max (ml/kg/min)	23.62±9.15	37.46±7.42	21.23±5.76	22.82±7.44
BMI (kg/m^2)	24.96±3.88	29.26±4.11	24.16±4.91	23.30±5.01
BF (%)	17.69±6.50	18.78±6.62	22.27±9.82	22.25±9.82
WHR (m)	0.97±0.07	0.92±0.14	0.89±0.18	0.93±0.07
FBS (mg/dl)	78.64±23.41	46.82±11.58	85.27±21.49	85.33±22.10
TC (mg/dl)	162.00±49.31	134.10±43.91	163.20±36.61	169.40±35.47
TG (mg/dl)	109.90±30.99	96.95±31.08	102.00±20.41	113.07±19.14
HDL (mg/dl)	24.60±8.51	33.81±6.38	29.53±6.55	29.54±6.57
LDL (mg/dl)	107.45±41.52	87.11±37.86	121.73±33.35	125.40±33.05
AI (mg/dl)	7.27±3.31±3.31	4.16±1.77	5.62±1.10	5.84±1.06

SBP: Systolic blood pressure. DBP: Diastolic blood pressure. VO2 max: Maximal oxygen consumption. BMI: Body mass index. BF: Body fat. WHR: Waist-to-hip ratio. FBS: Fasting blood sugar. TC: Total cholesterol. TG: Triglyceride. HDL: High-density lipoprotein. LDL: Low-density lipoprotein. AI: Artherogenic index.

Table-2: Changed score values and ANOVA test (n= 245).

Variables	Groups changed score values		ANOVA results	
	Interval group x±SD	Control group x±SD	F-values	p-value
SBP	-16.40±13.16	2.61±7.85	137.220	0.000*
DBP	-4.01±4.34	-1.07±0.17	42.059	0.000*
VO2max	13.85±9.94	1.59±3.54	199.262	0.000*
BMI	-0.70±0.82	0.14±0.40	92.991	0.000*
%BF	-9.91±4.75	-0.02±0.07	10.006	0.002*
WHR	-0.08±0.16	0.02±0.13	24.909	0.000*
FBS	-30.08±18.72	0.14±0.40	511.463	0.000*
TC	-22.71±28.59	6.20±7.94	160.104	0.000*
TG	-11.69±7.58	0.07±8.72	532.172	0.000*
HDL	8.70±12.15	0.01±0.33	28.181	0.000*
LDL	-19.80±12.15	3.67±3.42	171.679	0.000*
AI	-3.11±3.61	0.22±0.30	58.065	0.000*

*Significant p< 0.05.

SBP: Systolic blood pressure. DBP: Diastolic blood pressure. VO2 max: Maximal oxygen consumption. BMI: Body mass index. BF: Body fat. WHR: Waist-to-hip ratio. FBS: Fasting blood sugar. TC: Total cholesterol. TG: Triglyceride. HDL: High-density lipoprotein. LDL: Low-density lipoprotein. AI: Artherogenic index.

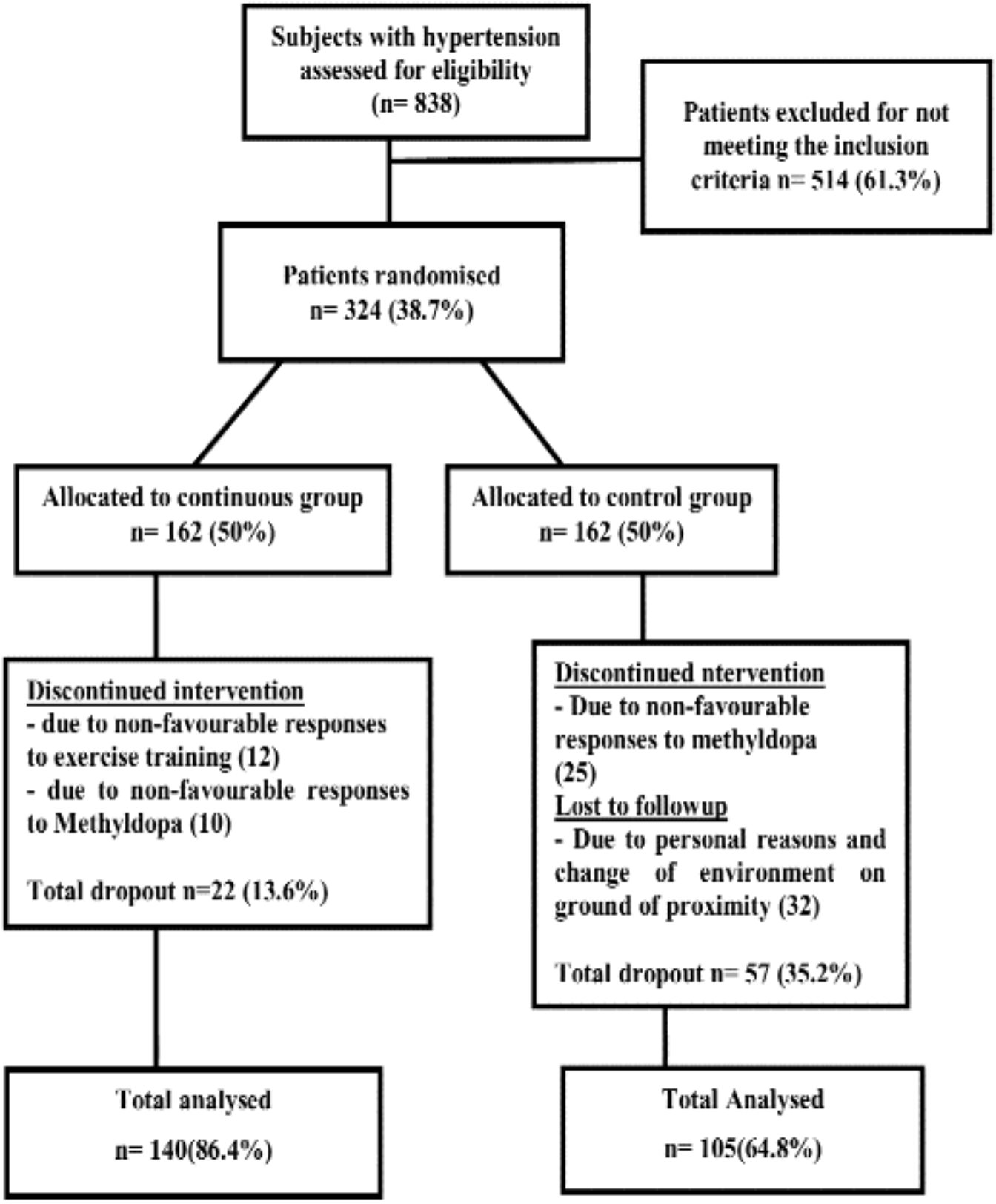

Figure-1: Study design flow chart.

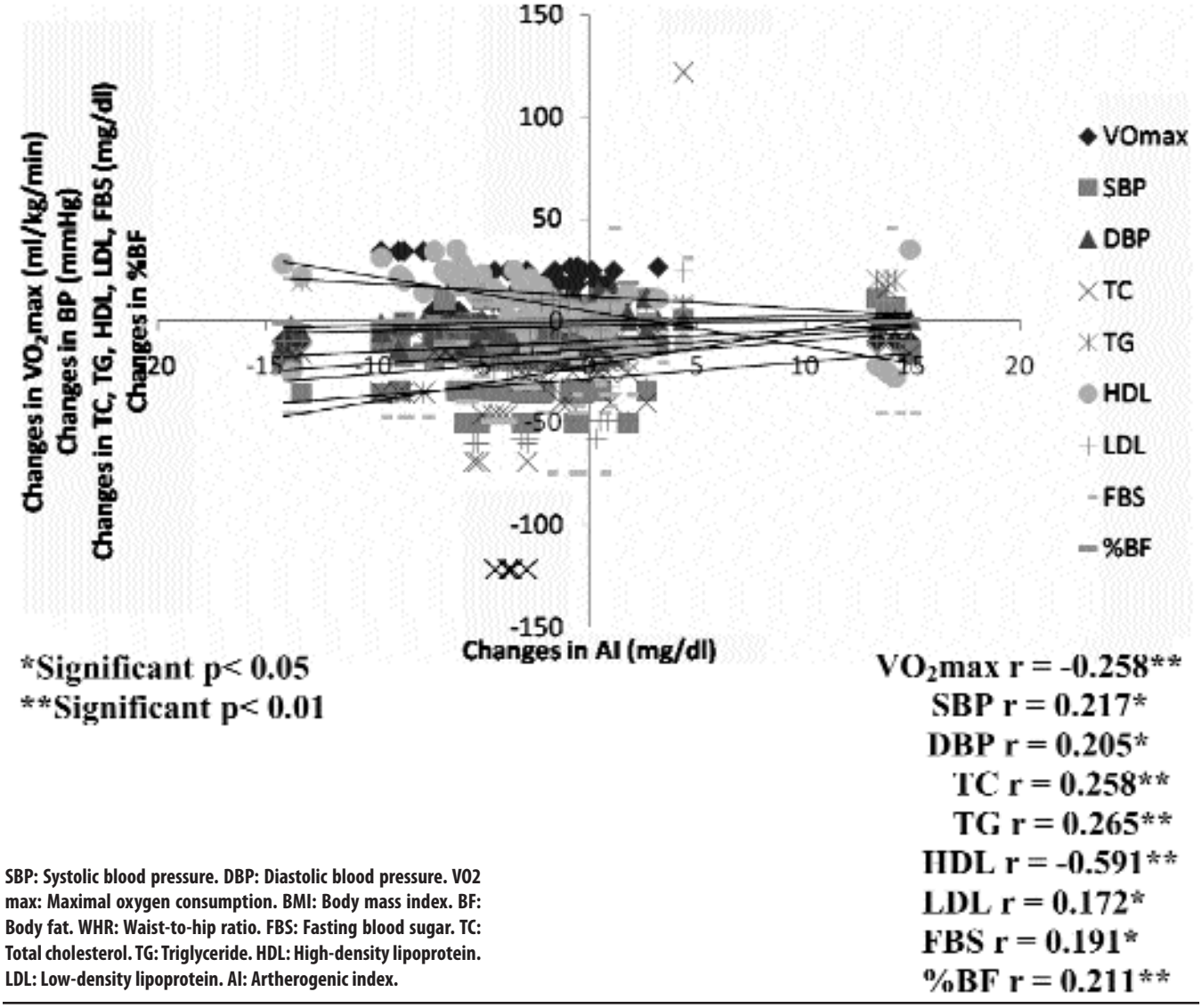

Figure-2: Correlation between training changes in variables, metabolic markers and index of adiposity (n=140).

cases, and 105 [42.9%] from the controls) completed the 8-week training programme, while 79 (24.38%) subjects (22 [27.8%] from cases, and 57 [72.2]) from controls) dropped out because of non-compliance, unfavourable responses to methyldopa and exercise training or incomplete data. The data of 245 subjects, as such, was used in the statistical analysis (Figure-1).

The subject's age ranged between 45 and 70 years. The mean age, height, weight, BMI and %BF among the cases were: 58.40±6.91 years; 167.78±7.81cm; 70.18±11.37kg; 24.96±3.88kg.m-2; and 17.69±6.50%). Among the controls they were: 58.27±6.24 years; 167.89±5.31cm; 68.47±17.07kg; 24.16±4.91kg.m-2; and 22.27±9.82%. There was no significant difference in age between the two groups (t=0.156, p<0.876).

Pre-test versus post-test mean values for various parameters were compared (Table-1). ANOVA test results indicated a significant reduction in the cases against the controls in SBP, DBP, %BF, BMI, WHR, FBS; TC, TG, HDL, LDL, AI and VO2max (Table-2).

Results indicated significant correlation between baseline VO2max and other variables such as: SBP (r= 0.143); DBP (r= 0.133); %BF (r= 0.128); TC (r= 0.228); TG (r= 0.157); HDL (r= 0.162); LDL (r= 0.322) and AI (r= 0.477). Training changes in VO2max significantly correlated with training changes in other parameters such as: SBP (r= -0.268); DBP (r= -0.237); %BF (r= -0.212);

BMI (r= -0.247); WHR (r= -0.247); FBS(r= -0.170); TC (r= -211); TG (r= -0.297); HDL (r= 0.190); LDL (r= -0.173) and AI (r= -0.258). Training changes in AI significantly correlated with training changes in other parameters such as: VO2max, SBP, DBP, %BF, FBS, TC, TG, HDL and LDL at p< 0.05 and p< 0.01 (Figure-2).

Discussion

To our knowledge, this is the first randomised, controlled trial examining the simultaneous impact of interval, moderate intensity, aerobic training on blood pressure, biomarkers of inflammation and metabolic markers in hypertension, particularly among pure black African subjects. However, the purpose of this study was to investigate the effects of interval training on VO2max, BP (SBP & DBP), FBS, indices of cholesterol metabolism (TC, TG, HDL, LDL and AI) and indices of adiposity (%BF, BMI and WHR). Results indicated significant correlation between baseline VO_2max and other variables (SBP, DBP FBS, TC, TG, HDL, LDL and AI). There were significant effects of interval training on VO_2max, SBP, DBP FBS, BMI, WHR, TC, TG, HDL, LDL and AI. Training changes in VO2max significantly correlated with change in SBP, DBP FBS, BMI, WHR, TC, TG, HDL, LDL and AI. Also, training changes in AI significantly correlated with change in VO_2max, SBP, DBP FBS, TC, TG, HDL, LDL and AI.

On VO_2max, result of the present study was in agreement with several others. The finding was consistent with a study which looked into the effect of aerobic exercise in patients with essential hypertension.[14] Twenty stage 1 and 2 hypertensives participated in a 12-week endurance ergometer at 50% VO2max, 3 to 5 times per week for 30 minutes. They reported significant increase in VO_2max at p<0.05. Another study was done on the effect of physical training on maximum aerobic capacity;[15] 31 (63±1 years), hypertensive (153±2/88±1mmHg) individuals participated in a 6 months aerobic exercise training at 75% VO_2max, 3 times weekly for 40 minutes. They reported a significant increase in maximal aerobic capacity (VO_2max:18.3±3.8 versus output of 20.7±4.2ml/kg/min, at p<0.017). Despite these outstanding results, the limitation of the two studies, however, was lack of control groups.

Findings from the present study revealed a significant decrease in SBP and DBP in the experimental groups over the placebo group. The favourable changes resulting from aerobic training on both SBP and DBP demonstrated in the present study was consistent with a study which investigated the effect of aerobic exercise and weight reduction intervention on 133 sedentary-hypertensive (SBP: 130-180mmHg; DBP: 85-110mmHg) males and females.[16] Participants were grouped into aerobic group, aerobic with weight reduction group and control group. Participants engaged in 6 months' treatment period. They reported a significant reduction in both SBP and DBP in the treatment groups compared to the placebo group. Another study[17] investigated the effects of aerobic exercise on elderly (≥60 years) hypertensive (SBP ≥140mmHg and DBP ≥90mmHg) 54 patients who were randomly assigned to exercise and control groups. The exercise group engaged in a 12-week treadmill exercise programme, while the controls did not. They reported significant decreased in SBP and DBP by 8.5±8.2 and 5.1±3.7mmHg at p<0.001.Their results concur with the finding of the present study.

One study investigated the effect of 6-month aerobic exercise on BP.[18] Thirty-five (22 Caucasians; 13 Afro-American) sedentary pre-hypertensives and hypertensive subjects. It reported non-significant changes in BP of both the Caucasians and Afro-American subjects.

A similar result to the present study on FBS was reported by a study which examined the effect of exercise and weight-loss on FBS in hypertension.[19] The study comprised 133 sedentary, overweight men and women with unmedicated high normal blood pressure, or stage 1 to 2 hypertension, who were randomly assigned to aerobic exercise only. It reported a significant reduction in FBS in the behavioural weight management programme. Another study examined the effect of mild exercise on FBS. Fifteen untrained obese hypertensive patients with a BMI ≥25kg/m^2 were placed on a low-calorie diet of 800cal/day and engaged in mild exercise. It reported a significant reduction in plasma levels of FBS and insulin at p< 0.001, and also a decrease in FBS and insulin by 11.8% and 58.4% respectively.

Our results are in agreement with several studies on lipid profile. One study had a total of 42 patients (23 men and 19 women) with white coat hypertension, meaning 24-h ambulatory BP 119.2±6.6 and 78.3±5.8mmHg, who were divided randomly into two groups: control (n= 20) (no exercise), and moderate-intensity exercise (n= 22).[21] The training group exercised three times per week at the prescribed intensity, using a treadmill. It reported significant reductions in clinical and ambulatory BP. It also reported significant reductions in plasma TC, LDL and TG. Besides, elevation of HDL was also noted.

Another study investigated the effect of exercise on

lipid profile of 10 patients with essential hypertension.[22] The subjects were on regimen of supervised mild exercise; a multi-stage exercise was done for 30 minutes three times weekly for 10 weeks. It 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. It concluded that mild exercise lowers blood pressure and improves the lipoprotein profile. However, other studies have reported contrary findings.[23,24] The differences could be attributed to the differences in exercise intensities, subjects' health status and pre-training (baseline) lipid profile status.

The present study indicates significant reduction in %BF in the case against the controls. The former group indicated a significant reduction in %BF. This finding was in agreement with the finding' of a study which also investigated the effect of aerobic exercise on %BF of mild to moderate obese hypertensive subjects.[25] Fourteen mild hypertensive obese subjects (SBP, 140/160 and DBP, 90/100mmHg) and 22 normotensive obese subjects, age ranging from 22 to 51 years and all subjects having BMI >26kg/m^2 were put on a mild hypocaloric diet and exercise on cycle ergometer and walking on treadmill, at an HR corresponding to the anaerobic threshold (AT) for 60 minutes, 3 times per week for a total period of 12 weeks. They were asked to maintain the exercise for one year. The study reported a significant decrease in %BF fat in the hypertensive and normotensive groups following 12 weeks training at $p<0.01$and during one year follow-up at $p<0.0001$ in the normotensive group.

A study on apparently healthy adolescents showed that BF seemed to be associated with a higher production of inflammatory proteins.[26] Associations between inflammatory proteins, pro-inflammatory cytokines, and adiposity measurements were examined, and it was found that acute-phase inflammatory proteins positively correlated with most measurements of BF.

The current study demonstrated a significant reduction in BMI in the cases over the controls. A study investigated the effect of 6-month aerobic exercise on BP.[18] Thirty-five (22 Caucasians; 13 Afro-Americans) sedentary pre-hypertensives and hypertensive subjects. It reported a significant decrease in BMI of both the Caucasians and the Afro-American subjects. Another study also investigated the effect of aerobic exercise on WHR of 14 mild to moderate obese hypertensive subjects.[25] It reported a significant decrease in WHR in the hypertensive and normotensive groups following 12 weeks training at $p<0.0005$ and $p<0.001$ respectively, and during one year follow-up at $p<0.05$ in the normotensive group, but not significant in hypertensive group in the one-year follow-up.

Conclusion

The therapeutic role of interval exercise training on BP reduction may be mediated through elevation of HDL; reduction/suppression of artherogenic metabolic markers and reduction in adiposity levels. Also, that interval training programme is an effective adjunct non-pharmacological multi-purpose management of hypertension.

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