Effects of Continuous Exercise Training on White Blood Cell Count in Men with Essential Hypertension *

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ABSTRACT

White blood cell (WBC) count is considered a biomarker of the inflammatory processes that result from vascular injury that actively contributes to the development of cardiovascular diseases, precisely hypertension. The positive role of exercise in the management of hypertension has long been established. However, the relationship between WBC count and hypertensive management, particularly in a non pharmacological technique seems ambiguous and unclear. The main purpose of the present study is to determine the effect of a continuous training programme on WBC count in male African subjects with essential hypertension. Two hundred and seventeen male patients with mild to moderate systolic blood pressure [SBP] and diastolic blood pressure [DBP] essential hypertension were age matched and grouped into experimental and control groups. The experimental group took part in an 8 week interval training (35-59% HR max reserve) programme of between 45 minutes to 60 minutes, while the control hypertensive group did not receive any exercise training during this period. Cardiovascular parameters (SBP, DBP & VO_2max) and WBC count were assessed. A students' t-test and Pearson correlation tests were used in data analysis. The findings revealed a significant decrease in WBC count, VO_2 max, SBP, and DBP after a continuous training programme. Also the WBC count was inversely related to VO_2max. The study concluded that a continuous training programme could be included in the management of hypertension and that the therapeutic effect of continuous exercise may be mediated through the suppression of inflammatory (WBC count) reaction.

Key words: hypertension, exercise, inflammation, white blood cell, Black Africa

INTRODUCTION

Hypertension is a major global health problem and a 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 events such as stroke, kidney disease, decreased disability adjusted life years and mortality.[1,2] Several studies have reported links between inflammation and hypertension;[3-8] many of these studies found an association between inflammatory markers such as WBC and hypertension, including its complications.[5-8]

A majority of the biological mechanisms that have been suggested to explain the effect of elevated WBC count on hypertension involves chronic low grade inflammation.[9] Inflammation alters endothelial function, resulting in inability to produce nitric oxide and prostacycline, which causes loss of the vascodilator, antithrombotic, and antiartherogenic

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properties of the vascular endothelium.[10,11] Also, stimulated leucocytes have an increased tendency to adhere to vascular endothelium, which may cause capillary leucocytosis, and subsequently increase vascular resistance.[12] An elevated WBC count may also be a marker of a state characterized by increased catecholamine levels or sympathetic nervous activities;[13] which can increase blood pressure and may eventually result in sustained hypertension.[14]

Studies have found WBC to be inversely related to the physical activity of men and women from diverse white racial backgrounds. There have been many reports on different pathways by which regular exercise reduces inflammation.[15,16] According to Fried et al.[17] and Halle et al.,[18] the potential common pathway may be the interleukins (IL) and tumour necrosis factor- (TNF-) which are both released in significant amounts from adipose tissue, particularly visceral adipose tissue. Their release is augmented by increased sympathetic stimulation which is down-regulated by regular physical activity; TNF- is a potent stimulator of IL-6 production and IL-6 is a potent stimulator for WBC production.[19] On the other hand, studies have reported that regular exercise induces anti-inflammatory actions; during exercise, IL-6 (interleukin-6) is produced by muscle fibres.[20-23] IL-6 stimulates the appearance in the circulation of other anti-inflammatory cytokines such as IL-1ra (interleukin-1 receptor antagonist) and IL-10 (interleukin-10) and inhibits the production of the pro-inflammatory cytokine, TNF-alpha. The suppression of inflammatory reaction by exercise may further result in biochemical, neural, and hormonal changes in the blood vessel walls that induce blood vessel relaxation. The blood vessels relax after each exercise session because of body warming effects, the local production of certain chemicals, such as lactic acid and nitric oxide, decreases in nerve activity and changes in certain hormones and their receptors.[24,25] Over time, as the exercise is repeated, there is growing evidence of a long-lasting effect.

Many studies have been conducted on the association between WBC count and hypertension, but few have objectively investigated the association between a physical training programme and the WBC count in the non pharmacological management of hypertension, particularly in the black African population. The purpose of the present study therefore is to investigate the relationship between a continuous training programme and WBC in the non pharmacotherapy of chronic essential hypertension in a black African population.[5-8,15,16]

METHODOLOGY

Subjects: The population for the study comprised male essential hypertensive subjects attending the hypertensive clinic of Murtala Muhammed Specialist Hospital, Kano, Nigeria. Subjects were fully informed about the experimental procedures, risks and protocol, after which they gave their informed consent in accordance with the American College of Sports Medicine (ACSM) [26] guidelines regarding the use of human subjects as recommended by the human subject protocol. Ethical approval was granted by the Ethical Committee of Kano State Hospitals Management Board.

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 were on a single antihypertensive medication were recruited.[26] They were sedentary and had no history of psychiatric or psychological disorders or abnormalities.

Exclusion criteria: Obese or underweight (BMI between 20 & 30 kg/m^2), smokers, alcoholics, diabetic, other cardiac, renal, and respiratory disease patients were excluded. Those who participated in vigorous physical activities and were above average physical fitness (VO_2max > 27 & > 33 ml/kg. min for over 60 and 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 age matched and randomly grouped into experimental (162) and control (161) groups.

Procedure

Research design: In the present study, the age matched randomized double blind independent groups design was used to determine the influence of the continuous training programme on cardiovascular parameters.

Pretest procedure

Wash out period: All subjects on antihypertensive drugs were asked to stop all forms of medication and these were replaced with placebo tablets (consisting mainly lactose and inert substance) in a double blind method.[28, 29] Also subjects, including those not on any antihypertensive medications, were placed on placebo tablets for one week (7 days); this is known as the 'wash-out period'. The purpose of the wash-out period was to get rid of the effects of previously taken antihypertensive drugs/medication. 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 and post-test procedures were conducted on the last day of the wash-out period.

Physiological measurements: The subjects resting heart rates (HR), SBP, and DBP were monitored from the right arm as described by Musa et al.[30] using an automated digital electronic BP monitor (Omron digital BP monitor, Medel 11 EM 403c; Tokyo Japan).

Anthropometric measurements: The subjects' physical characteristics (weight [kg] & height [m]) and body composition (body mass index [BMI] (kg/m^2)) assessment were done in accordance with the standardized anthropometric protocol.[31, 32]

Blood sample collection (venipuncture method): Both pre and post-treatment venous blood samples were obtained after a 12-hour overnight fast (fasting blood sample). A 5ml syringe was used for blood sample collection, using the procedure described by Bachorik. [33] About 5ml of blood was drawn from the antecubital vein of each subject under strict antiseptic conditions. One millilitre of the blood sample was immediately transferred into a special container containing an anticoagulant (heparin, 75U/ml) for the WBC count. All samples were stored in a refrigerator at -80°C until the time of analysis.[34] Following fasting blood collection and 3-4 hours prior to the stress test, all subjects were fed with a standardized hypertensive nutrient consisting of 16% protein, 54% carbohydrate and 35% fat and a moderate salt restriction of ⅓ of 1.73g (0.6g).[35]

White blood cell count: The WBC count was done using the Turks method as described by Dacie and Lewis.[36]

Stress test: The Young Mens Christian Association (YMCA) submaximal cycle ergometry test protocol was used to assess subjects' aerobic power (VO_2max) as described by ACSM.[37] The stress test (pre and post training) was conducted under the supervision of experts in basic life support care, and the emergency unit of the hospital was made ready to accommodate any incident that might occur during the stress test.

Test procedure

Training programme: Following the stress test and prior to the exercise training, all subjects in both the control and continuous groups were re-assessed by the physician and were prescribed with an antihypertensive drug; methyldopa (Aldomet) as necessary. Aldomet was preferred because it does not alter normal haemodynamic responses to exercise,[38] and it is a well-tolerated antihypertensive drug in Africa.[39] In addition, it is the one prescribed the most in Kano, where the study was conducted and had proved useful in the treatment of mild to moderately severe hypertension.[40] Subjects maintained these prescriptions with regular medical consultation and observation through-out the period of exercise training.

The continuous group (group 1): Subjects in the continuous group exercised on a bicycle ergometer at a low intensity of between 35-59% of their HR max as recommended by ACSM.[41] The starting workload was 100 kgm (17 watts) which was increased at a pedal speed of 50rpm to obtain a HR max reserve of 35%. This was increased in the first two weeks to and levelled up at 59% HR max reserve throughout the remaining part of the training period. The initial exercise session was increased from 45 minutes in the

first two weeks of training to and levelled up at 60 minutes throughout the remaining part of the training. Exercise sessions were maintained at three times per week throughout the 8 weeks training period.

The control group (group 2): Subjects in the control group were instructed not to undertake any vigorous physical activity during the 8-week period of study.

Post-test procedure

Wash out period: At the end of the 8-week training period, all subjects were asked to stop methyldopa (Aldomet) and were placed on placebo tablets for one week as in the pretest procedure.

Post-training SBP, DBP, WBC count, assessment feeding and a 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, 105 from control) completed the 8-week training programme. One hundred and six subjects (50 from continuous, 56 from control) had dropped out because of non-compliance, unfavourable responses to methyldopa and exercise training or had incomplete data; therefore, only the data for 217 subjects were used in the statistical analysis (figure 1).

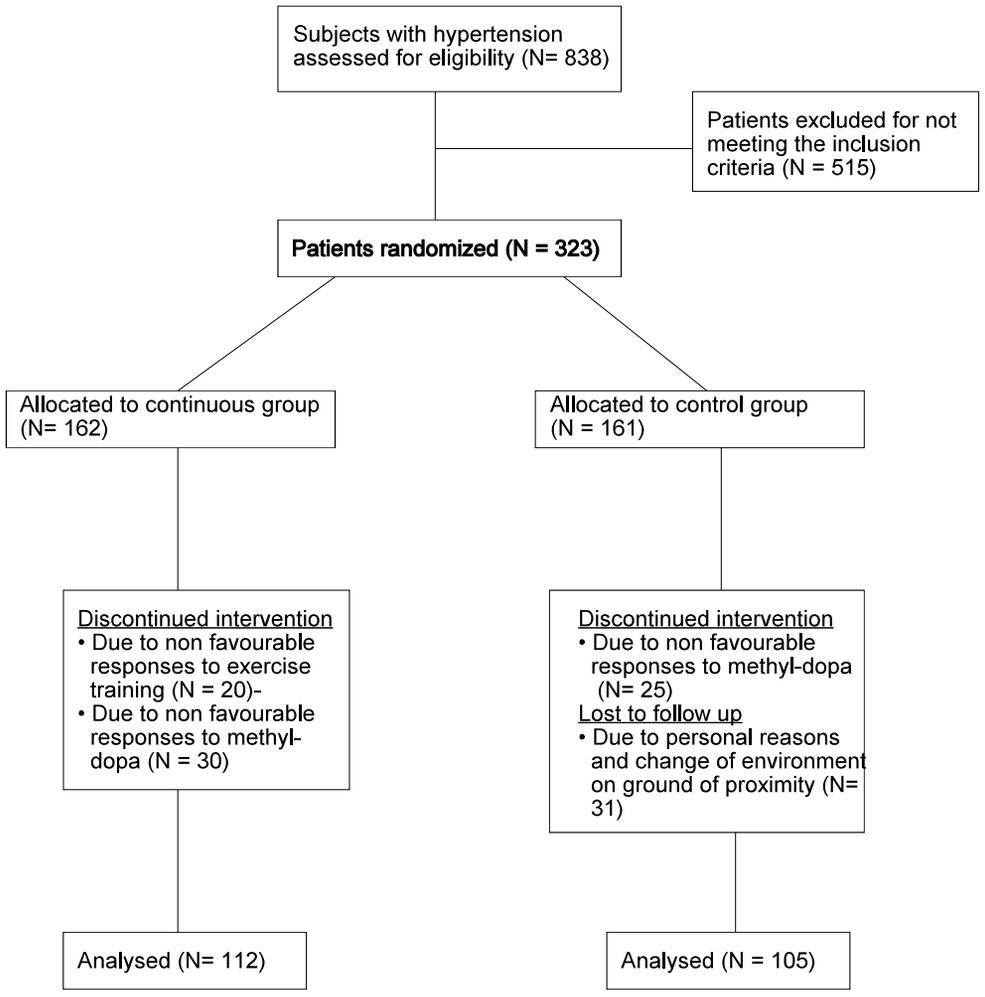

Figure 1. Study design flow chart

Statistical Analysis

Following data collection, the measured and derived variables were statistically analysed. The descriptive statistics (mean, standard deviations and % change) of the subjects physical characteristics, estimated VO_2 max, WBC count and cardiovascular parameters were determined. The Student's t-test and the Pearson product moment correlation test were computed for the variables of interest. All statistical analysis was performed on a Toshiba compatible microcomputer using the Statistical Package for the Social Sciences (SPSS) (Version 16.0 Chicago IL, USA). The probability level for all the tests was set at 0.05 to indicate significance.

RESULTS

The subjects were aged between 50 and 70 years. For the continuous exercise group mean age was 58.63±7.22 years, height 1.73±6.97m, weight 67.49±10.16 kg, and BMI 22.48±2.89 $kg.m^{-2}$, while for the control group, mean age was 58.27 ±6.24 years, height 1.68±5.31m, weight 68.47±17.07 kg, and BMI 23.37±5.31 $kg.m^{-2}$. 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 the groups. The physical characteristics of the subjects were comparable (table 1).

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

There was a significant negative correlation between changes in WBC count and VO_2max (r = -0.200) at $p < 0.05$.

Table 1. Groups mean ± SD base line characteristics and Independent t-test (N = 217)

Variables	Continuous group X ± SD	Control group X ± SD	t-values	p-values
Age (years)	58.63 ± 7.22	58.27 ± 6.24	0.390	.697
SBP(mmHg)	170.45 ± 15.57	160.87 ± 13.23	0.540	.600
DBP(mmHg)	97.56 ± 7.53	96.10 ± 2.61	0.530	.597
VO_2max (ml/kg/min)	20.69 ± 12.49	21.23 ± 5.76	0.406	.685
Weight (Kg)	67.48 ± 10.16	68.47 ± 17.07	-0.514	.608
BMI (Kg/m^2)	22.92 ± 2.20	23.37 ± 3.87	-1.060	.290

*Significant, $p < 0.05$

Table 2. Independent t-test between groups

	Continuous group		Control group		
Variables	Pretest X ± SD	Post-test X ± SD	Pretest X ± SD	Post-test X ± SD	p-values
SBP(mmHg)	170.45 ± 15.57	157.82 ± 23.91	160.87 ± 13.23	163.47 ± 14.88	.000*
DBP(mmHg)	97.56 ± 7.53	94.83 ± 7.21	97.17 ± 1.43	96.10 ± 2.61	.004*
VO_2max (ml/kg/min)	20.69 ± 12.49	28.68 ± 13.60	21.23 ± 5.76	22.82 ± 7.44	.000*
WBC count (x10/mm)	8.43 ± 1.80	7.65 ± 1.37	7.13 ± 1.3	8.21 ± 1.60	.000*

*significant, $p < 0.05$

DISCUSSION

Findings from the present study revealed a significant decrease in SBP, DBP and increase in VO_2 max in the experimental group over the control group. The favourable changes that resulted from aerobic training in both SBP and DBP demonstrated in the present study are consistent with several other studies[42,43,44] Also, the results of the present study indicated a significant reduction in the WBC count in the experimental group over the control group. There was a negative significant correlation between changes in the WBC count and VO_2max. Kullo et al.[45] investigated the effect of aerobic exercise on WBC count, though on patients with coronary heart disease (CHD). One hundred and seventy two asymptomatic men with CHD (age, 51 ± 9.3years) engaged in a symptomless graded treadmill aerobic exercise. They reported a significant reduction in WBC count and an inverse significant correlation with VO_2max (r = -0.22, p = 0.004) similar to the findings of the present study. Church et al.[46] also reported a similar finding, in a cross-sectional study

of 4057 men that examined the age-adjusted resting WBC count levels and the risk of a clinically significant elevation of white blood cell count across nine fitness-body fatness combinations. They reported that fitness was inversely related to the age-adjusted values of WBC count.

A contradictory finding was reported by Shankar et al.,[47] though on normotensive subjects. They studied the relationship between WBC count and physical activity in the development of hypertension on 2,459 hypertension-free women and men after they were adjusted and stratified by smoking and several other potential confounding factors and reported a non-significant effect of moderate physical activity twice a week on WBC count. The reasons for the contradiction in the findings between the present study and the previous study[47] might not be unconnected with the interracial differences that might exist in exercise responses to WBC count.[15, 48] Also the effect of the subjects' health status and condition cannot be ruled out. A previous study[47] investigated normotensive subjects as compared to subjects with hypertension in the present study. The effect of socio-demographic variables such as body weight, per cent body fat and body mass index could not be ruled out. In the present study, non obese subjects with hypertension were studied. However, studies have shown that most of the inflammatory reactions take place in the adipose tissues.[17, 18] The effect of types of exercise is also worth considering, the various modes, frequency and intensity of exercises elicit different physiological and psychological effects on the body.[49, 50] The present study utilized a laboratory low intensity continuous training programme.

However, it is generally accepted that the physiological mediator of low grade chronic inflammation and raised WBC count is the TNF-alpha, which has been proven to be down-regulated by regular physical activities and may be the cause for improved endothelial function. Another mechanism is that the posts exercise hypotension which is accompanied by a decrease in serum catecholamine's, norepinephrine, dopamine, cortisol, sympathetic nervous system, plasma rennin activity thus suppresses inflammatory reaction and finally down-regulates WBC count.[51,52]

CONCLUSION

Based on the results of the present study, it was concluded that a continuous exercise training programme is an effective non-pharmacological adjunct in the management of chronic essential hypertension and that the antihypertensive effect of continuous training may be through the suppression and down regulation of the WBC count as reported in the present study. However, the need clearly exists for related future studies to directly investigate the endothelial physiology response to exercise training. Also, studies to further investigate interracial, sociodemographic and gender responses to WBC count and exercise training are required.

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