

EFFECTS OF EIGHT WEEKS AEROBIC EXERCISE TRAINING PROGRAMME ON CARDIOVASCULAR PARAMETERS, PAIN AND WHITE BLOOD CELL COUNT IN CHRONIC LOW BACK PAIN PATIENTS

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ABSTRACT

The study sought to determine the effects of eight weeks interval aerobic exercise training programme on cardiovascular parameters, pain and white blood cell count in chronic low back pain (CLBP) patients in selected tertiary hospitals in Enugu State. Eighty age-matched subjects with CLBP were randomly assigned into experimental and control groups. Sixty subjects, experimental (33) and control (27) completed the study. The experimental group exercised on a bicycle ergometer three times weekly at moderate intensities of between 50 and 70% of their age predicted maximum heart rate for a period between 48 to 72 minutes. The control did not engage in any organized exercise programme. Pain intensity and plasma levels of white blood cell were assessed before and after eight weeks of treatment. The blood sample (5mls) was collected and analyzed. Data were analyzed using ANCOVA at $p < 0.05$ level of significance. Results showed significant groups mean effect for the estimated blood pressure (BP), heart rate (HR) body mass index (BMI), pain intensity and white blood cell (WBC) ($p < 0.05$) among the exercise group compared to the control. Exercise training programme should form part of the treatment programmes in the management of CLBP.

Key Words: aerobic exercise, blood pressure, heart rate, white blood cell count

INTRODUCTION

Pain is a discomfort caused by tissue injury or noxious stimulation, and typically leading to evasive action (O'Sullivan and Siegelmann, 2012; Saladin, 2012). The physiology of pain and the potential for reducing the pain sensations has not been fully investigated. The influence of higher brain centre's on the perception of pain can be an important tool in pain relief (Foster and Palstanga, 1998). When acute, pain is characteristically associated with behavioral arousal and a stress response consisting of increased blood pressure, heart rate, pupil dilatation, and levels of cortisol in the plasma. Local muscle contraction (e.g., limb flexion, abdominal wall rigidity) is also often present (Kasper et al., 2005; Porter, 2005).

Chronic (intractable) pain is disabling and is easily recognizable, but it is poorly understood. The pain

overwhelms the patient, and is often associated with anxiety, depression and insomnia (Clancy and McVicar, 2002). It is impossible to predict when chronic pain will end, it often gets worse rather than better, it is poorly controlled, and therapies are generally ineffective. Examples of chronic pain include: arthritis and cancer pains (Clancy and McVicar, 2002; Cunningham, 2000). Chronic pain can be so terrible and detrimental to one's life that some people would rather die than continue living with it.

White Blood Cells (WBCs) also called leukocytes or leucocytes are the cells of the immune system that are involved in defending the body against both infectious disease and foreign invaders (Brooks et al, 1996). Five different and diverse types of leukocytes exist, and several types (including monocytes and neutrophils) are phagocytic. All leukocytes are produced and



derived from a multipotent cell in the bone marrow known as a hematopoietic stem cell. They live for about three to four days in the average human body. Leukocytes are found throughout the body, including the blood and lymphatic system (Maton et al., 1997). The number of leukocytes in the blood is often an indicator of disease. There are several different types of white blood cells. They all have many things in common, but all are distinct in form and function. A major distinguishing feature of some leukocytes is the presence of granules. White blood cells are often characterized as granulocytes or agranulocytes. It is therefore, important to investigate the effects of eight weeks of interval aerobic exercise training programme on cardiovascular parameters, pain and white blood cell count in chronic low back pain patients.

MATERIALS AND METHODS

Subjects: This study recruited sedentary, non-diabetic subjects with chronic low back pain (CLBP) who were receiving treatment the General Outpatient clinic of National Orthopedic Hospital, Enugu, Nigeria and University of Nigeria Teaching Hospital (UNTH), Ituku Ozalla, Enugu State. A total of eighty subjects with CLBP were enrolled in the study. All participants gave informed consent to participate in the study following full explanation of the protocol. The study's protocol was based on the American College of Sports Medicine guidelines (Meier-Ewert *et al.*, 2004). Ethical approval was granted by the Research and Ethics Committee of the UNTH, Enugu and National Orthopedic Hospital, Enugu respectively.

Study design: This study employed randomized controlled trial design. Eligible participants were randomized using simple random assignment into the exercise group (experimental) and the control group respectively. The participants in the two groups were age matched. The experimental group participated in an interval aerobic exercise training programme for the duration of 8 weeks and the control did not engage in any organised exercise programme. At the end of the exercise training a post-test procedure was administered to all subjects. Laboratory investigations were done at

Safety Molecular Pathology Laboratory in the Faculty of Health Sciences and Technology University of Nigeria Enugu Campus between 8.00am and 10.00am. All subjects were placed on Tramadol analgesic (50mg 12 hourly) as prescribed by the orthopaedic surgeons for the duration of the training.

Inclusion Criteria: Subjects with LBP symptoms for at least 12 weeks and declared medically fit to undertake physical activity and exercise. Also, the absence of musculoskeletal disabilities that would affect the ability to tolerate the test considered.

Exclusion criteria: Subjects with cardiac, systemic, or inflammatory disease, medical history of serious injury, spinal surgery or malignant pathology, and obesity (a body mass index of over 30 kg/m²) because of its association with hypercortisolism (Orth *et al.*, 1998) were excluded from this study. Also those involved in vigorous physical activities and above averagely physically fit, such as sports men and women, were excluded. A total of 80 sedentary non-diabetic subjects with chronic low back pain satisfied the study (experimental [$n = 40$] and control [$n = 40$]). Sixty subjects (33 from experimental and 27 from control) completed the 8-weeks training programme.

Outcome variables: The study outcome measures included BP, HR, pain intensity, BMI, and plasma levels of WBC.

Pre-test procedure: The subjects' resting heart rate systolic blood pressure and diastolic blood pressure were measured from the right arm using sphygmomanometer and stethoscope and the heart rate measured by counting the pulse with the use of stopwatch. These measurements were monitored between 8.00 am and 9.00 am.

Anthropometric measurements: Subjects' physical characteristics (weight [kg] and height [m]) and body composition (body mass index [kg/m²]) assessment were carried out in accordance with standardized anthropometric protocol (Ware, 2004).



Assessment of pain: Subjects were in a comfortable sitting position and were presented with the visual analogue scale which they completed under the researchers' guidance.

Blood sample collection (Venipuncture method):

The pre-training venous blood samples were obtained between 8.00am and 9:00 am using 5 ml syringe, using the procedure described by Bachorik (1982). Blood was drawn according to standardized protocol. About 5ml of blood was drawn from each subject under strict antiseptic condition.

Biochemical measurements: Blood samples were centrifuged at 3000 rpm for 5 minutes and plasma harvested and stored frozen at -20°C until required for analysis (Barbieri *et al.*, 2003). Plasma levels of white blood cell count was measured as described by Dacie and Lewis in Lamina and Okoye (2009) at Safety Molecular laboratory, Enugu.

Stress test: The Young Men Christian Association (YMCA) submaximal cycle ergometry test protocol was used to assess subjects' fitness level for the exercise as described by Golding *et al.* (1989), America College of Sports Medicine (1995); Heyward (2002), and Howley and Franks (2003). The YMCA protocol uses two to four 3-minutes stage of continuous exercise, two HR-power output data points needed (steady state HR) of between 110 and 150 beats/min. Exercise test started with a five minute warm up at zero resistance in order to acquaint the subjects with the cycle ergometer.

According to Brook *et al.* (1996); Pollock and Wilmore (1990) middle aged, less fit, cardiac patient generally begins stress test exercise at 100 or 150 to 300 kgm.min⁻¹ (17w or 25w to 50w respectively) with power increments of 5-25 watts per stage. The first 3 minutes' work rate was set at between 100 and 150kg.m (17-25watts), (1 watt = 6kg.m.min⁻¹). The pedal speed was set at 50rpm (revolutions per minute) by setting the metronome between 68 and 100bpm (beats per minute), heart rate and blood pressure were measured within the last minute of each stage. If a HR of above 110 bpm was obtained in the first 3 minute, then only one additional 3-minute stage was performed by increasing the workload by 25 watts (150kgm). If

the second stage HR was less than 110bpm. Then 3rd or 4th stages 3 minutes were performed at additional workload of 25 watts (150kgm) up to 300kgm in order to obtain two HR between 110 and 150bpm. These two HR did not differ more than 5bpm, when they did, the test was extended by another minute or until a stable value was obtained. At the end of the test, five-minute recovery period (cool down) at zero resistance pedaling was administered. Post exercise BP and HR were monitored and recorded.

Intervention

The EG: Participants in the EG exercised on a bicycle ergometer at a moderate intensity of between 50-70% of their HR max that was estimated from 220 minus the age of the subject, at a work/rest ratio of 1:1 according to Howley and Franks (1992); America College of Sports Medicine (1998); and Nieman (2003). The subjects pedaled at a slow speed and zero resistance for 5 minutes as warm up exercise. The starting workload was 100 kgm (17 watts) which was increased at a pedal speed of 50rpm to obtain a HR max of 50% which was increased in the first two weeks to level up at 70% HR max throughout the remaining part of the training period. In the first two weeks, the duration was 48 minutes which was then increased to 72 minutes that was maintained throughout the remaining six weeks' period of the training programme. The training session was concluded with a cool-down exercise which was slow speed pedaling at zero resistance for 5 minutes.

The exercise duration was four 6-minutes work interspaced with 6-minute rest in the first two weeks (i.e. 24 minutes' exercise and 24 minutes' rest = 48 minutes), while in the last six weeks the exercise duration was six-6-minutes work interspaced by 6 minutes' relief (i.e. 36 minutes' exercise and 36 minutes' rest = 72minutes). At the rest intervals, subjects pedaled at zero resistance. The frequency of training was three times per week for eight weeks. The workload that gave the HR max was noted and recorded for subsequent training sessions. The exercise training lasted for eight weeks. The subjects' blood sample (5mls)





was collected before and after the 8 weeks’ aerobic exercise training and analyzed for biochemical parameters. The training was done in the morning hours between 8.00am and 10am.

The CG: Subjects in the control group were instructed not to undertake any vigorous physical activity during the period of study.

Statistical analysis: The descriptive statistics (Means and standard deviations) of the subjects’ parameters systolic and diastolic blood pressure, heart rate, body mass index, white blood cell and pain intensity were determined. The pre test and post test data of the two (2) groups were compared

using Student’s t-test analysis. All statistical analyses were performed on a Toshiba compatible microcomputer using the statistical package for the social science (SPSS), (version 17.0 Chicago IL, USA). Alpha level was set at $p < 0.05$.

RESULTS

Table 1 is the means and standard deviations of the subject’s physical characteristics. It shows the mean ages of the participants were between 46 and 51 years, while the mean height were between 1.65 and 1.67 meters, mean weight between 75 kg and 77 kg while the means of body mass index was between 27 and 29 kg/m².

Table 1: Physical characteristics of subjects (Mean± SD)

Anthropometric data	Exercise group n=33	Control group n=27 Mean± SD	Total N=60
Age (years)	46.52 ±11.83	50.11 ±10.53	48.13 ±11.32
Height (m)	1.67±0.10	1.65 ±0.07	1.66 ±0.09
Weight (kg)	75.82 ±13.29	76.89 ±5.40	76.30±10.44
BMI (kg/m ²)	27.16 ±4.52	28.39 ±2.87	27.72 ±3.95

BMI= body mass index

Table 2: Comparison of groups’ baseline characteristics of subjects (Students t-test)

Variables	Exercise group n= 33	Control group n= 27 mean± SD	t-value	p-value
Age (yrs)	46.52±11.8	50.11±10.53	-1.230	.224
SBP (mmHg)	131.64±15.01	126.44±18.96	1.186	.240
DBP (mmHg)	82.94±9.60	77.78±10.93	1.946	.056
HR (beat/min)	77.55±10.84	73.44±9.85	1.519	.134
BMI (kg/m ²)	27.16±4.62	28.39±18.91	1.41	.200
VAS	6.27±1.74	4.89±1.63	3.104	.003*
WBC	4.12±1.42	5.08±0.73	0.168	.002*

*Probability value less than 0.05 was considered significant

Keys: Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), pain level as measured by visual analogue scale [VAS], White blood cell (WBC),



Table 3: Comparison of groups’ outcome effects of exercise on variables (ANCOVA)

Variables	Exercise group pretest	Exercise group posttest n= 33	Control group pretest	Control group posttest n= 27	F-value	p-value
SBP (mmHg)	131.64±15.01	125.97±14.93	126.44±18.91	127.07±14.72	12.362	.001*
DBP (mmHg)	82.94±9.60	76.61±10.45	77.78±10.93	81.33±9.45	29.759	.000*
HR (beat/min)	77.55±10.84	72.27±11.64	73.44±9.85	80.78±9.76	30.398	.000*
BMI	27.16±4.62	26.39±4.61	28.39±18.91	28.46±3.13	11.076	.002*
VAS	6.27±1.79	3.55±1.64	4.89±1.63	4.67±1.59	103.382	.000*
WBC	4.12±1.42	4.75±1.61	3.88±0.71	5.08±0.73	8.778	.004*

Probability value less than 0.05 was considered significant

Table 4: Gender comparison of outcome effects of exercise on variables (ANCOVA), N=33

Variables	Male pretest	Male posttest n= 18	Female pretest	Female posttest n=15	F-value	p-value
SBP (mmHg)	136.00±12.23	131.72±11.98	126.40±16.72	119.067±15.54	10.359	.003*
DBP (mmHg)	83.28±9.45	77.83±9.54	82.53±10.09	75.13±11.61	1.035	.317
HR (beat/min)	81.83±13.21	76.00±12.74	72.40±2.13	67.80±8.57	0.128	.723
BMI (kg/m ²)	24.57±1.36	24.20±1.54	30.28±5.24	29.02±5.67	4.505	.042*
VAS	6.67±1.85	3.50±1.76	5.80±1.66	3.60±1.55	17.998	.000*
WBC	4.28±1.78	4.87±1.78	4.17±1.26	4.61±1.42	0.12	.724

Probability value less than 0.05 was considered significant

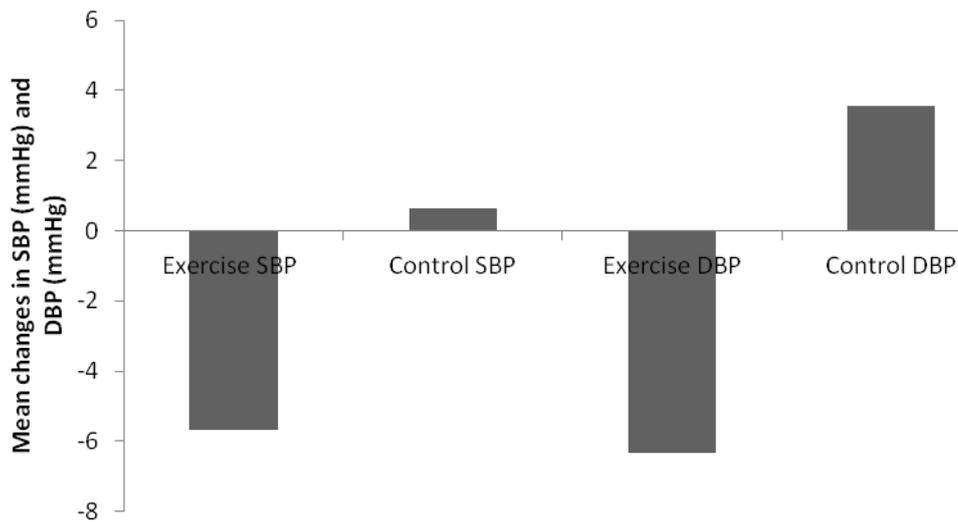


Fig. 1: Mean (Pre and post training) changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP)

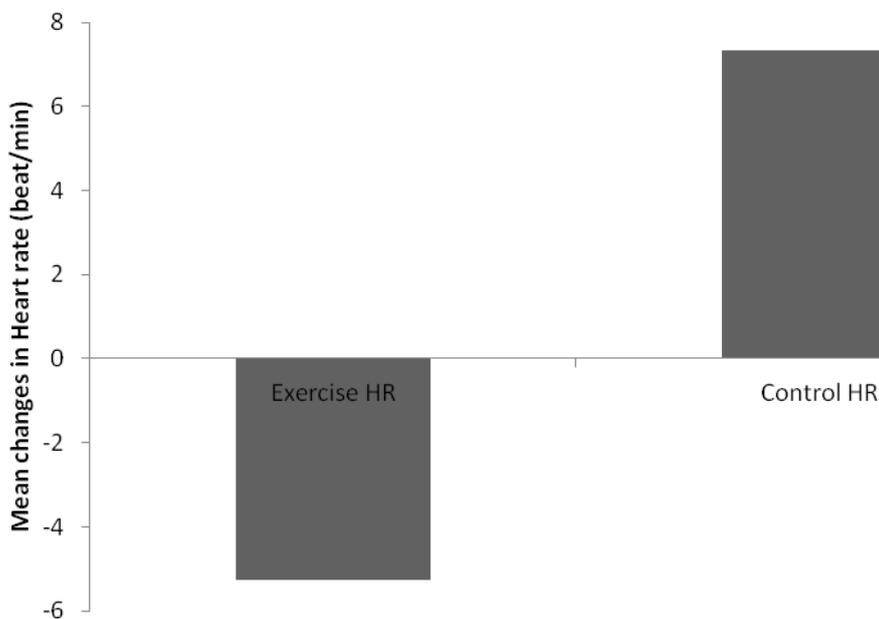


Fig. 2: Mean (pre and post training) changes in resting HR

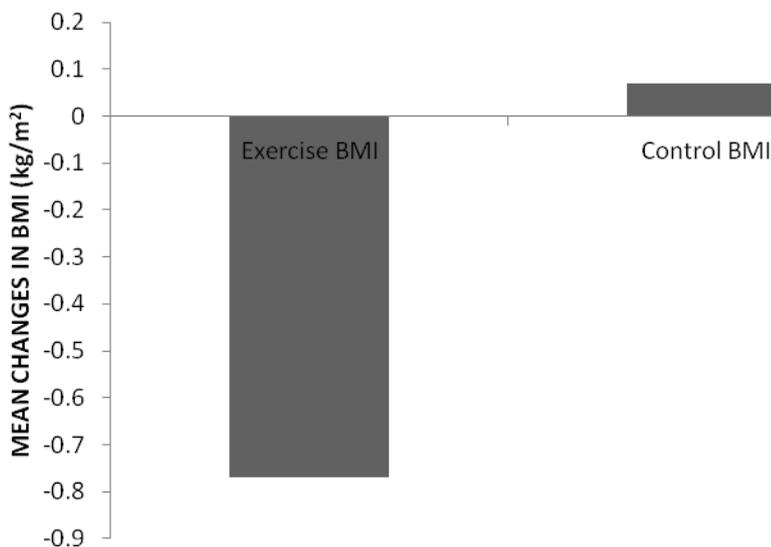


Fig. 3: Mean (pre and post training) changes in body mass index

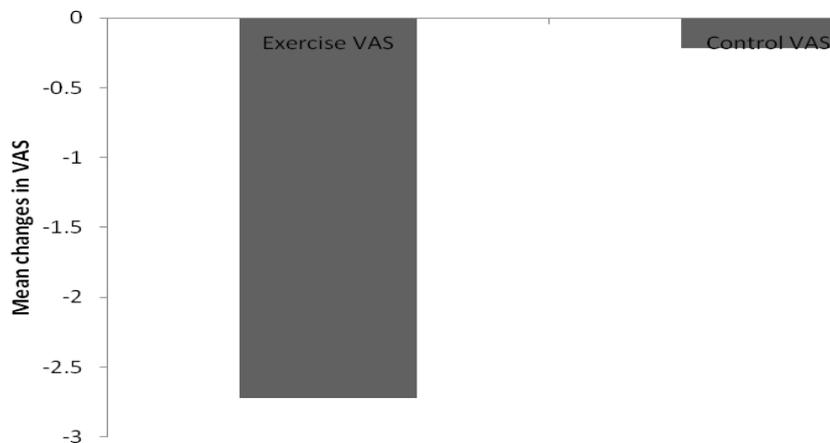


Fig. 4: Mean (pre and post training) changes in VAS

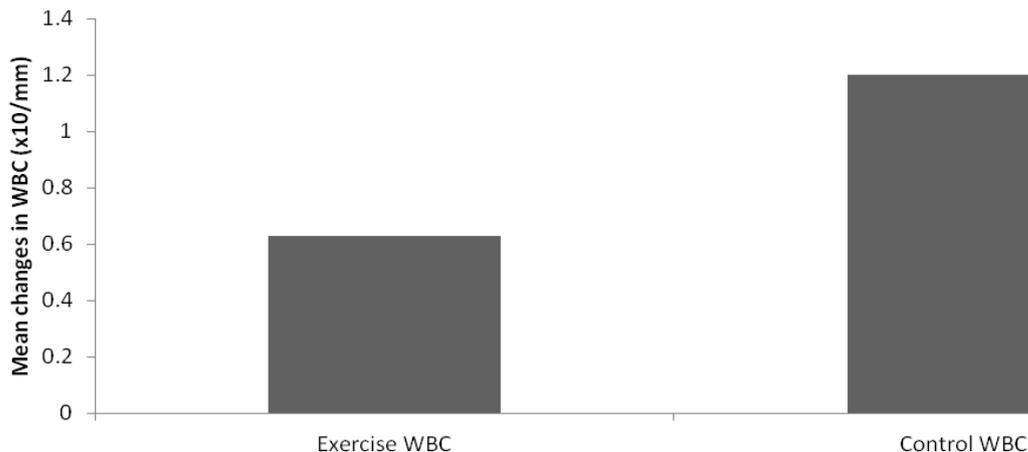


Fig. 5: Mean (pre and post training) changes in WBC

Discussion

Findings from the present study revealed a significant decrease in SBP and DBP in the experimental group over control group. This agrees

with a similar studies conducted by Molmen-Hansen (2012). and Guimarães *et al*, (2010). The researchers concluded that continuous and interval exercise training was beneficial for blood pressure control. The favorable changes resulting from

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aerobic training on both SBP and DBP as demonstrated in the present study is also consistent with several studies (Smith *et al.*, 2007; Westhoff *et al.*, 2007; Laterza *et al.*, 2007; Jones *et al.*, 2007).

Resting blood pressure is inversely correlated with acute pain sensitivity in healthy normotensives. Bruehl *et al.* (2002) reported that elevated SBP was associated with higher pain threshold in pain-free controls, but with lower pain threshold in LBP subjects. They concluded that the BP-pain sensitivity relationship is altered in chronic pain, suggesting dysfunction in pain regulatory systems, and that these alterations are not related to opioid dysfunction. The relationship between chronic pain and blood pressure is much less well understood. It has been reported in a number of studies that there may be a deficiency of endogenous opioids in chronic pain patients (Bruehl *et al.*, 1998). The blood pressure-pain relationship was studied by Bruehl *et al.* (1998). Their main finding was that in patients in whom the duration of the pain was relatively short (less than a year) there was a weak inverse correlation between the symptoms of pain and blood pressure, but in those who had been suffering from pain for more than 2 years the correlation was positive -- those who reported more frequent or intense pain had higher blood pressures. Maixner *et al.* (1997) found no relationship between blood pressure and sensitivity to acute pain in patients with temporomandibular joint disorders.

The probable mechanisms whereby the exercise training reduces blood pressure in this study could be related to neurohumoral, vascular and structural adaptations; sympathetic inhibition, decreased circulating catecholamine concentrations, decreased total peripheral resistance, improved insulin sensitivity, enhanced receptor sensitivity and alterations in vasodilators and vasoconstrictors as a result of exercise. Also, the “post exercise hypotensive effects” including relaxation and vasodilatation of blood vessels in the legs and visceral organ areas are venerable mechanism. Body warming effects, local production of certain chemicals, such lactic acid and nitric oxide; decreases in nerve activity and changes in certain hormones and their receptors are probable reasons

(Izdebska *et al.*, 2006; Mueller, 2007; Laterza *et al.*, 2007; Brook *et al.*, 1996).

Body mass index (BMI) is a measure of obesity. BMI below 20 kg/m² is indicative of underweight; 20 -24 kg/m² normal weight; 25 -29 kg/m² overweight; and over 30 kg/m² is obesity (Pollock and Wilmore, 1990). Overweight and obesity are important risk factors for chronic diseases morbidity, and mortality (DiPietro, 1995). The present study demonstrated a significant reduction in BMI in the exercise group over control. Studies (Jones *et al.* 2007; Takata *et al.*, 2003) have reported similar results on the positive effect of aerobic training on BMI.

A possible mechanism is that exercise training may decrease fat deposition, a factor linked to body weight and BMI (Keating *et al.*, 2012; Reid *et al.*, 1994; Hagberg, 1994; Wadden, 1997). It has been suggested that a dose response relationship exists between exercise volume and visceral adipose tissue (VAT) reduction, which has been attributed to a greater amount of energy expenditure leading to greater weight loss (Keating *et al.*, 2012). Multiple hypotheses might explain the link between overweight and obesity and musculoskeletal symptoms including, amongst others, increased mechanical demands and metabolic factors associated with obesity. Increased forces across the joints are likely to play a larger role in the relationship between a high BMI and weight-bearing joints (back and lower extremities) (Rechardt *et al.*, 2010; Wearing *et al.*, 2006; Viikari-Juntura *et al.*, 2008).

The present study revealed significant and considerable changes in the pain level (VAS) in exercise group over control group. The result of the present study is consistent with the findings of several studies (Hayden, van Tulder & Tomlinson, 2005; Joffe *et al.*, 2002; Liddle, Gracey & Baxter, 2007; Moffett *et al.*, 1999). Despite these outstanding results, the differences between the present study and previous studies were methodological and management differences, duration of studies and types of control subjects and participant activities level prior to recruitment. The positive role for increasing moderate physical



activity in the management and prevention of many chronic health conditions is now well established (Karmisholt and Gotzsche, 2005; Hu *et al.*, 1999). However, the American College of Sports Medicine (ACSM) (Alton *et al.*, 1998) recommends 30 min of low intensity aerobic activity 3–5 times a week to maintain a healthy lifestyle. Current literature suggests that exercise therapy aimed at improving return to work and normal activities is more effective for chronic LBP than bed rest (Garfin & Garfin, 2002; Hagen, Grasdahl & Eriksen, 2003).

However, research also suggests that individuals with chronic LBP should perform non-specific physical activity to reduce pain as opposed to specific back exercises (Hurwitz, Morgenstern & Chiao, 2005). Systematic reviews on the effect of exercise therapy on chronic LBP found that it was effective in decreasing pain and improving function [Hayden *et al.*, 2005; van Tulder, Koes & Bouter, 1997] and also effectively reducing recurrences in episodes of LBP (van Tulder *et al.*, 2000).

However, there is some evidence that a general exercise programme, which aims to increase individuals' confidence in the use of their spine and overcome the fear of physical activity, can be effective for patients with chronic back pain (of more than six months' duration) (Frost *et al.*, 1995). A randomized trial of a supervised exercise programme by Klaber *et al.* (1995) in a hospital setting reported significantly better outcomes at six months and two years for the exercise group compared with the control group.

Moffett *et al.* (1999) conducted a similar study evaluating the effectiveness of an exercise programme in a community setting for patients with low back pain to encourage a return to normal activities. They reported that the exercise group showed greater decreases in all measures of back pain and disability compared with the controls. At six weeks after randomisation, patients in the intervention group reported less distressing pain than the control group and a marginally significant difference on the Roland disability questionnaire scores. At six months the difference of the mean change scores of the Roland disability

questionnaire was significant, and at one year the differences in changes of both the Roland disability questionnaire and the Aberdeen back pain scale were significant.

The mechanism by which aerobic exercise relief pain may be through the opioid and non opioid pathways: The opioid pathway is through an increase in plasma β -endorphin levels, indicating involvement of the peripheral nervous system. Very little research has assessed both changes in plasma β -endorphin levels and pain perception; most of the research that has been conducted used aerobic exercise in young active males and found no correlations between β -endorphin levels and pain levels. Animal research shows a cross-tolerance between endogenous activation of the opioid system (through long-term voluntary exercise) and exogenous opioid administration. The non-opioid Mechanism is mediated via exercise influence on all aspects of the biopsychosocial model, affecting how an individual reports pain. Exercise activates large afferent fibers, and thus the mechanisms by which it relieves pain may involve the gate control theory and spinal inhibition. Additional theories include the relationship between activation of the motor cortex and descending inhibition (Bement, 2009; Kanarek *et al.*, 1998). Also, physical exercise keeps the musculoskeletal system in shape and promotes psychological well-being (Oldervoll *et al.*, 2001).

The present study indicated a significant reduction in WBC in the exercise group over control. This finding is in agreement with the report of several studies (Kullo *et al.*, 2007; Shankar *et al.*, 2004; Church *et al.*, 2009). Though, there has been a contradictory report on the mechanism by which regular exercise reduces WBC count. According to Fried *et al.* (1998); Halle *et al.* (1998) the potential common pathway may be the interleukins (IL). While multiple interleukins are likely to be involved, there is already strong evidence for the involvement of tumor necrosis factor- (TNF-) and IL-6. Both IL-6 and TNF-alpha are released in significant amounts from adipose tissue, particularly visceral adipose tissue. Their release from adipose tissue is augmented by increased sympathetic stimulation which is down-regulated



by regular physical activity (Mohamed-Ali, 2000). TNF- is a potent stimulator of IL-6 production and IL-6 is a potent stimulator for WBC production (McCarty, 1999). On the contrary, Pedersen and Bruunsgaard (2003); Pedersen (2006) reported that regular exercise induces anti-inflammatory actions.

It is generally at large 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. Another mechanism is that the post exercise hypotension which has been found to accompany decrease in serum catecholamines, norepinephrine, dopamine, cortisol, sympathetic nervous system, plasma rennin activity (Brooks *et al*, 1996; Hagberg, 1995; Duncan *et al*, 1986; Nelson *et al*, 1986), is responsible for suppressing inflammatory reaction and finally down-regulating WBC count.

Conclusion

Based on the results of this study the following conclusions were drawn. Exercise training relative to the individual's aerobic fitness capacity is feasible in subjects with chronic low back pain. Also that aerobic exercise (interval) is an important factor for the control pain, improving quality of life and averting the development of cardiovascular events (such as CHD, Stroke etc) in subjects with chronic low back pain.

The experimental group (interval exercise training programme) had a more profound significant effect than the control group (sedentary non exercising) with respect to estimated SBP, DBP & HR, BMI, pain intensity and WBC count. There was no significant gender effect with respect to DBP, HR and WBC. However, significant gender effect was recorded with respect to SBP, BMI and VAS.

Recommendations

Based on the findings of the present study, the following recommendations are advanced:

(1) The present study demonstrated a rationale bases for the adjunct role of long term moderate

intensity interval exercise training in pain modulation, and down regulation of blood pressure in the management of chronic low back pain. Therefore, orthopedic specialist and exercise specialists should feel confident in the use of this type of training in the adjunct management of chronic low back pain;

(2) There is need for more studies involving elderly, female and male chronic low back pain subjects of different black African and Nigerian background, to further clarify the effects of age, sex, race and genetics on low back pain.

Limitations of the Study

In the present study, attempts were made to control the effects of some intervening variables on the findings, but it was difficult to completely exclude their influences. The following limitations were therefore considered in the interpretation of the findings:

(1) A major constraint of this study was difficulty in monitoring the drugs and diet of the subjects who were strongly advised to avoid and desist from self medication. Their non-compliance with this instruction might affect the findings of the study;

(2) Another constraint was difficulty in monitoring the physical activity pattern of the subjects after the regular training programme. Therefore, the involvement of the subjects in other physical exercise aside the prescribed one in the training might affect the findings. The same applied to the control subjects.

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AUTHORS CONTRIBUTIONS:

Ezugwu U.A., Ezema C.I and Okoye G.C.were responsible for the design of the study and gathering of literature materials, Ezugwu U.A., Ezema C.I., Ativie R.N, Ikele C. Ojukwu, C.P. and Ekezie U. were responsible for the review of literature, drafting of the manuscript, analysis of the data and presentation of the data; Ezugwu U.A. and Ezema C.I were responsible for collection of data, Okoye G.C. supervised the research work. All the authors read the manuscript.

