ORIGINAL ARTICLE

EFFECT OF AEROBIC EXERCISE ON C-REACTIVE PROTEIN (CRP) AND INDEX OF ERECTILE FUNCTION IN SUBJECTS WITH HYPERTENSION AND ERECTILE DYSFUNCTION, KANO, NIGERIA

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ABSTRACT

BACKGROUND: Erectile dysfunction; the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance has been reported to be a problem in hypertensive and physically inactive individuals. Physical inability has been implicated in the etiology of vasculogenic erectile dysfunction and hypertension. The objective of this study was therefore to determine the effect of physical training on C-reactive protein and erectile function index in the management of erectile dysfunction in male subjects with hypertension.

METHODS: Sixty five male subjects with hypertension were age matched and grouped into continuous, interval and control groups. Subjects in the interval group involved in interval training (60-79% maximum heart rate; the continuous group involved in continuous training (35-59% HR max) for 8 weeks for duration of 45 - 60 minutes, while control group remain sedentary during this period. Serum C-reactive protein was assessed and the International Index of Erectile Function questionnaire was used in data collection. ANOVA, Bonferroni post hoc analysis and Spearman correlation test was used in data analysis.

RESULTS: The 65 age matched subjects were grouped into continuous (n=22; 61.78±7.79 years), interval (n=22; 62.11 ± 9.32 years) and control (n=21; 64.00± 8.53 years) groups. Findings of the study revealed a significant effect of exercise training on C-reactive protein, erectile function index, SBP, DBP and VO2 max of subjects with hypertension at p<0.05.

CONCLUSIONS: This study revealed that the down regulatory effect of exercise training on C-reactive protein, SBP, DBP and VO2 max may be the likely cause for improved erectile function in subjects with hypertension and erectile dysfunction. We recommend that therapeutic exercise should form part of the management modalities in hypertension and erectile dysfunction.

KEY WORDS: C-reactive protein; Erectile dysfunction; Exercise; Hypertension, Kano, Nigeria.

INTRODUCTION

Erectile dysfunction (ED) is a common problem, affecting more than half of all men between the ages of 40 and 70 years (1, 2, 3). ED has been defined by the National Institutes of Health Consensus Panel on Impotence as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance (4).

Numerous studies have shown that ED shares several modifiable risk factors with cardiovascular disease including atherosclerosis, hypertension, hyperlipidemia, diabetes mellitus, smoking, obesity and sedentary lifestyle (5-8). Data from several studies involving patients with cardiac disease have shown a high prevalence of ED (42–75%) (9-11). According to Feldman et al the most common etiology for organic ED is vasculogenic (12). Men with hypertension have a 15% probability of developing complete ED (increasing to 20% if they smoke).

Nitric Oxide (NO) released in response to sexual stimulation relaxes penile vascular smooth muscle by increasing the intracellular cyclic guanosine monophosphate (cGMP) concentration. Vasodilatation of erectile tissues allows the sinusoidal spaces to fill with blood, resulting in the attainment and maintenance of an erection (13). Higher levels of C-reactive protein (CRP) might increase blood pressure by reducing NO production in endothelial cells (14), resulting in vasoconstriction and increased production of endothelin-1 (15).

The influence and significance of lifestyle factors in erectile dysfunction (ED) have been demonstrated in cross-sectional and prospective, randomized, controlled trials. A review of several recent epidemiologic studies in several countries have shown that modifiable lifestyle or risk factors, including physical activity in particular, are directly related to the occurrence of ED (16).

Furthermore, the role of lifestyle changes (weight loss,
physical activity) demonstrated to be effective in modifying ED in moderately obese, sedentary men. It is a well established fact that sedentary lifestyle contributes to increased risk of cardiovascular diseases especially hypertension. Studies have shown that exercise training lowers blood pressure in hypertensive patients (17-20). The value of risk factor modification and lifestyle change in the clinical management of ED and concomitant cardiovascular illness was documented in other studies (16). However, few studies have actually investigated the effect of physical training in the management of ED. The objective of the present study was therefore to assess the therapeutic efficacy of exercise in the management of ED in hypertensive patients.

Subjects and Methods

Age matched randomized double blind independent groups design was used to determine the influence of the interval and continuous training program on cardiovascular parameters. Subjects’ age were arranged in ascending order (50 to 70 years) and then assigned to interval, continuous and control groups in an alternating pattern (age matched). One week wash out period was established and pretest was administered to all subjects on the last day of the wash out period. Following wash out and pretest assessment, all subjects were placed on methyl-dopa (aldomet), the interval and continuous groups involved in interval and continuous training programs for 8 weeks, while the control group remained sedentary during this 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.

Population for the study was male subjects with essential hypertension attending the hypertensive clinic of Murtala Mohammed Specialist Hospital (MMSH), Kano, Nigeria. Those complaining of ED of mainly lactose and inert substance in a single blind method (22). All subjects including those who were 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 in the Department of Physiotherapy of Murtala Mohammed Specialist Hospital (MMSH), Kano 8:00 - 10:00 am.

Subjects resting SBP and DBP were monitored from the right arm using an automated digital electronic BP monitor (Omron digital BP monitor, Model 11 EM 403c; Tokyo Japan). The measurements were taken between 8:00 - 10:00 am on each test day. Pre and post treatment venous blood samples were obtained between 8:00 am and 10:00 pm after about 12 hour overnight fast. Serum samples were transferred in to plastic containers, sealed and labeled. All samples were stored in a refrigerator at -80°C until analysis (23). The high sensitive C-reactive protein was determined qualitatively and semi-quantitatively using commercial latex agglutination method (Latex liquid reagents and manual by Dialab Produktion und Vertrieb Von Chemisch, Gesellschaft M.B.H). A titer (highest dilution showing positive result or lowest detection point) is then established at 0.2mg/l (values lower than 0.2 was regarded as 0.1mg/l).

Erectile function was assessed by completing questions 1 to 5 on the International Index of Erectile Function (IIEF), which is a multidimensional questionnaire (21). The IIEF score represents the sum of questions 1 to 5, with a maximum score of 25; a score of 21 or less indicates erectile dysfunction.

Stress test: The Young Men Christian Association (YMCA) sub maximal cycle ergometry test protocol was used to assess subjects’ aerobic power as described by American College of Sports Medicine (ACSM) (24); Golding et al. (25). The YMCA protocol uses two to four 3-minutes stages of continuous exercise, two Heart rate (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 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 maximum heart rate [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/min⁻¹, which was used to predict the subjects VO₂ max. This procedure was done for both pre and posttest stress test.

Training program: Following stress test and prior to the exercise training, all subjects in continuous, interval and control groups were re-assessed by a physician and were prescribed with methyldopa as necessary. Subjects maintained these prescriptions with regular medical consultation and observation throughout the period of sedentary, so also the control group during the period of sedentary.

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 reserve that was estimated 220 minutes for the age of a subject as recommended by ACSM (20). The starting workload was 100 kg (17 watts) which was increased at a pedal speed of 50 (revolution per minute) rpm to obtain a HR max 35% was increased in the first two weeks and level up at 59% HR max 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 level up at 60 minutes throughout the remaining part of the training.

The interval group (group 2): subjects in the interval group exercised on a bicycle ergometer at a moderate exercise intensity of between 60% and 79% HR max at a work/rest ratio of 1:1(20). Subjects pedaled at a speed of 50 rpm with the initial workload of 17 watts which was increased to HR of between 60% and 79% HR max. In the first two weeks, the intensity was 60% HR max which was then increased and level up at 79% HR max thought-out the remaining period of the training. The exercise session was increased from 45 minutes in the first two weeks and maintained at 60 minutes throughout the remaining period of the training program. The frequency of training was three times per week. The interval program was for 6 minutes work intervals interspaced with 6 minute relief intervals in the first two weeks while in the last 6 weeks the interval program was 6 minutes work. Intervals interspaced by 6 minutes relief. At the rest intervals, subjects pedaled at zero resistant.

Exercise session of three times per week was maintained throughout the 8 weeks period of training for both the interval and continuous groups.

The control group (group 3): subjects in the control group were instructed not to undertake any vigorous physical activity during the 8 weeks period of study.

During the 8 weeks training and sedentary period, all subjects (interval, continuous & control) were placed on methyldopa according to their pre recruitment doses. Aldomet was preferred because it does not alter normal hemodynamic responses to exercise (26). It is a well-tolerated and mostly prescribed antihypertensive drug in Nigeria (27), particularly Northern Nigeria where the study was conducted (28).

Posttest procedure

At the end of the 8 weeks training period, all subjects were asked to stop methyldopa (Aldomet) and were prescribed with placebo tablets in a single blinded method for one week. In the last day of the post training wash out period, fasting blood samples were collected as described earlier.

Posttest stress test: Stress test was also conducted at the last day of the posttest wash out period as described earlier.

Post training SBP, DBP, CRP assessment and stress test were conducted as described earlier in the pretest procedures using standardized protocols, techniques and methods and all subjects were presented with the IIEF questionnaire.

The coded responses on the IIEF were then entered in to computer and analyzed using the statistical package for the Social Science (SPSS) window version 16.0 Chicago, IL; USA. ANOVA and Temhane post hoc analysis was used (in the SPSS ANOVA, data were entered as ordinal data for CRP, IIEF and interval for SBP, DBP & VO₂max). The descriptive statistics (Means, standard deviations) of the subjects’ physical characteristics were analyzed. Spearman correlation was also performed. In ANOVA, the difference between the pre and posttest values (changed score) was used as the dependent variables. A value of P<0.05 was considered statistically significant.

RESULTS

Sixty five subjects (22 from interval, 22 from continuous & 21 from control group) completed the eight weeks training program. Ten subjects (3 from interval, 3 from continuous and 4 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 65 subjects were used in the statistical analysis.

The subject’s age ranged from 50 to 70 years with mean ± SD: interval (62.11± 9.32years); continuous (61.78± 7.79years) and Control (64.00 ±8.53years) groups. There was no significant groups’ difference in baseline physical characteristics and fasting blood sugar...
level (Table 1). However groups differ significantly in height.
Subjects’ baseline (pre-training) and post training values for variables of interest were checked. ANOVA results indicated that groups differ significantly in CRP ($F_{18.556, p=0.000}$) and IIRF ($F_{10.995, p=0.000}$). Bonferroni post hock indicated significant group differences in all variables. Figure 1 showed significant negative correlation between changes in CRP and IIEF score ($r=-0.547$) (Tables 2 and 3).

**Table 1.** Groups baseline physical characteristics, FBS (mean(X) ± SD) and ANOVA-test values (N = 65), Kano, Nigeria, 2007.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline physical characteristics &amp; FBS</th>
<th></th>
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<th>F-values</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Interval group n= 22</td>
<td>Continuous group n= 22</td>
<td>Control group n= 21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age(years)</td>
<td>62.11±9.32</td>
<td>61.78±7.79</td>
<td>64.00±8.53</td>
<td>1.152</td>
<td>0.323</td>
</tr>
<tr>
<td>Height(cm)</td>
<td>167.66±7.68</td>
<td>173.96±6.46</td>
<td>168.49±6.21</td>
<td>5.508</td>
<td>0.006</td>
</tr>
<tr>
<td>Weight(kg)</td>
<td>69.06±11.66</td>
<td>69.28±10.17</td>
<td>69.98±19.11</td>
<td>0.024</td>
<td>0.976</td>
</tr>
<tr>
<td>BMI(kg/m$^2$)</td>
<td>24.60±4.00</td>
<td>22.85±2.80</td>
<td>24.47±5.24</td>
<td>1.216</td>
<td>0.303</td>
</tr>
<tr>
<td>FBS(mmol/L)</td>
<td>4.30±1.26</td>
<td>4.63±0.91</td>
<td>4.60±1.25</td>
<td>0.547</td>
<td>0.582</td>
</tr>
</tbody>
</table>

**Fig 1.** Correlation between training changes in CRP and IIEF score, Kano, Nigeria, 2007.

**DISCUSSION**

This study indicated significant reduction in SBP, DBP and significant increase in VO$_{2\text{max}}$ as a result of exercise training; several previous studies have reported similar findings (29-31). This study also indicated significant effect of exercise on erectile dysfunction and significant negative correlation between IIEF and CRP as a result of exercise training.

The finding of the present study is in agreement with other studies (32-34), which reported significant reduction in CRP value following aerobic exercise and inverse correlation between CRP count and VO$_{2\text{max}}$ in healthy, mild to moderate hypertensive and coronary heart disease patients. Several other studies of large population cohorts, including the British Regional Heart Study (35), the Third National Health and Nutrition Examination Survey (36, 37), the Cardiovascular Health Study (38), the men’s Health Professionals Follow-up Study, the Nurses’ Health Study II (39) and the Health, Aging and Body Composition Study (Health ABC) (40), provided evidence for an inverse, independent dose–response relation between plasma CRP concentration and level of physical activity in both men and women.
Table 2: Distribution of pre and post test results (mean ± SD) by groups (N = 65), Kano, Nigeria, 2007.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Interval group</th>
<th>Continuous group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X±SD</td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td></td>
<td>Pretest</td>
<td>Posttest</td>
<td>Pretest</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>164.02±15.20</td>
<td>149.00±16.49</td>
<td>167.57±11.62</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>96.14±4.41</td>
<td>90.80±5.39</td>
<td>101.48±7.51</td>
</tr>
<tr>
<td>VO_{2} max</td>
<td>24.80±9.62</td>
<td>36.65±7.84</td>
<td>20.96±10.95</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>0.15±0.05</td>
<td>0.12±0.04</td>
<td>0.15±0.05</td>
</tr>
<tr>
<td>IIEF</td>
<td>10.91±5.49</td>
<td>14.55±4.65</td>
<td>8.18±3.96</td>
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</table>

The physiological basis for the therapeutic role of both continuous and interval exercise in the management of ED in hypertension as reported in the present study could be related to the biochemical, neural, and hormonal changes in the blood vessel walls that induce an acute and long-term blood vessel relaxation. The blood vessels may relax after each exercise session because of body warming effects, local production of certain chemicals, such as lactic acid and nitric oxide; decreases in nerve activity and changes in hormones and their receptors (41, 42). Over time, as the exercise is repeated, there is growing evidence that a long lasting effect on blood vessels. Chronic (regular, long-term) physical training may reduce basal concentrations of inflammatory markers. Data from cross-sectional observational studies have shown an inverse association between markers of systemic inflammation, physical activity and fitness status (35-43).

In conclusion, the finding of this study demonstrated that exercise improve erectile function in older hypertensive men with erectile dysfunction. This improvement was associated with amelioration of endothelial function through reduction in markers (CRP) of systemic vascular inflammation. Though the findings of this study provided a rational base for recommending exercise in the management of erectile dysfunction, there are some limitations which include failure to directly assess endothelial function, rather CRP level was used. Also few number of participants. These factors warrant more attention in future study.

Table 3. Groups changed scores (mean ± SD) and ANOVA-test values (N = 65), Kano, Nigeria, 2007.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Changed score values X±SD</th>
<th>F-values</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Interval group</td>
<td>Continuous group</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n= 22</td>
<td>n= 22</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>-15.02±14.07</td>
<td>-14.14±7.50</td>
<td>2.34±8.18</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>-5.34±4.90</td>
<td>-6.05±4.92</td>
<td>-1.14±1.99</td>
</tr>
<tr>
<td>VO_{2} max</td>
<td>13.21±8.42</td>
<td>6.57±5.08</td>
<td>1.34±3.18</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>-0.03±0.05</td>
<td>-0.02±0.04</td>
<td>0.01±0.03</td>
</tr>
<tr>
<td>IIEF</td>
<td>3.64±2.27</td>
<td>3.50±2.24</td>
<td>0.86±1.28</td>
</tr>
</tbody>
</table>
ACKNOWLEDGMENTS

All subjects with hypertension who participated in the study and staff of the Physiotherapy Department Murtala Muhammed Hospital, Kano, Nigeria.

REFERENCES

Effect of Aerobic Exercise on C-Reactive Protein

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