

CARDIAC AND PRESSOR FUNCTIONS IN EXERCISING YOUNG MEN FOLLOWING VITAMIN C SUPPLEMENTATIONO. O. Omodara^{1*} and S. I. Jaja²¹Department of Human Physiology, College of Medical Sciences, Abubakar Tafawa Balewa University, Bauchi, Nigeria.²Department of Physiology, College of Medicine, University of Lagos, Lagos, Nigeria.***Corresponding Author: O. O. Omodara**

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ABSTRACT

This study was conducted to investigate cardiac and pressor functions in exercising young men following vitamin C supplementation. Experiments were carried out on normotensive male subjects. A total of 20 subjects voluntarily participated in this study. Their ages ranged from 18 to 24 years consisting of ten (10) exercising subjects who were the test group, and ten (10) non – exercising subjects who were the control group. The exercising subjects in this study were individuals who were involved in regular physical exercise for not less than 3 hours per week. Each subject was given 300mg of vitamin C orally every day for six weeks (42 days). On day 1 (before the first dose of vitamin C) and on day 43 (a day after the last dose of vitamin C), cardiac and pressor parameters were measured. The results showed that in both exercising and non – exercising subjects, vitamin C supplementation significantly reduced the pressor parameters (systolic blood pressure -SBP, diastolic blood pressure -DBP and mean arterial blood pressure -MABP) while the difference in the changes in the pressor parameters between exercising and non – exercising subjects was not significant. Vitamin C supplementation significantly altered some of the cardiac parameters (P-wave duration - $P < 0.01$, QRS duration - $P < 0.001$, P-wave amplitude - $P < 0.01$, T-wave amplitude - $P < 0.02$, QT interval - $P < 0.001$, R-R interval - $P < 0.02$) in exercising subjects and (QRS duration - $P < 0.02$, T-wave amplitude - $P < 0.02$) in non – exercising subjects while the difference in the changes was not significant. In conclusion, these findings indicate that vitamin C supplementation has the potency to equilibrate the changes in the pressor and cardiac functions in exercising and non-exercising young men.

KEYWORDS: Vitamin C, Pressor, Electrocardiogram, Exercise, Antioxidant.**INTRODUCTION**

Physical exercise is any bodily activity that enhances or maintains physical fitness and overall health and wellness.^[1] It is performed for various reasons, including increasing growth and development, preventing aging, strengthening muscles and the cardiovascular system, honing athletic skills, weight loss or maintenance, and also enjoyment. Frequent and regular physical exercise boosts the immune system and helps prevent "diseases of affluence" such as cardiovascular disease, type 2 diabetes, and obesity.^[2,3] It may also help prevent stress and depression, increase quality of sleep and act as a non-pharmaceutical sleep aid to treat diseases such as insomnia, help promote or maintain positive self-esteem, improve mental health, maintain steady digestion and treat constipation and gas, regulate fertility health, and augment an individual's sex appeal or body image, which has been found to be linked with higher levels of self-esteem.^[4,5]

The beneficial effect of exercise on the cardiovascular system is well documented. There is a direct correlation between physical inactivity and cardiovascular mortality, and physical inactivity is an independent risk factor for the development of coronary artery disease. Low levels of physical exercise increase the risk of cardiovascular diseases mortality.^[6]

Children who participate in physical exercise experience greater loss of body fat and increased cardiovascular fitness.^[7] Studies have shown that academic stress in youth increases the risk of cardiovascular disease in later years; however, these risks can be greatly decreased with regular physical exercise.^[8] There is a dose-response relation between the amount of exercise performed from approximately 700 to 2000 kcal of energy expenditure per week and all-cause mortality and cardiovascular disease mortality in middle-aged and elderly populations. The greatest potential for reduced mortality is in the sedentary who become moderately active. Studies have shown that since heart disease is the leading cause of

death in women, regular exercise in aging women leads to healthier cardiovascular profiles. Most beneficial effects of physical activity on cardiovascular disease mortality can be attained through moderate-intensity activity (40% to 60% of maximal oxygen uptake, depending on age). Persons who modify their behavior after myocardial infarction to include regular exercise have improved rates of survival. Persons who remain sedentary have the highest risk for all-cause and cardiovascular disease mortality.^[9] According to the American Heart Association, exercise reduces blood pressure, LDL and total cholesterol, and body weight. It increases HDL cholesterol, insulin sensitivity, and exercise tolerance.^[10]

Vitamin C (ascorbic acid) is an essential micronutrient that is acquired primarily through the consumption of fruit, vegetables, supplements, fortified beverages, and fortified breakfast or "ready-to-eat" cereals.^[11] Vitamin C is a powerful aqueous-phase antioxidant that reduces oxidative stress^[12] and enhances endothelial function through effects on nitric oxide production.^[13] Antihypertensive effects of vitamin C were hypothesized as early as 1946,^[14] and many laboratory^[15,16] and human studies^[17,18] have established biological plausibility. Population-based observational studies have shown an inverse association between plasma vitamin C concentrations^[19] and vitamin C intake with blood pressure (BP),^[20] providing justification for trials evaluating vitamin C supplementation and BP reduction.

One of the vital roles of vitamin C is to act as an antioxidant to protect cellular components from free radical damage. Vitamin C has been shown to scavenge free radicals directly in aqueous phases of cells and circulatory system. Vitamin C has also proven to protect membranes and other hydrophobic compartments from such damage by regenerating the antioxidant form of vitamin E.^[21] Increased oxidative stress has been linked to impaired endothelial vasomotor function in atherosclerosis, and recent studies demonstrated that short-term ascorbic acid treatment improves endothelial function and may also benefit patients with coronary artery disease.^[22] Vitamin C, when acutely infused or chronically ingested, improves the defective endothelium-dependent vasodilation present in these clinical conditions. The mechanisms that might account for the ability of vitamin C to preserve nitric oxide (NO) include: ascorbate-induced decreases in low-density lipoprotein (LDL) oxidation, scavenging of intracellular superoxide, release of nitric oxide from circulating or tissue S-nitrosothols, direct reduction of nitrite to nitric oxide, and activation of either endothelial NO-synthase or smooth muscle guanylate cyclase. The ability of ascorbic acid supplements to enhance defective endothelial function in human disease provides a rationale for use of such supplements in these conditions. However, plausible mechanisms account for the effect, and to ensure that undesirable toxic effects are not present.^[23]

Earlier studies had shown that large doses of vitamin C when given orally and for at least 6 weeks reduced arterial blood pressure in hypertensive and non-hypertensive subjects.^[17,24,25] High levels of vitamin C in blood had been shown to be necessary to restore endothelium-derived nitric oxide (NO) action in hypertensive patients.^[26] On the other hand, other researchers have shown that a 4-week course of oral vitamin C (4g/day) or a single intravenous injection of vitamin C (2g) did not affect arterial blood pressure, stroke volume, cardiac output or peripheral resistance in healthy older men or patients with chronic heart failure. However, acute intravenous injection and not chronic oral vitamin C increased cardiovagagal baroreflex sensitivity in these patients.^[27,28,29] When given at pharmacological doses, vitamin C increased insulin-stimulated glucose uptake.^[30,31]

It is, however, not clear how vitamin C supplementation affect the cardiac and pressor functions of exercising young men. The aim of this study was to investigate the effect of 6-weeks vitamin C supplementation on the blood pressure, heart rate and changes in electrocardiogram (ECG) in exercising young men. Non-exercising young men served as control subjects.

MATERIALS AND METHODS

Inclusion Criteria: This study was carried out on normotensive male subjects in Idi-Araba area of Lagos state. A total of 20 subjects voluntarily participated in this study. The subjects were informed of the organization and details of the study and signed an informed consent form. Their ages ranged from 18 to 24 years consisting of ten (10) exercising subjects who were the test group, and ten (10) non-exercising subjects who were the control group. The exercising subjects in this study were individuals who were involved in regular physical exercise for not less than 3 hours per week.^[32] A brief case history was taken to provide information on subjects' cardiovascular and general health. All subjects had no known history of cardiovascular problem, and none was taking any medication as at the time of this study.

EXPERIMENTAL PROTOCOL

The experiment was carried out in Physiology Laboratory of College of Medicine, University of Lagos. The experiment was carried out in a fully air-conditioned room with temperature of about 18°C. Each subject was allowed to rest for about 10minutes in order to acclimatize to the room environment, and also allow cardiovascular parameters to return to resting levels. Anthropometric, blood pressure and pulse rate parameters were measured. ECG parameters were recorded in the supine position.

Anthropometric Measurements: Heights (in meters) of the subjects were measured using an inflexible measuring bar, and values recorded to the nearest 0.05m.

Body weights (in kilogram) were measured using a digital weighing scale.

Measurement of Blood Pressure: Blood pressures were obtained by auscultatory technique following the principle described by Beevers *et al.*^[33] using a mercury sphygmomanometer (U-MEC SPHYGMOMANOMETER, WENZHOU KANGJU MED. DEVICES LTD, CHINA). The first and fifth korotkoff heart sounds represented the systolic blood pressure (SBP) and diastolic blood pressure (DBP) respectively.^[34]

Measurements of Electrocardiographic Parameters: A 12-lead, 10 electrodes electrocardiographic (ECG) machine was used for this study (ECG-DG 2032, WENZHOU KANGJU MED. DEVICES LTD, CHINA). The electrodes were positioned as recommended by the American Heart Association.^[35] A paper speed of 25mm^s⁻¹ was used throughout the recording. The machine was standardized at each tracing to show a pen deflection of 10mmV⁻¹.

Each subject was given 300mg of vitamin C (VINCO PHARMACEUTICAL NIGERIA. LIMITED.) daily for six weeks (42 days).^[34] The vitamin C was administered orally. At the end of 42 days, the subjects returned to the laboratory, and the experimental protocol was carried out again.

DATA AND STATISTICAL ANALYSIS

All the parameters were measured in exercising and non-exercising subjects, values obtained were analyzed using Microsoft Excel Version 2013 and presented as Mean ± SEM (standard error of mean). Comparisons were carried out between both group using independent t-test; while comparisons within each group was done using paired t-test. P-value of less than 0.05 (P<0.05) was considered significant.

Body mass index (BMI) was calculated by dividing the body weight by the square of the height.

Body surface area (BSA) was calculated using the Mosteller formula:

$$\text{Body Surface Area} = \frac{\sqrt{\text{Height (cm)} \times \text{Weight (kg)}}}{3600}$$

The Pulse Pressure (PP) was calculated by finding the difference between the systolic blood pressure (SBP) and diastolic blood pressures (DBP).

Mean arterial blood pressure (MABP) = one-third of pulse pressure + diastolic blood pressure.^[37]

To determine heart rate, the R-R distance was measured and then inputted into the formula:

$$\frac{25\text{mm/sec} \times 60 \text{ beats/minute}}{\text{R-R interval (mm)}}.$$

Where: R-R is the distance between two successive R peaks, 25mm/sec is the calibration of the ECG machine. In this study, all ECG parameters were determined from chest lead, V₄, of the ECG recording and analyzed.

The rate pressure product (RPP) was measured using the formula: systolic blood pressure (mmHg) × heart rate (beats/min),^[38] to determine the rate of myocardial oxygen consumption.

RESULTS

Table 1: Comparison of the anthropometric measurements of exercising and non-exercising young men before Vitamin C supplementation.

	Non-Exercising (Mean± SEM)	Exercising (Mean ± SEM)
Age(years)	20.10 ± 0.67	21.40 ± 0.50
Weight (kg)	62.28 ± 1.79	67.97 ± 3.11
Height (m)	1.74 ± 0.02	1.76 ± 0.02
BMI (kg/m ²)	20.75 ± 0.56	21.94 ± 1.03
BSA (m ²)	1.74 ± 0.03	1.83 ± 0.09

Table 1 shows a summary of the anthropometric measurements of exercising and non-exercising young men before vitamin C supplementation. Table shows that all anthropometric measurements were similar in the two groups.

Table 2: Comparison of pressor parameters of exercising and non- exercising young men before Vitamin C supplementation.

	Non-Exercising (Mean± SEM)	Exercising (Mean ± SEM)
SBP(mmHg)	114 ± 4.00	110 ± 2.98
DBP (mmHg)	73.00 ± 3.35	66.50 ± 2.59
PP (mmHg)	41.00 ± 2.33	43.50 ± 2.79
MABP (mmHg)	86.67 ± 3.41	81.00 ± 2.39
RPP (units)	8739 ± 685.36	7114 ± 375.92

n=20

Table 2 shows a summary of the comparison of pressor parameters Between exercising and non - exercising subjects. Results show that all measured parameters were similar.

Table 3: Comparison of electrocardiographic parameters of exercising and non-exercising young men before Vitamin C supplementation.

	Non-Exercising (Mean \pm SEM)	Exercising (Mean \pm SEM)
P-wave amplitude (millivolt)	0.08 \pm 0.01 ^a	0.12 \pm 0.02 ^b
QRS amplitude (millivolt)	2.48 \pm 0.20	2.75 \pm 0.19
T-wave amplitude (millivolt)	0.45 \pm 0.05	0.59 \pm 0.09
P-R interval (seconds)	0.18 \pm 0.01	0.18 \pm 0.01
ST segment (seconds)	0.08 \pm 0.01	0.06 \pm 0.01
QT Interval (seconds)	0.35 \pm 0.01	0.36 \pm 0.01
P-wave duration (seconds)	0.10 \pm 0.008	0.10 \pm 0.007
T-wave duration (seconds)	0.17 \pm 0.010	0.19 \pm 0.007
QRS duration (seconds)	0.04 \pm 0.03 ^a	0.05 \pm 0.03 ^b
R-R Interval (seconds)	0.81 \pm 0.04 ^a	0.95 \pm 0.05 ^b
HEART RATE (beats/min)	76.30 \pm 4.31 ^a	64.70 \pm 3.01 ^b

a= statistically significant as compared to Exercising Subjects

b= statistically significant as compared to Non-Exercising Subjects

n=20, P<0.05

*Table 3 shows the summary of electrocardiographic parameters between exercising and non - exercising subjects before vitamin c supplementation. Results show that **P-wave amplitude, QRS duration and R-R interval** were all higher ($P<0.05$) in exercising subjects, while **Heart Rate** was lower ($P<0.05$) in exercising subjects. All other measured parameters were similar.*

Table 4: Effect of Vitamin C supplementation on pressor parameters in non-exercising and exercising young men.

Parameters	Non-Exercising		(c) Δ Mean \pm SEM	Exercising			P-Levels		
	(a)Pre-suppl	(b)Post-suppl		(d)Pre-Suppl	(e)Post-Suppl	(f) Δ Mean \pm SEM	(a)vs(b)	(d)vs(e)	(c)vs(f)
SBP(mmHg)	114.00 \pm 4.00	107.00 \pm 2.99	-7.00 \pm 2.11	110 \pm 2.98	101.80 \pm 3.12	-8.20 \pm 1.47	<0.001	<0.001	NS
DBP(mmHg)	73.00 \pm 3.35	69.00 \pm 2.78	-4.00 \pm 1.52	66.50 \pm 2.59	61.30 \pm 2.49	-5.20 \pm 1.09	<0.05	<0.01	NS
PP(mmHg)	41.00 \pm 2.33	38.00 \pm 2.21	-3.00 \pm 2.43	43.50 \pm 2.79	40.50 \pm 2.41	-3.00 \pm 1.63	NS	NS	NS
MABP(mmHg)	86.67 \pm 3.41	81.67 \pm 2.66	-5.00 \pm 1.31	81.00 \pm 2.39	74.80 \pm 2.46	-6.20 \pm 0.96	<0.01	<0.001	NS
RPP	8739 \pm 685.36	7894 \pm 528.04	- 845.00 \pm 398.50	7114 \pm 375.92	7535 \pm 480	4.21 \pm 405.66	NS	NS	NS

Table 5: Effect of Vitamin C supplementation on electrocardiographic parameters in non- exercising and exercising young men.

Parameters	Non-Exercising		(c) Δ Mean \pm SEM	Exercising			P-Levels		
	(a)Pre-suppl	(b)Post-suppl		(d)Pre-Suppl	(e)Post-Suppl	(f) Δ Mean \pm SEM	(a)vs(b)	(d)vs(e)	(c)vs(f)
P-wave duration(s)	0.10 \pm 0.008	0.10 \pm 0.006	-0.001 \pm 0.01	0.10 \pm 0.007	0.08 \pm 0.006	-0.02 \pm 0.004	NS	<0.01	NS
QRS duration (s)	0.04 \pm 0.003	0.03 \pm 0.002	-0.01 \pm 0.003	0.05 \pm 0.003	0.04 \pm 0.002	-0.013 \pm 0.002	<0.02	<0.001	NS
T-wave duration(s)	0.17 \pm 0.01	0.19 \pm 0.011	0.02 \pm 0.01	0.19 \pm 0.007	0.17 \pm 0.01	-0.02 \pm 0.01	NS	NS	NS
P-wave amplitude(mV)	0.081 \pm 0.01	0.085 \pm 0.011	0.004 \pm 0.01	0.121 \pm 0.02	0.085 \pm 0.013	-0.036 \pm 0.01	NS	<0.01	<0.05
QRS amplitude(mV)	2.48 \pm 0.20	2.22 \pm 0.11	-0.26 \pm 0.25	2.75 \pm 0.19	2.95 \pm 0.13	0.21 \pm 0.17	NS	NS	NS
T-wave amplitude(mV)	0.45 \pm 0.05	0.37 \pm 0.03	-0.08 \pm 0.04	0.59 \pm 0.09	0.46 \pm 0.06	-0.13 \pm 0.042	<0.02	<0.02	NS
PR interval (s)	0.182 \pm 0.01	0.166 \pm 0.008	-0.016 \pm 0.01	0.18 \pm 0.01	0.19 \pm 0.009	0.01 \pm 0.01	NS	NS	NS
ST segment (s)	0.082 \pm 0.01	0.096 \pm 0.014	0.014 \pm 0.01	0.06 \pm 0.01	0.09 \pm 0.01	0.03 \pm 0.013	NS	NS	NS
QT interval (s)	0.35 \pm 0.01	0.33 \pm 0.006	-0.02 \pm 0.01	0.363 \pm 0.006	0.328 \pm 0.0095	-0.035 \pm 0.005	NS	<0.001	NS
R-R interval (s)	0.81 \pm 0.04	0.83 \pm 0.04	0.026 \pm 0.03	0.95 \pm 0.05	0.83 \pm 0.04	-0.12 \pm 0.04	NS	<0.02	NS
Heart Rate (b/min)	76.30 \pm 4.31	73.40 \pm 3.40	-2.90 \pm 2.83	64.70 \pm 3.01	73.60 \pm 2.95	8.90 \pm 3.32	NS	NS	NS

DISCUSSION

Table 3 shows the comparison of the electrocardiographic measurement between non-exercising and exercising young men before vitamin C supplementation. This shows that P-wave amplitude, QRS duration and R-R interval were higher in exercising subjects than non-exercising subjects before vitamin C supplementation. Higher P-wave amplitude implies higher voltage during atrial contraction. Higher QRS duration implies decrease in rate of conduction of impulses within the ventricles. Higher R-R interval showed a decrease in rate of conduction of impulses from the atrium to the ventricles and thus, translates to the decrease in heart rate observed in exercising young men. The heart rate of exercising subjects was lower ($P < 0.05$) than the non-exercising subjects. Similar findings had been documented in previous studies in athletes.^[39,40] Studies indicate that the sinoatrial node and atrioventricular node are suppressed by an increase in vagal tone in athletes thereby giving rise to sinus bradycardia and heart block.^[41] Participation in sports activity and regular physical training which is associated with physiological, structural and electrical change in the athletes' heart that enable sustained increases in cardiac output for prolonged periods.^[42] ECG changes in athletes are common and usually reflect structural and electrical remodeling of the heart as an adaptation to regular physical training.^[43,44]

Table 4 shows the effect of vitamin C supplementation on pressor parameters of non-exercising and exercising young men. This shows that vitamin C supplementation reduced the SBP, DBP and MABP of both non-exercising and exercising subjects. Similar findings had been documented in previous studies by Jaja *et al.*^[34] Vitamin C has been observed to have a negative correlation with blood pressures.^[19,45,46] Other researchers had attributed the pressor lowering effect of vitamin C to its antioxidant effect^[12,47] or to its ability to enhance nitric oxide bioavailability and activity^[26] which in turn induces vasodilatation. Nitric oxide induces vasodilatation by increasing the concentration of cyclic guanosine monophosphate (cGMP) in vascular smooth muscle.^[48] Human coronary and peripheral arteries show endothelial dysfunction in a variety of conditions, including atherosclerosis, hypercholesterolemia, smoking and hypertension. This dysfunction manifests as a loss of endothelium dependent vasodilatation to acetylcholine infusion or shear stress, and is typically associated with decreased generation of nitric oxide (NO) by the endothelium.^[23] Vitamin C, when acutely infused or chronically ingested, improves the defective endothelium-dependent vasodilatation present in these clinical conditions.^[23]

In other researchers' explanation of the mechanism by which vitamin C supplementation decreases blood pressure, ascorbate increases intracellular concentrations of tetrahydrobiopterin, a cofactor of endothelial nitric oxide synthase, which enhances production of nitric

oxide—a potent vasodilator.^[49] Furthermore, there is evidence that vitamin C improves nitric oxide bioactivity.^[49,50] Moreover, in short-term human trials, vitamin C supplementation has been shown to improve endothelial function of both brachial^[51,52] and coronary^[53] arteries. Although plasma vitamin C concentration was not measured in this study, other studies have shown that following an acute or chronic dose, plasma vitamin C level increased.^[27] Oral vitamin C therapy has been shown to reduce oxidative stress and increase nitric oxide bioavailability.^[27,54] Vitamin C may also cause vasodilatation by inhibiting calcium entry into vascular smooth muscle cells and thus preventing increased vascular resistance.^[55]

Table 4 also shows that there is no statistically significant difference between the changes in pressor parameters observed before and after vitamin C supplementation in both non-exercising and exercising subjects.

Table 5 shows the effect of vitamin C supplementation on electrocardiographic measurement of non-exercising and exercising young men. This shows that in both groups of subjects, vitamin C supplementation reduced T-wave amplitude and QRS duration. Reduced T-wave amplitude implies lower voltage during ventricular repolarization, while reduced QRS duration implies increase in rate of conduction of impulses within the ventricle. Also, in exercising subjects, vitamin C supplementation reduced P-wave duration, P-wave amplitude, QT interval and R-R interval. This is similar to the findings documented by Bednarz *et al.*^[56]

Also, there is a statistically significant difference between the changes in P-wave amplitude observed before and after vitamin C supplementation in both non-exercising and exercising subjects.

In conclusion, this study showed that the change in pressor and most of the cardiac functions observed in exercising subjects following vitamin C supplementation is similar to that of non-exercising subjects, suggestive that vitamin C supplementation has the potency to equilibrate the changes in the pressor and cardiac functions in exercising and non-exercising young men.

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