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EFFECT OF PRE-INGESTION OF COLA NITIDA ON POST EXERCISE HEART RATE IN THE PHASES OF THE MENSTRUAL CYCLE

Omorogiuwa A* and Ogbonmwan E

Department of Physiology, School of Basic Medical Sciences, College of Medical Sciences University of Benin.

ABSTRACT: *Cola nitida and estrogen, a predominant hormone of the follicular phase of the menstrual cycle have been documented to have some cardiovascular effects. Although at normal resting state, cardiovascular effects such as changes in heart rate may not obvious. This study is therefore aimed at assessing post-exercise heart rate adjustment time in subjects who ingested Cola nitida during the follicular and luteal phases of the menstrual cycle. Sixty-four healthy volunteers with 32 subjects in the follicular phase and 32 subjects in the luteal phase of the menstrual cycle were studied. The thirty two subjects in each phase were further sub-divided into 4 subgroups with 8 subjects each group. The first groups of subjects were not given cola nitida while the remaining groups of subjects were given 100mg/kg, 200mg/kg and 400mg/kg of Cola nitida respectively. All subjects had their serum estrogen concentrations and base line heart rates assessed using standard methods before administering Cola nitida. 90 minutes post ingestion of Cola nitida, subjects were exposed to exercise for 35 minutes. The heart rates of subjects in sitting position were recorded every minute until they returned to baseline values. Results were presented as mean ± SD, $p < 0.05$ was considered to be statistically significant. Overall the percentage of subjects that experienced tachycardia was more in the luteal phase compared to follicular phase, although it was not statistically significant ($p > 0.05$) and the dose of Cola nitida ingested was observed to be inversely proportional to the heart rate adjustment time.*

KEYWORDS: *Cola Nitida*, Menstrual Cycle, Follicular, Luteal, Exercise, Heart Rate

INTRODUCTION

The menstrual cycle is essentially made up of two distinct phases with an ovulation phase interfaced between these two distinct phases. The distinct phases are the follicular which is estrogen dominated and the luteal phase which is progesterone dominated. The dominance of these sex hormones in these phases of the menstrual cycle is more obvious during the latter part of the phases. In other words women in the late follicular phase have more serum estrogen concentration than women in the early follicular phase. Similarly, women in the late luteal phase have more serum progesterone concentration than women in the early luteal phase. Estrogen affects the cardiovascular system through the activation of estrogen receptors resulting in activation of endothelial nitric oxide synthase with subsequent arterial vasodilation (Mendelsohn, 2002). He also opined that advanced atherosclerosis and certain progestins may attenuate some of the protective effects of estrogen.

In southern Nigeria, *Cola nitida* (kola nut) is a common associate of remarkable ceremonies such as marriages and christening. It has been used in folk medicine as an aphrodisiac and an appetite suppressant, enabling African soldiers who chew them to travel long distances without food (Trindall, 1997). *Cola nitida* like other cola such as *garcinia kola* and *cola acuminata* is composed of protein, phenolics, flavonoids, magnesium, copper, essential amino acids (

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arginine, proline, cysteine) and anti-nutrient factors such as saponins and oxalate (Dah-Nouvlessounon et al., 2015). It is generally accepted that the concentration of vitamin C in the indigenous wild fruits is higher than that in exotic fruits (Wehmeyer, 1966).

Somorin (1973) reported that caffeine, theobromine and theophiline are found in kola nut and the caffeine content is often considered to be the agent responsible for the physiological or clinical effect of kola nut in man and other mammals (Chukwu et al, 2006).

Caffeine stimulates heart function (Dodd et al., 1991), blood circulation and release of epinephrine (adrenaline) from the adrenal gland (Anderson et al., 1994; Bangsbo et al., 1992).

The American Heart Association recommends individuals to practice physical exercises in most days of the week, every day if possible, with intensity ranging from moderate to strenuous, according to their physical capability, for a period of 30 minutes or more(Pearson et al ., 2002). Regular exercises improve blood lipid, control insulin resistance, reduce cardiovascular risk factors (Gremeaux et al., 2012), and lower the incidence of cardiovascular diseases and mortality (Mora et al., 2007; Scherr et al., 2011). At the end of the exercise, special attention should be paid to heart rate behavior because of its prognostic value (Cole et al., 1999; Watanabe et al., 2001; Nishime et al., 2000). The smaller the heart rate variation, the higher the relative risk of developing a cardiovascular disease.

This study is aimed at assessing the role of estrogen dominated follicular phase of the menstrual cycle on post exercise heart rate adjustment time in subjects who ingested varying doses of *Cola nitida*.

MATERIALS AND METHODS

Plant material

Cola nitida seeds where purchased from Uselu market in Benin, Edo state, Nigeria. They were subsequently authenticated in the department of Plant Biology and Biotechnology of the University of Benin, Nigeria,

Subjects

A total of 64subjects who were students of a tertiary institution in Benin volunteered for the study. The 64 subjects were equally divided into two groups A and B. Group A were subjects in the Follicular phase of the menstrual cycle, while group B were subjects in the Luteal phase of the menstrual cycle.

Group A thus had 32 subjects and were subsequently sub-divided into 4 subgroups as follows

A_0 ; n = 8, A_1; n = 8, A_2; n = 8 and A_3; n = 8.

Similarly, Group B had 32 subjects and were subsequently sub-divided into 4 subgroups as follows

B_0; n = 8, B_1; n = 8, B_2; n = 8 and B_3; n = 8.

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Ethical clearance

Ethical approval was obtained from the Ethics and Research Committee of Saint Philomena's Catholic hospital. Informed consent was also obtained from the subjects.

Inclusion criteria: Regular menstrual cycle of 28 days

Exclusion criteria: History of peptic ulcer diseases, Palor, HbSS, Pregnancy, use of contraceptives, history of alcohol use, history of previous use of cola nitida, history of use of tobacco or any other illicit drug.

Phases of the menstrual cycle studied

The Follicular phase of the menstrual cycle was defined as the 12th day of the cycle while the Luteal phase of the menstrual cycle was defined as the 24th day.

Menstrual profile

A questionnaire was used to extract menstrual profile of subjects for the study.

Estrogen assay

Estrogen was assayed by radioimmunoassay (Bayer) on the 12th day for those in the follicular phase and on the 24th day for those in the Luteal phase of the menstrual cycle.

Administration of *Cola nitida*, heart rate measurement and exercise protocol

Prior to exercise base line hear rate was measured using Omron HEM-705CP. Subsequently subjects were either not given *Cola nitida* or given appropriate doses of *Cola nitida*; subjects in subgroup A_0 were not given *Cola nitida* and they served as control for the follicular phase, while subjects in groups A_1, A_2 and A_3 were given 100mg/kg, 200mg/kg and 400mg/kg respectively. Subjects in subgroup B_0 were not given *Cola nitida* and they served as control for the luteal phase, while those in groups B_1, B_2 and B_3 were given 100mg/kg, 200mg/kg and 400mg/kg respectively. 90 minutes after the ingestion of *Cola nitida* subjects were asked to warm up for 5 minutes and mount the thread mill with 2% inclination at 5mph for 30 minutes. The heart rates of subjects were measured every minute using Omron HEM-705CP until they returned to baseline values.

STATISTICAL ANALYSIS: Results were presented in tables and graphs as mean ± S.E.M using Microsoft excel 2007 Statistical analyses were done using Fisher's exact test and Students't-test; $p < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Menstrual profile

Table 1: Menstrual profile of subjects

Parameters	Follicular phase (n=32)	Luteal phase (n=32)
Age (years)	19.21±2.96	18.21±3.02
Age at Menarche (years)	10-13	11-13
Katamania (Days)	3-7	2-5
Menstrual Cycle Length (Days)	28	28

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Table 2: The estrogen concentrations in Mean ± SD of the groups in the Follicular phase of the menstrual cycle.

Parameter	A_0 (n=8)	A_1 (n=8)	A_2 (n=8)	A_3 (n=7)
Estrogen (pg/ml)	290.80±18.79	277.4 ± 18.74	311.3 ± 14.44	306.60 ± 23.33

Table 3: The estrogen concentrations in Mean ± SD of the groups in the Luteal phase of the menstrual cycle.

Parameter	B_0 (n=8)	B_1 (n=8)	B_2 (n=8)	B_3 (n=7)
Estrogen (pg/ml)	81.75 ± 4.76	96.13 ± 6.52	101.9 ± 7.97	95.86 ± 3.20

In the group of subjects in the follicular phase; one subject out of the eight subjects in the sub-group required to chew 400mg/kg of cola nitida declined because she could not chew and ingest the necessary quantity of cola nitida. Thus seven subjects participated in this group as against 8 subjects in the other groups. A similar finding was observed in the luteal phase group. The reason was essentially because of the unique bittertaste of the *Cola nitida*.

Table 4: Percentage of subjects that experienced post exercise tachycardia after ingestion of Cola nitida during the phases of the menstrual cycle

Doses of *Cola nitida*	**Baseline Heart rate**	**Follicular phase**	**Luteal phase**
Nil dose	66-82 beats/min	1 (12.5%) ; n = 8	2 (25.0%) ; n = 8
100mg/kg	62-78 beats/min	1 (12.5%) ; n = 8	2 (25.0%); n = 8
200mg/kg	68-80 beats/min	2 (25.0%); n = 8	4 (50.0%); n = 8
400mg/kg	63-76 beats/min	2(28.5%); n = 7	4 (57.4%); n = 7

In both phases of the menstrual cycle, there was a similar pattern of percentage increase of subjects who experienced tachycardia as the doses of *Cola nitida* increased. The caffeine content of *Cola nitida* plays a significant role in its physiologic action. Caffeine effects neurotransmission at both central and peripheral sites, primarily due to its antagonistic action at adenosine receptors (Rall(a),1990; Rall(b), 1982) thus increasing norepinephrine release. Norepinephrine serves as the neurotransmitter of the sympathetic nervous system, providing a vasoconstrictor influence on blood vessels and increasing both heart rate and contractility. Caffeine may therefore increase BP and heart rate by diminishing the inhibitory influence of adenosine at sympathetic terminals. In addition, caffeine may stimulate sympathetic drive via increased activity of the locus coeruleus, which is correlated with increased sympathetic nerve activity (Elam et al., 1986).

Nevertheless, the number of subjects who experienced tarchycardia in the luteal phase seemed to be more than subjects in the follicular phase. However, overall as shown in table 5, this was only empirical.

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Table 5: Relationship between post-exercise tachycardia and phases ofthe menstrual cycle

Phases of the menstrual cycle	Tarchycardia	Normocardia	Total
Follicular phase	6	25	31
Luteal phase	12	19	31
Total	18	44	62

Using the Fisher's exact test, there was no statistical difference ($p > 0.05$) between the number of subjects observed to have tachycardia in the follicular phase and the number of subjects in the luteal phase. In other words the phase of the menstrual cycle does not determine the number of subjects that will have tachycardia.

Table 6: Post exercise heart rate adjustment time following ingestion of

***Cola nitida* during the phases of the menstrual cycle**

Doses of *Cola nitida*	Heart rate adjustment time (Beats/min)		p values
	Follicular phase	Luteal phase	
Nil dose	5.25 ± 0.25 (n = 8)	5.63 ± 0.26 (n = 8)	$p < 0.05$
100mg/kg	4.00 ± 0.00 (n = 8)	4.13 ± 0.23 (n = 8)	$p > 0.05$
200mg/kg	3.13 ± 0.14 (n = 8)	4.25 ± 0.16 (n = 8)	$p < 0.05$
400mg/kg	3.14 ± 0.14 (n = 7)	3.75 ± 0.20 (n = 7)	$p < 0.05$

Heart rate adjustment time is the time taken for the heart rate of a subject to return to the baseline value. From the study the dose of *Cola nitida* ingested is inversely proportional to the adjustment time. The heart rate recovery time was also less in the follicular phase of the menstrual cycle. Thus even though the increased doses of cola nitida increased the heart rate in the both phases of the menstrual cycle the recovery time was shorter in the follicular phase of the menstrual cycle. Thus the protective effect of estrogen on the cardiovascular system was more efficient with increased heart rate. Heart rate is mediated primary by the direct activity of the autonomic nervous system (ANS), specifically through the sympathetic and parasympathetic branches activities over the sinus node auto- rhythmicity with predominance of the vagal activity (parasympathetic) at rest, that is progressively inhibited since the onset of exercise (Marcos and Claudio, 2003). The heart rate response n the onset of exercise represents the integrity of the vagus nerve and the recovery on the post-exercise transit also denotes important prognostic information; by the way, individuals that have a slow heart rate recovery in the first minute post-exercise have increased mortality risk (Marcos and Claudio, 2003). In the study done by Mont el al. (2009), people who did long-term regular training showed bradycardia in frequent stability, while the mechanism of resting bradycardia was reported to be influenced by the acceleration of the parasympathetic nervous system activity of the heart. Thus the high serum estrogen concentration in the follicular phase may have accelerated the parasympathetic nervous system to reduce the heart rate adjustment time especially at higher doses of *Cola nitida*.

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CONCLUSION

The follicular phase of the menstrual cycle has a better post-exercise heart rate adjustment time compared to the luteal phase and this may be protective against cardiovascular diseases. This advantage is traceable to the high serum estrogen concentration during this phase. Furthermore the autonomic effect on the heart is directly proportional to the dose of *cola nitida* consumed.

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