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Antioxidant Vitamins and Free Radical Status in Nigerian Pre-Eclamptic Women*

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Abstract: The status of antioxidant vitamins (vitamins A, C and β -carotene) and free radical (malonyl dialdehyde) were determined in 100 pre-eclamptic and 100 normotensive pregnant women from the 24th week of pregnancy and 100 normotensive non pregnant Nigerian women. The mean values of these antioxidant vitamins were significantly lower ($p < 0.05$) in the pre-eclamptic, compared with the normotensive pregnant and normotensive non-pregnant women respectively. The free radical level, on the contrary, was significantly higher ($p < 0.05$) in the pre-eclamptic, compared to the normotensive pregnant and normotensive non-pregnant women respectively. However, the levels of these indices in both the normotensive pregnant and normotensive non-pregnant groups were within a very close range and the difference between the two groups were not significant ($p > 0.05$). These results suggest that increase in the free radicals and decrease in the antioxidant vitamins concentrations are characteristic features of pre-eclamptic pregnancy. The specific point in pregnancy course that the free radical starts to rise and the antioxidant vitamins begin to decrease is a subject of further study.

Key words: Antioxidant-vitamins, free-radical, pre-eclampsia, normotensive pregnancy

INTRODUCTION

Pre-eclampsia is a multisystem disorder peculiar to pregnant women. It is a progressive disease with a variable mode of presentation and rate of progression. Pre-eclampsia remains the most common medical complication of pregnancy and a major cause of maternal and perinatal morbidity and mortality worldwide (Moodley, 1993; Sibai *et al.*, 2005). The precise aetiology and pathophysiology of this disease remains an enigma (Calder and Dunlop, 1995; Wagner, 2004). However, the pathophysiological mechanism of this disease has been reported to be characterized by the constriction of some peripheral arterioles, leading to increased peripheral resistance and arterial hypertension (Seydoux *et al.*, 1990; Bellany *et al.*, 2007). According to Sibai *et al.* (2005) key findings support a causal or pathogenetic model of superficial placentation driven by immune maladaptation, with subsequently reduced concentrations of angiogenic growth factors and increased placental debris in the circulation; and that women at risk are identified on the basis of epidemiological and clinical risk factors, but the diagnostic criteria of preeclampsia is unclear, with no known biomarker.

According to Conde-Agudelo *et al.* (2008), the risk of pre-eclampsia was increase in pregnant women with urinary tract infection and periodontal disease; and that there were no associations between pre-eclampsia and infections. Moreover, maternal endothelial dysfunction, such as reduced vascular prostacyclin production, has been reported to be implicated in patients with pre-eclampsia

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(Cunningham and Linahemer, 1990; Sibai *et al.*, 1995; Brown and Buddle, 1996). This endothelial dysfunction may be caused by the process and products of lipid peroxidation, which is known to be associated with pre-eclamptic condition (Walsh and Wang, 1993). Lipid peroxidation generates free radical species, such as reactive oxygen products and malonyl dialdehyde. Reactive oxygen species generated from lipid peroxidation include superoxide radicals (O_2^-), peroxide radicals (HO_2^-) and singlet oxygen (O).

The peroxides obtained from lipid peroxidation vasoconstrict the human placental vessels specifically by stimulating thromboxane production and decreasing prostacyclin synthesis (Sibai *et al.*, 1995; Walsh and Wang, 1993; Lawoyin and Ani, 1996). Malonyl dialdehyde levels have been used as index of lipid peroxidation (Sharpe *et al.*, 1994). Lipid peroxidation, in biochemical systems, has been reported to be inhibited in the presence of antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and glutathione-s-transferase), vitamins (vitamins A, C, α -tocopherol and β -carotene) as well glutathione (Mayes, 1990; Sies and Krinsky, 1995).

This study estimates the status of some antioxidant vitamins and a free radical, malonyl dialdehyde, in Nigerian pre-eclamptic patients. The relationship between these indices and lipid peroxidation, as implicated in pre-eclamptic condition is discussed.

MATERIALS AND METHODS

Venous blood was collected from 200 volunteer pregnant women and 100 non-pregnant women who reported for check-up at the antenatal clinic of the University of Calabar teaching hospital (UCTH), Calabar, Nigeria. Out of the 200 pregnant women (in their second and third trimester), 100 were diagnosed pre-eclamptic ($\geq 140/90$ mm Hg), while the remaining 100 were normotensive (BP range between 100/60-130/80 Hg). The blood pressure of the non-pregnant women ranges between 110/60-120/80 mm Hg. All the women used for this study were between the ages of 25-35 years old. This experiment was carried out in accordance with the guidelines of the Institutional Human Research Ethics Committee.

Serum samples were separated from the whole blood after coagulation and used for the estimation of antioxidant vitamins (vitamins A, β -carotene and vitamin C) and free radical (malonyl dialdehyde).

Vitamin A and β -carotene were estimated by the method of Bessey *et al.* (1946) while ascorbic acid (vitamin C) was estimated by the modified method of Scharffert and Kingsley (1995). Malonyl dialdehyde was estimated using the method described by Rumley and Paterson (1998). All absorbance readings were taken with Coleman Junior IIA linear absorbance spectrophotometer. Student's t-test was used to evaluate the significance of the difference between the mean values of pre-eclamptic women with normotensive pregnant and non-pregnant women respectively. A significant change was accepted at $p < 0.05$.

RESULTS

The mean values of vitamin A in pre-eclamptic, normotensive pregnant and non-pregnant women were 43.2 ± 5.1 , 95.2 ± 10.2 and 78.3 ± 8.0 $\mu\text{g dL}^{-1}$, respectively; the levels of β , carotene in the corresponding groups were 259.7 ± 30.5 , 571.4 ± 118.8 and 470.4 ± 108.4 $\mu\text{g dL}^{-1}$, respectively. The levels of vitamin C were 56.7 ± 6.1 , 96.6 ± 9.6 and 84.1 ± 4.8 $\mu\text{g dL}^{-1}$, respectively. Malonyl dialdehyde levels in pre-eclamptic, normotensive pregnant women were 1.8 ± 0.1 , 0.4 ± 0.1 and 0.5 ± 0.1 nmoles dL^{-1} , respectively (Table 1).

These results show that the mean antioxidant vitamin levels were significantly lower ($p < 0.05$) in pre-eclamptic women compared to the respective values in normotensive pregnant and non-pregnant groups. On the other hand, the level of malonyl dialdehyde in pre-eclamptic group was significantly

Table 1: Serum antioxidant vitamins and MDA levels in pre-eclampsia

Group	Vit. A (μdL^{-1})	β -carotene ($\mu\text{g dL}^{-1}$)	Vit. C (μdL^{-1})	MDA (nmoles dL^{-1})
Normotensive non-pregnant (I)	78.3 \pm 8.0	470.4 \pm 108.4	84.1 \pm 4.8	0.5 \pm 0.1
Normotensive pregnant (II)	95.2 \pm 10.2*	571.4 \pm 118.8*	96.9 \pm 9.6	0.4 \pm 0.1
Pre-eclamptic (III)	43.2 \pm 5.1**	259.7 \pm 30.5**	56.7 \pm 6.1**	1.8 \pm 0.1**

Values are presented as mean \pm SD; *p<0.05 compared with I; **p<0.05 compared with II; n = 100

higher (p<0.05) than the levels in normotensive pregnant and non-pregnant groups. However, the differences in the levels of the antioxidant vitamins and free radical between the normotensive pregnancy and normotensive non-pregnant groups were not of any appreciable significance.

DISCUSSION

The results of this study show that the level of malonyl dialdehyde (a free radical product of lipid preoxidation) is raised under pre-eclamptic condition, resulting in a reduction in the levels of antioxidant vitamins. Malonyl dialdehyde levels, as earlier reported by Sharpe *et al.* (1994), are used as an index of lipid peroxidation caused by oxidative activities. The increase in the levels of malonyl dialdehyde under pre-eclamptic condition, observed in this study, indicates the complication of lipid peroxidation. This result is in agreement with the observation of Walsh and Way (1993) that lipid preoxidation is incriminated in pre-eclampsia.

Antioxidant vitamins have been reported to be mobilized in the body to inhibit lipid peroxidation and complement antioxidant enzymes to scavenge reactive free radical species (Mayes, 1990; Sies and Krinsky, 1995; Redman, 1993). The decreased levels of antioxidant vitamins observed in this study may be due their mobilization to interfere with lipid peroxidation and scavenge the reactive free radical species, in an attempt to protect the system against oxidative stress associated with pre-eclampsia. Vitamins A, C and β -carotene are known to act synergistically with α -tocopherol to inhibit lipid peroxidation (Sies and Krinsky, 1995; Redman, 1993; Bucttner, 1993; Chew, 1995). These reports justify the decreased levels of the antioxidant vitamins reported in this study. However, the specific stage in pregnancy that the free radical starts to rise and the antioxidant vitamins begin to fall is yet to be established.

From these results, supplementation of diets with antioxidant vitamins could be suggested for pre-eclamptic patients so as to augment the decreased antioxidant level and reduce the concentration of reactive species in the maternal circulatory system. This can serve as a measure of preventing maternal and fetal morbidity associated with pre-eclampsia.

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