ELSEVIER

European Journal of Obstetrics & Gynecology and Reproductive Biology 93 (2000) 37–39

EUROPEAN JOURNAL OF OBSTETRICS & GYNECOLOGY AND REPRODUCTIVE BIOLOGY

www.elsevier.com/locate/ejogrb

Original Article

Vitamin E and C in preeclampsia

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Received 19 July 1999; received in revised form 4 November 1999; accepted 27 December 1999

Abstract

Vascular endothelial damage has been implicated in the pathophysiology of preeclampsia. Lipid peroxidation may be involved in the process and essential nutrients that can scavenge free radicals, such as vitamin E and C, operate in concert. Antioxidant vitamins E and C were estimated in 30 preeclamptic and 30 normotensive pregnant women. Significantly lowered levels of vitamins E and C were observed in preeclamptic women as compared to controls ($P<0.001$ and $P<0.05$ respectively). In patients with preeclampsia antioxidant nutrients may be utilized to a greater extent to counteract free radical-mediated cell disturbances, resulting in a reduction in serum antioxidant levels.

Keywords: Vitamin C; Vitamin E; Antioxidants; Free radicals; Preeclampsia

1. Introduction

In addition to the enzymic mechanism of the radical removal, essential nutrients that can scavenge free radicals, such as vitamin E and C, constitute a strong line of defense in retarding free radical induced cellular damage [1]. Vascular endothelial damage is known to play a role in the pathophysiologic mechanism of preeclampsia and free radical mediated lipid peroxidation may be involved in the process [1,2]. Several observations support this concept, including an increase in lipid peroxidation products [1,2] and a decrease in antioxidant activity [1,2] in preeclampsia compared with normal pregnancy. Randomized controlled trials have shown that vitamin C and E supplementation may be beneficial in the prevention of preeclampsia in women at increased risk of the disease [3]. Antioxidant nutrients counteract these free radical disturbances and, thereby, protect cell membranes against free radical mediated lipid peroxidation [1]. Hence, the present study was planned to investigate the plasma levels of vitamin C and vitamin E in patients with preeclampsia.

2. Material and methods

Thirty normotensive pregnant and 30 preeclamptic women attending antenatal clinics at Pt. B.D. Sharma PGIMS, Rohtak (India) were recruited after they gave informed consent. Inclusion criteria was: Age 18–35 years, primigravida who visited hospital during first trimester, 28–40 weeks gestation, absence of labour contractions, absence of any other medical complication (such as renal disease, primary hypertension, cardiovascular disease, connective tissue disease) concurrent with preeclampsia. Preeclampsia was defined as described in classification approved by the International Society for the study of Hypertension in Pregnancy [5]. Under this classification, hypertension is defined as one diastolic blood pressure readings $\geq$110 mmHg or two consecutive diastolic blood pressure readings $\geq$90 mmHg $\geq$4 h apart. Significant proteinuria is defined $>$300 mg protein in a 24-h urine collection or, if this is not available, 1+ proteinuria by dipstick on two consecutive occasions $>$4 h apart. With these definitions the following classification of pre-

0301-2115/00/$ – see front matter
PII: S0301-2115(00)00243-8

Table 1
Clinical characteristics of study groups (Results expressed as mean values)

	Normotensive pregnant (n=30)	Preeclampsia (n=30)
Age (yr)	21±5.6	23.5±6.2
Hemoglobin (g%)	9.6±2.0	9.3±1.25
Gestational age at presentation (wk)	30.1±2.0	30.3±2.5
Age of assessment age at delivery (wk)	38.2±	36.4±3.9
Proteinuria	Nil	+(in all patients)
Mean arterial BP (mmHg)	80±8	118±9
Birth weight (g)	2500±275	2211±794

eclampsia was derived: Hypertension in combination with proteinuria developing after 20 weeks' gestation in a previously normotensive nonproteinuric woman. Overnight fasting samples were collected before starting antihypertensive therapy. Patients were excluded from the study if they had abnormal levels of serum creatinine (>1.5 mg/dl); or had a history of vitamin E or C supplementation or use of aspirin or antihypertensive drugs. Vitamin E was measured spectrofluorometrically [2]. Vitamin C was estimated spectrophotometrically [6]. Data was analyzed statistically using student's *t*-test.

3. Results

Table 1 shows the clinical data on the preeclamptic women and healthy controls and Table 2 gives the fetal outcome of preeclamptic women. The plasma levels of vitamin C were significantly decreased in patients with preeclampsia as compared to controls ($P<0.05$). Also, vitamin E levels were low in preeclampsia as compared to controls ($P<0.001$), Table 3.

Table 2
Fetal outcome in preeclamptic women

	Preeclamptic women (n=30)
Live birth	23
Still birth	7
Gestational age at delivery (wk)	36.4±3.9[a]
Birth weight (g)	2211±794[a]
Mode of delivery:	
Normal	21
Em. LSCS	5
Vacuum extraction	4
Apgar score	
1 min	6/10
5 min	7/10

[a] ±S.D.

Table 3
Vitamins in preeclampsia (μmol/l, mean±S.D.)

	Normotensive pregnant (n=30)	Preeclampsia (n=30)
Vitamin C	60.18±23.27	45.99±5.68
Vitamin E	23.63±0.97	10.63±0.87

4. Discussion

Vascular endothelial damage is known to play a role in the pathophysiologic mechanisms of preeclampsia [2,3]. It has been suggested that free radical mediated lipid peroxidation may be involved in endothelial damage seen in preeclampsia [2,3,6,7]. Excess free radical disturbances are typically accompanied by increased utilization of antioxidants, resulting in a decrease in their concentrations. In the present study, we observed a fall in both vitamin C as well as vitamin E levels in preeclampsia as compared to normotensive controls. Our results are in agreement with those reported in literature [4]. Wang determined vitamin E levels longitudinally throughout normal pregnancy and observed a progressive increase in vitamin E concentrations which was most prominent between 24 and 32 weeks [8]. While others have reported decreased vitamin E levels during preeclampsia and normal levels in normotensive pregnant women [3,4,9]. It appears that water-soluble antioxidant nutrients (reduced vitamin C) may be initially consumed, followed by lipid-soluble antioxidants (alpha-tocopherol). Also, it has been reported that vitamin C regenerates vitamin E by non enzymic mechanism [10].

In addition, vitamin C and E have been demonstrated to inhibit superoxide anion production in the pig coronary artery suggesting that beneficial effects antioxidant vitamins are related, in part, to alterations in vessel redox status [11]. Furthermore, vitamin C treatment improves endothelial nitric oxide action in patients with coronary artery disease [11,12]. The decrease in antioxidant nutrient levels observed in this study indirectly supports the concept that free radical-mediated lipid peroxidation and related antioxidant consumption may be involved in the pathophysiologic mechanisms of preeclampsia. Human defenses against oxidative stress and free radical damage primarily consist of antioxidant-enzymes and nutrients. The antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase) are synthesized in the body, and their concentrations, cannot be easily influenced. In

contrast, antioxidant nutrient levels can be simply manipulated by dietary or pharmacologic supplementation. The concept of increase utilization of vitamin C and E in preeclampsia women raises the possibility of a potential protective role for antioxidant nutrients in preeclampsia. Various antihypertensive drugs (methyl dopa, labetolol or atenolol) along with diuretics have been evaluated in at least 15 randomized trials, but revealed no such benefit of preventing preeclampsia [13]. Magnesium, zinc, or fish oil supplementation, antioxidant nutrient supplmentation (vitamin C, E, allopurinol) trials have also revealed minimal-to-no benefit [9,13,14]. A randomized controlled trial investigated the effect of supplementation with vitamin C and E on plasma markers of vascular endothelial activation (plasminogen-activator inhibitor-1, PAI-1) and placental insufficiency (PAI-2) and the occurrence of preeclampsia [3]. Vitamin C and E supplementation was associated with a 21% decrease in PAI-1/PAI-2 ratio during gestation. In the intention-to-treat cohort, preeclampsia occurred in 17% women in the placebo group and 8% in the vitamin group, thereby suggesting that supplementation with vitamin C and E may be beneficial in the prevention of preeclampsia in women at increased risk of the disease. While another randomized controlled trial of antioxidant therapy (vitamin E, vitamin C and allopurinol) have shown that lipid peroxide levels were not significantly altered, however uric acid levels decreased and vitamin E levels increased significantly. Also, these dosages did not improve fetal outcome [9,13,14].We have demonstrated that superoxide anion formation was increased and glutathione levels are lowered in preeclampsia and glutathione levels are lowered in preeclampsia as compared to normotensive pregnant women [15,16]. It can be inferred from these studies that the beneficial effects of the antioxidants (vitamin C and E) were related to their ability to decrease production of superoxide. Vitamin C may also increase prostacyclin production and lower blood pressure [12,17]. The findings of the present study demonstrating lower vitamin C and E status in preeclampsia fit well with these previous observations.

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