PLASMA ANTIOXIDANT VITAMINS AND LIPID PEROXIDATION PRODUCTS IN PREGNANCY INDUCED HYPERTENSION

G.M.Rao *, Sumita P*, Roshni M* and M.N. Ashtagimatt*.

* Department of Biochemistry, Center for Basic Sciences Kasturba Medical College Bejai, Mangalore 575 004

ABSTRACT

It has been suggested that antioxidant systems are impaired in pregnancy induced hypertension and hence patients are exposed to oxidative stress. In order to investigate the relationship between lipid peroxidation and certain antioxidant parameters in blood of pregnancy induced hypertension (PIH) cases, 25 normotensive and 23 PIH samples were studied. In the present study, thiobarbituric acid reactive substances showed a tendency to increase, however the increase remained statistically insignificant. Plasma ascorbic acid level remained unaltered and Vitamin E showed a tendency to increase in the study group. The findings implicate oxidative stress in the disease and cite the biochemical rationale for clinical trials of antioxidants to prevent and treat pregnancy induced hypertension.

KEY WORDS

Vitamin C, Vitamin E, Lipid peroxidation & PIH

INTRODUCTION

Damage From free radicals has been implicated in many pathological conditions. It is envisaged that increased free radical activity arises from increased production of free radicals or deficiency in protective antioxidant systems. Pregnancy induced hypertension (PIH) is associated with endothelial dysfunction (1). Such dysfunction could be caused by oxidative stress. The unsaturated lipids and thiol containing proteins in cell membranes are susceptible to free radical attack. There are reports about increased free radical activity in PIH(2). But little is known about the part played by changes in specific antioxidants. Several lines of evidence indicate that adverse changes in structure and Junction of maternal vascular endothelium accounts for the vascular activity, activation of coagulation cascade and multisystem damage in preeclampsia. Multiple circulating factors may provoke the spectrum of endothelial changes, including lipoproteins(3). Placental hypoxia or ischemia could result in release of products in to maternal circulation which then initiates the maternal pathological changes. Lipid peroxidation products are candidate factors that may mediate disturbances of other maternal vascular endothelium. Rodgers et al (4) reported that

preeclamptic sera contains cytotoxic factors that damage endothelial cells. The identity of these cytotoxic factors is not known, but lipid peroxides are likely candidates as suggested by Hubel et al (5).

Vitamin E is a lipid soluble and chain breaking antioxidant. Several studies found lower plasma Vitamin E in patients with PIH (6). Ascorbate is the water soluble antioxidant vitamin, reacts rapidly with superoxide and peroxy radicals and even more rapidly with hydroxyl radicals to give semidehydroascorbate. Furthermore deficiency of Vitamin C causes impaired immune responses (7).

In this study, two extra cellular antioxidants Vitamin E and Vitamin C and RBC-Thiobarbituric acid reactive substances are assessed to reflect the oxidative stress across the cell membrane. RBC are selected because it is easily accessible and may be affected in PIH (hemolysis). It is rich in thiol functions, which are potentially involved in attack from and protection against free radicals.

MATERIALS AND METHODS

All chemicals used in the study were of Research Grade and purchased in India.

There were two study groups, healthy pregnant with normal blood pressure and pregnant with pregnancy-induced hypertension. Sample was collected from the subjects in the third trimester. No cases of chronic hypertension or superimposed preeclampsia were included in the study. None of the women had received antihypertensive medication until the samples were

Author for Correspondence

Dr. Gayatri M. Rao

Department of Biochemistry, Center for Basic Sciences Kasturba Medical College Bejai, Mangalore 575 004

taken.

Blood sample was collected by vein puncture, in heparinised bottles, on one occasion. The sample was centrifuged at 3600 r.p.m. to separate the cells and plasma. RBC was washed with saline phosphate buffer (3 times) and the buffy coat of WBC was removed. Packed RBC was suspended in saline phosphate buffer (v/v).

Plasma: Vitamin C: colorimetric method (8) and Vitamin E (9)

RBC: Thiobarbituric acid reactive substance (TBARS) was estimated by the method of Stocks and Dormandey (10)

Statistical analysis was done by Student 't' test.

RESULTS AND DISCUSSION

Results of the study are documented in Table No.1. As expected diastolic blood pressure of the study group was significantly increased ($P = 0.000$). Lipid peroxidation was enhanced in hypertensive complications of pregnancy as judged by the elevated levels of TBA reactive substance. Plasma Vitamin C levels showed a tendency to decrease in PIH when compared with that of the normal. Plasma Vitamin E remained statistically insignificant with higher mean values in PIH versus control.

Reduced ascorbate is quite effective in protecting plasma lipids and susceptible molecules from peroxidation. Plasma ascorbate level decreases gradually throughout normal pregnancy. A decrease in mean plasma ascorbate concentration in PIH relative

to normal pregnancy are seen (11) and the present values also agree with the same. High availability of unsaturated lipid could contribute to a predisposition to enhance lipid peroxidation. Several recent studies have reported that there is no evidence for increased lipid peroxidation in PIH (12).

Maternal levels of plasma Vitamin E and RBC -lipid peroxides were increased in pregnancy (13). The reason for increased Vitamin E levels may be due to common carrier system for vitamin E, cholesterol and triglycerides, the level of which are increased during pregnancy (14, 15). Gestational increase of estrogen is thought to promote hepatic production of very low density lipoprotein- triglycerides (5). The results of the present study suggest that the plasma antioxidant vitamins are not affected much in PIH.

REFERENCE

1. Tsukatani, E. (1983). Etiology of EPH-gestosis from the view point of dynamics of vasoactive prostanoids. Lipid peroxides and vitamin E. Acta. Obstet. Gynaecol. Jpn. 35: 713-720.
2. Pober, J.S., Cotran, R.S. (1990), Cytokines and endothelial cell biology. Physiol. Rev. 70, 427-451.
3. Hubel, CA., Lyall, F., Weissfeld, L., Gandley, R.E., Roberts, JM, (1998), Small low density lipoproteins and vascular cell adhesion molecule are increased in association with hyperlipidemia in pre-eclampsia. Metabolism. 47, 1281-1288.
4. Rodgers, G.M, Taylor, R.N., Roberts, JM (1988), Preeclampsia is associated with a serum factor cytotoxic to human endothelial cells. Am. J Obstet. Gynecol. 159, 908- 914.
5. Hubel CA., Roberts, JM, Taylor, R.N., Musci, T.J., McLaughlin, M.K. 1999), Lipid peroxidation in pregnancy: New perspectives on preeclampsia. Am. J Obstet. Gynecol. 61, 1025-1034.
6. Burton, G. W (1994), Vitamin E : Molecular and biological junction. Proc. Nutr. Soc. 53, 251-262.
7. Jacob, R.A., Keley, D.S., Painetto, F.S.. (1991), Immunocompetence and oxidant defense during ascorbate depletion of healthy men. Am. J Clin. Nutr. 53, 194-200.
8. Tietz, N. W (1986), Methods of determination of ascorbic acid. In : Text book of Clinical biochemistry, Edited by N. W Tietz, WB. Saunders company, Philadelphia London, Toronto 960- 962.
9. Bieri, J.G, Teets, L, Belavady, B., Andrews, E.L (1964), Serum Vitamin E levels in a normal adult population in Washington D.C Area. Proc. Soc. Exptl. Biol. Med. 117, 131-133.

TABLE No.1

Parameters	Normal (Mean± SE)	PIH (Mean± SE)
Age (Years)	24.61±0.7	27±1.35
Gestational age (weeks)	39.07 ± 0.22	36.19±0.97
Systolic BP (mm Hg)	113.76±1.95	152±2.05*
Diastolic BP (mm Hg)	76.48±1.62	105.3± 1.97
Lipid peroxidation (μmols / dl)	1.07±0.18	1.52±0.22
Vitamin C (μmols / dl)	6.55±0.63	6.24±1.43
Vitamin E (mg / dl)	4.02±2.16	5.15±1.89
* p = 0.000		

10. Stocks, J, Dormandy, T.L (1971), The autooxidation of human red cell lipids induced by H₂O₂. *Br. J. Hematol.* 20, 95-111
11. Mikhail, MS, Anyaegbunam, A., Garfinkel, D., Palan, D., Basu, J, Romerey, SL (1994), Preeclampsia and antioxidant nutrients: Decreased plasma levels of reduced ascorbic acid, α -tocopherol and β -carotene in women with preeclampsia. *Am. J Obstet. Gynecol.* 171, 150-157.
12. Regan, CL, Levine, R.J., Baird, D.D., Ewell, M.G., Martz, KL, Sibai, B.M, Rokach, J, Lawson, J.A., Fitzgerald, G.A. (2001), No evidence for lipid peroxidation in severe preeclampsia. *Am. J. Obstet. Gynecol.* 185(3), 572-578.
13. Schiff, E., Friedman, SA., Stampfer, M, Kao, L, Barret, P.H, Sibai, B.M (1996), Dietary consumption and plasma concentration of Vitamin E in pregnancies complicated by preeclampsia. *Am. J Obstet. Gynecol.* 175, 1024-1028.
14. Wang, Y, Walsh, SW, Zhang, J, Jingdige, G. (1991), Maternal levels of prostacyclin, thromboxane, vitamin E and lipid peroxides throughout normal pregnancy. *Am. J Obstet. Gynecol.* 165, 1690-1694.
15. Traber, MG. (1994), Determinants of plasma Vitamin E concentrations. *Free. Radic. Biol Med.* 16; 229- 239. 0