Original Article

Lipid Peroxidation and Antioxidant Status in Preeclampsia

Rokeya Begum[1]

Abstract

Background: *Preeclampsia is the most common and major medical complication of pregnancy with a high incidence of maternal and foetal morbidity and mortality. During pregnancy abnormally increased lipid peroxidation and free radical formation as well as significantly decreased antioxidants production in maternal blood may lead to pathogenesis of preeclampsia. So, we designed this study as little information is known about lipid peroxidation and antioxidant level in preeclampsia.* ***Objectives:*** *To assess the serum malondialdehyde (MDA) level as a lipid peroxidation product and vitamin E (antioxidant) level in women with preeclampsia as well as in normal pregnancy and to compare the values.* ***Materials and Methods:*** *The study was conducted on 60 women aged from 25 to 35 years in the department of Biochemistry, Budi Kemuliaan Maternity Hospital (BKMH) in Jakarta during the period April to July 2004. Twenty were normal pregnant women and 20 were preeclamptic patients. For comparison age matched 20 apparently healthy nonpregnant women were included in the study. The study subjects were selected from outpatient department (OPD) of Obstetrics and Gynaecology of BKMH in Jakarta. Serum MDA (lipid peroxidation product) level was measured by thiobarbituric acid reactive substances assay (TBRAS) method and vitamin E was estimated spectroflurometrically. Data were analyzed by unpaired Student's t test between the groups by using SPSS version 12.* ***Results:*** *The mean serum MDA levels were significantly higher in normal pregnancy and also in preeclampsia than that of nonpregnant control group women ($p<0.001$). Again the serum MDA levels were significantly higher in preeclampsia than that of normal pregnant women ($p<0.001$). The serum vitamin E levels were significantly lower in preeclampsia and also in normal pregnancy than that of nonpregnant control women ($p<0.001$). Moreover, the serum vitamin E levels were significantly lower in preeclampsia compared to that of normal pregnancy which was also statistically significant ($p<0.001$)* ***Conclusion:*** *As in preeclamptic group level of oxidation product is high and antioxidant level is low, it can be assumed that in preeclampsia, serum antioxidants are excessively utilized to counteract the cellular damage mediated by free radicals production and deficient antioxidants as well as increased lipid peroxidations may be the important factors in the pathogenesis of preeclampsia.*

Key words: *Preeclampsia, Lipid peroxidation, Antioxidant*

J Enam Med Col 2011; 1(2): 56-59

Introduction

Pregnancy is the physiological state accompanied by a high energy demand of bodily functions in which many changes occur in the milieu interior of the body. Biochemical changes also occur in the blood during normal pregnancy and become exaggerated in preeclampsia.[1] Preeclampsia is one of the most common complications during pregnancy, affecting up to 1-7% pregnant women around the world. The incidence of preeclampsia is 16-25% in first pregnancies and 12-15% in subsequent pregnancies in some countries. Preeclampsia accounts for around 16% in UK.[2] In Indonesia it was one of the most

1. Professor, Department of Physiology, Enam Medical College, Savar, Dhaka
Correspondence *Rokeya Begum, Email: rokeyaphysio@yahoo.com*

common and major causes of maternal and foetal morbidity and mortality during the last decade. Preeclampsia is the condition that happens after 20th week of gestation and characterised by high blood pressure, proteinuria and oedema or both.[2,3] Lipid peroxidation and formation of free radicals occur at low level in normal pregnancy. The peak level of lipid peroxidations occurs in the second trimester of pregnancy, but vitamin E concentration progressively increases till the end of pregnancy. The lipid peroxidations and free radical formation in normal pregnancy are controlled by adequate response of antioxidants that tries to minimize the cellular damage.[4,5] Antioxidants are the compounds that dispose, scavenge and suppress the formation of the free radicals or oppose their actions.[6,7] Preeclampsia is associated with endothelial damage which is caused by oxidative stress. Oxidative stress progressively increases during preeclampsia and results in increased formation of lipid peroxides, reactive oxygen species and superoxide anion radicals which lead to endothelial destruction and dysfunctions, platelet and neutrophil activation.[8-10] Placental hypoxia is a strong stimulator of endothelin synthesis and secretion, promotes the production of oxygen free radicals and lipid peroxides and these peroxides may enhance the vessel contractility and reduces uteroplacental blood flow. Altered lipid synthesis leading to decrease in prostaglandin I and thromboxane A2 ratio causes vasospastic phenomenon in kidney, uterus, placenta and brain as seen in preeclampsia.[9-12] In health, oxidation by free radicals and neutralization by antioxidants remain in balance. But If the reactive oxygen species (ROS) are in abundance, oxidative stress occurs which is thought to be the causative factor in pathogenesis of preeclampsia.[13,14]

Little information is known about the serum lipid peroxides and vitamin E in preeclampsia. For the aforesaid reasons the present study has been undertaken to study the serum malondialdehyde (MDA) and antioxidant vitamin E in women with preeclampsia, in normal pregnancy and also in healthy control for comparison.

Materials and Methods

This cross sectional comparative study was carried out in the department of Biochemistry of Budi Kemuliaan Maternity Hospital in Jakarta during the period April 2004 to July 2004. A total number of 40 cases aged from 25 to 35 years with gestational period more than 30 weeks were selected for the study. Twenty were normal pregnant women (Group B_1) and 20 were diagnosed preeclamptic patients (Group B_2). Twenty age matched apparently healthy normal nonpregnant women were enrolled as control (Group A). Subjects with diabetes, obesity, dyslipidaemia, liver disease and history of taking antioxidant drugs were excluded from the study. After selection of the subjects, the objectives, benefits, risk and procedure of the study were explained in details to the subjects and informed written consents were obtained from them. A detailed personal, family, medical, socioeconomic and drug history of the subjects were recorded in a preformed questionnaire. With all aseptic precautions 05 (five) mL of venous blood was collected in EDTA containing tubes from antecubital vein by sterile disposable syringe. Serum was separated by centrifugation at 3000 rpm for 15 minutes and stored at -20^0 C for further studies. Serum MDA level was measured by thiobarbituric acid reactive substances assay (TBRAS). Serum vitamin E level was estimated spectroflurometrically. The optical densities of serum MDA and vitamin E were measured at 530 nm and 280 nm respectively using spectrophotometer. Statistical analyses were done by Statistical Package of Social Service (SPSS) version 12. Data were expressed as mean ± SD. The results were analyzed by unpaired Student's t test between the groups. P value <0.05 was accepted as level of significance.

Results

The mean serum MDA levels were significantly higher ($p<0.001$) in both B_1 and B_2 groups in comparison to that of control group A. This value was twice in preeclampsia group (Group B_2) as compared to the normal pregnant group B_1 which was also statistically significant ($p<0.001$) (Table I and Table II).

The mean serum vitamin E levels were significantly lower in Group B_1 and B_2 in comparison to that of control group A. Again mean serum vitamin E in Group B_2 was half the level of Group B_1 which was also statistically highly significant ($p<0.001$) (Table I and Table III).

Table II shows the comparison of serum MDA levels between groups and Table III shows the comparison of serum vitamin E levels between groups.

Table I: Serum MDA and vitamin E levels in different groups (n = 60)

Parameters	Group A (n = 20)	Group B_1 (n = 20)	Group B_2 (n = 20)
MDA (in nmol/mL)	1.23 ± 0.54	3.64 ± 0.12	7.28 ± 1.05
Vitamin E (in µmol/L)	7.43 ± 1.40	5.75 ± 1.24	2.69 ± 0.17

Table II: Comparison of serum MDA levels between groups (n = 60)

Groups	MDA level (nmol/mL)	P values
A vs B1	1.23 ± 0.5 and 3.64 ± 0.12	< 0.001
A vs B2	1.23 ± 0.5 and 7.28 ± 1.05	< 0.001
B1 vs B2	3.64 ± 0.12 and 7.28 ± 1.05	< 0.001

Table III: Comparison of serum vitamin E levels between groups

Groups	Vitamin E level (µmol/L)	P values
A vs B_1	7.43 ± 1.40 and 5.75 ± 1.24	< 0.001
A vs B_2	7.43 ± 1.40 and 2.69 ± 0.17	< 0.001
B1 vs B_2	5.75 ± 1.24 and 2.69 ± 0.17	< 0.001

Discussion

In the present study significantly higher level of lipid peroxidation product i.e. serum MDA values were found in normal pregnancy as well as in preeclampsia compared to that of nonpregnant women. Serum MDA value was also significantly higher in preeclampsia than that of normal pregnant women. These findings are in consistence with those of some other researchers.[3,4,7,16] They reported that lipid peroxidation increases during normal pregnancy. But lipid peroxides and free radicals productions are more in preeclampsia than normal pregnancies and may be the important factors in pathogenesis of preeclampsia. Some investigators of different countries reported that primary defect in preeclampsia is the reduced foetoplacental perfusion that will lead to placental hypoxia.[8,9,11,17] They suggested placental hypoxia promotes lipid peroxidation that causes vascular endothelial damage and these may be implicated in the pathophysiology of preeclampsia. It has been postulated that in normal pregnancy the placental tissue also produces lipid peroxides. But the degree of lipid peroxidation is significantly lower in late pregnancy than in early pregnancy as because the antioxidant production is higher in late pregnancy than in early pregnancy which counteract the action of lipid peroxides production.[5,6,15,18] Some research workers reported that increased lipid peroxides in preeclampsia might be related to increased placental thromboxane formation which causes increased cyclooxygenase activity that would increase the free radical formation.[6,11,16,19] These findings are in agreement with the findings of other studies.[4,7,10.11] Several studies demonstrated that preeclampsia is associated with increased utilization of antioxidants.[8,10,19,21]

In the present study, the plasma levels of vitamin E were significantly lower in preeclampsia and in normal pregnancy than that of healthy nonpregnant women. These findings are in agreement with the findings of other research workers.[8,9,12,22] They suggested that insufficient antioxidant capacity leads to oxidative stress and subsequently oxidative injury, endothelial damage and dysfunction occur both in maternal and placental tissues. Several studies demonstrated that decreased level of vitamin E in preeclampsia is due to its increased consumption in exerting its action and may also be due to decreased absorption from the intestine as a result of increased vasoconstriction.[4,8,11,20,21,22]

Vitamin E is the major lipid soluble chain breaking antioxidant, has been documented to prevent oxidative damage of the cell membrane and decrease platelet aggregation by a nonoxidative mechanism. The vitamin E is a potent antioxidant that protects the cell membrane against enzyme activity, free radicals or highly reactive degradation products during pregnancy.[6,9,10,21,23]

The results of the present study are in consistence with the previous studies. They suggested that significant rise in lipid peroxides with decreased vitamin E levels are possible causative factors for the pathogenesis

of preeclampsia. In preeclamptic women antioxidants may be utilized to a greater extent to counteract the free radical mediated cellular changes, resulting in the reduction of plasma antioxidant levels.

This study reveals that increased lipid peroxides and vitamin E deficiency are the risk factors and may be linked to increased oxidative stress in deficient subjects to cause preeclampsia. Therefore, early detection of these parameters may be useful to reduce the occurrence of preeclampsia and to prevent the oxidative damage and thereby improve the maternal and foetal outcome.

Acknowledgement

The author of this study acknowledges the partial financial support from World Health Organization. Author thanks the staff of the Biochemistry, Obstetrics and Gynaecology departments of Budi Kemuliaan Maternity Hospital and also all those who volunteered as subjects for the study.

References

1. Dutta DC. Hypertensive disorders in pregnancy. In: Konar HL (ed). Textbook of Obstetrics. 5th edn. Kolkata: New Central Book Agency (P) Ltd., 2001: 234-255.
2. Chesley LC. Diagnosis of preeclampsia. Obstet Gynaecol 1985; 65: 433-335.
3. Nelson GH, Zuspan FP, Milligan LT. Defect of lipid metabolism in toxaemia of pregnancy. Am J Obstet Gynaecol 1989; 114: 582-588.
4. Wickens D, Wilikins MH, Lunce J, Ball G, Dormandy TL. Free radical oxidation products in normal and abnormal pregnancy. Ann Clin Biochem 1998; 18: 158-162.
5. Poranen AK, Ekblad U, Uotila P, Ahotupa M. Lipid peroxidation and antioxidants in normal and pre-eclamptic pregnancies. Placenta 1996; 17: 401-405.
6. Yand W, Walsh SW. Antioxidant activities and mRNA expression of superoxide dismutase, catalase and glutathione peroxidase in normal and preeclamptic placenta. J Soc Gynaecol Investig 1996; 3: 179-184.
7. Simmi K, Sharina BD. Vitamin E and preeclampsia. Euro J Obstet & Gynaeco Reprod Biol 2000; 93(1): 37-39.
8. Packer L, Landviks. Vitamin E, introduction to biochemistry and health benefits. New York Academy of Science 1998: 1-6.
9. VanWijk MJ, Kublickiene K, Boer K, VanBavel E. Vascular function in preeclampsia. Cardiovasc Res 2000; 47: 38-48.
10. Lorentsen B, Henrikson T. Plasma lipids and vascular dysfunction in preeclampsia. Semin Reprod Endocrinol 1998; 16(1): 33-39.
11. Barden A, Ritchie J, Walters B, Michael C, Rivera J, Mori T, Croft K, Beilin L. Study of plasma factors associated with neutrophil activation and lipid peroxidation in preeclampsia. Hypertension 2001; 38(4): 8003-8008.
12. Sekiba K, Yoshiolka T. Changes of lipid peroxidation and superoxide dismutase activity in the human placenta. Am J Obstet Gynecol 1997; 135: 368-371.
13. Hubel CA, Roberts JM, Taylor RN et al. Lipid peroxidation in pregnancy: new perspective on preeclampsia. Am J Obstet Gynecol 1989; 161: 1025-1034.
14. Chappel LC, Seed PT, Briley A, Kelly SRN, Frank J, Hunt BJ et al. A longitudinal study of biochemical variables in women at risk of preeclampsia. Am J Obstet Gynecol 2002; 187(1): 127-136.
15. Utoila JT, Tuimala RJ, Aarmio TM, Pyykko KA, Ahotupa MO. Findings on lipid peroxidation and antioxidant function in hypertensive complications of pregnancy. Br J Obstet Gynaeco 1993; 100: 270-276.
16. Mutlu Turkoglu U, Ademoglu E, Ibrahimoglu I, Aykac, Toker G, Uysal M. Imbalance between lipid peroxidation and antioxidant status in preeclampsia. Gynaecol Obstet Invest 1998; 46: 37-40.
17. Ozan H, Licol Y, Cengiz C, Ediz B. Plasma antioxidant status and lipid profile in women with preeclampsia. J Obstet Gynaecol Res 2002; 28: 274-279.
18. Saha S, Abraham R, Daniel M, Subakir SB. Oxidant antioxidant imbalance in preeclampsia. Hum Reprod 1998; 43(1): 133-139.
19. Aksoy H, Taysi S, Altinkaynak K, Bakan E , Kumtepe Y. Antioxidant potential and transferrin, ceruloplasmin and lipid peroxidation in women with preeclampsia. J Investig Med 2003; 51: 284-287.
20. Wakatsuki A, Ikenoue N, Okatani Y, Shinohara K, Fukaya T. Lipoprotein particles in preeclampsia: susceptibility to oxidative modification. Obstet Gynaecol 2000; 96((1): 55-59.
21. Jain SK, Wise R. Relationship between elevated lipid peroxides, vitamin E deficiency and hypertension in preeclampsia. Mol Cell Biochem 1995; 151: 33-38.
22. Yagi K. Assay for lipid peroxide level and its clinical significance. In: Yagi K (ed). Lipid peroxides in biology and medicine. NewYork, 1982: 233-242.
23. Madazli R, Benian A, Gumata K et al. Lipid peroxidation and antioxidants in preeclampsia. Eur J Obstet Gynaecol & Reprod Biol 1999; 85(2): 205-208.