ijcrr
Vol 03 issue 11
Category: Research
Received on:06/09/11
Revised on:09/09/11
Accepted on:11/09/11

LIPID PEROXIDATION IN PREGNANCY INDUCED HYPERTENSION

Padmasree Dantu

Department of Biochemistry, Maharajah's Institute of Medical Sciences, Nellimarla, Vizianagaram, Andhra Pradesh

E-mail of Corresponding Author: docpadmaamc@yahoo.co.in

ABSTRACT

Pre-eclampsia is due to reduced placental perfusion and a consequent maternal disorder characterized by endothelial dysfunction caused by lipid peroxidation due to oxidative stress secondary to reduced placental perfusion. An oxidative stress is said to occur when the peroxidant injury due to lipid peroxides such as Malondialdehyde and secondary degeneration products of lipid peroxidation overwhelms the antioxidant defence. The study was undertaken to find out the levels of Serum Malondialdehyde in Pregnancy induced Hypertension (PIH).

A study was carried out among a total of 60 cases of PIH, distributed among the gestational periods of 27-40 weeks. Controls were 75 normal pregnants and 30 non-pregnants. Serum Malondialdehyde (MDA), Serum Total Cholesterol (TC), Serum Triglycerides (TG), Serum High-density Lipoprotein Cholesterol (HDLC), Serum Low-density Lipoprotein Cholesterol (LDLC), Serum Very Low-density Lipoprotein Cholesterol (VLDLC) were estimated. Other investigations done were Urine Protein, Serum Creatinine, Serum Uric acid, Serum Glutamate Oxaloacetate Transaminase (SGOT), Serum Glutamate Pyruvate Transaminase (SGPT) and Serum Bilirubin in support of diagnosis. Malondialdehyde showed a definite increase with increasing period of gestation in normal pregnant controls along with Serum Total Cholesterol, Serum Triglycerides, and Serum Very Low-density Lipoprotein Cholesterol. In non-pregnant controls, Malondialdehyde, Lipids and Lipid sub fractions were within the normal range. Serum Malondialdehyde did not show any definite variation in relation to severity of disease like mild without proteinuria, mild with proteinuria and severe PIH, but showed a definite increase with increasing period of gestation 27-30 weeks, 31-35 weeks and 36-40 weeks. Serum Total Cholesterol, Serum Triglycerides, Serum Very Low-density Lipoprotein cholesterol showed a definite increase with increasing period of gestation in Pregnancy induced Hypertension.

Key words: Endothelial dysfunction, Malondialdehyde, Oxidative stress.

INTRODUCTION

The major pathogenic mechanism in PIH is endothelial dysfunction related to reduced placental perfusion.

Figure 1

Imbalance between vasodilator and vasoconstrictor endothelial factors as well as between thrombotic, fibrinolytic mediators and growth promoting substances leads to endothelial dysfunction. The major mechanism that promotes release of vasodilatory factors such as Nitric Oxide (NO), Prostacyclin (PGI2) and

Endothelium Derived Hyper polarising Factor (EDHF) is the sheer stress blood flow on the endothelial surface.[1] Endothelial vasoconstrictors are Endothelin-1 and others like arachidonic acid products generated with cyclo-oxygenase participation: Prostaglandin F2, Thromboxane A2, Superoxide anion and Angiotensin II.[2] Oxidative stress is the term used to describe any challenge in which pro-oxidants predominate over antioxidants.[3,4] Oxidative damage of polyunsaturated fatty acids is lipid peroxidation [5,6], which causes a reduction in membrane fluidity, permeability and lowered NO synthesis leading to hypertension.[7] Lipid peroxidation has been implicated in the pathological process of PIH.[8,9] It is a chain reaction providing a continuous supply of free radicals that initiate further peroxidation. The primary molecular products of lipid peroxidation are unstable and aldehydes that are secondary stable products like Malondialdehyde (MDA) are produced which act as cytotoxic messengers. Lipid peroxidation of placenta has been studied as a model for phenomenon of aging. In PIH, there is increased lipid peroxidation in the maternal circulation and in the placenta (mitochondrial lipid peroxidation). MDA was assessed as a marker of lipid peroxidation and an index of degree of polyunsaturated fatty acid peroxidation. Increased placental VLDLC and LDLC could participate in endothelial dysfunction in PIH. A placental oxidant-antioxidant imbalance might cause the release of lipid peroxidation products into the circulation with subsequent damage of endothelium and increase of circulating lipid peroxide, which by themselves are able to induce smooth muscle constriction and increased pressor responsiveness to Angiotensin II. The increased susceptibility to oxidative stress of syncitiotrophoblast plasma membranes might be due either to reduced antioxidant system or to an abnormality of the lipid composition of the membranes.[10] Thus Serum MDA assay is useful to monitor the course of the disease.

MATERIALS AND METHODS

Serum MDA was quantitated by 2-Thiobarbituric acid (TBA) method by (Keisatoh)[11], a colorimetric assay and a more specific method. The lipid peroxide content was estimated as MDA equivalent of TBA assay values, which measured total MDA (free and bound). Normal range of Serum MDA is 1.6-2.8 nmol/ml. The standard calibration curve is linear up to 20nmol/ml. Other lipid parameters; TC by Zak's method (normal 140-240 mg/dl), TG by Glycerol-3-Phosphate Oxidase / N-Ethyl-N-Sulfopropyl-n-anisidine (GPO/ESPAS) (normal 80-180 mg/dl), HDLC by Burstein.M&Scholnick M.R method (normal 30-70 mg/dl), LDLC by Friedwald formula (normal 50-170 mg/dl)& VLDLC by calculation (normal 5-25 mg/dl). Along with the above investigations, Serum Creatinine, Serum Uric acid, SGOT, SGPT, Serum Bilirubin and Urine Protein were analyzed as part of the study.

RESULTS

The distribution of controls and cases: Non-pregnant controls: 30, Pregnant controls: 75 (I trimester: 21, II trimester: 24 and III trimester: 30). PIH cases: 60 (mild PIH without proteinuria: 15, mild PIH with proteinuria: 15 and severe PIH: 30).

Table 1

Non-pregnant controls: The Mean and Standard deviation (SD) values of Lipids were (TC 160 ± 9.17 and TG 80 ± 11.6) and Lipid sub fractions were (HDLC 50 ± 11.3, LDLC 94 ±7.46 and VLDLC 16 ±

2.33). The Mean and SD of MDA for the mean age (in years) 25± 5 were 1.88 ± 0.42 showed a range of 1 - 2.4 nmol/ml.

Pregnant controls: The Mean and SD values of Lipids were (TC 182.96 ± 19.53 and TG 119.04 ± 25.06) and Lipid sub fractions were (HDLC 50.08 ± 9.34, LDLC 109.07 ± 15.76 and VLDLC 23.80 ± 5.01) and that of MDA were 3.01 ± 0.84. In pregnant controls, study of MDA, Lipids and Lipid sub fractions related to gestational age: in I trimester, values of MDA were 1.9 ± 0.43, TC 162 ± 9.7, TG 88 ± 8.04, HDLC 48 ± 7.92, LDLC 96.4 ± 2.16 and VLDLC 17.6 ± 1.60. In II trimester, the values of MDA were 3 ± 0.43, TC 180 ± 15.7, TG 120 ± 15.7, HDLC 52 ± 7.46, LDLC 104 ± 6.11 and VLDLC 24 ± 3.15. In III trimester, MDA values were 3.8 ± 0.15, TC 200 ± 9.17, TG 140 ± 14.4, HDLC 50 ± 11.37, LDLC 122 ± 8.40 and VLDLC 28 ± 2.89.

PIH cases: Table 2

Figure 2

Statistical analysis: P-values were calculated for various parameters. Those of MDA, TC, TG and VLDLC are

Table 3

P-values of HDLC and LDLC in the three trimesters of normal pregnants and in mild and severe PIH are >0.05.

DISCUSSION

Lipid peroxidation in healthy non-pregnant and pregnant women: MDA, TC, TG, HDLC, LDLC and VLDLC were within the normal range in non-pregnant controls. MDA, TC, TG and VLDLC showed no significant variation between non-pregnants and I trimester pregnants. Significant increase observed in II trimester and highly significant increase in III trimester of MDA, TC, TG and VLDLC values compared to non-pregnants.

Lipid peroxidation in mild and severe cases of PIH: No significant variation of MDA, TC, TG and VLDLC among mild cases (without or with proteinuria) and severe PIH was observed. The values showed a highly significant increase in mild and severe PIH compared to both pregnant and non-pregnant controls.

Lipid peroxidation related to the period of gestation in PIH: MDA, TC, TG, and VLDLC showed significant increase in 31-35 weeks and 36-40 weeks compared to 27-30 weeks. Moderately significant increase in 36-40 weeks compared to 31-35 weeks and highly significant increase in 27-40 weeks PIH cases compared to I, II and III trimester normal pregnants and non-pregnants.

The highest MDA (lipid peroxide) in the study was 6.1nmol/ml.

The severity of lipid peroxidation among different gestational age groups of PIH varied as follows.

36-40 weeks PIH > 31-35 weeks PIH > 27-30 weeks PIH

6 nmol/ml > 5.9 nmol/ml > 5.6 nmol/ml

The results of the present study are in consistent with those of another two studies.[12, 13]

Table 4 & Table 5

Increase in lipid peroxidation was observed in PIH compared to healthy non-pregnant and normal pregnant controls and is consistent with the observation that in women with PIH, a compromise in placental blood flow leads to oxidative stress. Thus the estimation of Serum MDA forms a good marker of lipid peroxidation in PIH.

CONCLUSION

Compromised placental perfusion from vasospasm is almost certainly a major culprit in the genesis of increased perinatal

morbidity and mortality associated with PIH, which is due to oxidative stress and lipid peroxidation. Serum Malondialdehyde assay is useful to monitor the course of the disease process and treatment regimen prescribed.

ACKNOWLEDGEMENTS

The author is thankful to Mr. D.S.S.K. Raju, Assistant Professor, Department Of Biochemistry, MIMS, Vizianagaram, for his timely help.

The sustained support of the members of the author's family can never be sufficiently acknowledged.

REFERENCES

1. Born, M and Smith, T et al., Clinicians manual on endothelium and cardiovascular disease. London Science press, 1996.
2. Gavras, H and Gavras, L., endothelial function in cardiovascular disease. The role of Bradykinin. London Science. Press, 1996.
3. Jones, D.P. and Delong, M.J. Detoxification and protective functions of nutrients. Biochemical and physiological aspects of human nutrition. Ed. Stipanuk, MHWB Saunders Company, Philadelphia. P. 901-916, 2000.
4. Sies, H. Oxidative stress: Introductory remarks. Oxidative stress. Ed. Sies, H. Orlando, Florida: Academic press, p. 1-10, 1985.
5. Ashok Mulchandani et al., Anal Biochem. 225,277-282, 1995.
6. Eum. J. B Boyle, J.A and Hearnsberger, J.O. J. Food Sci 59, 251-255, 1994.
7. Mutlu, T urkoglu, U. et al., Plasma nitric oxide metabolites and lipid peroxide levels in preeclamptic pregnant women before and after delivery. Gynecol. Obstet. Invest, 48(4), 247-50, 1999.
8. Hallwell, B. and Gutteridge, J.M.C. Free radicals in Biology and Medicine 2ndEd Clarendon/oxford Univ. Press Oxford/Newyork, 416-494, 1989.
9. Halliwell B., Haemostasis 1, 118-126, 1993.
10. Cester, N. et al., Pregnancy induced hypertension: a role of peroxidation in microvillus plasma membranes. Mol. Cell. Biochem, 23, 131 (2), 151-5, Feb 1994.
11. Keisatoh., Serum lipid peroxide in cerebro vascular disorders determined by a new colorimetric method. Clin Chim. Acta, 90, 37-43, 1978.
12. Minoru Ishihara, et al., Studies on lipid peroxide of normal pregnant women and of patients with toxemia of pregnancy. Clin. Chim. Acta, 84, 1-9, 1978.
13. Mohanty, et al., VIII Annual National Conference, Ambicon, 1999.

Table 1 shows analysis of results according to groups

1	Comparative study related to	Non-pregnant & pregnant controls
2	Case study related to	Severity of PIH
3	Case study related to	Period of gestation in PIH
4	Case study related to	Lipids and sub fractions in PIH

Table 2 shows MDA, Lipid and Lipid sub fractions (Mean ± S.D) in mild and severe PIH

Category	MDA nmol/ml	TC mg/dl	TG mg/dl	HDLC mg/dl	LDLC mg/dl	VLDLC mg/dl
Mild PIH with out proteinuria	5.82 ± 0.19	278.66 ± 8.23	232.2 ± 10.4	49.06 ± 8.6	183.1 ± 12.02	46.4 ± 2.09
Mild PIH with proteinuria	5.80 ± 0.19	278.2 ± 9.4	229.7 ± 9.7	51.8 ± 6.7	180.4 ± 11.55	45.9 ± 1.94
Severe PIH	5.84 ± 0.19	280.6 ± 9.02	232.4 ± 9.3	49.4 ± 4.92	184.64 ± 10.04	46.36 ± 1.83

Table 3 Shows P-value data obtained by statistical analysis.

Groups	P-value
Non-pregnant vs. 1st trimester pregnant controls	>0.05*
Non-pregnant vs. 2nd trimester pregnant controls	<0.01**
Non-pregnant vs. 3rd trimester pregnant controls	<0.001***
1st trimester vs. 2nd trimester pregnant controls	<0.01**
2 nd trimester vs. 3rd trimester pregnant controls	<0.05*
1 st trimester vs. 3rd trimester pregnant controls	<0.001***
Non-pregnant & pregnant controls vs. moderate & severe PIH cases	<0.001***
Non-pregnant & pregnant controls vs. 27-40 weeks PIH cases	<0.001***
Mild (both groups) vs. severe PIH cases	>0.05*
27-30 weeks PIH vs. 31-35 weeks PIH cases	<0.01**
3I-35 weeks PIH vs. 36-40 weeks PIH cases	<0.05*
27-30 weeks PIH vs. 36-40 weeks PIH cases	<0.01**

* Moderately Significant ** Significant *** Highly significant

Table 4 Shows consistency of the present study with other studies in PIH in relation to severity of the disease

Year	Study	Mild PIH with out proteinuria	Mild PIH with proteinuria	Severe PIH
1978	Minoru Ishihara et al	6.7 ± 0.9	6.66 ± 0.8	6.71 ± 0.9
1999	Mohanty et al	5.7 ± 1.4	5.66 ± 0.12	5.74 ± 0.1
2001	Present study	5.82 ± 0.19	5.8 ± 0.19	5.84 ± 0.19

Table 5 Shows consistency of the present study with other studies in PIH with increasing period of gestation

Year	Study	27-30weeks PIH	31-35weeks PIH	36-40 weeks PIH
1978	Minoru Ishihara et al	6 ± 0.4	5.8 ± 0.8	7 ± 0.9
1999	Mohanty et al	5 ± 0.5	5.8 ± 0.12	5.9 ± 0.14
2001	Present study	5.6 ± 0.09	5.9 ± 0.10	6 ± 0.07

Figure 1 shows consequences of endothelial dysfunction in decreased placental perfusion.

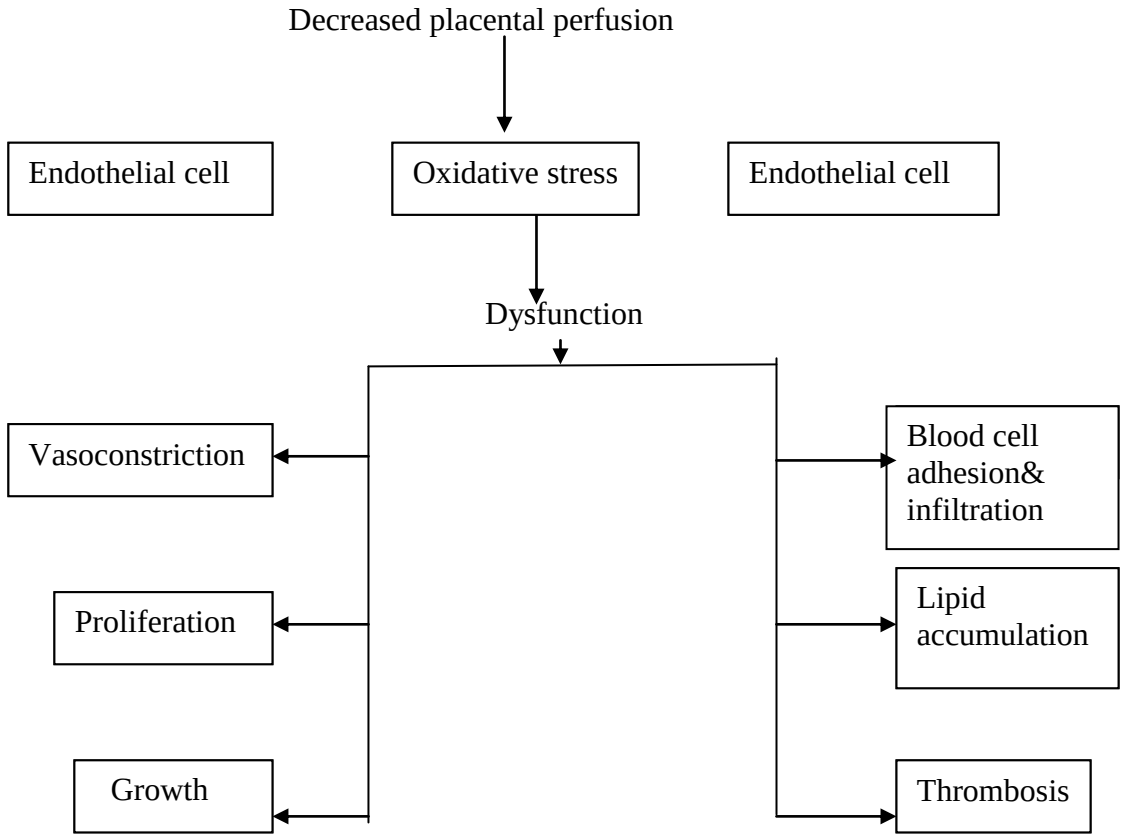

Figure 2 shows MDA, Lipids and Lipid parameters in the order of increasing period of gestation in PIH.