

Evaluation of Oxidative stress in preeclampsia

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Summary: Twenty five preeclamptic, 25 normotensive pregnant and 25 healthy nonpregnant women were analysed with regard to serum lipid profile, malonaldehyde (MDA), superoxide dismutase (SOD) and vitamin E. In preeclampsia significant increase in prooxidant (MDA) was observed as compared to controls. MDA showed a significant correlation to the level of blood pressure. Serum cholesterol and triglycerides were increased in normotensive pregnant and increased still higher in preeclampsia, but, no significant correlation could be found between MDA and cholesterol levels. A significant fall in antioxidants (SOD and vitamin E) was noted in preeclampsia as compared to control. Therefore, an increased lipid peroxidation and lowered antioxidant status may be involved in the pathogenesis of preeclampsia.

Introduction

Current concepts of preeclampsia have been focused on dysfunction of maternal vascular endothelium as the central pathogenetic factor of the disease (Hubel et al, 1989). Since hyperlipidaemia and increased lipid peroxidation have been reported in preeclampsia, involvement of free radicals in preeclampsia may be associated with endothelial dysfunctioning (Hubel et al, 1989; Poter and Nestel, 1979; Novak et al, 1989). This metabolic effect of lipid peroxides may imbalance the prostacyclin and thromboxane production which could account for the blood pressure and coagulation changes in the disease. Amongst various antioxidants, vitamin E the most potent antioxidant, may scavenge these free radicals and help in protection of the endothelial membrane in preeclampsia (Ehrenkranz, 1980). The present project is therefore aimed at evaluating the lipid profile, extent of lipid peroxidation and antioxidant status in preeclampsia.

Methods

Seventy five Indian women in the age group 18 to 48 years, consisting of 25 healthy nonpregnant, 25 normotensive pregnant and 25 preeclamptics attending/ admitted in Obstetrics Ward of Postgraduate Institute of Medical Sciences, Rohtak (India) were selected for the study. Informed consent was obtained from these subjects and the study was approved by the ethical committee of the Institute. These subjects were screened for diabetes mellitus, renal disease, primary hypertension and if present were excluded from the study. Dietary history was taken to rule out any dietary deficiency of vitamin E in these patients. Study samples were taken from these patients

before starting any hypertensive medication by venepuncture under aseptic conditions. The samples were assayed for malonaldehyde (MDA), (thiobarbituric acid reaction by Placer et al, 1960), superoxide dismutase (SOD) (by Misra and Fridovich 1972), vitamin E by spectrofluorometric method (Duggan, 1950) and serum total cholesterol and triglyceride were estimated enzymatically.

The results were statistically analysed using student's t-test and regression analysis was carried out.

Results

Lipid peroxidation was enhanced in preeclamptic women as judged by elevated levels of MDA as compared to control ($p < 0.001$), (Table 1). A significant correlation was noted between the levels of MDA and mean arterial blood pressure in case of preeclamptic group ($p < 0.001$, $r = 1.386$). However, there was no significant correlation between cholesterol and mean arterial blood pressure ($p = N.S.$, $r = 1.49 \times 10^{-2}$). Also, no correlation could be found between MDA and serum total cholesterol ($p > 0.1$, $r = 0.9 \times 10^{-5}$). Serum cholesterol and triglyceride levels were significantly raised in preeclamptic women though modest elevation was also observed in normotensive women (Table 1). Superoxide dismutase activity was significantly lowered in preeclamptic women compared to controls ($p < 0.001$). The levels of vitamin E were measured in the 3 groups to assess the non-enzymic antioxidant status. A highly significant fall in vitamin E levels was seen in preeclamptic women as compared to the two control groups ($p < 0.001$). The vitamin E/ cholesterol ratio showed a significant fall in preeclampsia compared

Table I.
Serum lipid profile, MDA, SOD and Vitamin E levels in various groups (mean \pm SE)

Variables	Nonpregnant (n=25)	Normotensive pregnant (n=25)	Preeclamptic (n=25)
MDA (nmol/ml)	1.04 \pm 0.02	1.68 \pm 0.12	2.806 \pm 0.18
Cholesterol (mmol/L)	7.8 \pm 0.18	8.9 \pm 0.81	10.5 \pm 0.94
Triglyceride (g/L)	0.95 \pm 0.09	1.59 \pm 0.03	2.66 \pm 0.15
SOD (E.U.)	256.0 \pm 6.95	184.7 \pm 6.12	173.0 \pm 2.96
Vitamin E (umol/L)	25.75 \pm 0.89	23.63 \pm 0.97	10.63 \pm 0.87
Vitamin E/cholesterol ratio (S.E.)	3.30 (0.59)	2.60 (0.12)	1.0 (0.1)

Difference in all values are significant at all levels ($p < 0.001$)

to that in control ($p < 0.001$). But, no significant correlation could be found between vitamin E and cholesterol ($p > 0.01$, $r = 0.000728$).

An increase in MDA levels and a fall in vitamin E levels was observed in preeclamptic women (Table I). No significant correlation could, however, be observed between MDA and vitamin E levels ($p > 0.1$, $r = 0.0033$).

Discussion

Serum lipids have been reported to be increased in pregnancy and still higher levels are reported in preeclampsia by Hubel et al (1989). The hyperlipidaemia has been attributed to the endocrinal response in these conditions. In the present study, we have observed higher lipid levels in preeclampsia as compared to normotensive pregnant women. This increased lipid level may increase the susceptibility of polyunsaturated fatty acids to peroxidative damage presumably by the free radicals (Rolando, 1980) that may lead to the formation of malonaldehyde (MDA). Several investigators have reported increased MDA or other products of lipid peroxidation in preeclampsia (Poter and Nestel 1979; Novak et al, 1989; Tsukatani, 1983). In the present study, lipid peroxidation product (MDA) was significantly increased in preeclampsia as compared to control group. Nevertheless, the hyperlipidaemia may contribute to increased lipid peroxidation, the precise mechanism by which the oxidant stress is increased in preeclampsia remains to be established.

There are conflicting evidences as to the status of vita-

min E in pregnancy and preeclampsia (Tsukatani, 1983; Uotila et al, 1993). It had been observed by Tsukatani (1983) that serum vitamin E levels increase with advancement of pregnancy, but, the concentration of vitamin E is lower in preeclampsia than in normal pregnancy. In contrast, Uotila et al (1993) have reported an increase in vitamin E levels in preeclampsia that may be attributed to compensatory increase in response to increased peroxide load. Lowered levels of vitamin E in normotensive pregnant as compared to nonpregnant and marked decrease in preeclamptic women as compared to controls was observed in the present study (Table I). This might be because of increased requirements. Nonetheless in relation to lipid levels and lipid peroxide levels in preeclampsia, this requirement may obviously be of some significance. This contention is supported by the evidence that concentration of vitamin E is lower in preeclampsia than in normal pregnant (Scrinshaw et al, 1949). On the other hand decreased activity of SOD in pregnancy may be due to reduced enzyme production or inactivation of this enzyme (Novak et al, 1989). This may be speculated because of the accumulation of toxic products produced during pregnancy.

Relation of increased lipid peroxidation or free radical in the pathogenesis of preeclampsia remains to be established. Recent evidence indicates involvement of the endothelial cell dysfunction in the pathophysiology of preeclampsia (Sukimori et al, 1992). Lipid peroxides are cytotoxic to endothelial cells (Tsukatani, 1983). Also, Lipid peroxides inhibit prostacyclin synthetase, removing the defense against proaggregatory and vasoconstrictile ac-

tivity of thromboxane A_2 (Moncada et al, 1976). The vasoconstriction thus produced can worsen hypertension by means of ischaemic injury to the cells and subsequent peroxidation leading to a vicious cycle. It is also likely that superoxide anion produced during platelet aggregation or degradation of lipid peroxides may inactivate endothelium derived relaxation factor (EDRF, NO), reduced the release of prostacyclin and further impede the vasorelaxant influence of the endothelium (Gryglewski et al, 1986). To our knowledge no reports are available in literature regarding beneficial effects of dietary supplementation of vitamin E during the progression of preeclampsia. Studies are underway in this relation in our laboratory.

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