Plasma lipid and lipoprotein concentrations in pregnancy induced hypertension

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Abstract

Objectives: Aim of this study was to evaluate implication of pregnancy induced hypertension on maternal plasma lipid, lipoprotein, apolipoprotein concentrations and lipid peroxidation products by a comparison of normal pregnancy vs. preeclampsia.

Design and methods: Thirty-four women with preeclampsia and 32 healthy pregnant women (controls) in the third trimester were recruited for this study.

Results: In the preeclamptic group plasma total triglyceride, low density lipoprotein cholesterol (LDL-C), malondialdehyde (MDA) and apolipoprotein B (apo-B) were significantly increased, while plasma high density lipoprotein cholesterol (HDL-C) was significantly decreased compared to that of control group. There was no significant difference in total cholesterol and apolipoprotein A1 (apo-A1) concentrations.

Conclusion: Our findings suggest that preeclampsia share some metabolic characteristics with coronary artery disease such as dislipidemia and increased lipid peroxidation. However lipoprotein concentrations may be better biochemical markers of dislipidemia in the preeclamptic state than the corresponding apolipoproteins.

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1. Introduction

Preeclampsia is a hypertensive disorder of pregnancy, characterized by vasospasm, proteinuria, edema and is the leading cause of maternal, fetal and neonatal mortality and morbidity [1]. Different factors, molar pregnancy, multifetal gestations, certain chromosomal alterations of the fetus, familiar history of hypertension, diabetes mellitus, chronic hypertension, increased oxidative stress, and renal disease have been associated with preeclampsia [1]. In addition, endothelial cell injury and impaired endothelial function are important in the pathogenesis of preeclampsia [2].

Serum lipids have a direct effect on endothelial function. Lipid peroxides are normally present in lipoproteins and seem to contribute to vascular tone regulation through stimulation of the arachidonic acid enzymatic pathways [1,2]. Pregnancy is associated with physiologic hyperlipidemia. In normal pregnancy, this feature is not atherogenic and is believed to be under hormonal control [2]. Although no agreement exists in the literature about changes in LDL and HDL-C in preeclampsia, different lines of evidence indicate that abnormal lipid metabolism is not merely a manifestation of preeclampsia, but that it is directly involved in its pathogenesis [1,2].

Differences in the pattern of plasma oxidant/antioxidant balance in women with preeclampsia remain unestablished, but lipid peroxides have been found to be elevated in preeclampsia, and there appears to be some correlation between lipid peroxide levels and the severity of preeclampsia [2,3]. MDA, a metabolite of lipid peroxides detectable in plasma, was used as an indicator of lipid peroxidation [3].

The present study investigates the relationship of plasma lipids (cholesterol, triglyceride), lipoproteins (LDL-C and
HDL-C), apoproteins (apo-A1, apo-B), and plasma MDA levels, an indicator of lipid peroxidation, and their potential involvement in the pathophysiology of pregnancy induced hypertension.

2. Material and methods

Two groups of age matched women were selected for this study, including 34 preeclamptic and 32 healthy women with uncomplicated pregnancy. Preeclamptic and healthy pregnant women were recruited from those referred to the Obstetric and Gynaecology department of the Turgut Ozal Medical Center in Malatya, Turkey.

Patients with preeclampsia were defined by criteria of hypertension, proteinuria, edema and reversal of hypertension and proteinuria after pregnancy [1]. Characteristics of the groups are detailed in the Table 1.

Fasting venous blood samples were collected from subjects between 8:00 AM and 10:00 A.M. Plasma was separated from blood anticoagulated with heparin. 24 h urine was collected in bottles containing Na₂B₄O₇ (500mg/1000 mL urine) as preservative. Plasma and urine samples were stored at −80°C until the time of assay.

The levels of plasma total cholesterol, triglyceride and HDL-C were measured enzymatically (Beckman Synchorn LX 20 auto analyser-USA). Apo A1 and apo-B levels in plasma were determined by immunoturbidimetric assay (Behring-Nephelometer-100 analyser, Frankfurt-Germany). LDL-C were calculated from Friedewald Formulas. Plasma lipid peroxidation was determined by the amount of malondialdehyde analyzed spectrophotometrically [3].

The results are presented as mean values ± SEM. Independent t-test was used for statistical significance. A level of \( p < 0.05 \) was accepted as statistically significant. SPSS 10.0 program was used for statistical analyses (SPSS Inc, Chicago, Illinois, USA). The study was approved by the local Ethics Committee, and all participants gave informed consent.

3. Results

In preeclamptic subjects, the mean systolic and diastolic pressure and proteinuria were significantly higher than that of controls, whereas no significant differences were found in age, gestational age, plasma protein and hemoglobin (Table 1).

Plasma triglyceride, LDL-C, MDA (\( p < 0.001 \)) and apo-B (\( p < 0.05 \)) levels were significantly higher in pre-eclamptic subjects than in controls, whereas the plasma HDL-C concentrations were significantly lower in pre-eclamptic cases than in the control group (\( p < 0.01 \)). Total cholesterol and apo-A concentrations were not statistically different (Table 1 and Fig. 1).

4. Discussion

According to the most recent hypothesis, preeclampsia is a generalized inflammatory state where several plasma factors that regulate endothelial functions are altered [1,2]. An endothelial hyperstimulation is initially provoked, eventually leading to severe endothelial dysfunction, and resulting in disseminated microangiopathic disease with vasospasm and hypercoagulation [2].

It is known that preeclampsia is associated with hypertriglyceridemia [1]. We also confirmed the increases in the level of triglyceride in preeclampsia. In addition, in our study, significantly high LDL-C, MDA and low HDL-C concentrations were found in preeclamptic Turkish women. However, higher total cholesterol levels in the preeclamptic group did not reach significant level. These results are consistent with the findings reported in studies of other populations. Recently, it was reported that patients with preeclampsia had lower mean serum HDL-C and higher mean triglyceride concentrations than the control group in the Finnish and Peruvian population [4,5].

The endothelial dysfunction in preeclampsia could originate from oxidative stress as well as dislipidemia. Free radicals can be generated by many different enzymatic processes. They are extremely reactive and interact with polyunsaturated fatty acids to produce lipid peroxides with a much longer half-life [1–3].

Increased MDA levels found in our study, show similar results to that of other studies [3,6]. This increase in MDA is strongly related to lipid peroxidation caused by oxidative...
stress, and is expected to affect various tissues and organ systems, including vascular endothelium. When oxidative stress reaches a certain level, cellular damage occurs, including structural damage in cellular membranes, in mitochondrial and nuclear DNAs and impairment of enzymatic functions at multiple levels. Oxidative stress can have an affect mainly on vessels endothel and on many tissues and organs both locally and systematically. During these processes, other molecules involved in vasodilatation such as nitric oxide are inhibited by high lipid peroxide concentration [1,2]. We think, all of these circumstances might be the cause of the ethiopathogenesis of hypertension in preeclampsia.

It is well known that apo-B is a protein component of a variety of lipoproteins which are VLDL, IDL, LDL and lipoprotein (a). In the present study, levels of apo-B concentrations in preeclamptic group were high as LDL-C. However, levels of HDL and apo A1 were not concomitant. HDL levels were found significantly low, while apo A1 levels did not show significant difference in preeclamptic group when compared to that of control group. In our opinion, this can be originate from polymorphism of Apo A1 of HDL and/or functional disorder of HDL. Apoprotein polymorphism of lipoproteins in diabetics have been studied previously [7,8]. Erbagci, et al. reported low HDL-C levels in diabetic patients without a concomitant decrease in Apo A1 levels [8]. We have not found any literature on this point in preeclamptic patients. Although it is anticipated a concomitant HDL and Apo A1 levels, our results suggest that lipoprotein concentrations appear to be better biochemical markers of dislipidemia in the preeclamptic state than the corresponding apolipoproteins.

Generation of lipid peroxides in preeclampsia is supposed to be initiated in the placenta [1,9]. This could result from ischemic and inflammatory phenomena in the fetomaternal interphase. Isolated trophoblastic villi produce increased amounts of lipid peroxides when cultured under hypoxic conditions [9]. Arbogast and Taylor [10] have postulated that the evidence of atherogenesis in placental spiral arteries taken from preeclamptics is suggestive of multiple cell cycles of cell death and reendothelization. Intracellular lipid accumulation in vascular and kidney endothelial cells is well established. Endothel cell activation or injury has been shown directly or indirectly leading to the activation of leukocytes and platelets and the formation of lipid-laden foam cells. High LDL and VLDL cholesterol exposure results in a thrombogenic cascade of events where macrophages, leukocytes and activated platelets trigger an inflammatory response which is further inviting cytokines and adhesion molecule activation. Consequently, these observations are consistent with the thesis that elevations of maternal circulating lipids may play a role in poor placental implantation and/or reductions in placental perfusion in early pregnancy.

In conclusion, our data also suggest that an abnormal lipid metabolism and particularly high triglycerides, LDL-C and lipid peroxides, and low HDL-C concentrations may contribute to promotion of oxidative stress and vascular dysfunction seen in preeclampsia.
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References