Electron Microscopic Study of the Effects of Preeclampsia on the Placental Endothelial Cells Ultra Structures during Pregnancy

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Abstract

Background: Preeclampsia occurs in 3-5% of pregnancies and is a major cause (12-20 %) of maternal mortality in developed countries. It is the leading cause of preterm birth and intra-uterine growth restrictions (IUGR).

Objective: The study was designed to determine and demonstrate the ultra structural changes of endothelial cells in placenta of women suffering from hypertensive disease.

Patients & Methods: Placental samples were obtained from two groups of pregnant women groups (preeclamptic and normal pregnant women). The specimens were fixed in 2.5% gluteraldehyde and preceded for electron microscopic examination.

Results: Placenta of women with preeclampsia has shown marked degenerative changes in both endothelial and trophoblastic cells. These changes were represented by precipitation of fibrin with the accumulation of platelets in capillary lumen. Abundance of collagen fibers precipitate in the apical region of both endothelial cells and trophoblasts, with thickening of endothelial basement membrane.

Conclusion: All histological changes or lesions obstruct the continuous conduction from maternal surface of the trophoblasts through fetal capillary endothelium causing endothelial dysfunction.

Key words: Preeclampsia, endothelial cell, ultrastructures.

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Introduction

Preeclampsia (PE) is a complication of human pregnancy characterized by hypertension, proteinuria and edema. PE is highly associated with pregnancy related risks for the mother due to general endothelial dysfunctions and to the fetus due to the severely compromised uterine blood supply [(1)]. Epidemiological studies from isolated populations [(2)] or large population cohorts [(3&4)] have yielded direct evidence that PE increases risk for cardiovascular diseases for both mother and offspring later in life.

Resistance sized arteries (100-400µm) are mainly involved in the regulation of peripheral vascular resistance, blood pressure and blood flow to the target organ [(5)]. Their vascular endothelium in this circulation primarily serves to assure blood supply to every organ according to the physiological needs. The mechanism underlying the alteration in vascular resistance and the role of vascular endothelium in preeclampsia have been investigated intensively [(6)] yet, we still lack the knowledge of the changes in the ultrastructuars of endothelial cells that leads to endothelial dysfunction in preeclampsia, which is the aim of this study.

Methods:

1. Patients:

This work was carried out in the Department of Obstetrics & Gynecology, and E.M department in at AL- Alkadymia Teaching Hospital in Baghdad, for a period of ten months, from Oct. 2007 to the July 2008. This study was conducted on 50 women, they were in early labor and all sharing the following criteria:

1. All were singleton pregnancies.
2. Their parities were between zero- four.
3. All had full term pregnancies, confirmed by known last menstrual period and early ultrasound report.They were divided into two groups. The first group (normal or

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1. No history of medical problems, smoking or drug intake.

2. No history of obstetrical problems.
3. Their newborns had birth weight within the 10^{th} percentile of the individualized birth weight ratio.

The second group (patients group) consisted of 35 women with pregnancies complicated by intrauterine growth restriction (IUGR) and had the following additional criteria:

1. All had history of risk factors of complicated current pregnancy with pre-eclampsia or history chronic hypertension.
2. Examination of these women revealed inadequate fundal growth.
3. They had an ultrasonographic evidence of (IUGR), deviation from an appropriate growth percentile depending on biparietal diameter, head and abdominal circumferences measurements, with amniotic fluid index of less than 10cm.
4. Their newborns had birth weight less than the 10^{th} percentile of the individualized birth rate ratio.

Tissues Preparation:

Placental tissue samples were obtained from the outer area of the maternal surface of the placenta and cut into small pieces (2x2x2 mm) , prefixed in 2.5% Gluteraldehyde in phosphate buffer pH(7.2). The specimens were prepared for semi-thin sections of 0.5- 1*u*m, stained with 1% Methylene blue and special stain consists of Azar II and Basic fuchsin[7]

Results:

Endothelial cells and trophoblsts shows variable necrotic changes in all patients groups as in the following figures:-

- Figure (1) shows the following degenerative changes

1. Fibrin deposition in the lumen of blood capillary.
2. Small nutritional vesicles in the cytoplasm of endothelial cells.
3. Thickening and hyalinization of the apical region of trophoblastic cells.

- Figure (2,3) shows the following changes:

1. Rupture and hemorrhage in some regions of internal intema of blood capillary.
2. Abundance of collagen fibers deposition with the thickening of the basement membrane of endothelial cells.
3. Mitochondrial swelling and fragmentation of the rough endoplasmic reticulum of endothelial cells.

- Figure(4) shows the following necrotic changes:

1. Apoptotic degeneration of trophoblastic nuclei.
2. Mitochondrial swelling mainly those located between folds of membranes of trophoblastic cells.
3. Platelets accumulation and thrombosis of RBC were found in the lumen of blood capillary.

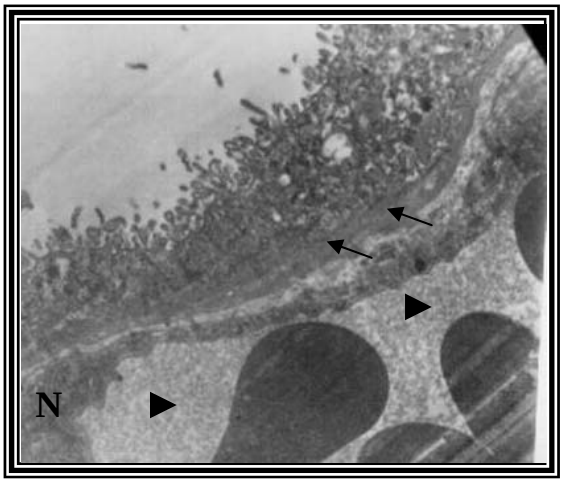

Figure 1: Blood capillary and trophobalstic cells of preeclamptic women showing; fibrin deposition in the lumen of blood capillary (▶) , Hyalinization of the apical region of the trophoblast (⟶).
N: nucleus of endothelial cells
Uranyl acetate and lead citrate 3400x.
X3400
Uranyl acetate and lead citrate 6200x

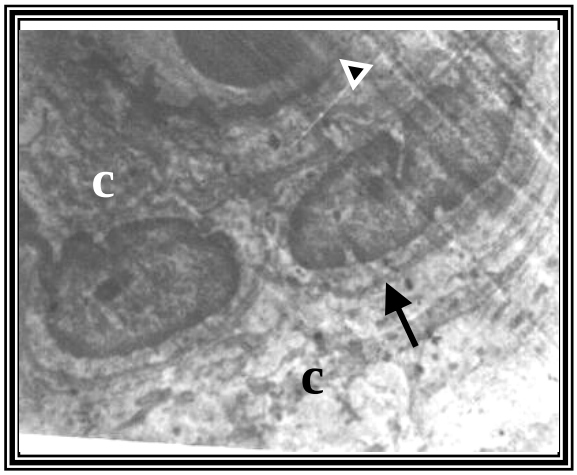

Figure 2: Blood capillary of preeclamptic women showing rupture of internal intema (▶). Collagen fiber deposition (co), thickening of the basement membrane (⟶).Uranyl acetate and lead citrate 4400x**.**

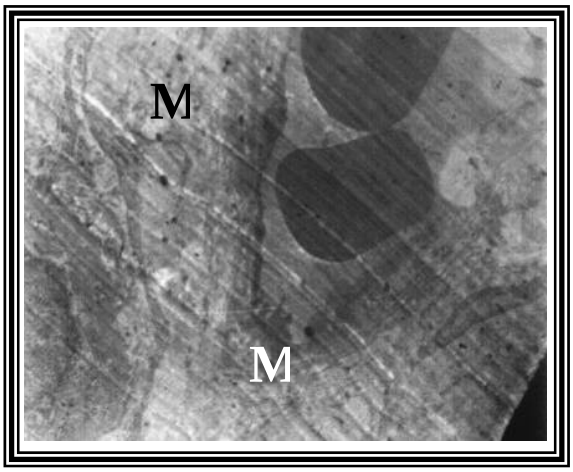

Figure 3: Blood capillary of preeclamptic women showing thickening of endothelial layer, swelling mitochondria (**M**).
Uranyl acetate and lead citrate 4400x

Figure 4: Blood capillary and trophoblasts of preeclamptic women showing apoptotic nuclei of trophoblastic cells (▶), platelets aggregation (⟶), mitochondrial swelling (➤) Uranyl acetate and lead citrate 3400x**.**

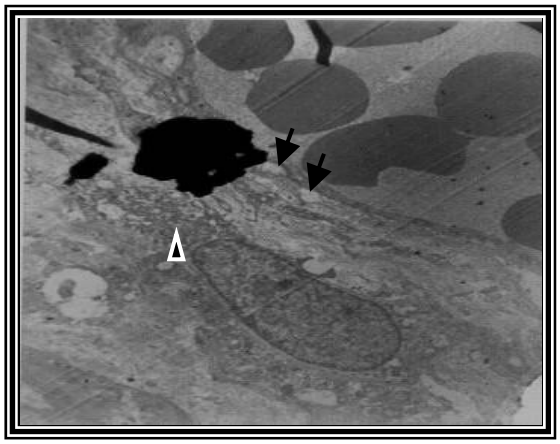

Figure 5: Endothelium of blood capillary and trophoblasts of preeclamptic women showing
- proteinous vesicles in torphoblast (▶)
- collagen deposition (co)
- pinocytic vesicles (⟶)

Uranyl acetate and lead citrate 3400x.

Discussion:

The endothelium, a single cell layer lining all blood vessels, is severely compromised in PE; In fact, endothelial dysfunction is considered as a pathogenic hallmark in this complication [(8).] In this study the aggregation of platelets in capillary blood lumen reflects the dysfunction of this normally protective "antihypertensive and antiplatlets" layer, and may explain most of clinical findings of the maternal disorders. Intemal changes, thickening of the basement membrane of endothelial cells, fibrin deposition and platelets aggregation found in this study may explain the diminish and sometimes almost occlude the vascular lumen. These lesions are most strikingly seen in placenta taken from women suffering from hypertensive complications of pregnancy but also seen in diabetic women placenta [(9)].

Pinocytic vesicles that originate in the plasma membrane seen in our samples refer to the nutrition substance, moreover, the presence of fibrotic changes in the region between endothelial cells basement membrane and apical redilated, regions of the trophoblasts will hinder fetal nutrition and oxygenation, which will be associated with fetal hypoxia[(10)] .

Normally the uteroplacental arteries are invaded by endovascular trophoblast and remodeled into dilated, inelastic tube without maternal vasomotor control. This process takes place via apoptotic changes [(11),] so the increment in apoptotic trophoblast seen in this study may have caused reduction in the number of normal trophoblast in the uterine villi. These changes affect the histological barrier comprises: trophoblast, fetal capillary and there basal lamina.

The increment in the proteinous substances of trophoblast could be explained according to the previous study by Campell *et al* [12], they suggest that proteinous substances in trophoblast disturbed cell-cell communication between trophoblast and the maternal endothelium and may be responsible for the deficient endovascular invasion seen in preeclampsia.

Conclusions:

1. Proteinous precipitate in trophoblast altered the endothelial function, since they affect cell-cell communication between trophoblast and endothelial cells.

2. Fibrin precipitate and accumulation of platelets may caused obstruction of blood capillary lumen and, thereby will affect endothelial functions.

3. Increment apoptotic trophoblast may inflict endothelial dysfunction.

4. Collagen precipitate between apical regions of trophoblast and endothelial basement membrane hinder nutritional exchange between endothelial cells and trophoblast.All these histological changes or lesions obstruct the continuous conduction from maternal surface of the trophoblast through fetal capillary endothelium causing endothelial dysfunction.

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