The Role of 3D Power Doppler Ultrasound in Assessment of Placental Bed Vascularity in Pre-Eclampsia

Thesis
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دور موجات الدوبلر الفوق صوتية ثلاثية الأبعاد فى تقييم الأوعية الدموية المشيمية الرحمية فى حالات تسمم الحمل

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فى أمراض النساء والتوليد

مقدمة من

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Summary

Preeclampsia is a pregnancy-specific syndrome characterized by new-onset hypertension and proteinuria, occurring usually after 20 weeks' gestation. Although the etiology remains unknown, placental hypoperfusion and diffuse endothelial cell injury are considered be the central pathologic events ***(Vadillo-Ortega et al., 2011).***

The 3D power Doppler allows the assessment of the architecture of the placental tree. Such information is very important considering that problems on the normal development of the placenta, as well as the reduction on its FIs, are usually associated with alterations in fetal growth, amniotic fluid volume, and Doppler flowmetric parameters of the umbilical artery ***(Hata et al., 2011).***

This case-control study was conducted in Department of obstetrics and gynecology of Maternity hospital-Ain Shams University in a period started from July 2010 to December 2011.

A number of 80 pre-eclamptic patients at (32-36) weeks of pregnancy were included in the study. Before the investigation, patients gave a written informed consent and confirmed that they meet all inclusion crieteria. 80 patients acted as control.

Acknowledgment

First of all, all gratitude is due to ***Allah*** *for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

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Alshaimaa Yassin Abdelkhalik

Introduction

Preeclampsia is a pregnancy-specific syndrome characterized by new-onset hypertension and proteinuria, occurring usually after 20 weeks' gestation. Although the etiology remains unknown, placental hypoperfusion and diffuse endothelial cell injury are considered to be the central pathologic events ***(Vadillo-Ortega et al., 2011).***

Preeclampsia is classified into mild and severe types and, in its extreme, may lead to liver and renal failure, disseminated intravascular coagulopathy, and central nervous system abnormalities, including seizures ***(Sibai et al., 2010).***

Because the only cure is delivery, preeclampsia is associated with high maternal and neonatal mortality and morbidity. Worldwide, preeclampsia and eclampsia are estimated to be responsible for approximately 14% of maternal deaths per year (50,000-75,000) ***(Chames et al., 2010).***

Despite its impact on maternal and child health, efforts to predict and prevent the disease have been disappointing. Numerous strategies (low-dose aspirin, calcium, and vitamin C and E supplementation) have been shown to be of little benefit. Because our understanding of the pathogenesis of this disease is incomplete, these preventive strategies were proposed based on

pathogenetic hypotheses that did not withstand the test of time (***Hofmeyr et al., 2009)***.

Many investigators believe that the placenta is the trigger for endothelial cell injury. Placental hypoperfusion or ischemia in preeclampsia has many causes. Preexisting vascular disorders such as hypertension and connective tissue disorders can result in poor placental circulation ***(Baweja et al., 2011)***.

However, most women who develop preeclampsia are healthy and do not have underlying medical conditions ***(von Dadelszen et al., 2011).***

The shallow placentation noted in preeclampsia is a result of the inability of trophoblasts to invade the decidual vessels this invasion of the decidual arterioles is incomplete. The invasive cytotrophoblasts fail to replace tunica media, resulting in mostly intact arterioles that are capable of vasoconstriction ***(Vigil-De Gracia et al., 2009).***

The ultrasonography is a non-invasive method that allows the study of several placental parameters since its formation. Through two-dimensional ultrasonography, the placenta can be assessed according to thickness and maturity ***(Chen et al., 2006).***

The three-dimensional ultrasonography (3DUS) is one of the most recent technological advances in diagnostic medicine ***(Michal Pomorski et al., 2011).***

One of the recent applications of 3DUS is related to the vascularization assessment of organs and structures through three-dimensional power Doppler (3DPD) ***(Michal Pomorski et al., 2011).***

The 3D power Doppler allows the assessment of the architecture of the placental tree. Such information is very important considering that problems on the normal development of the placenta ***(Hata et al., 2011).***

3D power Doppler indices are:

Vascularization Index (VI)*:*

- Vascularization index is a dimensionless measurement and gives information about the blood flow (color areas) in the placenta and spiral arteries in studied volume.

Flow Index (FI)*:*

- Flow index is also a dimensionless measurement with information about the intensity of blood flow.
- It is calculated as a ratio of weighted color values (amplitudes) to the number of color values.

Vascularization Flow Index (VFI)*:*

- Vascularization flow index is the combined information of vascularization and mean blood flow intensity.
- It is another a dimensionless index calculated by dividing weighted color values (amplitudes) by the total voxels minus background voxels.

Studying 3DPD parameters in pre-eclamptic pregnancies in comparison to normal cases will help in finding its role in prediction of pre-eclampsia ***(Ivica Zalud et al., 2007).***

Aim of the Work

Measurement of placental blood flow in pre-eclamptic patients in comparison with normal pregnancies by 2D indices and 3D power Doppler indices.

Chapter (1):

Preeclampsia

Definition:

Preeclampsia is a pregnancy-specific syndrome characterized by new-onset hypertension and proteinuria, occurring usually after 20 weeks' gestation. Although the etiology remains unknown, placental hypoperfusion and diffuse endothelial cell injury are considered to be the central pathologic events ***(Vadillo-Ortega et al., 2011).***

Preeclampsia is classified into mild and severe types and, in its extreme, may lead to liver and renal failure, disseminated intravascular coagulopathy, and central nervous system abnormalities, including seizures. Because the only cure is delivery, preeclampsia is associated with high maternal and neonatal mortality and morbidity ***(Sibai et al., 2010).***

Worldwide, preeclampsia and eclampsia are estimated to be responsible for approximately 14% of maternal deaths per year (50,000-75,000). Despite its impact on maternal and child health, efforts to predict and prevent the disease have been disappointing. Numerous strategies (low-dose aspirin, calcium, and vitamin C and E supplementation) have been shown to be of little benefit. Because our understanding of the pathogenesis of this disease is incomplete, these preventive strategies were

proposed based on pathogenetic hypotheses that did not withstand the test of time. Recently, a number of investigators demonstrated and confirmed that an imbalance in angiogenic molecules play a major role in the pathogenesis of preeclampsia, raising the possibility that these molecules may be targeted for preventive measures and possible palliative therapy ***(Lindheimer et al., 2008).***

Preeclampsia as a Two-Stage Disorder:

The abnormal interfaces between maternal, paternal, and fetal tissues may cause preeclampsia have led to hypotheses that the syndrome is a two-stage disorder. There is a spectrum to include "maternal and placental preeclampsia" ***(August et al., 2011).***

Stage 1 is caused by faulty endovascular trophoblastic remodeling that causes the stage 2 clinical syndrome (Fig. 1). There certainly is evidence that some cases of preeclampsia fit this theory. Importantly, stage 2 is susceptible to modification by preexisting maternal conditions that include cardiac or renal disease, diabetes, obesity, or hereditary influences. Such compartmentalization seems artificial, and it seems logical that there likely is a continuous process. Preeclampsia is clinically more realistically a continuum of worsening disease ***(Redman et al., 2011).***

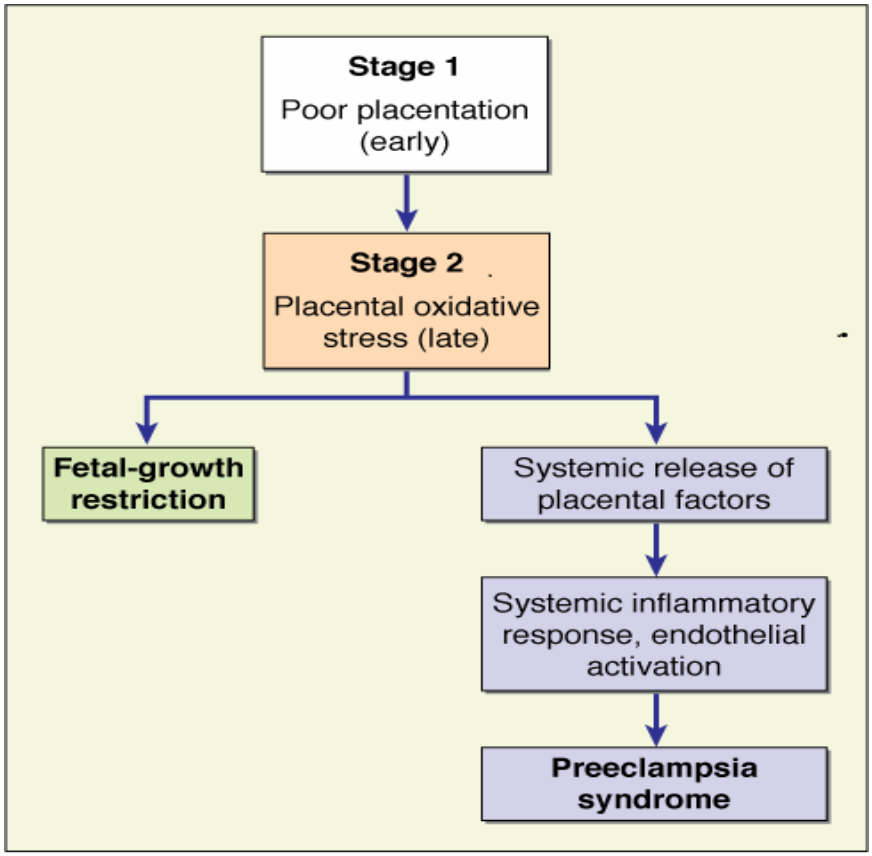

Fig. (1): Preeclampsia as a Two-Stage Disorder (Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY: Williams Obstetrics, 23rd ed. 2010: http://www.accessmedicine.com).

Schematic outlines the theory that the preeclampsia syndrome is a "two-stage disorder." Stage 1 is preclinical and characterized by faulty trophoblastic vascular remodeling of uterine arteries that causes placental hypoxia. Stage 2 is caused by release of placental factors into the maternal circulation causing systemic inflammatory response and endothelial activation ***(Redman et al., 2011)*.**

Pathophysiology:

The general consensus is that preeclampsia is an endothelial cell disorder resulting in mild-to-severe microangiopathy of target organs such as brain, liver, kidney, and placenta ***(Lain et al., 2009).***

While hypertension may be the most common presenting symptom, it should not be viewed as the initial pathogenetic process. Evidence of other organ involvement before hypertension becomes fulminant is not uncommon. Several circulating markers of endothelial cell injury have been shown to be elevated in women who develop preeclampsia before they became symptomatic. These include endothelin, cellular fibronectin, plasminogen activator inhibitor-1, and altered prostacyclin/thromboxane profile ***(Sibai et al., 2011).***

Evidence to date suggests that oxidative stress; circulatory maladaptation; inflammation; and humoral, mineral, and metabolic abnormalities may all contribute to endothelial dysfunction and pathogenesis of preeclampsia ***(Reddy et al., 2011).***

Many investigators believe that the placenta is the trigger for endothelial cell injury. Evidence suggests that hypoperfused placentas produce various factors that are capable of injuring endothelial cells. Recent data suggest that circulating factors

that interfere with the action of vascular endothelial growth factor (VEGF) and placental growth factor (PlGF) play a major role in maternal manifestation of the disorder) ***(Redman et al., 2011).***

Placental hypoperfusion or ischemia in preeclampsia has many causes. Preexisting vascular disorders such as hypertension and connective tissue disorders can result in poor placental circulation. In cases of multiple gestation or increased placental mass, it is not surprising for the placenta to become underperfused. However, most women who develop preeclampsia are healthy and do not have underlying medical conditions. In this group of women, abnormally shallow placentation has been shown to be responsible for placental hypoperfusion ***(Magee et al., 2008).***

Placentation in Preeclampsia:

The shallow placentation noted in preeclampsia is a result of the inability of trophoblasts to invade the decidual vessels. In normal pregnancies, a subset of cytotrophoblasts called invasive cytotrophoblasts migrate through the implantation site and invade decidua tunica media of maternal spiral arteries and replace its endothelium in a process called pseudovascularization ***(Kee-Hak Lim et al., 2009).***

As a result of these changes, these vessels undergo transformation from small muscular arterioles to large capacitance, low-resistance vessels. This allows increased blood flow to the maternal-fetal interface. Remodeling of these arterioles probably begins in the first trimester and ends by 18-20 weeks' gestation. However, the exact gestational age at which the invasion stops is unknown ***(Robert Pijnenborg et al., 2007).***

In preeclampsia, this invasion of the decidual arterioles is incomplete. The invasive cytotrophoblasts fail to replace tunica media, resulting in mostly intact arterioles that are capable of vasoconstriction. Histologic evaluation of the placental bed demonstrates few cytotrophoblasts beyond the decidual layer. The trophoblast differentiation along the invasive pathway involves alteration in the expression of a number of different classes of molecules, including cytokines, adhesion molecules, extracellular matrix, metalloproteinases, and the class Ib major histocompatibility complex molecule, HLA-G ***(Redman et al., 2011).***

Abnormal Trophoblastic Invasion:

In normal implantation, shown schematically in (Fig. 2), the uterine spiral arterioles undergo extensive remodeling as they are invaded by endovascular trophoblasts. These cells