RECENT ADVANCES IN HIGH RISK PREGNANCY

Dilip Kumar Dutta

Federation of Obstetric & Gynaecological Societies of India

JAYPEE

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HIGH RISK PREGNANCY

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Preface

In the last decade, a lot of advances in the management of high-risk pregnancies have been understood; but till date, evidence-based information is available only in 30-40% conditions, encountered in clinical practice.

Till date, the major challenges faced by obstetricians to diagnose and treat preterm birth, pre-eclampsia, diabetes, thyroid disease in pregnancy, etc. And to diagnose this problem, imaging techniques which includes hormone assays, USG, Doppler study, neonatal ventilatory support and steroids, etc. are adopted in spite of not knowing what is the exact time to use these tools to manage these clinical problems.

In view of above facts, the editor took initiative to select various experts to write chapter in details to get evidence-based information and along with their original works.

This book not only highlights various topics in medical complications of pregnancy but also focuses various issues and treatment modalities in obstetric complications in details.

I am very much grateful to FOGSI who has allowed to me publish this book during 52 AICOG at Guwahati, 2010. My sincere thanks to M/s Jaypee Brothers Medical Publishers (P) Ltd., New Delhi who published this book.

Lastly, I felt that obstetricians involved in the high-risk pregnancy will be benefited not only to manage high-risk cases but also to get all current information on high-risk pregnancy.

At last, I am very grateful to my wife Dr Banani Dutta, my son Dr Indranil Dutta, and my daughter Miss Ipsita Dutta for their help to prepare this book.

Dilip Kumar Dutta

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Section – I
Obstetrics Complications

CHAPTER

1 Pre-eclampsia and Eclampsia

PN Nobis

Pre-eclampsia is a commonly encountered disorder during pregnancy. It is a multisystem disorder affecting almost all the vital systems of the body. It is unique to human pregnancy.[1] Pre-eclampsia and eclampsia are associated with a high maternal and perinatal mortality and morbidity worldwide. The term pre-eclampsia is used to describe a wide spectrum of patient who may have only mild elevation in blood pressure (BP) or severe hypertension with various organ dysfunction.[2] The etiopathogenesis of pre-eclampsia is still illusive and hence management is early detection, symptomatic treatment and delivery at an opportunate time.

Pre-eclampsia is primarily defined as gestational hypertension plus proteinuria.[3] Proteinuria is defined as concentration of > 300 mg/24-hour period, or a concentration of 30 mg/dl (1+on dipstik) or more in at least at two random urine samples collected 4 hours apart. The concentration of urinary protein in random urine sample correlate poorly with proteinuria found in 24-hours urine. Therefore, the definitive test to diagnose proteinuria should be quantitative protein excretion in a 24 hour period.[2]

Edema is not regarded as a criteria for diagnosis of pre-eclampsia. However, sudden appearance of gross edema with hypertension and proteinuria heralds onset of severe pre-eclampsia.

The incidence of pre-eclampsia varies from 3 to 7 percent of all pregnancies. Pre-eclampsia may superimpose in pregnancy with essential hypertension. When pre-eclampsia is superimposed in those cases of chronic essential hypertension blood pressure rises high, there appears significant proteinuria. It is estimated that 25% of hypertensive women develop pre-eclampsia[4], while another estimate put it as 70%.[2]

Risk Factor for Development of Pre-eclampsia

- Maternal age < 20 or > 35 years of age.
- Family history of hypertension, pre-eclampsia, eclampsia
- Primigravida

- Hydatidiform mole
- Multiple pregnancy
- Pre-existing hypertension
- Diabetes mellitus
- Pre-existing kidney disease
- Obesity
- Previous history of pre-eclampsia or eclampsia
- Fetal hydrops
- Pre-existing vascular disease, thrombophilia
- Fetal trisomy.

ETIOLOGY AND PATHOPHYSIOLOGY

The etiology of pre-eclampsia is still eluding the obstetricians. In different times several etiological factors have been suggested, but no one could satisfy the scientific world. Few widely discussed theories are mentioned here.

PLACENTAL BED

Pre-eclampsia is peculiar to pregnancy. Trophoblast and the placenta with or without a fetus play the central role in the genesis of pre-eclampsia. It is well known that during normal pregnancy trophoblastic cells invade the spiral arteries and brought about vascular changes like breaking down the endothelium, internal elastic lamina and the muscular coat replaced mostly by fibrinoid material.[5] These changes take place during the first trimester of gestation. Again in early second trimester there occurs a second wave of trophoblastic invasion transforming the arteries of the myometrial segment. These physiological changes transform the spiral arteries into wide sinusoids, increasing blood supply to the fetus and the placenta. In pre-eclampsia only one half to two-thirds of the spinal arteries undergo these changes and second wave of invasion fail to occur.[6] Extent of failure of trophoblastic invasion of the spiral arteries correlate with the severity of hypertension. These typical vascular lesions of the placental bed is termed as "acute atherosis", because of appearance of foam cell in the vessel wall.[7] But it is not specific to pre-eclampsia only. Similar changes are observed in intrauterine growth restriction (IUGR) also. Endothelial damage is observed through out the maternal fetal boundary in decidua outside the placental bed also.[8]

The reason behind the abnormal placentation is not known. Different suggestions have been put forward. These include reduced expression of histocompetable antigen HLA C, cytokine regulation of integrin expression and local cellular inflammatory reaction.

Oxidative Stress

Another popular theory regarding etiopathogenesis of pre-eclampsia is oxidative stress. The increased production of reactive oxygen species can damage the cell membrane, protein and DNA. Cytokines, tumor necrosis factor α (TNFα) and interleukins contribute to the oxidative stress of pre-eclampsia. It is observed that oxidative stress from reduced placental perfusion lead to endothelial dysfunction in pre-eclampsia.

Nitric oxide is an important free redical. It has an unpaired electron in its outer orbital. The unpaired electron makes the molecule highly reactive and it readily combines with oxygen to produce nitrogen dioxide, a potent oxidizing agent.[9] Normally vascular endothelium regulates release of vasoactive substances which control thromboresistance and tone in the vessel wall. Moreover, it inhibits blood coagulation by synthesizing thrombomodulin and heparin sulphate.[9] Vascular endothelial dysfunction is likely to be a principal abnormality leading to pathophysiological menifestations of different organ systems. During normal pregnancy, maternal vasculature demonstrates decreased responsiveness to vasoactive peptides like angiotensin II. But in pre-eclampsia vessels show hyper-responsiveness to these hormones. Vascular reactivity and altered coagulation system are result of endothelial dysfunction. The cause of vascular endothelial dysfunction is not clear. It might be that oxidative stress is responsible to a great extent.

Some other factors have also been implicated in the genesis of pre-eclampsia. These are, to name few, platelet activation, circulating lipids, some dietary elements and genetic factor. Circulating lipids have diverse effects on vascular endothelium. Low density lipoprotein (LDL) oxidation may play some role in endothelial dysfunction.[10] Several studies have shown platelet activation in association with pre-eclampsia. There occurs increased release of thromboxane, a potent vasoconstrictor prior to onset of the disease. Studies have been conducted to explore relation of dietary deficiency or excess in the genesis of pre-eclampsia. These studies include role of vitamin C and E. Calcium deficiency is thought to cause gestational hypertension.[11,12]

Calcium supplementation was tried to prevent pre-eclampsia without definite result. Fish oil was given to modify the abnormal prostaglandin balance. But fish oil was also found to be ineffective in preventing onset of pre-eclampsia.[13]

An inherited maternal component is thought to increase the susceptibility of some women to develop pre-eclampsia,[14] wide range of studies have been carried out to find a link between pre-eclampsia and genetic abnormality. But results so far, are in consistent.

Investigation

Complete blood count should be carried out as microangiopathic anemia may be present.

Platelet count is important and a count $<100,000/mm^3$ is significant. It should be repeated twice weekly during the period of observation. When thrombocytopenia is present fibrinogen level, prothrombin time and partial thromboplastin time should be evaluated. Abnormality might be due to disseminated intravascular coagulopathy or consumptive coagulopathy complicating severe pre-eclampsia.

Renal function – there is about 25 percent reduction of glomerular filtration rate (GFR) in pre-eclampsia due to vasospasm and glomerular capillary endothelial swelling. Uric acid level is more sensitive than serum creatinine level. Serum uric acid level of > 5 mg/dl is abnormal.

In hepatic function mild elevation of serum transaminase is common in pre-eclampsia. In early stage bilirubin level is rarely elevated.

Classification

Pre-eclampsia can be classified into mild and severe varities. In mild variety blood pressure remain below 160/110 mm Hg. In severe variety systolic blood pressure is 160/110 mm Hg or above recorded at least on two occasions 6 hours apart and the patient being at rest. Blood pressure should be recorded preferably in sitting position or in lying down position with a 30 degree tilt of the body, so that the heart remains at the same level with the BP cuff.

Twenty-four hours urinary protein is $\geq$ 5 gm and 24 hours urinary output is 400 ml or less. Patient complains of blurring of vision and epigastric pain, nausea and vomiting. Other more serious findings are abnormal liver function tests, thrombocytopenia and pulmonary edema. Liquor volume is usually less (oligohydramnios) with intrauterine growth restricted fetus. Severe pre-eclampsia may lead to eclampsia.

Aspartate aminotransferase (SGOT) and lactate dehydrogenase level may be elevated. Elevated liver enzymes is a part of HELLP syndrome, a severe complication of pre-eclampsia.

Examination of urine for proteinuria by dipstick method is not dependable. If the dipstick test shows proteinuria of $\geq$ 2+, quantitative estimation of protein in 24 hours collection of urine should be performed. Proteinuria of $\geq$ 300 mg/day is significant.

Management

Termination of pregnancy is the definitive step to cure from pre-eclampsia. The decision to deliver the baby is taken for the best interest of the mother. Few

factors need consideration before taking the decision to deliver the baby. These are severity of pre-eclampsia, duration of gestation, maternal and fetal conditions.

Management of mild pre-eclampsia: A patient with mild pre-eclampsia can be treated as out patient. However, for proper evaluation of maternal and fetal conditions and for ensuring adequate monitoring these patients may need hospitalization. Adequate monitoring is required because they are at risk of developing severe pre-eclampsia, abruption of placenta. The fetus may be in a compromised state due to reduced utero-placental blood flow and/or intrauterine growth restriction. Hospitalization of a patient with mild pre-eclampsia remote from term enhances fetal survival.

In hospital patient is allowed to take average diet. Sedative or antihypertensive drugs are not used. There is report that use of antihypertensive drug may lead to reduce birth weight.[16] Subsequent management depends upon gestational age and maternal response. Monitoring of the mother and the fetus is important during her stay in hospital.

- Patient is asked to report immediately if she feels headache, visual disturbances or epigastric pain.
- Blood pressure should be checked every 4 hours during the day.
- Measurement of weight at least twice weekly to detect sudden excessive weight gain.
- Urinary output in 24 hours should be measured weekly.
- Laboratory investigations include measurement of urinary protein, hematocrit, platelet count and liver function test to be repeated twice a week. These investigations are important because thromobocytopenia and abnormal liver function may develop even with mild pre-eclampsia.

Delivery

In woman with favorable cervix at or near term labor should be induced with oxytocin drip or with prostaglandin. Pregnancy should not be allowed to continue beyond term. In women with mild pre-eclampsia remote from term pregnancy is allowed to continue till 37 weeks, under strict monitoring, for better fetal survival.

Between 34 to 37 weeks of pregnancy induction of labor is indicated in patients with IUGR, ruptured membrane or in anticipation of fetal jeopardy, evident from monitoring procedures. During the period of observation induction is carried out in patients completing 40 weeks of gestation or after 37 weeks with favourable cervix and when there appears signs of worsening of maternal and fetal condition.

For evaluation of fetal condition following are important

- Daily fetal movement count.