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Gestational hypertension and preeclampsia for the practicing clinician

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Abstract

Hypertensive disorders of pregnancy is one of the leading causes of maternal morbidity and mortality. In this article, the definition, classification, and pathophysiology of the different forms of HDP and the management is discussed.

Key words: pre-eclampsia, eclampsia, hypertensive disorders in pregnancy

Introduction

Hypertension in pregnancy is defined as persistently elevated systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or if previous blood pressure is known 20 mmHg rise in systolic blood pressure or 10 mmHg in diastolic blood pressure. When managing pregnant patients with hypertension, blood pressure has to be measured accurately (Box 1).

Gestational hypertension is defined as the new onset of hypertension after 20 weeks gestation without any maternal or fetal features of preeclampsia, followed by the return of blood pressure to normal within 3 months postpartum. Preeclampsia is a hypertensive disorder in pregnancy characterized by cytokine mediated endotheilial damage leading to placental malperfusion and maternal multi-organ involvement. Preeclampsia is associated with increased risk for developing chronic diseases such as hypertension, coronary heart disease, and stroke in later life for the mother.

Box 1. Measurement of blood pressure in pregnancy

- Should be measured at rest
- Measured in left lateral or seated position using the appropriate cuff size
- Measurement should be confirmed by repeated readings
- BP measurement should be repeated in at least 4 hours

Classification and diagnosis of preeclampsia

Preeclampsia is classified based on gestational age by the International Society for the Study of Hypertension in Pregnancy (ISSHP)[1] into preterm (delivery <37 weeks of gestation), the term (delivery ≥37 weeks of gestation), and postpartum pre-eclampsia.[2]

The criteria to diagnose preeclampsia has undergone a series of changes to include both maternal and fetal factors (Box 2).[3] Proteinuria is evaluated by either a urine dipstick result ≥2+, a 24-hour urine collection sample value of ≥300 mg, or a urine protein to creatinine ratio of 0.3mg/dl or greater. Hematological manifestations include thrombocytopenia, defined as a platelet count <150 x10^9. Other organs affected could be the liver and kidney. Although elevated blood pressure is found, it may not be present in every case and proteinuria might not be present in all patients.

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Box 2. Diagnosis of pre-eclampsia

1. **Pre-eclampsia (de novo)** is gestational hypertension accompanied by one or more of the following new-onset conditions at ≥20 weeks' gestation:

a) Proteinuria

b) Other maternal end-organ dysfunction, including:

- Neurological complications (e.g., eclampsia, altered mental status, blindness, stroke, clonus, severe headaches, or persistent visual scotomata)
- Pulmonary oedema
- Haematological complications (e.g., platelet count <150 x10^9, DIC, haemolysis)
- Acute kidney injury (AKI) (serum creatinine ≥90 ≥mol/L or ≥1 mg/dL)
- Liver involvement (e.g., elevated transaminases such as ALT or AST >40 IU/L) with or without right upper quadrant or epigastric abdominal pain)

c) Uteroplacental dysfunction (e.g., placental abruption, angiogenic imbalance, fetal growth restriction, abnormal umbilical artery doppler waveform analysis, or intrauterine fetal death).

2. **Pre-eclampsia (Superimposed on chronic hypertension)**
Among women with chronic hypertension, development of new proteinuria, another maternal organ dysfunction(s), or evidence of uteroplacental dysfunction (as above).

Screening for preeclampsia

There are risk factors that may help in identifying women who are at increased risk of developing preeclampsia.[4] (Box 3)

Box 3. Risk factors for developing preeclampsia

Factors identified as "high risk" for developing preeclampsia (one or more risk factors)

- Previous hypertensive disorder (before pregnancy)
- Chronic kidney disease or kidney impairment
- Multifoetal gestation
- Preexisting chronic hypertension
- Preexisting diabetes mellitus
- Autoimmune disorders (SLE, antiphospholipid syndrome)

Factors identified as "moderate risk" **for developing preeclampsia** (two or more risk factors)

- Advanced maternal age (>40years)
- Obesity (BMI ≥35)
- Nulliparity
- Family history of preeclampsia
- Interpregnancy interval of ten or more years
- Conception through assiated reproductive technology
- Systolic blood pressure >130 mmHg and/or diastolic blood pressure > 80 mmHg

Though the above risk factors are taken into consideration when determining the need for prevention of preeclampsia, the best method to predict preeclampsia would be to use an individualized algorithm.[5]

Predicting preeclampsia

Circulating angiogenic factors such as soluble fms-like tyrosine kinase 1 (sFlt-1) and placental growth factor (PlGF) have been discussed as biomarkers that can predict preeclampsia. Both these molecules are mainly produced in the placenta and are indicators of placental health. The use of the sFlt-1/PlGF ratio in diagnosing preeclampsia, determining fetal outcomes, severity of disease, and timing of birth is not recommended at present. Many major international guidelines suggest the use of the ratio in combination with a standard clinical assessment to help rule out proteinuric pre-eclampsia or pre-eclampsia requiring delivery within the next 7 (for the sFlt-1/PlGF ratio) or 14 days (for Triage PlGF), in women with suspected pre-eclampsia between 20 and 34 + 6 weeks gestation.[3]

Preventing preeclampsia

Aspirin at 150mg daily from 12 weeks to 36 weeks is recommended.[3] The use of aspirin was supported by many studies including the Aspirin for Evidence-Based PREeclampsia (ASPRE) prevention trial. The ASPRE is a multicentre, randomized, double-blind placebo-controlled trial of 1,776 women with pre-eclampsia.[6]

The role of calcium supplementation in the prevention of pre-eclampsia is well documented. A meta-analysis of 13 trials including 15,730 women published in the Cochrane database and several other metanalysis revealed a significant reduction in preeclampsia with calcium supplementation especially in patients with low calcium intake.[7,8]

The role of exercise in the prevention of preeclampsia has been documented. A meta-analysis of 27 trials found that exercise of at least 260 metabolic equivalents of task minutes/week reduced the development of pre-eclampsia by 25%.[9]

At present there is insufficient evidence to demonstrate the effectiveness of vitamins C and E, fish oil, garlic supplementation, vitamin D, folic acid, or sodium restriction for reducing the risk of pre-eclampsia.[10]

Management

The management of hypertension is crucial. Hypertension typically worsens with gestation. Severe hypertension (≥160/110 mmHg) may lead to intracerebral hemorrhage, eclampsia, and placental abruption. Treatment aims to reduce blood pressure to a target range of 140-155/90-105 mmHg.[11] This is considered an emergency and protocol-based management is advised depending on facilities available.[4] Medications commonly used in the treatment of severe hypertension include intravenous labetalol, intravenous hydralazine, or oral immediate-release nifedipine. Seizure prophylaxis in patients with severe pre-eclampsia is done using intravenous magnesium sulfate therapy.

Mild to moderate hypertension should be managed with medication to keep the blood pressure 130-138 mmHg/80-88mmHg. Oral medications used in pregnancy include methyldopa, labetalol, and nifedipine. These agents are typically available in private and state-sector hospitals in the country. Patients may complain of severe headaches and ankle oedema with nifedepine. Labetalol is contraindicated in asthma. Methyldopa, a slow-acting drug compared to the above two drugs causes peak results at 72 hours. Methyldopa causes lethargy and drowsiness and may worsen depression.[12]

Antepartum management and timing of delivery in preeclampsia

The definite treatment of preeclampsia is delivery. The timing should be guided by fetal and maternal factors. The decision should be a collective decision between the obstetrician, physician, neonatologist, and the patient. The well-being of the fetus plays a major role in determining the timing of the delivery. Fetal evaluation should include ultrasonography of the amniotic fluid index, estimated fetal weight, and antenatal testing. Adverse factors in the fetus includes sustained reversed end-diastolic flow of the umbilical artery. Continuing pregnancy until 37 weeks is carried out while closely monitoring the pregnant mother and the fetus in patients with either well-controlled gestational hypertension or preeclampsia without severe features in the setting of normal antepartum testing. Patients with preeclampsia with severe features at or beyond 34 0/7 weeks gestation undergo delivery after maternal stabilization. Delivery before 34 0/7 weeks gestation, if indicated, should be supported by the administration of antenatal steroids for fetal lung maturation.

The mode of delivery depends on maternal and fetal factors. In severe pre-eclampsia, the need for urgent delivery has increased the risk of cesarean sections, however, if delivery can be achieved in a reasonable time frame vaginal delivery should be encouraged. Induction of labour and risk of emergency LSCS is common with pregnancies complicated with hypertension in pregnancy.

Maternal factors that favour delivery vs expectant management include uncontrolled blood pressure, continued headaches/visual disturbance or right upper quadrant/epigastric pain despite repeated medical management, myocardial infarction, stroke, pulmonary edema, HELLP syndrome, eclampsia, or suspicion of placental abruption or bleeding with no other diagnosis.

Magnesium sulphate is the drug of choice for the prevention and treatment of eclampsia. It is also used as a neuroprotective agent for the fetus when delivery is anticipated before ≥33+6 weeks.[13]

Long term management

Patients who have had preeclampsia are at increased risk of cardiovascular diseases. All major guidelines suggest cardiovascular risk screening in patients with preeclampsia. Patients who have had hypertensive disorders in pregnancy have a 2-5 times higher risk of hypertension in later life, compared to patients with no hypertensive disorders during pregnancy.[14]

Patients with preeclampsia are at risk of ischemic stroke, chronic kidney disease, and vascular dementia.[15] The patients with preeclampsia need regular follow-up, continuous screening for cardiovascular diseases, and lifestyle modifications.

Infants born to mothers with preeclampsia have a higher possibility of having adverse neuro developmental outcomes, increased risk for CVD higher blood pressure, and increased risk of stroke.[16]

Conclusion

Early prediction and prevention are needed for the management of pre-eclampsia. As PE could result in maternal and fetal risks early identification and proper management are crucial.

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Key points

- Hypertension should be defined as a systolic BP (SBP) ≥140 mmHg and/or (DBP) ≥90 mmHg, based on an average of at least two office measurements.
- Low-dose aspirin is recommended to be taken at preferably before 16 weeks and discontinued by 36 weeks for the prevention of preeclampsia after risk stratification.
- Severe hypertension in pregnancy (i.e., SBP ≥160 mmHg or DBP ≥110 mmHg) requires urgent antihypertensive therapy.
- The decision to deliver in preeclampsia depends on maternal and fetal well-being.
- Annual medical review following hypertensive pregnancy is recommended after the initial postpartum review as preeclampsia confers a higher risk of cardiovascular diseases to the mother.

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