REVIEW ARTICLE

Pattern of Treatment Approaches for Preeclampsia During Pregnancy

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Abstract

Preeclampsia is a hypertensive disorder that is now predictable during its advanced stage of severity and that may cause risk to the life of the mother and fetus. Preeclampsia is a condition categorized by increase in systolic blood pressure from ≥140 mmHg and diastolic blood pressure from ≥90 mmHg on checking at least two times within 4 hours after 20 weeks of pregnancy for those women previously having normal blood pressure and other parameters like with or without proteinuria ≥0.3 gm test in urine within 24 hour or the ratio of protein /creatinine more than 0.3 mg/dl and thrombocytopenia, changes in renal functioning, hepatic dysfunction. In developing countries, preeclampsia is defined as a chief cause of maternal and perinatal mortality rates. Preeclampsia may be responsible for causing premature cardiovascular diseases, such as chronic hypertension, ischemic heart disease, and stroke to the mother or pregnant women, whereas children born from women having preeclampsia are at increased risk of such diseases like stroke, congestive heart failure, and metabolic disorder in adult life. For the management of preeclampsia, major factors that are necessary to maintain is screening of women at high risk and prevention from reoccurrence. Three groups of current preeclampsia management are (Preventive measures of preeclampsia, Primary examination, and management).

Keywords: Preeclampsia, Thrombocytopenia, Hypertensive disorder, Maternal mortality.
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Introduction

Date from 2200 BC German authors, the first report reference for eclampsia detected in Egypt. Eclampsia is a Greek word that originates from "eclampsia," which means "bright light." Earlier eclampsia was a disease categorized by sudden seizures, late pregnancy, and termination at delivery. Late 19th century, Experts found that glomerulonephritis is characterized by proteinuria.[1] The childbearing women were searched for seizures and Urinary alterations, which show evidence of proteinuria in them. Increased blood pressure levels were observed in these women with the help of the blood pressure measuring method. Earlier, the information about proteinuria and arterial high blood pressure being responsible for the preceding onset of seizures is not available sufficiently. So, "preeclampsia," a hypertensive disorder, was now predictable during its advanced stage of severity, and that may cause risk to the life of the mother and fetus.[2]

Preeclampsia is a condition categorized by increase in systolic blood pressure from ≥140 mmHg and diastolic blood pressure from ≥90 mmHg on checking at least two times within 4 hours after 20 weeks of pregnancy for those women previously having normal blood pressure and other parameters like with or without proteinuria ≥0.3 gm test in urine within 24 hour or the ratio of protein /creatinine more than 0.3 mg/dl and thrombocytopenia, changes in renal functioning, hepatic dysfunction.[3] The ranges for blood pressure from mild to severe is considered by the National High Blood Pressure Education Program Working Group Report on high blood pressure in pregnancy guidelines, are normal range of blood pressure is 140/90 mmHg, mild hypertension is 140/90 to 150/109 mmHg and severe hypertension >160/ >110 mmHg. Severe preeclampsia is defined as increased levels of blood pressure and proteinuria or any signal for end-organ damage. Preeclampsia can be deadly for both mother and child.[4] In developing countries, preeclampsia is defined as a chief cause of maternal and perinatal mortality rate. Preeclampsia may be responsible for causing premature cardiovascular disease, such as chronic hypertension, ischemic heart disease, and stroke in the mother or pregnant women, whereas child born from women having preeclampsia are at increased risk of such diseases like stroke, congestive heart failure, and metabolic disorder in adult life. Delivery is the only healthful treatment in preeclampsia. Continual management is essential for reducing maternal and fetal complications or maintaining the risk-benefit relation of induced preterm delivery. For the management of preeclampsia, major factors that are necessary to maintain are screening of women at high risk and prevention from reoccurrence.[5]

Preeclampsia Management Guidelines

Three groups of current preeclampsia management are

- Preventive measures of preeclampsia,
- Primary examination
- Management

Some parameters like high blood pressure, kidney disorders or Asherson's syndrome may rule out women at high risk of preeclampsia.[6] Management may include cessation of smoking habit, change in dietary supplements and also required maintenance of medicine for improvement in pre-existing kidney disorders and cessation of teratogenic agents like warfarin, ACE inhibitors (angiotensin-converting enzyme inhibitor) and others that cause potential risk to a fetus. Required parameters for detection of preeclampsia are kidney function test, liver functioning, electrolyte balance and measurement of blood pressure. NICE guidelines suggest low-dose aspirin should prescribed before 12 weeks of pregnancy to 36 weeks of pregnancy to those women who are at high risk for developing preeclampsia. Those women having low levels of calcium in their diet require calcium supplementation of dose ≥1 g/day and it is also effective in reducing the chances of developing preeclampsia.[7]

Antenatal care and Intrapartum care

Multi-disciplinary process is followed to manage preeclampsia that may include the obstetrician, midwife, anesthetic, physician, hematologist and pediatrician team as necessary.8

Antihypertensive drugs

Antihypertensive drugs are the best treatment to choose for the reduction and maintenance of systolic blood pressure range to below 150 mmHg and diastolic blood pressure range between 80 to 100 mmHg, as given in Table 1. Blood pressure may drop shortly on the commencement of treatment the blood pressure may get drop shortly and regular dose maintenance is necessary to reduce the cause of fetal distress that may affected by uteroplacental circulation.[9]

Some antihypertensive drugs are methyldopa, labetalol, and calcium channel blockers like nifedipine are used as prophylaxis for preeclampsia. Intravenous medication may also be effective in the treatment of hypertensive disorders. Labetalol is a superior choice among antihypertensive agents, and it belongs to the mixed alpha/beta adrenergic antagonist class. Its two oral doses should be recommended. Take at least 30-minute lap for the administration of the second dose after the first dose is administered. Medication should be administered intravenously on the failure of oral treatment to produce an effect or have less tolerability. Labetalol is contraindicated in patients with bronchial asthma and substitutes used are atenolol, metoprolol, methyldopa and nifedipine (contraindicated before 20 weeks of gestation). Antihypertensive agents are warned in cardiac disease. Hydralazine, a muscle relaxant, is the second best choice for antihypertensive agents. A bolus infusion on every 5 minutes needs regular measurement of blood pressure.

Table 1: Antihypertensive agents with dose

Drug	*Dose*
First-line antihypertensive drugs	
Methyldopa	0.5–3 gm/day, PO/BD
Labetalol	200–1200 mg/day, PO/BD or TDS 20–40 mg, Intravenously
Second line antihypertensive drugs	
Nifedipine	10–30 mg by oral route
Verapamil	80 mg ,TDS, by oral route
Clonidine	0.1–0.6 mg/day, BD
Alternative choice	
Hydralazine	50–300 mg/day, BD, TDS
Prazosin	0.5–5 mg
Oxprenolol (beta blocker)	20–160 mg
Diaz-oxide	30–50 mg, on every 5–15 minutes intravenously (Podymow T et al. 2011, Lowe SA et al. 2009)

In the management of severe preeclampsia, regular fetal monitoring is necessary.[10]

Methyldopa is often suggested for mild to moderate hypertensive disorder (National High Blood Pressure Education Program. 2000). Drowsiness is a common side effect on methyldopa and May be more problematic for women are not hospitalized as compared to hospitalized women. Methyldopa may also be responsible for causing depression, a threat not correctly calculated during the period of gestation. Substitutes for methyldopa are calcium antagonists and labetalol. Atenolol should be escaped to reduce the circumstances of fetal growth restriction. ACE inhibitors (angiotensin-converting enzyme inhibitors) and angiotensin receptor antagonists are both contraindicated in pregnancy.[11]

Fetal monitoring

For the elimination of IUGR risk, continual detection of fetal growth, amniotic fluid level and umbilical sonography are required to be done at the initial stage of preeclampsia and performing these tests every 2 weeks is necessary to maintain pregnancy conservatively.[12]

Delivery

The only cure for preeclampsia is to deliver a baby and this decision should take on the mother's stabilize condition. Mild or moderate preeclampsia condition, increases need to deliver baby between 34 to 37 weeks period of gestation by considering the mother and fetus condition, risk factors and proper availability of facilities for a neonatal intensive care unit. On the developing condition of severe preeclampsia, early delivery becomes a priority over treatment or fetal wellbeing.[13,14]

The choice for deliver a baby whether vaginal or cesarean

is depends upon the laboratory parameters. Delivery is necessary when there is an incident of fetal suffering, problem in maintaining the mother's blood pressure, eclampsia, sinking biological chemistry parameters or suffering of the mother. Cesarean section is not usually considered for delivery, but it may be preferred at the period of gestation less than 32 weeks. Vaginal delivery can be considered after 34 weeks of gestation because of PGE2 and PGF2a, which are vaginal prostaglandins and it may appreciate the delivery properly. Maintenance of antihypertensive medication or therapy should be necessary at the time of detection and childbirth. During labor, the therapy goal is to reduce or prevent seizures and to maintain blood pressure.[15]

Fluid management

Management for accurate input/output fluid balance is necessary because iatrogenic fluid overload is responsible for maternal death in preeclampsia. The level of plasma volume is decreased and chances of pulmonary edema are increased in the preeclampsia patient so close monitoring for preeclampsia patient is necessary. The total fluid input should limit 80 mL/hour or approximately about 1-mL/kg/hour. High concentration of oxytocin used as a part of total fluid input when required. Low urine output (oliguria) is responsible for the early delivery. In order to avoid early delivery oliguria should not precipitate. Diuretics are used for women having confirmation for pulmonary edema.[16]

Anticonvulsant therapy

In severe preeclampsia management, magnesium sulfate (MgSO4) is a therapeutically effective agent and also control seizures. Magnesium sulfate indicated to be replaced by other agents are benzodiazepines (diazepam), anticonvulsant agent (phenytoin), or combination of chlorpromazine, promethazine, and pethidine. For reduction in maternal and neonatal complications due to eclampsia, magnesium sulfate is a therapeutically active agent. The First loading dose 4g of magnesium sulfate (MgSO4) is administered intravenously over 15 to 20 minutes and the dose 2g of magnesium sulfate on reoccurrence of seizures and further, the maintenance dose of 1 g/hour should administered for 24 hours after childbirth. MgSO4 also speed up the lung development of baby. Due to the risk of organ failure, detection should be necessary for magnesium sulfate therapy in ICU (intensive care unit). According to Glasgow score of 15 on each 4 hour observation for deep tendon reflexes, rate of breathing less than 12 minutes, urine outflow more than 30 mL/hour are necessary. The overdose of MgSO4 causes immobility, numbness, atrioventricular block and decreased rate of breathing. The overdose of magnesium sulfate (MgSO4) required the termination of the infusion, and administer injection of calcium gluconate, and the level of magnesium in the blood should be measured. On absence of biceps reflex and decreased rate of breathing required termination of magnesium sulfate treatment.[17]

Corticosteroids

Corticosteroids play important in maintaining pregnancy consequences and are responsible for the formation of fetal lungs or lung maturation. It acts as a neuroprotective agent for preterm fetuses. Corticosteroid therapy is mainly useful in preterm baby for reducing breathing problems in infants and help in the proper growth of infant fetal health outcomes. The physician prescribes corticosteroids between 24 and 36 weeks of pregnancy and for those women having their deliveries near next week. Corticosteroid therapy used in pregnancy are betamethasone intramuscularly and dexamethasone intravenously. Both betamethasone and dexamethasone have same level of effectiveness.[18]

Antiplatelet therapy

Acetylsalicylic acid is a cyclo-oxygenase inhibitor having anti-inflammatory, antiplatelet effects. Aspirin low dose is only effective therapy for the treatment of preeclampsia. WHO recommends a low dose of aspirin in pregnancy from 12th week to till delivery and prescribes low dose of aspirin is 75–100 mg [National Institute for Health and Care Excellence (NICE) 2015, WHO. 2013]. The Pregnancy Task Force Report for hypertension is issued by ACOG in, which it recommended that aspirin low dose should be prescribed daily in the beginning of the 1st trimester of pregnancy in women with chance of preterm delivery or previous pregnancy associated with the history of preeclampsia as given in Table 2. Aspirin low dose, which is 81mg/day should be given as prophylaxis for patients with high risk of pregnancy between 12 weeks and 28 weeks of period of gestation which should be continued till delivery. Studies confirmed the importance of low-dose aspirin is suitable for high-risk of preeclampsia in pregnant women, preterm preeclampsia and the incidence of severe preeclampsia. The dose of aspirin should be more than 100 mg and also prescribed after 16th week of pregnancy is also valuable for the treatment of preeclampsia.[19]

Prenatal care

Ensuing delivery, the movement of extracellular fluid increases the intracellular volume and subsequently increases the pressure in the blood. The fluid change increases the chance of pulmonary edema, cerebral edema and eclampsia.[20]

During pregnancy prenatal follow up is necessary in pregnant women who suffer from hypertension to ensure the proper solution of high blood pressure. During their pregnancy, those women have suffered from preeclampsia are to be guided that they are at increased risk of developing cardiovascular and renal disease later in life. Patient discharge should be done by daily close monitoring of blood pressure.[21]

The blood pressure should be <160/110mmHg for prevention of brain injury, b-blockers, calcium blockers and ACE inhibitors should be used for management. In postpartum period use of methyldopa is avoided due to

Table 2: Doses, routes of antiplatelet drugs

Betamethasone	*12 g IM, 2 doses, 24-hour interval*
Dexamethasone	10 mg IV, 2 doses, 24-hour interval.

their potential cause depression and psychosis. Women are discharged from hospital when their blood pressure is 140/90 mmHg or less with or without treatment and the result of blood test normal or improved. On daily or alternate days bases the blood pressure in the hospital should checked till 2nd weeks of postpartum. Antihypertensive therapy will carry on till the blood pressure reduced down 130/80 mm of Hg.[22]

Those pregnant women diagnosed with severe preeclampsia have a chance of recurrence of preeclampsia in their next pregnancy. Pregnant women who had early onset of preeclampsia they need to undergo test of the antiphospholipid syndrome. It is necessary to consult the results of preeclampsia with a physician for future pregnancy. Usually, hypertension and/or proteinuria are cured within 6th week postpartum.[23]

For all those women offered with pew-conceptual counseling essential for high blood pressure, as definite antihypertensive medications such as ACE inhibitors are teratogenic and altered pre-conceptually.

Conclusion

Preeclampsia is a condition that categorized by increase in systolic blood pressure from 140 mmHg and diastolic blood pressure range from 80 to 100 mm Hg on checking at least two times within 4 hours after 20 weeks of pregnancy for those women previously having normal blood pressure and other parameters like with or without proteinuria 0.3 gm test in urine within 24 hours or the ratio of protein /creatinine more than 0.3 mg/dl and thrombocytopenia, changes in renal functioning, hepatic dysfunction. The Pregnancy Task Force Report for hypertension is issued by ACOG in which it recommended the aspirin low dose should be prescribed daily in the beginning of the 1st trimester of pregnancy in women with a chance of preterm delivery or previous pregnancy associated with the history of preimperial hypertension. Prenatal follow-up is necessary in women who had early onset of pregnancy. They need to undergo test of the antiphospholipid syndrome.

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