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Original Research Paper

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MANAGEMENT OF PRE-ECLAMPSIA: ISSUES FOR ANAESTHETISTS

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ABSTRACT The role of anaesthetist for anaesthetic management for preeclamsia is very crucial. Anaesthetist's responsibility starts before the surgery at the moment of stabilizing patient's hemodynamic status and guiding to an obstetrician about administration of antihypertensives and seizure prophylaxis. The anaesthetic problems in these may be due to the effects on the cardiovascular, respiratory, neurologic, renal, haematologic, hepatic and uteroplacental systems. Labetolol, hydralazine, diazoxide and nifedipine is considered as the most common used drugs. Magnesium sulphate is the most effective agent for seizure prophylaxis. Platelet transfusion threshold is determined as 50000/mm3 in acutely bleeding patient. Cerebral haemorrhage remains the commonest cause of death in this group and hence rapid and effective treatment of hypertension to prevent haemorrhagic stroke is needed in these patients. As aetiology is largely unknown, preventative measures and screening tools are lacking and management is directed at the control of clinical manifestations. Delivery remains the only definitive treatment.

KEYWORDS : Hypertensive disorders of pregnancy, pre-eclampsia, eclampsia, HELLP syndrome, magnesium sulphate

INTRODUCTION

Preeclampsia is a multisystem disorder of unknown etiology characterized by development of hypertension to the extent of 140/90 mm Hg or more with proteinuria after the 20th week in a previously normotensive and nonproteinuric woman. The disease is responsible for considerable morbidity and mortality, complicating 5–8% of pregnancies. Deaths are due to intracranial haemorrhage and cerebral infarction, acute pulmonary oedema, respiratory failure and hepatic failure or rupture. Severe maternal complications include antepartum haemorrhage due to placental abruption, eclampsia, cerebrovascular accidents, organ failure and disseminated intravascular coagulation.

The most recent revised classification for hypertensive disorders in pregnancy is by the International Society for the Study of Hypertension in Pregnancy (ISSHP) in 2014:

1. Chronic hypertension
2. Gestational hypertension
3. Pre-eclampsia – de novo or superimposed on chronic hypertension
4. White coat hypertension.

Literature search and selection

We performed an electronic search in Google Scholar, PubMed and Cochrane databases for original and review articles on HDP from 1998 to 2018. The search terms include 'hypertensive disorders of pregnancy', 'pre-eclampsia', 'eclampsia' and 'pregnancy-induced hypertension'. Only full text articles were reviewed. The current evidence and guidelines around HDPs are summarised.

DIAGNOSTIC CRITERIA OF PREECLAMPSIA

Hypertension: An absolute rise of blood pressure of at least 140/90 mm Hg, if the previous blood pressure is not known or a rise in systolic pressure of at least 30 mm Hg, or a rise in diastolic pressure of at least 15 mm Hg over the previously known blood pressure is called pregnancy-induced hypertension.

Edema: Demonstration of pitting edema over the ankles after 12 hours bed rest or rapid gain in weight of more than 1 lb a week or more than 5 lb a month in the later months of pregnancy may be the earliest evidence of preeclampsia. However, some amount of edema is common (physiological) in a normal pregnancy.

Proteinuria: Presence of total protein in 24 hours urine of more than 0.3 g or more than or equal to 2+ (1.0 g/L) on at least two random clean-catch urine samples tested more than or equal to 4 hours apart in the absence of urinary tract infection is considered significant.

Test for protein in urine by multiple reagent strip (dipstick) as follows: Trace = 0.1 g/L; 1+ = 0.3 g/L; 2+ = 1.0 g/L; 3+ = 3.0 g/L; 4+ = 10.0 g/L.

INCIDENCE: The incidence of preeclampsia in hospital practice varies widely from 5% to 15%. The incidence in primigravidae is about 10% and in multigravidae 5%. Imperfect documentation and lack of uniformity in the diagnostic criteria are the responsible factors in variation of its frequency.

Aetiopathogenesis-

The basic concepts of the aetiology of HDPs could be that these women are exposed to chorionic villi for the first time (in primiparity), exposed to a superabundance of chorionic villi (as with twins or hydatidiform mole), have a pre-existing vascular disease and are genetically predisposed to hypertension developing during pregnancy. Sibai et al. have listed the currently plausible potential causes as an abnormal trophoblastic invasion of uterine vessels, immunological intolerance between maternal and foeto-placental tissues, maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy, dietary deficiencies and genetic influences.

In normal implantation, endovascular trophoblasts invade the uterine spiral arteries. In pre-eclampsia, there is incomplete trophoblastic invasion; the magnitude of defective trophoblastic invasion of the spiral arteries correlated with the

severity of the hypertensive disorder. The nitric oxide system is also affected in HDP. Pre-eclampsia is associated with decreased endothelial nitric oxide synthase expression, which increases cell permeability. There may be life-threatening thrombocytopaenia caused by platelet activation, aggregation and consumption. This may persist up to 5 days after delivery.

There may also be neonatal thrombocytopaenia. Dietary deficiencies and excesses have been blamed as the cause of eclampsia. Supplementation with various elements such as zinc, calcium, and magnesium has been suggested to prevent pre-eclampsia. Obesity is a potent risk factor for pre-eclampsia. Hereditary hypertension is linked to pre-eclampsia; preclampsia–eclampsia is highly heritable in sisters, daughters, granddaughters and daughters-in-law and is hence thought to have a congenital/familial component. There is also a 60% concordance in monozygotic female twin pairs, and HLA-DR4 has been thought to be linked to pre-eclampsia.

MANAGEMENT OF HDP

GENERAL MANAGEMENT (MEDICAL AND NURSING)

Supportive care: (i) to prevent serious maternal injury from fall, (ii) prevent aspiration, (iii) to maintain airway and (iv) to ensure oxygenation.

Patient is kept in a railed cot and a tongue blade is inserted between the teeth. She is kept in the lateral decubitus position to avoid aspiration. Vomitus and oral secretions are removed by frequent suctioning, oxygenation is maintained through a face mask (8–10 L/minute) to prevent respiratory acidosis.

Detailed history is to be taken from the relatives, relevant to the diagnosis of eclampsia, duration of pregnancy, number of fits and nature of medication administered outside.

Examination: Once the patient is stabilized, a thorough but quick general, abdominal and vaginal examinations are made. A self-retaining catheter is introduced and the urine is tested for protein. The continuous drainage facilitates measurement of the urinary output and periodic urine analysis.

Monitoring: Half hourly pulse, respiration rate and blood pressure are recorded. Hourly urinary output is to be noted. If undelivered, the uterus should be palpated at regular intervals to detect the progress of labour and the fetal heart rate is to be monitored. Immediately after a convulsion, fetal bradycardia is common.

Fluid balance: Crystalloid solution (Ringer's solution) is started as a first choice. Total fluids should not exceed the previous 24 hours urinary output plus 1000 mL (insensible loss through lungs and skin). Normally, it should not exceed 2 litres in 24 hours. Infusion of balanced salt solution should be at the rate of 1 mL/kg/h.

Antibiotic: To prevent infection, Ceftriaxone 1 g IV twice daily is given.

When the diagnosis is preeclampsia, the gestational age, as well as the level of BP, influences the use of antihypertensive therapy. At term, women with preeclampsia are likely to be delivered, treatment of hypertension (unless severe) can be delayed, and BP can be reevaluated postpartum. If preeclampsia develops remote from term, and expectant management is undertaken, treatment of severe hypertension is initiated, and BP can usually be safely lowered to 140/90 mm Hg with oral medications as methyldopa, labetalol, nifedipine or isradipine, and some -adrenoceptor blockers (metoprolol, pindolol, and propranolol) and low dose diazoxide.

Sibai et al. evaluated the effectiveness of labetalol, an 1 and non-selective -blocker), in the treatment of severe HDP in 200 nulliparous patients at 26–35 weeks gestation. In the women given labetalol, there were significantly lower mean BPs, and no differences in mean pregnancy prolongation, gestational age at delivery and birth-weight from normal. The caesarean delivery rates and the number of infants admitted to special care nurseries were similar. The treatment regimen for labetalol is a 20-mg intravenous bolus dose followed by 40 mg if not effective within 20 min, followed by 80 mg every 20 min up to a maximum dose of 300 mg.

Hydralazine is also used to control severe hypertension; it is remarkably effective in the prevention of cerebral haemorrhage. It is indicated if the systolic pressure >160 mmHg or the diastolic pressure >105 mmHg. It is administered at 5–10 mg doses at 15–20 min intervals until a satisfactory response is achieved.

Nifedipine, 10 mg oral to be repeated in 30 min, has also been used. Compared with hydralazine, fewer doses were required to achieve BP control without increased adverse effects. It has potent and rapid antihypertensive effects, and some women develop worrisome hypotension.

Sodium nitroprusside is not recommended unless there is no response to hydralazine, labetalol or nifedipine. A continuous infusion is begun with a dose of 0.25 g/kg/min increased as necessary to 5 g/kg/min. Foetal cyanide toxicity may occur after 4 h.

Treatment and prevention of seizures (eclampsia)

Magnesium sulphate is an effective anticonvulsant agent in severe pre-eclampsia and eclampsia, without producing central nervous system depression in either the mother or the infant. It is usually given during labour and for 24 h postpartum, as this period is the most likely time for convulsion to develop. It is not given to treat hypertension. Magnesium is cleared by renal excretion. Magnesium intoxication is avoided by ensuring that the urine output is adequate, the patellar or biceps reflex is present and that there is no respiratory depression. Plasma magnesium levels must be checked periodically.

Eclamptic convulsions are prevented by plasma magnesium levels maintained at 4–7 mEq/L (4.8–8.4 mg/dL or 2.0–3.5 mmol/L). To establish a prompt therapeutic level, the initial intravenous infusion of 4–6 g is followed by continuous infusion at 2–3 g/h, and the initial intramuscular injection of 10 g is followed by 5 g every 4 h. Observe for toxic symptoms. As the plasma magnesium level reaches 10 mEq/L, patellar reflexes disappear – this sign serves to warn of impending magnesium toxicity. As the plasma levels rise above 10 mEq/L, respiratory depression develops. At plasma levels of 12 mEq/L or more, respiratory paralysis and arrest follow. For mild-to-moderate respiratory depression, treatment is with calcium gluconate, 1 g and withholding further magnesium sulphate. The effects of IV calcium may be short lived. Severe respiratory depression and arrest have to be treated with prompt tracheal intubation and mechanical ventilation.

Other regimens are: (1) Lytic cocktail (Menon 1961) using chlorpromazine, promethazine and pethidine. (2) Diazepam (Lean) and (3) Phenytoin.

Compared to other regimes, magnesium sulfate has got the following benefits:

(i) it controls fits effectively without any depression effect to the mother or the infant. (ii) reduced risk of recurrent convulsions (9%) (iii) significantly reduced maternal death rate (3%) and (iv) reduced perinatal mortality rate.

Status eclampticus: Thiopentone sodium 0.5 g dissolved in 20 mL of 5% dextrose is given intravenously very slowly. The procedure should be supervised by an expert anesthetist. If the procedure fails, use of complete anesthesia, muscle relaxant and assisted ventilation may be employed. In unresponsive cases, cesarean section in ideal surroundings may be a lifesaving attempt.

Fluid therapy

Routine administration should be with lactated ringer solution at the rate of 60 ≤-125 mL/h (1–2 mL/kg/h), unless unusual fluid loss from vomiting, diarrhoea, diaphoresis or excessive blood loss at delivery occur. Haemo-concentration and reduced central venous and pulmonary capillary wedge pressures require attempts to expand the blood volume to relieve vasospasm and to reverse organ deterioration. Infusion of large fluid volumes enhances the maldistribution of extravascular fluid and increase the risk of pulmonary and cerebral oedema. Invasive haemodynamic monitoring is required to prevent the serious complication of fluid overload, pulmonary oedema.

Labour analgesia

Epidural blockade is the preferred method of labour analgesia. It may obtund the sympathetic response to labour pain and thus limit blood pressure increases during labour. Severe pre-eclampsia is not a contraindication to epidural analgesia but should be avoided if there is a low and/or rapidly falling platelet count. Recommendations as to what is an acceptable platelet count for neuraxial blockade vary.

In general, neuraxial blockade is likely to be safe at platelet counts greater than 100 x 10-9/L and is generally not recommended below platelet counts of 50 x 10-9/L. However individual maternal risk factors and local resource issues are important when deciding on the most appropriate method of providing analgesia. In women with contraindications to regional blockade, analgesia should be provided by alternative means, such as patient controlled intravenous opioid analgesia.

Anaesthesia for caesarean birth

Neuraxial anaesthesia is the preferred anaesthetic technique for delivery by caesarean section (Level 1+). Single-shot spinal, combined-spinal epidural, and epidural anaesthesia have all been used effectively. There is no evidence that one technique has an advantage over the other.

Hypotension requiring vasopressor medication during neuraxial anaesthesia is less common in women with pre-eclampsia than in healthy women. If hypotension occurs, it may be successfully managed with titrated doses of intravenous ephedrine (3–5 mg bolus) or phenylephrine (50–100 μg bolus) [61, 67] (Level 1+).

The use of adrenaline-containing local anaesthetic solutions for epidural boluses to provide surgical anaesthesia appears to be safe, and is widely used to minimise systemic absorption of local anaesthetics. There has been a single case report of a hypertensive crisis with absorbed adrenaline, emphasising the need for close observation of these women.

General anaesthesia in women with pre-eclampsia- Intubation may be more difficult due to oedema of the upper airways and decreased pulmonary compliance may impair ventilation.

Indications for general anaesthesia:

Contraindication to regional blockade e.g. low platelets, coagulopathy Post-ictal patient with obtunded level of consciousness or in patient with recurrent seizures Presence of pulmonary oedema associated with hypoxia Patient refusal of a regional anaesthetic technique

The pressor response to laryngoscopy can lead to a dangerously high surge in blood pressure that may lead to intracranial haemorrhage. It is essential that measures to attenuate this response are undertaken prior to induction and extubation. Magnesium (0.5-1g bolus), labetalol (25-50mg bolus) and potent parenteral opioids (e.g. alfentanil 1-2mg bolus) have all been successfully used.

Antacid and antiemetic premedication (ranitidine and metoclopramide) should be administered prior to caesarean delivery and antihypertensive and anticonvulsive drugs should be continued perioperatively. If the woman has received magnesium sulphate, muscle relaxation must be carefully monitored since magnesium may prolong the action of neuromuscular blocking agents. The routine use of ergometrine and syntometrine is avoided due to their hypertensive propensity and syntocinon is advised. Nonsteroidal anti-inflammatory drugs should be withheld due to potential adverse effects on renal and platelet function. Paracetamol may need to be withheld if there is laboratory evidence of significant liver dysfunction.

Recovery

While many women will recover rapidly following delivery, close observation and monitoring is imperative since some may deteriorate and there is a risk of post-partum seizures in up to 44% of women with severe pre-eclampsia. Post-operative care should be provided on a maternity high dependency unit or intensive care unit as indicated. Careful attention to fluid balance, antihypertensive therapy and blood and biochemical status should be maintained. Magnesium sulphate is typically continued for 24 hours following delivery.

Post-partum review

Women with hypertensive disorders of pregnancy should be followed up. Antihypertensive medication may need stopping, changing or reducing in dose. Post-partum antihypertensive treatment may be required for 2-6 weeks after which it may be weaned off with careful review. Women who experience hypertension in their first pregnancy are at increased recurrence risk of 19% for gestational hypertension, 32% for pre-eclampsia, and 46% for pre-eclampsia superimposed on pre-existing chronic hypertension.

Monitorization Options

Blood pressure measurement should be done carefully and correctly. Intra-arterial blood pressure measurement enables continuous blood pressure recording, facilitates repeated blood sampling shows cardiac output by minimally invasive cardiac output monitors. Transthoracic echocardiography provides structural and functional information about cardiac performance, diastolic function, and responses to interventions.

American College of Obstetricians and Gynecologists (ACOG) listed invasive monitorization indications in obstetric patients as follows:

1. Septic patients with refractory hypotension and/or oliguria
2. Unexplained or refractory pulmonary edema or persistant oliguria
3. Gestational hypertension with pulmonary edema or oliguria
4. Cardiovascular decompansation intraoperatively
5. Massive blood or volume lost or replacement
6. ARDS
7. Shock with unknown etiology
8. New York Heart Association Class III or IV cardiac disease
9. Perioperative or peripartum coronary artery disease.

Acute Pulmonary Edema

Pulmonary edema refers to an excessive accumulation of fluid

in the pulmonary interstitial and alveolar spaces. It may develop in up to 2.9% of pregnancies complicated by preeclampsia. Oxygen supplementation either via non-invasive ventilation devices or intubation and ventilation are used depending on the severity of the respiratory compromise. Morphine sulphate should be administered intravenously at a dose of 2 to 5 mg to reduce the adrenergic vasoconstrictor stimuli to the pulmonary arteriolar and venous beds.

Furosemide administered intravenously to promote diuresis. Head elevation should also be used. Pulmonary edema may occur 30% of cases with preeclampsia in the antenatal period. In addition to the therapy discussed above, a multidisciplinary careful decision about delivery should be done with new-born specialists.

Oliguria and Acute Renal Failure

Oliguria in the postpartum period may occur in the partriurent who has normal renal functions. Steyn et al. assessed the effects of low dose dopamine for oliguria in severe eclampsia. It is suggested that dopamine should first be tested in non-pregnant women with very low urine output before it is considered for trials with pregnant women because of the potential for severe adverse effects if the dose is exceeded. Prerenal and intrarenal pathology (acute tubular necrosis) accounts for 83-90% of all cases of acute renal failure in preeclampsia. Renal damage secondary to these pathologic changes is seen most commonly in preeclampsia and usually resolves completely after delivery. The management of acute renal failure in the setting of preeclampsia should focus on reversible conditions as dehydration. Blood pressure control, correcting fluid and electrolyte imbalance, and maintaining adequate nutrition is supportive. Persistent acidemia, hyperkalemia, volume overload and uraemia are indications for renal replacement therapy.

Cerebral Hemorrhage and Stroke

Cerebral hemorrhage has been reported to be the most common cause of death in patients with eclampsia. Stroke is known to be the most common cause of death (45%) in women with HELLP syndrome who receive traditional nonsteroid obstetric and medical management. Hypertension may persist in the postpartum period. These patients deserve immediate and special attention in intensive care units and antihypertensive therapy to reduce their risk of such neurological events.

Postpartum Plasmapheresis in Severe Preeclampsia

Scwartz et al. reported a case of severe preeclampsia in which hemolysis and rapid platelet consumption persisted after delivery. Exchange plasmapheresis with fresh frozen plasma were begun on the eighth postpartum day, but the hemolysis and rapid platelet consumption did not begin to improve until the 12th postpartum day.

The authors proposed the use of plasmapheresis in highly selected cases of severe preeclampsia with hemolysis and thrombocytopenia that do not resolve after delivery. In 1986 fourteen cases of plasmapheresis with fresh frozen plasma for maternal indications in selected cases of preeclampsia and eclampsia were reviewed and the possible role of plasmapheresis in treating the selected cases is emphasized.

Martin et al. assessed the postpartum use of plasma exchange with fresh-frozen plasma in a group of seven women with severe preeclampsia-eclampsia and HELLP syndrome that persisted <72 hours after delivery. Within 48 hours of exchange plasmapheresis, they achieved a decreasing trend in lactate dehydrogenase levels and platelet counts increased 4.5 times after 72 hours.

Conclusion

HDP are common in India; various risk factors increase the occurrence. The basic management objectives should be facilitating the birth of an infant who subsequently thrives and complete restoration of health to the mother.

For patients with preeclampsia an anaesthesist should be aware of the following:

1. Preoperative assesment of the preeclamptic patient involves fluid balance hemodynamic situation, coagulation profile and careful airway examination.
2. Neuraxial anesthetic techniques, when feasible, are strongly preferred to general anesthesia for preeclamptic parturients.
3. Tracheal intubation may be difficult due to mucosal edema. Difficult airway management devices should be readied for intubation. Adequate sedation and analgesia is needed to control the stress response to intubation.
4. Emergence from anaesthesia should be handled carefully to avoid hypertension, aspiration and acute pulmonary edema.
5. Invasive monitoring for guiding successful fluid management are supportive.
6. Multiple organ failure can be prevented by obsevation of high risk severe preeclamptic patients in intensive care unit setting in antenatal and postnatal period.

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