**Name of journal: World Journal of Anesthesiology**

**ESPS Manuscript NO: 6483**

**Columns:** **REVIEW**

**Preeclampsia and eclampsia: Etiopathogenesis and perioperative management**

Srivastava U *et al*. Preeclampsia and eclampsia

Uma Srivastava, Veena Asthana, Amrita Gupta

**Uma Srivastava,** Department of Anaesthesia and Critical Care, S N Medical College, Agra-282002, Uttar Pradesh, India

**Veena Asthana,** Department of Anaesthesia, HIMS, Dehradun-248140, Uttarakhand, India

**Amrita Gupta,** Lecturer Department of Anaesthesia and Critical Care, S N Medical College, Agra-282002, Uttar Pradesh, India

**Author contributions:** Srivastava U, Asthana V and Gupta A contributed equally to this work; Gupta A collected literature; Srivastava U and Asthana V wrote the paper.

**Correspondence to: Dr. Uma Srivastava, Professor,** Department of Anaesthesia and Critical Care,S N Medical College, Agra-282002, Uttar Pradesh, India.drumasrivastava@rediffmail.comS

**Telephone:** +91-98-37246746 **Fax:** +91-98-37246746

**Received:** October 20, 2013  **Revised:** December 11, 2013

**Accepted: March 03, 2014**

**Published online:**

**Abstract**

Preeclampsia is a pregnancy specific syndrome of elusive etiology, developing in 2nd trimester and associated with high maternal and perinatal morbidity and mortality. The spectrum ranges from mild preeclampsia with no systemic involvement to multi-system involvement. The course is unpredictable and delivery is the only curative treatment. Elevated blood pressure (> 160/110 mmHg) should be reduced gradually to a safe level (140/90) using antihypertensive drugs. Prophylaxis and treatment of convulsions using MgSO4 is indicated for severe preeclampsia. Fluid therapy is controversial due to potential delicate balance between constricted plasma volume and risk of fluid overload and pulmonary oedema secondary to increased capillary permeability and reduced colloid osmotic pressure. Single shot spinal anaesthesia is the technique of choice for caesarean delivery unless contraindicated. General anaesthesia is indicated in patients with coagulopathy or eclampsia but is associated with risk of difficult airway and exaggerated sympathetic response during laryngoscopy. Epidural analgesia and anaesthesia is safe in absence of coagulopathy.

© 2014 Baishideng Publishing Group Co., Limited. All rights reserved.

**Key words:** Preeclampsia; Eclampsia; Regional anaesthesia; Caesarean section; Fluid therapy

**Core tip:** Preeclampsia and eclampsia constitute the commonest life-threatening complications of pregnancy characterized by hypertension and proteinuria presenting after 20 wk of gestation. In the severe form the condition is challenging for anaesthetists due to involvement of almost every system. The chief problems include hypertension, thrombocytopaenia, renal dysfunction, contracted plasma volume, reduced colloid osmotic pressure, leaky capillaries, oedema of airway and larynx *etc*. Fluid management is complex and carries risk of pulmonary oedema. HELLP syndrome and eclampsia are associated with high maternal mortality. For caesarean section spinal anaesthesia is technique of choice unless contraindicated. Epidural analgesia is good for labor pain.

Srivastava U, Asthana V, Gupta A. Preeclampsia and eclampsia: Etiopathogenesis and perioperative management.

**Available from:**

**DOI:**

**INTRODUCTION**

Preeclampsia is a multisystem disorder affecting 5%-10% women during 2nd trimester of pregnancy. It is characterized by hypertension and proteinuria and affects 3%-7% primiparas and 1%-5% multiparas. It is a principal cause of maternal mortality and morbidity worldwide constituting about 16% of peripartum deaths[1]. The condition is life threatening to foetus in addition to mother. Although the exact etio-pathogenesis remains to be determined, the placenta is undoubtedly involved, as termination of pregnancy is the only curative treatment. The preeclampsia may increase the risk of premature cardio-vascular disease such as hypertension, ischemic heart disease and stroke is later life[2,3]. Multidisciplinary team approach involving obstetrician, anaesthetist and pediatricians is required for management[4-6].

**CLASSIFICATION OF HYPERTENSIVE DISEASES OF PREGNANCY**

The National High Blood Pressure Education Programme Working group (2000)[7] classified hypertensive disorders as follows.

***Gestational hypertension***

Systolic BP ≥ 140 or Diastolic BP ≥ 90 mmHg for 1st time during pregnancy; No Proteinuria; BP returns to normal within 12 wk post partum; Final diagnosis only post partum; May have some features of preeclampsia for example epigastric pain or thrombocytopaenia.

***Preeclampsia***

BP ≥ 140/90 mmHg after 20 wk of gestation; Proteinuria ≥ 300 mg/24 h or ≥ 1+ dipstick in a random urine sample.

***Eclampsia***

Seizures that cannot be attributed to any other cause in a woman with preeclampsia.

***Superimposed preeclampsia on chronic hypertension***

New onset proteinuria ≥ 300 mg/d in hypertensive women but no proteinuria before 20 wk of gestation; Sudden increase in proteinuria or BP or decrease in platelet count to < 100000/mm3 in women with hypertension and proteinuria before 20 wk of gestation.

***Chronic hypertension***

BP > 140/90 before pregnancy or diagnosed before 20 wk of gestation not attributable to gestational trophoblastic disease or hypertension first diagnosed after 20 wk of gestation and persistent after 12 wk postpartum.

Preeclampsia is denoted as mild when only hypertension and proteinuria are present. Oedema is no longer considered to be diagnostic criteria. Severe preeclampsia is defined as the one of the following features in presence of preeclampsia: Systolic BP of 160 mmHg or higher, diastolic BP of 110 mmHg or higher on two occasions at least six hours apart; Proteinuria of more than 5 g in 24 h; Headache; Visual disturbances; Oliguria; Pulmonary oedema; Upper abdominal pain; Thrombocytopaenia; Convulsions; Serum creatinine level raised; Impaired liver functions; Intrauterine growth retardation of foetus.

**RISK FACTORS FOR DEVELOPMENT OF PREECLAMPSIA**

Young and nulliparas; Genetic predisposition; Multifoetal pregnancy; History of preeclampsia in previous pregnancy; Family history of preeclampsia; Obesity, diabetes; Afro-American race

**PATHOGENESIS OF PREECLAMPSIA**

The pathogenesis of preeclampsia involves a number of maternal, placental and foetal factors, the exact mechanism of which is still not clearly known. These include[8]:(1) placental implantation with abnormal trophoblastic invasion of uterine vessels; (2) immunological factors; (3) maternal maladaptation to cardio-vascular or inflammatory changes of normal pregnancy; and (4) genetic factors.

During normal trophoblastic invasion in normal pregnancy spiral arteries of uterus are transformed from high resistance vessels into low resistance vessels and stop responding to vasoconstrictors. Abnormal trophoblastic invasion in preeclampsia results in failure of spiral vessels to dilate. These vessels became more responsive to vasoconstrictors. This results in chronic placental ischemia and oxidative stress[9]. Placental ischaemia causes fetal complications like intra uterine growth retardation (IUGR) and death. Oxidative stress leads to endothelial cell activation with secretion of free radicals, oxidized lipids and cytokines which causes wide spread endothetial dysfunction[10,11]. Four fold increase of circulating endothetial cells has been reported in preeclampsia patients[12]. Endothelial dysfunction causes: (1) vascular hyperpermeability[13,14] resulting in oedema, proteinuria; (2) vasospasm resulting in hypertension, oliguria, seizures, liver ischaemia, abruption; and (3) activation of coagulation resulting in thrombocytopaenia. Endothetial dysfunction is main factor responsible for clinical effects on various organ systems like liver, brain and kidney. It also promotes microangiopathic haemolytic anaemia.

There is also increased secretion of thromboxane (vasoconstrictor) and reduced secretion of prostacyclines (vasodilator). The imbalance in normal ratio of thrombaxane and prostacycline[15] coupled with reduced production of nitric oxide, which is a potent dilator favours increased sensitivity to angiotensin II and ultimately leads to widespread vasoconstriction[16] and endothelial injury and platelet activation and consumption[14].

**PHYSIOLOGIC DERANGEMENTS IN VARIOUS SYSTEMS**

The effects are variable and depend upon the duration and severity.

***Cardio- vascular system and plasma volume***

Chief effects are hypertension, increased systemic vascular resistance, hyperdynamic circulation with low or normal cardiac output and hyperdynamic left ventricular function. Contracted plasma volume together with incompetent endothelial barrier, hypoalbuminemia and low colloid osmotic pressure lead to peripheral oedema. Despite water and sodium retention, hypovolaemia is present because of loss of fluids and proteins in the extra vascular compartment. Haemocencentration is the hallmark of preeclampsia.

Maternal plasma volume expansion which accompanies normal pregnancy is attenuated in preeclampsia. Deficit of 600-800/m2 has been reported[17]. Colloidal osmotic pressure is significantly reduced in preeclampsia due to reduced proteins levels compared to normal pregnancy being 14 mmHg. (22 mmHg in normal pregnancy and 25-28 in nonpregnant population)[18,19].

***Central nervous system***

Hyperreflexia, irritability, headache, visual disturbances, altered mental status may be present in severe preeclampsia. Encephalopathy, convulsions, raised intracranial tension and even post seizure coma may be seen. Pathogenesis of convulsions is disputed but it possibly occurs as a result of cerebral vasospasm, oedema, encephalopathy, microinfarcts or haemorrhage[20]. Intracranial hemorrhage is commonest cause of maternal mortality[21].

***Respiratory system***

Mucosal and airway oedema, along with laryngeal oedema is common in severe preeclampsia. Pulmonary oedema can occur in about 3% of patient[22] and is common after delivery. It is multifactorial; due to left ventricular dysfunction or failure, pulmonary capillary leak and due to reduced colloid osmotic pressure gradient.

***Kidneys***

Swelling of capillary endothelial cells is hallmark of renal pathology. GFR is reduced and serum creatinine and uric acid are raised. Oliguria and acute tubular necrosis may occur but renal failure is rare except in HELLP syndrome.

***Liver***

Involvement of liver is mild except in severe preeclampsia complicated by HELLP syndrome. Ischemic lesions, raised liver enzymes, hypo-albuminaemia and subcapsular hepatic hematoma may be seen.

***Coagulation***

Thrombocytopaemia (Platelet count < 100000/mm3) may be present in 18% of cases with severe preeclampsia. Platelet function may also be affected. Platelet aggregation is reduced compared to normally present finding of increased aggregation in pregnancy.

***Uterine activity and foetus***

Uterine activity is increased resulting in premature labor. Because of reduction in intervillous blood flow, increased vascular resistance and increased viscosity of blood secondary to haemoconcentration, placenta may show early aging, calcification, infarcts and abruption. Chronic placental hypoperfusion with loss of autoregulation is also seen[23]. There may be intrauterine growth retardation, death and premature delivery.

**COMPLICATIONS OF SEVERE PREECLAMPSIA**

Eclampsia is defined as the development of convulsions and/or unexplained coma during pregnancy or postpartum in patients of preeclampsia. The convulsions may occur during ante-partum period, during labor or post-delivery[20]. The overall incidence is 1-2000 deliveries in developed countries and 1-200-1600 in developing countries[8].

The convulsions are generalized and there are no reliable symptoms (except symptom of preeclampsia) or tests that can predict development of convulsions. Eclampsia is associated with risk of maternal death in 0%-1.8% parturients in developed countries[24-26]. Risk of maternal death is higher in developing countries primarily due to recurrent seizures, lack of proper antenatal[27] or ICU care[26]. Eclamptic convulsions should be immediately controlled with thiopental (50-100 mg), diazepam (2.5-5 mg), midazolam (1-2 mg) or Mgso4 (2-4 g) intravenously. Airway support, oxygenation and protection from aspiration pneumonites should also be done[28-30]. Recurrence of convulsions should be prevented by infusion of MgSO4.

***HELLP syndrome (Haemolysis, elevated liver enzymes and low platelets)***

Usually develops after 36 wk of gestation in women with severe preeclampsia. The incidence may be as high as 20%[28]. The symptoms are vague and patient may present with malaise, epigastric pain, nausea, vomiting and jaundice. Its severity ranges from a mild self limiting condition to a multi-organ involvement (DIC, liver and renal failure, pulmonary and cerebral oedema) with high foetal and maternal mortality[29,30]. The diagnostic criteria[31] are haemolysis (defined by abnormal peripheral blood smear and increased serum bilirubin), increased liver enzymes (aspartate aminotransferase level ≥ 70 U/L, LDH > 600 U/L) and a low platelet count (< 100000/mm3. It’s diagnosis calls for immediate delivery[8,29]. Administration of systemic steroids has been shown to reduce the risk of neonatal respiratory distress syndrome.

**MANAGEMENT OF PREECLAMPSIA**

The definite treatment is delivery of foetus and placenta. Until this can be accomplished, the main objective is to control the disease process, treat hypertension and prevent convulsions[8,28,29,32]. Early hospitalization with bed rest and regular clinical, cardio-tochographic study and lab investigations are useful to tailor the management of severe preeclampsia.

**INDICATIONS FOR EXPEDITED DELIVERY**

Uncontrolled severe hypertension not responding to treatment; Eclampsia; HELLP syndrome; Acute pulmonary oedema; Abruptio placentae; Foetal distress.

**CONTROL OF BLOOD PRESSURE**

Antihypertensive treatment is not indicated for mild preeclampsia as prolonged treatment with antihypertensive drugs may be associated with foetal growth retardation particularly in women with mild or moderate preeclampsia[33]. But if BP is persistently elevated, risk of hemorrhagic stroke increases. Most guidelines recommend antihypertensive medication when systolic BP is > 160 mmHg and diastolic > 110 mmHg and lowering of systolic BP to 140-150 mmHg and diastolic BP to 90-100 mmHg is desirable. A gradual reduction in BP is recommended at the rate of 10-20 mmHg every 10-20 min[34] as sudden precipitous fall may result in maternal and foetal complications. The aim is not to normalize the BP but to reduce to a safe level. However, there is no international consensus regarding choice of drug[5]. The choice is usually made depending upon experience of clinician with the particular drug[35]. Most commonly used drugs are labetalol (oral or IV), oral nifedipine and intravenous hydrallazine. Currently labetalol is most frequently used drug. Hydrallzine is frequently used by obstetricians but side effects like tachycardia, headache, postural hypotension and vomiting limits it use[6]. Nifedipine is also used but should be avoided where MgSO4 has been used as profound hypotension may occur.

***Dosage schedule of anti-hypertensive drugs***

Hydralazine 5-10 mg IV every 20-30 min or 5-20 mg per hour as continuous infusion following 5 mg IV bolus; labetalol 10-20 mg IV or 20-60 mg per hour as continuous infusion 50-100 mg per oral; nitroglycerine 10 µg per minute IV titrated to response.

**MANAGEMENT AND PROPHYLAXIS FOR CONVULSIONS**

MgSO4 is the drug of choice for both control and prophylaxis of convulsions[36]. MgSO4 is a tocolytic, anticonvulsant and mild generalized vasodilator. Its mode of action is not clearly known but is thought to act by releasing spasm of cerebral vasculature and by blocking calcium influx through NMDA subtype of glutamate channel. Whether or not all patients require prophylactic MgSO4, is debated. However most obstetricians use in severe preeclampsia when there is evidence of involvement of CNS, as evidenced by presence of severe persistent headache, visual disturbances, hyperreflexia and following a convulsion. It reduces risk of convulsions in 58% of patients[36]. But it should only be used in hospitalized women[18]. The dose is 4-6 g IV given slowly over 10-20 min followed by continuous infusion of 1-2 g/h. Monitoring during magnesium therapy includes: urine output (> 30 mL/h), deep tendon reflex, respiration and level of consciousness. Chances of toxicity increase with impaired renal functions, so doses should be reduced. Magnesium has low therapeutic index (Table 1). Early signs of toxicity are nausea, feeling of warmth, somnolence, double vision slurred speech and weakness. In case of any manifestation of toxicity, the infusion should be stopped and calcium gluconate (10 mL, 10%) should be given if needed along with supportive treatment.

***Role of anaesthetist in management of pre-eclampsia and eclampsia***

Chief role of anesthetist is to provide safe labor analgesia and anesthesia for caesarean delivery. Other roles are in resuscitation, ICU management including invasive monitoring and limitation of complications[6,29,30,34].

**ANALGESIA FOR LABOR AND DELIVERY**

Use of lumbar epidural analgesia for the severely preeclamptic or eclamptic patients when convulsions are under control is recommended both by obstetricians and anesthetist. Several advantages offered by this technique[29] include: (1) complete relief from labor pain without any neonatal depression; (2) ideal obstetric conditions for vaginal delivery especially for preterm babies; (3) suitable for operative vaginal delivery; (4) decreases circulating levels of catecholamine’s; (5) improves intervillous blood flow; (6) stabilizes BP to a modest level; (7) attenuates hypertensive response to pain; and (8) anesthesia can be extended for caesarean delivery.

The concerns for epidural analgesia include possibility of hypotension and rarely epidural haematoma. With judicious hydration and gradual induction of block, hypotension may be minimized[6,29]. Hydration must be done with great caution and 500-1000 mL of crystalloid is usually adequate[28,29]. In patients with mild preeclampsia 1-1.5 liters of balanced salt solution can be used. The block may be initiated with 6–10 mL of dilute local anesthetic with opioid. Bolus may be repeated if no hypotension noted. CSE has also been shown to be safe in severely preeclamptic patients[37].

**ANAESTHESIA FOR CAESAREAN SECTION**

Management of anaesthesia in patients with severe preeclampsia or eclampsia is challenging for anaesthetists. Emergency caesarean section is often required due to worsening of mother’s condition or due to foetal distress with limited time for optimization. But BP must be controlled and fluid volume must be optimized before proceeding for anaesthesia. It is important to have a flexible anaesthetic plan with more than two options as condition may change rapidly[38]. Detailed preanaesthetic evaluation including severity of condition, systemic involvement, fluid status and airway assessment should be done. Use of prior pharmacological therapy must be enquired. Complete blood count, BUN, creatinine and liver functions tests should be obtained especially if HELLP syndrome is suspected. Routine coagulation screening is not necessary[39]. But if coagulopathy is suspected clinically by history of easy bruising ecchymoses or petechial haemorrhage, coagulation studies should be done. Platelet count should be available before neuraxial analgesia or anesthesia in severe preeclampsia.

**REGIONAL ANAESTHESIA**

Choice of anesthesia should be individualized depending upon patient’s condition. Single shot spinal, combined spinal epidural or epidural anesthesia, all may be utilized[34] provided meticulous attention is paid to fluid management, hypotension and prevention of aorto-caval compression. Traditionally spinal anaesthesia was not employed for caesarean section in severely preeclamptic parturients. It was considered unsafe due to fear of severe hypotension induced by sympathetic block risking fetal safely. Another concern was development of pulmonary oedema following prophylactic IV fluids or fluids given to treat hypotension[40]. Therefore obstetric anaesthetist preferred epidural over spinal with the view that slow incremental doses of local anesthetic through epidural catheter would result in slow ascent of block and thus minimize the risk of sudden hypotension. However, retrospective analysis [41], prospective studies[42-45] and some editorials[46,47] strongly supported the use of spinal anesthesia in severe preeclampsia in absence of any contraindication and if epidural catheter had not already been placed for labor analgesia. The studies demonstrated lesser degree of hypotension when compared with healthy parturient receiving spinal for caesarean section[42-45]. Spinal anaesthesia with usual doses of local anaesthetic is now recommended as anaesthetic technique of choice for parturients with severe preeclampsia unless contraindicated[23,34,48,49]. Fast onset of block combined with certainty are critical advantages in emergency situation. Although spinal anesthesia can cause greater degree of hypotension than epidural anesthesia, the hypotension is short lived and can be easily treated with vasoactive drugs[23,50]. In addition, requirement of vasopressors was not found to be increased after spinal, epidural[51] or combined spinal epidural anaesthesia[52]. Before institution of block, patients with mild preeclampsia tolerate prehydration (10-15 mL/kg of crystalloid) well[28-30,38]. Most patients with severe pre-eclampsia can be prehydrated with 500-1000 ml of crystalloid if urine output is adequate[29].

Spinal anaesthesia is controversial in the setting of eclampsia[6] due to risk of convulsions[53] although has been used in a patient with difficult airway[54]. Some advocate use of epidural or general anaesthesia[55] for eclampsia. Epidural anaesthesia is indicated if woman is haemodynamically stable, is fully conscious, convulsions are controlled, has no neurological deficit and has no contraindication[29].

***Regional analgesia/anesthesia and risk of haemorrhage***

There is no absolute platelet count below which neuraxial analgesia or anaesthesia is contraindicated. But it is generally agreed that platelet count above 75000/mm3 in absence of other coagulation abnormality would not be associated with problems of haemorrhage with neuraxial technique[45,56]. Rate of fall of plate count is also important and neuraxial block may be contraindicated if the count falls rapidly over a short period[29,30]. Decision to place epidural catheter must be individualized, but catheter should be removed only when platelet count has normalized.

***Intravenous volume and fluid management***

The vasculature in preeclampsia has been described as ‘constricted and porous’. Volume expansion although is advocated on the rationale that it is contracted, however there is no evidence to support the notion that it will be effective in presence of raised afterload[57]. There may be advantage in expanding maternal circulating volume, but there can be potential hazard of development of pulmonary oedema especially when renal function is impaired[19,40]. Therefore fluid administration should be done carefully utilizing clinical and urine output monitoring with invasive monitoring only in certain cases. Severe preeclampsia is associated with complex set of haemodynamic changes[38] central venous pressure (CVP) may not correlate well with pulmonary capillary wedge pressure (PCWP). Often CVP may be low but PCWP may be quite high. In addition with fluid infusion, rise in PCWP may be earlier than that of CVP, and may remain disproportionately high[58,59]. Hence fluid management against CVP measurement is not recommended as it may lead to overhydration in most cases[60]. If CVP alone is monitored, volume expansion of CVP up to 5 mmHg or less is sufficient[38], because CVP- PCWP gradient can be as high as 8-10 . The higher CVP may result in overload[61].

In patients with oliguria (urine output < 300-500 mL/d), after excluding hypovolaemia as a cause, fluid challenge with 250-500 mL of crystalloid is given over 20 min. If patient responds by increase in urine output, additional fluid bolus may be repeated cautiously before regional block. If no response to initial fluid bolus, CVP/PCWP monitoring is recommended[60].

Consensus is that, invasive monitoring is not essential for safe fluid management in all patients of preeclampsia[38]. PCWP monitoring is recommended in patients with hypertension refractory to treatment, pulmonary oedema and oliguria not responding to modest fluid load[29,60,62].

There is no clear data regarding ideal volume and type of fluid[40,38,60]. Use of crystalloid may further reduce colloid osmotic pressure whereas colloids may lead to volume overload after delivery due to fluid mobilization owing to their longer half life[19]. Colloids may be preferred when there is cardio-respiratory or renal compromise.

***General anaesthesia***

General anesthesia is indicated in severe preeclampsia with HELLP syndrome, eclampsia, coagulopathy, cerebral oedema and in patients who refuse regional anaesthesia. The risks include: (1) potentially difficult airway due to airway and laryngeal oedema; (2) exaggerated sympathetic response to laryngoscopy and intubation and also during extubation; (3) Aspiration of gastric contents; (4) potentiation of neuromuscular block especially non-depolarizer block owing to prior use of MgSo4; and (5) impaired placental blood flow.

Before induction of anesthesia, BP must be controlled because untreated hypertension increases risk of cerebral haemorrhage, pulmonary congestion, hepatic and renal dysfunction and reduction in placental perfusion. Thiopental and succinylcholine are most frequently used and usually a smaller endotracheal tube is required. Presser response to laryngoscope may be attenuated using lignocaine, fentanyl, labetalol, nitroglycerine or magnesium sulphate. Laryngeal oedema resulting in failed intubation is fortunately rare but well described in preeclampsia[63]. The duration of single dose of succinyl choline is usually not affected by previous use of MgSO4[29], but doses of non-depolarizing muscle relaxants must be reduced. Use of peripheral nerve stimulator is recommended[29]. Atracurium is a preferred agent[64]. Ergotamine should be avoided and if required oxytocin infusion should be used[34].

**POSTOPERATIVE MANAGEMENT**

Management should be done in high dependency unit or transferred to ICU if required. The patients with severe preeclampsia are prone to convulse or develop pulmonary oedema within 24 h of delivery. If MgSO4 was given, it should be continued for 24-48 h. If required oral antihypertensive medication should also be given. Pain must be controlled by epidural or other route. Strict intake output chart should be maintained for at least 24 h or until diuresis develops.

**CONCLUSION**

Despite advancement in understanding of etiopathogenesis and management, preeclampsia and eclampsia still remain a leading cause of maternal mortality. Multidisciplinary care with early reference to anaesthesiologists who have clear knowledge of pathophysiology and are well trained in resuscitation and monitoring and critical care management may help in limiting complications and improve outcome.

**REFERENCES**

1 **Khan KS**, Wojdyla D, Say L, Gülmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. *Lancet* 2006; **367**: 1066-1074 [PMID: 16581405 DOI: 10.1016/S0140-6736(06)68397-9]

2 **McDonald SD**, Malinowski A, Zhou Q, Yusuf S, Devereaux PJ. Cardiovascular sequelae of preeclampsia/eclampsia: a systematic review and meta-analyses. *Am Heart J* 2008; **156**: 918-930 [PMID: 19061708 DOI: 10.1016/j.ahj.2008.06.042]

3 **Bellamy L**, Casas JP, Hingorani AD, Williams DJ. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. *BMJ* 2007; **335**: 974 [PMID: 17975258 DOI: 10.1136/bmj.39335.385301.BE]

4 **Cantwell R**, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, Harper A, Hulbert D, Lucas S, McClure J, Millward-Sadler H, Neilson J, Nelson-Piercy C, Norman J, O'Herlihy C, Oates M, Shakespeare J, de Swiet M, Williamson C, Beale V, Knight M, Lennox C, Miller A, Parmar D, Rogers J, Springett A. Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. *BJOG* 2011; **118** Suppl 1: 1-203 [PMID: 21356004 DOI: 10.1111/j.1471-0528.2010.02847.x]

5 **Uzan J**, Carbonnel M, Piconne O, Asmar R, Ayoubi JM. Pre-eclampsia: pathophysiology, diagnosis, and management. *Vasc Health Risk Manag* 2011; **7**: 467-474 [PMID: 21822394 DOI: 10.2147/VHRM.S20181]

6 **Dyer RA**, Piercy JL, Reed AR. The role of the anaesthetist in the management of the pre-eclamptic patient. *Curr Opin Anaesthesiol* 2007; **20**: 168-174 [PMID: 17479015 DOI: 10.1097/ACO.0b013e328136c1ac]

7 Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol* 2000; **183**: S1-S22 [PMID: 10920346]

8 **Cunningham FG**, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams Obstetrics . Williams Obstetrics. 23rd ed, New York, McGraw Hill, 2010. Available from: URL: http: //accessmedicine.mhmedical.com/book.aspx?bookId=350

9 **Holthe MR**, Staff AC, Berge LN, Lyberg T. Leukocyte adhesion molecules and reactive oxygen species in preeclampsia. *Obstet Gynecol* 2004; **103**: 913-922 [PMID: 15121565 DOI: 10.1097/01.AOG.0000124806.39111.ba]

10 **Maynard SE**, Min JY, Merchan J, Lim KH, Li J, Mondal S, Libermann TA, Morgan JP, Sellke FW, Stillman IE, Epstein FH, Sukhatme VP, Karumanchi SA. Excess placental soluble fms-like tyrosine kinase 1 (sFlt1) may contribute to endothelial dysfunction, hypertension, and proteinuria in preeclampsia. *J Clin Invest* 2003; **111**: 649-658 [PMID: 12618519]

11 **Levine RJ**, Maynard SE, Qian C, Lim KH, England LJ, Yu KF, Schisterman EF, Thadhani R, Sachs BP, Epstein FH, Sibai BM, Sukhatme VP, Karumanchi SA. Circulating angiogenic factors and the risk of preeclampsia. *N Engl J Med* 2004; **350**: 672-683 [PMID: 14764923 DOI: 10.1056/NEJMoa031884]

12 **Grundmann M**, Woywodt A, Kirsch T, Hollwitz B, Oehler K, Erdbruegger U, Haller H, Haubitz M. Circulating endothelial cells: a marker of vascular damage in patients with preeclampsia. *Am J Obstet Gynecol* 2008; **198**: 317.e1-317.e5 [PMID: 18068139 DOI: 10.1016/j.ajog.2007.09.049]

13 **Myers JE**, Hart S, Armstrong S, Mires GJ, Beynon R, Gaskell SJ, Baker PN. Evidence for multiple circulating factors in preeclampsia. *Am J Obstet Gynecol* 2007; **196**: 266.e1-266.e6 [PMID: 17346549 DOI: 10.1016/j.ajog.2006.10.875]

14 **Walsh SW**. Plasma from preeclamptic women stimulates transendothelial migration of neutrophils. *Reprod Sci* 2009; **16**: 320-325 [PMID: 19087976 DOI: 10.1177/1933719108327594]

15 **Wang YP**, Walsh SW, Guo JD, Zhang JY. The imbalance between thromboxane and prostacyclin in preeclampsia is associated with an imbalance between lipid peroxides and vitamin E in maternal blood. *Am J Obstet Gynecol* 1991; **165**: 1695-1700 [PMID: 1750462 DOI: 10.1016/0002-9378(91)90017-L]

16 **Spitz B**, Magness RR, Cox SM, Brown CE, Rosenfeld CR, Gant NF. Low-dose aspirin. I. Effect on angiotensin II pressor responses and blood prostaglandin concentrations in pregnant women sensitive to angiotensin II. *Am J Obstet Gynecol* 1988; **159**: 1035-1043 [PMID: 3189434]

17 **Hays PM**, Cruikshank DP, Dunn LJ. Plasma volume determination in normal and preeclamptic pregnancies. *Am J Obstet Gynecol* 1985; **151**: 958-966 [PMID: 3885738 DOI: 10.1016/0002-9378(85)90675-1]

18 **Sibai BM**. Diagnosis and management of gestational hypertension and preeclampsia. *Obstet Gynecol* 2003; **102**: 181-192 [PMID: 12850627 DOI: 10.1016/S0029-7844(03)00475-7]

19 **Wasserstrum N**. Issues in fluid management during labor: maternal plasma volume status and volume loading. *Clin Obstet Gynecol* 1992; **35**: 514-526 [PMID: 1521381 DOI: 10.1097/00003081-199209000-00011]

20 **Sibai BM**. Diagnosis, prevention, and management of eclampsia. *Obstet Gynecol* 2005; **105**: 402-410 [PMID: 15684172 DOI: 10.1097/01.AOG.0000152351.13671.99]

21 **Simolke GA**, Cox SM, Cunningham FG. Cerebrovascular accidents complicating pregnancy and the puerperium. *Obstet Gynecol* 1991; **78**: 37-42 [PMID: 2047065]

22 **Mabie WC**, Ratts TE, Ramanathan KB, Sibai BM. Circulatory congestion in obese hypertensive women: a subset of pulmonary edema in pregnancy. *Obstet Gynecol* 1988; **72**: 553-558 [PMID: 2971147]

23 **Henke VG**, Bateman BT, Leffert LR. Focused review: spinal anesthesia in severe preeclampsia. *Anesth Analg* 2013; **117**: 686-693 [PMID: 23868886 DOI: 10.1213/ANE.0b013e31829eeef5]

24 **Douglas KA**, Redman CW. Eclampsia in the United Kingdom. *BMJ* 1994; **309**: 1395-1400 [PMID: 7819845 DOI: 10.1136/bmj.309.6966.1395]

25 **Mattar F**, Sibai BM. Eclampsia. VIII. Risk factors for maternal morbidity. *Am J Obstet Gynecol* 2000; **182**: 307-312 [PMID: 10694329 DOI: 10.1016/S0002-9378(00)70216-X]

26 **Chames MC**, Livingston JC, Ivester TS, Barton JR, Sibai BM. Late postpartum eclampsia: a preventable disease? *Am J Obstet Gynecol* 2002; **186**: 1174-1177 [PMID: 12066093 DOI: 10.1067/mob.2002.123824]

27 **Katz VL**, Farmer R, Kuller JA. Preeclampsia into eclampsia: toward a new paradigm. *Am J Obstet Gynecol* 2000; **182**: 1389-1396 [PMID: 10871454 DOI: 10.1067/mob.2000.106178]

28 **Broveman FR**. Pregnancy associated diseases. In: Stoelting’s Anesthesia and Coexisting Diseases, 5th ed. Churchill Livingstone 2009; 557-580

29 **Gaiser RR**, Gutsche BB, Cheek TG. In: Shnider and Levinson’s Anesthesia for Obstetrics. Hughes SC, Levinson G, Rosen MA, editors, 4th ed. Lippincoll willianes and wilkins 2002; 297-321

30 **Bimbach DJ**, Browne IM. Anesthesia for obstetrics in Millers Anesthesia 7th ed Miller RD, editor. Churchiull Livingstone. 2010; 2203-2240

31 **Sibai BM**. The HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): much ado about nothing? *Am J Obstet Gynecol* 1990; **162**: 311-316 [PMID: 2309811 DOI: 10.1016/0002-9378(90)90376-I]

32 **Turner JA**. Diagnosis and management of pre-eclampsia: an update. *Int J Womens Health* 2010; **2**: 327-337 [PMID: 21151680 DOI: 10.2147/IJWH.S8550]

33 **von Dadelszen P**, Ornstein MP, Bull SB, Logan AG, Koren G, Magee LA. Fall in mean arterial pressure and fetal growth restriction in pregnancy hypertension: a meta-analysis. *Lancet* 2000; **355**: 87-92 [PMID: 10675164]

34 **Dennis AT**. Management of pre-eclampsia: issues for anaesthetists. *Anaesthesia* 2012; **67**: 1009-1020 [PMID: 22731893 DOI: 10.1111/j.1365-2044.2012.07195.x]

35 **Duley L**, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. *Cochrane Database Syst Rev* 2006; **(3)**: CD001449 [PMID: 16855969]

36 **Altman D**, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, Smith D; Magpie Trial Collaboration Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. *Lancet* 2002; **359**: 1877-1890 [PMID: 12057549 DOI: 10.1016/S0140-6736(02)08778-0]

37 **Ramanathan J**, Vaddadi AK, Arheart KL. Combined spinal and epidural anesthesia with low doses of intrathecal bupivacaine in women with severe preeclampsia: a preliminary report. *Reg Anesth Pain Med* 2001; **26**: 46-51 [PMID: 11172511]

38 **Ramanathan J**, Bennett K. Pre-eclampsia: fluids, drugs, and anesthetic management. *Anesthesiol Clin North America* 2003; **21**: 145-163 [PMID: 12698838 DOI: 10.1016/S0889-8537(02)00054-8]

39 **Leduc L**, Wheeler JM, Kirshon B, Mitchell P, Cotton DB. Coagulation profile in severe preeclampsia. *Obstet Gynecol* 1992; **79**: 14-18 [PMID: 1727573]

40 **Engelhardt T**, MacLennan FM. Fluid management in pre-eclampsia. *Int J Obstet Anesth* 1999; **8**: 253-259 [PMID: 15321120 DOI: 10.1016/S0959-289X(99)80106-X]

41 **Hood DD**, Curry R. Spinal versus epidural anesthesia for cesarean section in severely preeclamptic patients: a retrospective survey. *Anesthesiology* 1999; **90**: 1276-1282 [PMID: 10319773 DOI: 10.1097/00000542-199905000-00009]

42 **Aya AG**, Mangin R, Vialles N, Ferrer JM, Robert C, Ripart J, de La Coussaye JE. Patients with severe preeclampsia experience less hypotension during spinal anesthesia for elective cesarean delivery than healthy parturients: a prospective cohort comparison. *Anesth Analg* 2003; **97**: 867-872 [PMID: 12933418 DOI: 10.1213/01.ANE.0000073610.23885.F2]

43 **Clark VA**, Sharwood-Smith GH, Stewart AV. Ephedrine requirements are reduced during spinal anaesthesia for caesarean section in preeclampsia. *Int J Obstet Anesth* 2005; **14**: 9-13 [PMID: 15627532 DOI: 10.1016/j.ijoa.2004.08.002]

44 **Aya AG**, Vialles N, Tanoubi I, Mangin R, Ferrer JM, Robert C, Ripart J, de La Coussaye JE. Spinal anesthesia-induced hypotension: a risk comparison between patients with severe preeclampsia and healthy women undergoing preterm cesarean delivery. *Anesth Analg* 2005; **101**: 869-75, table of contents [PMID: 16116006 DOI: 10.1213/01.ANE.0000175229.98493.2B]

45 **Dyer RA**, Piercy JL, Reed AR, Lombard CJ, Schoeman LK, James MF. Hemodynamic changes associated with spinal anesthesia for cesarean delivery in severe preeclampsia. *Anesthesiology* 2008; **108**: 802-811 [PMID: 18431115 DOI: 10.1097/01.anes.0000311153.84687.c7]

46 **Santos AC**, Birnbach DJ. Spinal anesthesia in the parturient with severe preeclampsia: time for reconsideration. *Anesth Analg* 2003; **97**: 621-622 [PMID: 12933372]

47 **Santos AC**, Birnbach DJ. Spinal anesthesia for cesarean delivery in severely preeclamptic women: don't throw out the baby with the bathwater! *Anesth Analg* 2005; **101**: 859-861 [PMID: 16116004]

48 **ACOG Committee on Obstetric Practice**. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists. *Int J Gynaecol Obstet* 2002; **77**: 67-75 [PMID: 12094777]

49 **American Society of Anesthesiologists Task Force on Obstetric Anesthesia**. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. *Anesthesiology* 2007; **106**: 843-863 [PMID: 17413923]

50 **Visalyaputra S**, Rodanant O, Somboonviboon W, Tantivitayatan K, Thienthong S, Saengchote W. Spinal versus epidural anesthesia for cesarean delivery in severe preeclampsia: a prospective randomized, multicenter study. *Anesth Analg* 2005; **101**: 862-88, table of contents [PMID: 16116005 DOI: 10.1213/01.ANE.0000160535.95678.34]

51 **Sharwood-Smith G**, Clark V, Watson E. Regional anaesthesia for caesarean section in severe preeclampsia: spinal anaesthesia is the preferred choice. *Int J Obstet Anesth* 1999; **8**: 85-89 [PMID: 15321150 DOI: 10.1016/S0959-289X(99)80003-X]

52 **Wallace DH**, Leveno KJ, Cunningham FG, Giesecke AH, Shearer VE, Sidawi JE. Randomized comparison of general and regional anesthesia for cesarean delivery in pregnancies complicated by severe preeclampsia. *Obstet Gynecol* 1995; **86**: 193-199 [PMID: 7617349 DOI: 10.1016/0029-7844(95)00139-I]

53 **Ebirim LN**, Lagiri B, Buowari YD. Progression of pre-eclampsia to eclampsia under spinal anaesthesia. *Adv Biomed Res* 2012; **1**: 74 [PMID: 23326804]

54 **Nafiu OO**, Salam RA, Elegbe EO. Anaesthetic dilemma: spinal anaesthesia in an eclamptic patient with mild thrombocytopenia and an "impossible" airway. *Int J Obstet Anesth* 2004; **13**: 110-113 [PMID: 15321416 DOI: 10.1016/j.ijoa.2003.10.005]

55 **Moodley J**, Jjuuko G, Rout C. Epidural compared with general anaesthesia for caesarean delivery in conscious women with eclampsia. *BJOG* 2001; **108**: 378-382 [PMID: 11305544 DOI: 10.1111/j.1471-0528.2001.00097.x]

56 **Sharma SK**, Philip J, Whitten CW, Padakandla UB, Landers DF. Assessment of changes in coagulation in parturients with preeclampsia using thromboelastography. *Anesthesiology* 1999; **90**: 385-390 [PMID: 9952141 DOI: 10.1097/00000542-199902000-00009]

57 **Winer N**, Tsasaris V. [Latest developments: management and treatment of preeclampsia]. *J Gynecol Obstet Biol Reprod* (Paris) 2008; **37**: 5-15 [PMID: 18054175]

58 **Bolte AC**, Dekker GA, van Eyck J, van Schijndel RS, van Geijn HP. Lack of agreement between central venous pressure and pulmonary capillary wedge pressure in preeclampsia. *Hypertens Pregnancy* 2000; **19**: 261-271 [PMID: 11118399 DOI: 10.1081/PRG-100101987]

59 **Bolte AC**, van Geijn HP, Dekker GA. Management and monitoring of severe preeclampsia. *Eur J Obstet Gynecol Reprod Biol* 2001; **96**: 8-20 [PMID: 11311756 DOI: 10.1016/S0301-2115(00)00383-3]

60 **Young P**, Johanson R. Haemodynamic, invasive and echocardiographic monitoring in the hypertensive parturient. *Best Pract Res Clin Obstet Gynaecol* 2001; **15**: 605-622 [PMID: 11478818 DOI: 10.1053/beog.2001.0203]

61 **Young PF**, Leighton NA, Jones PW, Anthony J, Johanson RB. Fluid management in severe preeclampsia (VESPA): survey of members of ISSHP. *Hypertens Pregnancy* 2000; **19**: 249-259 [PMID: 11118398 DOI: 10.1081/PRG-100101986]

62 **Clark SL**, Cotton DB. Clinical indications for pulmonary artery catheterization in the patient with severe preeclampsia. *Am J Obstet Gynecol* 1988; **158**: 453-458 [PMID: 3348302 DOI: 10.1016/0002-9378(88)90003-8]

63 **Munnur U**, de Boisblanc B, Suresh MS. Airway problems in pregnancy. *Crit Care Med* 2005; **33**: S259-S268 [PMID: 16215346 DOI: 10.1097/01.CCM.0000183502.45419.C9]

64 **Khan ZH**. Preeclampsia/eclampsia: an insight into the dilemma of treatment by the anesthesiologist. *Acta Med Iran* 2011; **49**: 564-574 [PMID: 22052138]

**P-Reviewers:** Gabriele T, Kvolik S, Safavi M **S-Editor:** Ma YJ **L-Editor:** **E-Editor:**

**Table 1 Effects of increasing plasma magnesium level**

|  |  |
| --- | --- |
| **Plasma Mg level (mEq/L)** | **Clinical effects** |
| 1.5-2.0 | Normal level |
| 4.0-4.8 | Therapeutic range |
| 5.0-10.0 | Prolong P-Q interval, wide QRS |
| ≥ 10.0 | Loss of deep tendon reflex |
| ≥ 15.0 | Respiratory paralysis |
| 25.0 | Cardiac arrest |