Peripartum management of the pre-eclamptic patient

Pre-eclampsia is a common problem in pregnancy which can present at any time to any delivery suite. This article summarizes current best practice to enable the multidisciplinary team to deliver appropriate timely management to achieve best outcomes for both mother and baby.

Pre-eclampsia is defined as hypertensive disease in pregnancy, developing after 20 weeks' gestation, with associated significant proteinuria. It is a multi-organ disease that can lead to morbidity and mortality of both the mother and fetus. Although incidence of the disease is decreasing in the UK, currently estimated at 2–8% (Royal College of Obstetricians and Gynaecologists, 2012), it is still the second leading cause of direct maternal death in the most recent Centre for Maternal and Child Enquiries report (0.83 deaths per 100 000 births) (Cantwell et al, 2011).

Acute maternal complications include kidney failure, coagulopathy, intracerebral haemorrhage and pulmonary oedema. Long-term morbidity may include postnatal hypertension and an increased lifelong cardiovascular risk (Bellamy et al, 2007). Fetal complications include increased rates of preterm delivery (8–10% of preterm births are accredited to hypertensive disease (Slattery et al, 2008)), intrauterine growth restriction (Rasmussen and Irgens, 2006), placental abruption and perinatal death (5% of non-congenital abnormality stillbirths are attributed to pre-eclamptic mothers (Confidential Enquiry into Maternal and Child Health, 2009)).

Risk factors for pre-eclampsia in pregnancy include chronic kidney disease, previous pregnancy-induced hypertension, autoimmune disease, diabetes, nulliparity, increased maternal age and chronic hypertension (National Institute for Health and Clinical Excellence, 2010). These women require prompt antenatal identification and subsequent counselling.

Anaesthetic management of such complex patients requires a good understanding of the pathophysiology of pre-eclampsia. Early recognition and aggressive treatment can decrease fetal and maternal morbidity and mortality.

Table 1. Blood pressure and proteinuria classification

Blood pressure classification	Mild	Diastolic 90–99 mmHg and/or systolic 140–149 mmHg
	Moderate	Diastolic 100–109 mmHg and/or systolic 150–159 mmHg
	Severe	Diastolic >110 mmHg and/or systolic >160 mmHg
Proteinuria assessment	24-hour urine collection	>300 mg/mmol
	Protein:creatinine ratio	>30 mg/mmol

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Diagnosis and classification

The two components of pre-eclampsia are hypertension and proteinuria present after 20 weeks' gestation.

New-onset hypertension can be further classified into mild (diastolic 90–99 mmHg and/or systolic 140–149 mmHg), moderate (diastolic 100–109 mmHg and/or systolic 150–159 mmHg) and severe (diastolic above 110 mmHg and/or systolic above 160 mmHg) (*Table 1*). Blood pressure measurement should be carried out using an appropriately sized cuff. Hypertension can be diagnosed if two consecutive readings, 4 hours apart, confirm the above criteria. Hypertension without proteinuria is termed gestational hypertension or pregnancy-induced hypertension.

Proteinuria should be ruled out in any pregnant woman presenting with hypertension. A basic test can be done using an automated reagent strip. If 1 plus or more of protein is present, a 24-hour urine collection should be carried out, or a spot urinary protein:creatinine ratio. Significant proteinuria is more than 300 mg over 24 hours or a urinary protein:creatinine ratio of greater than 30 mg/mmol. Severe proteinuria is defined as more than 5 g over 24 hours or 3 plus on a reagent strip (National Institute for Health and Clinical Excellence, 2010).

Pre-eclampsia is categorized as severe when there is severe hypertension and/or symptoms and/or haematological and/or biochemical abnormalities. Being a multi-organ disease, symptoms of pre-eclampsia can manifest in several ways, but those more commonly described include headache, visual disturbances, oliguria, dypsnoea, epigastric pain, vomiting, sudden onset peripheral oedema and seizures. Haematological and biochemical abnormalities seen include thrombocytopenia, raised liver transaminases, bilirubin, urate, and abnormal urea and electrolytes.

Eclampsia is a potentially fatal convulsive condition associated with pre-eclampsia.

Pathophysiology of pre-eclampsia

Although not fully understood, the disease process is thought to begin when the cytotrophoblasts (fetal cells responsible for placental implantation) incorrectly implant into the wall of the uterus and the maternal vasculature. The spiral arteries, normally responsible for supplying the endometrium during menstruation, fail to convert to achieve utero-placental circulation. In response to chronic placental insufficiency, vasoactive substances are released from the placenta in an attempt to increase the blood supply. This alters the balance between thromboxane and prostacyclin in the mother. The process results in maternal hypertension, vasospasm, increased endothelial permeability, platelet aggregation and thrombophilia (Uzan et al, 2011), the multisystem consequences of which are depicted in *Table 2*. Essentially it is this inadequate placental blood supply that causes intrauterine growth restriction and in extreme cases intrauterine death.

HELLP syndrome

Haemolysis, elevated liver enzymes and low platelets (HELLP syndrome) is considered a complication of severe pre-eclampsia occurring in 10–20% of cases (Haram et al, 2009). HELLP syndrome presents without hypertension in 20% of cases and can present in the postnatal period in 30% of cases. Morbidity (1–10%) and mortality rates are increased in the presence of HELLP and prompt diagnosis and management is essential. Although the pathophysiology is not clear, it is thought that activation of the coagulation pathway leads to platelet consumption and microangiopathic haemolytic anaemia. Ischaemic changes occur in the liver, and periportal necrosis ensues. Symptoms classically include right upper quadrant pain, nausea and vomiting. Treatment and management is aimed at timely delivery, and control of pre-eclampsia (Weinstein, 2005).

Management aims

There are usually local guidelines available based on the National Institute for Health and Clinical Excellence (2010) guideline. A multidisciplinary approach is key in reducing both maternal and fetal morbidity. Obstetricians, anaesthetists, haematologists, midwives, critical care doctors and neonatologists all have a role to play as part of the clinical team. Team-work and good communication is essential in managing these complex patients where ultimately the only cure is delivery of the fetus.

Factors involved in the management of these patients are described below.

Management of hypertension

This will depend on the severity of hypertension and most units will have local guidelines. Oral labetolol (an alpha and beta adrenergic antagonist) is considered first-line treatment and can reduce the blood pressure in up to 80% of cases (*Table 3*). It can be administered intravenously if indicated. Intravenous hydralazine (a direct-acting smooth muscle relaxant) and oral nifedipine (a dihydropyridine calcium-channel blocker) are alternative options. In particularly resistant cases, these three agents can be used in combination. Blood pressure reduction should be seen within an hour of treatment; if this is not the case then another agent should be considered. Careful monitoring should be carried out when administering intravenous agents such as labetalol and hydralazine as they can cause a sudden drop in blood pressure. The aim of treatment is to drop the systolic blood pressure below 150 mmHg and/or the diastolic below 100 mmHg. The Centre for Maternal and Child Enquiries has recommended that a systolic reading above 150 mmHg should be treated immediately (Cantwell et al, 2011).

Table 2. Multisystem effects of pre-eclampsia

Central nervous system	Eclampsia (seizures)
	Cerebral haemorrhage (stroke)
	Cerebral oedema
	Cortical blindness
	Retinal oedema
	Retinal blindness
Renal system	Renal cortical necrosis
	Renal tubular necrosis
Respiratory system	Pulmonary oedema
	Laryngeal oedema
Liver	Jaundice
	HELLP syndrome (haemolysis, elevated liver enzymes and lowered platelets)
	Hepatic rupture
Coagulation system	Disseminated intravascular coagulation
	Microangiopathic haemolysis
Placenta	Placental infarction
	Placental abruption
Baby	Death
	Preterm birth
	Intrauterine growth restriction

From Duley et al (2006)

Table 3. Stepwise pharmacological approach to the management of hypertension in pre-eclampsia

Drug		Dose
Labetolol	Oral	200 mg hourly until desired effect (max 1600 mg total dose)
	Intravenous	20 mg bolus, followed by 40 mg bolus 10 minutes later, then 80 mg bolus every 10 minutes until desired response, maximum 220 mg total dose
Hydralazine	Intravenous	5–10 mg intravenously every 15–20 minutes
Nifedipine	Oral	10 mg orally (immediate-release), maximum 120 mg/day

Fluid management

Careful fluid management is vital in these patients. Owing to capillary wall damage, fluid leaks into the extravascular compartment, causing pulmonary and peripheral oedema. The patient is at particular risk post-delivery when endothelial function returns to normal and a potentially large fluid shifts occur. Again different protocols exist, but it is generally recommended that patients should be fluid restricted and maintenance fluid should be limited to 80 ml/hr (National Institute for Health and Clinical Excellence, 2010) with fluid challenges only given after careful consideration. Urine output of as low as 0.25 ml/kg/hr can be acceptable. If the patient remains persistently oliguric, is haemodynamically unstable or the situation is complicated by haemorrhage, invasive monitoring should be considered.

Prevention of eclampsia

Following the MAGPIE trial (Altman et al, 2002) it is now recommended that all patients with severe pre-eclampsia or severe hypertension should be treated with intravenous magnesium sulphate if birth is planned within 24 hours. The treatment regimen should be commenced in accordance with this trial as well as local guidelines. Magnesium 4 g should be given intravenously over 5 minutes followed by an intravenous infusion of 1 g/hr for the following 24 hours. Clinical monitoring of deep tendon reflexes and respiratory effort, rather than biochemical measurement of magnesium levels, is recommended. Alternative anticonvulsant therapy is usually not required in these patients.

Eclamptic seizures are usually short and self-limiting. General management should include a generic ABCD (airway, breathing, circulation, disability) approach. A further bolus dose of 2–4 g magnesium can be given intravenously, or the rate of infusion can be increased to 1.5 g/hr. It is important that the clinician, when assessing these patients, should consider other causes of seizures before a diagnosis of eclampsia is made. Treatment should continue well into the postnatal period and until blood pressure returns to normal.

Labour analgesia

A multimodal approach to labour analgesia should be adopted, although epidural analgesia is often regarded as the treatment of choice. Not only does it augment blood pressure reduction but it also provides a route of anaesthesia for caesarean section should it become necessary. Coagulopathy needs to be excluded before considering central neuraxial blockade, as thrombocytopenia is not uncommon in these patients. Guidance for acceptable levels of platelets required to perform central neuraxial blockade is from expert opinion only, in the obvious absence of clinical trials. A platelet count above 100×10^9/litre is considered safe, while below this, a full coagulation screen should be ordered. If the coagulation screen is normal, then it is thought reasonable to proceed if the platelet count is above 75×10^9/litre. In mild or moderate pre-eclampsia, it would be acceptable to site an epidural with coagulation and full blood count results available within 6 hours. In severe pre-eclampsia or HELLP syndrome central neuraxial blockade should not be performed without more up-to-date coagulation and platelet results (Cook et al, 2011). If coagulopathy is present and prevents the siting of an epidural, alternative options should be considered such as remifentanil patient-controlled analgesia.

Timing of delivery

This is often a difficult decision and again a multidisciplinary approach is crucial.

Before 34 weeks' gestation, women with pre-eclampsia should be managed conservatively if at all possible. Thresholds should be agreed upon by the obstetricians on admission of these patients to labour ward, and these will help guide any decisions regarding delivery. These thresholds will include biochemical, haematological and clinical markers. Markers such as refractory hypertension, or a worsening maternal or fetal clinical picture may expedite delivery. However, delivery should not be undertaken until discussions between obstetricians, anaesthetists and neonatologists have taken place. A course of maternal corticosteroids should ideally be completed before delivery, to aid fetal lung maturation.

Delivery should be offered to pre-eclamptic patients with severe hypertension who are more than 34 weeks' gestation, once the blood pressure has been controlled and a course of corticosteroids (if indicated) has been completed.

Women over 37 weeks' gestation with mild to moderate pre-eclampsia should be offered delivery within 24–48 hours (National Institute for Health and Clinical Excellence, 2010).

Timing of delivery is often guided by fetal wellbeing. These patients should receive cardiotocography, an ultrasound to assess fetal growth and amniotic fluid volume, and umbilical artery Doppler velocimetry. Depending on the severity of the disease, these tests will be repeated to a greater or lesser extent, and will aid the decision to deliver.

Delivery

Once the decision to deliver has been made, then an anaesthetic plan should be formulated. The choice of general *vs* regional anaesthesia will depend on consideration of the risks *vs* the benefits of each procedure. In pre-eclamptic patients even intravenous access, patient positioning, monitoring and anatomical landmarks may be challenging, and all of these should be optimized before starting any sort of anaesthesia. In cases of severe pre-eclampsia invasive arterial monitoring should be seriously considered.

In most cases regional anaesthesia is the ideal approach to providing anaesthesia for caesarean section, especially as general anaesthesia carries theoretically higher risks. Regional anaesthesia is contraindicated in the presence of coagulopathy and, as discussed previously, coagulation and full blood count test results should be available

within 6 hours of performing regional anaesthesia, or immediately before in a patient with severe pre-eclampsia. In a case of extreme fetal distress, clear communication between obstetricians and anaesthetists should occur in order to avoid the higher risks of general anaesthesia. The choice between a slower, more controlled but less predictable epidural anaesthetic and a more predictable, faster onset spinal anaesthetic should be considered in each individual case. Pre-spinal, fluid pre-loading should be done with extreme caution or even avoided totally. The normal predictable drop in blood pressure following spinal anaesthetic is often absent in these cases. Circulating vasoconstrictors maintain arteriolar vasoconstriction when sympathetic tone is blocked by the spinal anaesthetic. A vasopressor agent, such as phenylephrine, should be available, but pre-emptive infusions may be unnecessary. Infusion doses and bolus doses should be administered very cautiously in light of potential increased sensitivity.

In addition to the risks of general anaesthesia for the obstetric population, patients with pre-eclampsia may have an increased risk of a difficult airway as a result of airway oedema. A thorough airway examination should be carried out before induction of anaesthesia and, if indicated, an awake fibreoptic intubation can be performed via the oral route – the nasal route should be avoided because of increased venous congestion. As with any potentially difficult airway, positioning should be optimal, an additional anaesthetist should be present if possible, and a difficult airway trolley should be nearby. An exaggerated sympathetic response to laryngoscopy can occur, which can precipitate intracerebral bleeding in severe cases, and therefore this response should be avoided or attenuated with the use of pharmacological agents such as alfentanil, remifentanil, lidocaine or a short-acting beta-blocker. This response is also important to consider when contemplating extubation and a similar pharmacological approach should be considered. Magnesium will prolong non-depolarizing neuromuscular blockade and neuromuscular monitoring should be used to ensure complete reversal before extubation. It is also essential to remember that airway oedema could have progressed during the operation and care should be taken at extubation, ensuring a leak on cuff deflation.

Of the routine uterotonics used, ergometrine, an ergot alkaloid often used to stimulate uterine contraction, should be avoided in pre-eclampsia because of its potential to cause profound hypertension.

Postoperative care

Although definitive treatment of pre-eclampsia is delivery of the baby, risk from pre-eclampsia and its complications can persist for several hours or days postpartum. There is also a significant proportion of pre-eclamptic patients (approximately 20%) whose first presentation is in the postnatal period (Uzan et al, 2011). Management of these patients should be as for antenatal presentation. The major issue in this period is often fluid overload, and the potential to develop pulmonary oedema. A stringent fluid regimen should be adhered to, with a total input of 80 ml/hr along with strict measurement of urine output. Input should also include all intravenous infusions and oral intake. A decrease in urine output is not unusual following the stress response of surgery, but can be associated with syntocinon infusions. Fluid challenges in response to low urine output states should be avoided and only prescribed after discussion with senior clinicians. Indeed morbidity from pre-renal failure in this population is much less common than from pulmonary oedema. If fluid overload is suspected, then judicious use of diuretics can be considered (Martin et al, 1999). Where applicable, leaving epidural catheters in situ post-delivery is recommended to allow continued epidural analgesia while avoiding the sympathetic stimulation associated with pain.

The most appropriate place for postpartum care should be a multidisciplinary decision and critical care involvement may be required. The decision will often depend on whether there is a high dependency unit on the labour ward able to deliver a higher level of care. If the labour ward team feels the patient requires a higher level of care than is available on the labour ward, the patient should be promptly referred for critical care.

Recent advances

Pre-eclampsia is persistently one of the leading causes of direct maternal death in the UK and therefore a large amount of research continues to be undertaken on the disease and its prevention. A Cochrane review showed that in those mothers with high risk factors for developing pre-eclampsia, aspirin 75 mg orally daily reduces the incidence of developing the disease (Duley et al, 2007). In the acute setting, antiplatelet therapy can augment haemorrhage, so it is not recommended for those with only mild to moderate risk factors. Further Cochrane reviews have supported calcium supplementation in those who have a low dietary calcium (Atallah et al, 2010) but have shown no supporting evidence for the use of nitric oxide donors (Meher and Duley, 2007), diuretics (Churchill et al, 2007) or fish oils (Makrides et al, 2006).

Most ongoing research is based upon predicting and identifying individuals at high risk of developing pre-eclampsia, with the aim of focused primary prevention. Studies have looked at the presence of various vasoactive substances such as endoglin, vascular endothelial growth factor and sFlt-1 during the first or second trimester with the potential to develop antagonists against such factors (Ahmed, 2011). Potential inhibitors of sFlt-1 are statins, and the Birmingham StAmP trial is a double-blinded prospective trial aimed at ameliorating early onset pre-eclampsia, with the administration of pravastatin. Having started in 2012, this trial is still in the recruitment phase and results are not expected for some time.

Dyer at al (2008) have looked at various cardiac output monitors in patients with pre-eclampsia. The work implies that although mean arterial pressure drops cardi-

ac output may remain constant and intervention, e.g. phenylephrine bolus, may not be required. It raises a potential question about whether cardiac output monitoring should be used in these cases to guide fluid and vasopressor administration.

Conclusions

Pre-eclampsia remains one of the leading causes of fetal and maternal morbidity and mortality. When evaluating these patients it is important to be aware of the multisystem nature of the disease. Use of best evidence and local guidelines based on national guidelines is recommended in the management of these patients. When approaching such patients a clinical checklist (*Table 4*) can act as an aide memoire so that all clinical implications of the disease are considered. The optimal timing of delivery will be a multidisciplinary decision, requiring clear communication and teamwork between the specialties involved. The perioperative care of the pre-eclamptic patient remains a challenge but knowledge and understanding of the pathophysiology of the disease will help make it more successful. **BJHM**

Table 4. Checklist for management of pre-eclampsia

Confirmation of diagnosis	Proteinuria
	Hypertension
Classify severity of condition	Mild
	Moderate
	Severe
Ensure effective blood pressure control	Maintain systolic blood pressure below 150 mmHg
	Escalate treatment in a stepwise approach
	Consider early epidural
Consider eclampsia prevention	Magnesium prescribed for all severe cases
Enforce strict fluid management	Maintenance fluid 80 ml/hr
	Avoid fluid boluses
Optimal delivery timing	Communicate with all relevant specialties
Assess coagulopathy	Bloods within last 6 hours
	Bloods within 2 hours for severe cases
	Suitable for regional anaesthesia
Consider invasive monitoring	Arterial line?
	Central venous pressure line?
Airway	Detailed and repeated airway assessment
Decide on postpartum care location	Labour ward high dependency care
	Critical care
Multidisciplinary approach	Continual liaison and reassessment with the multidisciplinary team

KEY POINTS

- Appropriate recognition and treatment of pre-eclampsia decreases maternal and fetal morbidity and mortality.
- A systolic blood pressure above 150 mmHg should be treated.
- A checklist can be a helpful reminder when managing a pre-eclamptic patient.

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