17 July 2009

Severe pre-eclampsia and types of anaesthetics

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Introduction

Pre-eclampsia is a disease that complicates about 5-8% of all pregnancies. It is associated with significant morbidity and mortality and is still listed as one of the top 3 causes of maternal morbidity and mortality globally.

As would be expected, the management of pre-eclampsia poses a great challenge to the obstetrician. And when pre-eclampsia progresses to its severe form, the risk of morbidity and mortality (to both the mother and the foetus) increases substantially. Following from this, these patients often present for emergency caesarean section.

In this setting, there is often limited time for resuscitation and optimisation of clinical condition. Thus, this also poses a great challenge to the obstetric anaesthetist, in particular, with respect to pre-operative optimisation, choice of a safe anaesthetic and maintenance of intra-operative stability to ensure delivery of a healthy neonate and to minimise maternal morbidity and mortality.

Definition

Pre-eclampsia is a hypertensive disorder of pregnancy that occurs after 20 weeks of gestation. It is defined as a systolic blood pressure of 140 mmHg or greater or a diastolic blood pressure of 90 mmHg or greater on 2 or more occasions at least 4 hours apart with proteinuria (1+ or more on urine dipstix or greater than 0,3g protein in a 24-hr urine specimen).

Severe pre-eclampsia is defined as pre-eclampsia with one or more of the following:

- Systolic blood pressure of 160 mm Hg or higher or a diastolic blood pressure of 110 mmHg or higher on 2 or more occasions, 6 hours apart.
- Proteinuria, with excretion of 5g or more of protein in a 24-hour urine specimen or 3+ or greater on two random samples collected four or more hours apart;
- Oliguria, with excretion of less than 500 mL of urine in 24 hours;

- Pulmonary edema or cyanosis;
- Impairment of liver function;
- Visual or cerebral disturbances;
- Pain in the epigastric area or right upper quadrant;
- Decreased platelet count;
- HELLP syndrome;
- Intrauterine growth restriction.

Risk Factors

- Maternal factors:
  -Chronic hypertension
  -Renal disease
  -Diabetes mellitus
  -Obesity
  Primigravida
  -Previous history or family history (especially mother) of pre-eclampsia

- Pregnancy Associated Factors:
  -Multiple pregnancies
  -Molar pregnancy
  -Congenital anomalies (eg. trisomy 13, triploidy), etc.

Pathophysiology

- Endothelial cell dysfunction has been implicated in the pathogenesis of pre-eclampsia. Numerous hypotheses have been proposed for this endothelial cell dysfunction. Incomplete trophoblastic invasion into the spiral arteries has been implicated resulting in failure of the blood vessels to dilate and vessel thrombosis with reduced placental perfusion (the first stage of the development of pre-eclampsia). The second stage is the response to the reduced perfusion that leads to maternal and fetal affectation.

Clinical manifestations and complications

- -Cardiovascular and respiratory system: The intravascular volume is depleted. The total peripheral resistance is increased which leads to increased left ventricular work that can predispose to left ventricular dysfunction and pulmonary oedema. Increased risk of myocardial ischemia.
- -Airway: These patients can always be a potentially difficult intubation due to upper airway oedema.
- -Central nervous system: Patients can present with headaches, visual disturbances and irritability. Pre-eclampsia may be complicated with tonic clonic seizures, which is known as eclampsia. Cerebrovascular accidents may occur.
- -Gastrointestinal system: Patients may develop hepatic subcapsular haemorrhages.- maybe related to edema or ischemia or low platelets
- -Renal: Patients can develop renal failure.
- -Haematological system: Thrombocytopenia can occur. Patients may present with the HELLP syndrome.
- -Foetal-placental unit: Intra-uterine growth restriction (IUGR) can occur. There is an increased risk of abruptio placentae.

Obstetrical management of severe pre-eclampsia

- -Blood pressure control: Use of oral anti-hypertensives :
  - Ist line – alpha methyldopa
  - 2nd line – calcium channel blockers eg. nifedipine
  - 3rd line – hydralazine
  - 4th line – alpha blockers eg. prazosin

If immediate lowering of BP required, IV agents used eg. labetalol, nitroglycerine, sodium nitroprusside. However, aim to lower BP over 1 to 2 hours, with a maximum of 20% decline from baseline.

- -Seizure prophylaxis: Patients are put on an intravenous infusion of magnesium sulphate for 24hours to reduce the risk of developing eclampsia. (Sibai regime used locally – 6g Magnesium sulphate loading dose over 20-30 minutes, then 2g magnesium sulphate per hour for 24 hours).
- -Foetal monitoring: This includes the cardio-tocograph (CTG).
- -Mode and timing of delivery: The decision to deliver the foetus has to be individualised to the patient. Factors affecting delivery include gestational age (may need maternal steroid supplementation for fetal lung maturity), favourability of the cervix, maternal condition (blood pressure control, coagulopathy, worsening thrombocytopenia, etc.) and foetal condition (foetal distress, IUGR), etc.

Anaesthetic Management

- The anaesthetic management has to be individualised to the patient. These include either a regional anaesthetic technique or a general anaesthetic.

Regional anaesthesia:

- Provided there is no contraindication to a regional anaesthetic, it is the preferred mode of anaesthesia as it provides excellent analgesia, avoids airway manipulation, allows early maternal bonding with the newborn and the route of administration lessens the risk of neonatal respiratory depression.

- CONTRAINDICATIONS TO REGIONAL ANAESTHESIA INCLUDE:
  - patient refusal
  - coagulopathy
  - local infection
  - hypovolemia
  - raised intracranial pressure, depressed level of consciousness
  - hypersensitivity to local anaesthetics
  - fixed cardiac output states
- Regional anaesthesia includes spinal anaesthesia, epidural anaesthesia and combined spinal epidural anaesthesia.
- Drugs commonly used in our setting include a mixture of bupivicaine (a local anaesthetic, usually a dose of about 9mg) and fentanyl (an opioid, dose range usually between 10ug to 25ug).
- Spinal anaesthesia is usually associated with a rapid onset of action and the associated sympathectomy may cause a significant drop in the blood pressure. It is this effect that has traditionally led to the concern and reservation about the use of spinal anaesthesia in severe pre-eclampsia. However, recent research (see 'literature review' below) has suggested more favourable outcomes with spinal anaesthesia, and hence, it has started to gain more popularity.

It is worth noting that a systolic blood pressure of less than 100 mmHg or a reduction of greater than 20% in the mean arterial blood pressure from the baseline mean arterial pressure are undesirable as these are usually associated with impaired organ perfusion (of added concern in the parturient is impaired utero-placental perfusion). This hypotension is promptly treated with vasopressors (ephedrine or phenylephrine).

Epidural anaesthesia usually involves a mixture of a local anaesthetic and an opioid. This is associated with a slower and more gradual onset of action and hence a gradual and less dramatic drop in blood pressure. This has

traditionally made it the regional anaesthetic of choice in severe pre-eclampsia.

However, recent research (see 'literature review' below) may not support this. Epidural anaesthesia may also be used pre-operatively, as a mode of analgesia for the patient in labour. The epidural can then be 'topped up' to establish a higher level of anaesthesia, should the patient require a caesarean section. The epidural can also be continued in the post-operative period for post-op analgesia and blood pressure control. However, the epidural has to be monitored in at least a high care setting.

Combined spinal epidural anaesthesia - the spinal anaesthetic has a rapid onset of action (as would be required for a patient presenting for caesarean section) and the epidural can be subsequently used when the spinal anaesthetic starts to wear off (eg. for post-op analgesia and blood pressure control).

For all of the above mentioned regional anaesthetic techniques, there exists the possibility that the regional anaesthetic may fail to work (for various reasons eg. technical difficulties, uneven distribution of local anaesthetic/'patchy block', etc.). In this event, it may be required to convert from a regional anaesthetic to a general anaesthetic technique.

General anaesthesia:

General anaesthesia is usually reserved for those patients who have a contraindication to a regional anaesthetic technique (see above). The advantages of general anaesthesia are its rapid onset of action and its reliability as a mode of anaesthesia.

General anaesthesia, however has its own disadvantages and potential dangers. Firstly, pregnant patients can rapidly drop their haemoglobin oxygen saturation (upon initiation of general anaesthesia) due to a reduced functional residual capacity (the oxygen reservoir) and an increased oxygen demand. This means that once the patient is under general anaesthesia, there is very limited time to intubate the patient before desaturation starts to

occur. As a result, these patients need to be adequately pre-oxygenated before commencement with general anaesthesia.

Secondly, all pregnant patients are regarded as 'full stomachs' ie. they are at high risk for aspiration of gastric contents when general anaesthesia is induced (which results in the loss of protective airway reflexes). To minimise this risk, the patient is given sodium citrate (an antacid) just prior to entering the operating theatre (all parturients that are going to receive an anaesthetic are given sodium citrate as even a regional anaesthetic may be converted to a general anaesthetic). Also, a rapid sequence induction is performed.

Thirdly, the pregnant patient is regarded as a potentially difficult intubation due to upper airway oedema, enlarged breasts that may impair laryngoscopy, etc. In severe pre-eclampsia, the degree of upper airway oedema may be greater, making intubation more challenging. Thus, the anaesthetist needs to be prepared for a difficult intubation (eg. use of difficult intubation trolley).

The other problem is the 'intubation response'. This is the sympathetic nervous system response to intubation, including hypertension and tachycardia. This could prove detrimental to the patient with severe pre-eclampsia. As a result, the intubation response needs to be 'blunted' ie. the intubation response is minimised by the use of various drugs including opioids (eg. alfentanil) or beta-blockers (eg. esmolol) with a rapid onset of action, magnesium, lignocaine, etc.

Also, some of the anaesthetic agents (especially intravenous opioids) used may cross the placental membrane and cause respiratory depression in the neonate.

Literature Review

There have been numerous studies (both retrospective and prospective) that have compared the different types of anaesthesia administered to patients with severe pre-eclampsia or pre-eclampsia.

Prospective studies:

Aya et al (2003) compared the haemodynamics of spinal anaesthesia in patients with severe pre-eclampsia versus normotensive patients (n= 60) presenting for elective caesarean section. The risk of hypotension was found to be about six times less in the severe pre-eclampsia group. Also, the normotensive group had increased vasopressor requirements. It was argued that the smaller neonates (due to intra-uterine growth restriction) in the severe pre-eclampsia group may have had a lesser degree of aortocaval compression and hence a lesser degree of hypotension.

Visalyaputra et al (2005) compared spinal versus epidural anaesthesia in patients (n=100) with severe pre-eclampsia presenting for emergency or elective caesarean section. Hypotension was found to be more frequent in the spinal group, but not of significant duration and easily correctable. Vasopressor requirements were found to be more in the spinal group. However, the neonatal outcome (assessed by APGAR scores and umbilical artery pH) was found to be similar in both groups.

Sharwood-Smith (1999) et al also compared spinal versus epidural anaesthesia in patients (n=28) with severe pre-eclampsia. The haemodynamic changes and the neonatal outcomes were found to be similar between the two groups.

Wallace et al (1995) compared regional versus general anaesthesia in patients (n=80) with severe pre-eclampsia presenting for elective or emergency caesarean section. The maternal and neonatal outcomes were found to be similar in the two groups. It was also concluded that if steps were taken to ensure a careful approach to either type of anaesthetic, there were no marked differences in haemodynamics between the two groups.

Dyer et al (2003) compared spinal versus general anaesthesia in patients (n=70) with pre-eclampsia presenting for emergency caesarean section with a 'nonreassuring' foetal heart trace. Maternal haemodynamics were similar between the 2 groups. Neonatal umbilical artery pH was found to be lower in the spinal group but 5 minute APGAR scores between the 2 groups were similar.

Retrospective studies:

In one of the larger retrospective studies, Hood et al (1999) compared spinal versus epidural anaesthesia in patients (n=138) with severe pre-eclampsia presenting for caesarean section. The magnitude of maternal blood pressure declines was similar between the 2 groups. Maternal and neonatal (APGAR score) outcomes were also similar.

Okafor et al (2005) compared spinal versus general anaesthesia in patients (n=125) with pre-eclampsia and eclampsia. The maternal and foetal mortality was found to be high in the general anaesthetic group. Lack of equipment and inexperienced management were attributable factors.

Thus, it can be seen, that there is a paucity of studies focusing on emergency cases. In our setting, the vast majority of patients present for emergency surgery.

Most of the above studies were conducted on elective patients, where there was adequate time for pre-operative optimisation of clinical condition, including blood pressure control. Also of note, the majority of these studies were conducted in other countries, and as a result, it may be difficult to extrapolate the results of these studies and apply it to our patient population.

	SPINAL	EPIDURAL	GENERAL
Aya	Y		
Sharwood-Smith	Y	Y	
Hood	Y	Y	
Visalyaputra	N	Y	
Dyer	Y		Y
Wallace	Y	Y	Y
Okafor	Y		N

Suggested management

A suggested possible Mx for patients with severe pre-eclampsia would include:

- Provided there is no contraindication, regional anesthesia would be the anesthetic of choice.
- In the emergency setting, spinal (eg. 9mg bupivicaine + 10ug fentanyl) would probably be the best option.
- Labouring patients should ideally be on an epidural (0,0625 to 0,1% bupivicaine + 2ug/ml fentanyl).
- Epidural 'top ups' for OT, time permitting.
- Non emergency, consider CSE.
- If GA, important points to note :
    - Be prepared for difficult intubation
    - Blunt the intubation response eg. alfentanil (10 – 30ug/kg), magnesium (30mg/kg), lignocaine (1-1,5mg/kg), esmolol, etc.
    - Analgesia – longer acting opioids post delivery eg. morphine, pethidine
    - Keep MAP within 20% of baseline – use of vasopressors including phenylephrine and ephedrine
- Mx often individualised however!

Conclusion

The parturient with severe pre-eclampsia is at high risk for morbidity and mortality. To complicate matters further, in our setting, the vast majority of these patients present for emergency caesarean section. Thus, these patients pose an immense challenge to the attending obstetrician and anaesthetist.

As a result, lots of research has gone into the anaesthetic practice dealing with these patients. Of recent, some of these studies have shown conflicting results when compared to previous anaesthetic practices.

However, before we start applying these new results to our patient population, there is a need for more local research in the field.

Till we get more clear directives, Mx has to be individualised based on clinical judgement.

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