Pre-eclampsia and the anaesthetist

Parveez Peer
Kailash Bhatia

Abstract

Pre-eclampsia is a multisystem disorder of pregnancy that forms an integral part of the spectrum known as hypertensive diseases of pregnancy, occurring after 20 weeks of gestation. Its incidence seems to be increasing globally and it remains the fourth most common cause of direct maternal deaths in the UK. Intra-cerebral haemorrhage, pulmonary, liver and renal dysfunctions are recognized complications of pre-eclampsia that contribute to maternal morbidity and mortality. Measurement of specific maternal angiogenic factors such as placental growth factor (PGF) and soluble fms-like tyrosine kinase-1 (sFlt-1) may aid in the diagnosis and management of this condition. Strict blood pressure control using anti-hypertensive medications, fluid restriction, magnesium sulphate for seizure prophylaxis and timely delivery remain the key strategies to decrease maternal morbidity. Neuraxial anaesthesia, provided the coagulation status is normal, is the preferred technique for delivery. If general anaesthesia is used, emphasis should be on preparing for a difficult airway and ablation of the pressor response of laryngoscopy and intubation.

Keywords Anaesthesia; intra-cranial haemorrhage; magnesium sulphate; neuraxial; pre-eclampsia; pregnancy

Royal College of Anaesthetists CPD Matrix: 2B01, 2B02, 2B03, 2B05, 3B00

Introduction

Pre-eclampsia is a multisystemic hypertensive disorder occurring after 20 weeks of pregnancy. Globally the incidence of pre-eclampsia is increasing and is estimated to be around 10%, whereas the incidence is around 5% in the UK.[1] Nine out of 78 direct maternal deaths (12.8% or 0.42/100,000 maternities) were attributed to pre-eclampsia in the last Confidential Enquiries into Maternal Deaths and Morbidity 2009–2012 report (EMBRRACE-UK) making it the fourth leading cause of direct maternal deaths in the UK.[2] Though mortality from pre-eclampsia is decreasing, maternal morbidity due to the multisystemic nature of the disease and fetal morbidity (prematurity, small for gestation age (SGA), respiratory distress syndrome, stillbirth and death) necessitate a multidisciplinary approach in the diagnosis and management of this condition.

Parveez Peer *MBBS FRCA DESA is a Fellow in Obstetric Anaesthesia at Central Manchester University Hospitals and St Mary's Hospital, Manchester, UK. Conflicts of interest: none.*

Kailash Bhatia *MBBS FRCA EDRA DA DNB is a Consultant Anaesthetist at Central Manchester University Hospitals and St Mary's Hospital, Manchester, UK. Conflicts of interest: none.*

Learning objectives

After reading this article, you should be able to:

- classify pre-eclampsia
- state the risk factors and the manifestations of pre-eclampsia
- explain the management of pre-eclampsia in the delivery suite
- describe the anaesthetic management of a woman with pre-eclampsia

Diagnostic criteria

The updated diagnostic criteria for pre-eclampsia are listed in Box 1.

Eclampsia is defined as seizures that cannot be attributed to other causes in a woman with pre-eclampsia. It occurs in 1% of women with pre-eclampsia.

Pre-eclampsia needs to be differentiated from gestational hypertension, which is characterized by new onset of hypertension (>140/90 mmHg) after 20 weeks' gestation without significant proteinuria or end organ damage and return of blood pressure within 6–12 weeks postpartum. Progression from gestational hypertension to pre-eclampsia occurs in almost 25% of women.

Chronic hypertension refers to hypertension before pregnancy or before 20 weeks' gestation without a known cause and persists after 12 weeks postpartum. It complicates between 1% and 5% of pregnancies but this is on the rise with increasing maternal age, increasing obesity and increasing in vitro-fertilization pregnancies.

Pre-eclampsia superimposed on chronic hypertension is when a woman with chronic hypertension develops new signs or symptoms of pre-eclampsia.

Classification

Pre-eclampsia can be classified based on blood pressure measurements or based on gestation age, though now it is agreed that there may be an overlap of these two.

Pre-eclampsia classification based on blood pressure is as follows.

- Mild – SBP 140–149 and/or DBP 90–99 mmHg.
- Moderate – SBP 150–159 or DBP 100–109 mmHg.
- Severe – SBP 160 mmHg or higher, or DBP 110 mmHg or higher.

Early-onset and late-onset pre-eclampsia classification based on gestation age is as follows.

- Early-onset pre-eclampsia (<34 weeks' gestation age) – early-onset pre-eclamptic women are more likely to develop severe pre-eclampsia, HELLP syndrome (Haemolysis, Elevated Liver enzymes, Low platelet count) and eclampsia. Their fetuses are at higher risk of preterm delivery and death compared to late-onset pre-eclampsia. There is strong association between African and American race, congenital anomalies and pre-existing hypertension with early-onset pre-eclampsia.
- Late-onset pre-eclampsia (≥34 weeks' gestation age) – younger maternal age, nulliparity, diabetes mellitus and other maternal co-morbidities are associated with late-onset disease.

Diagnostic criteria for pre-eclampsia

Hypertension diagnosed after 20 weeks of gestation, with previous normal blood pressure (BP), which returns to normal within 6–12 weeks postpartum.

1) High blood pressure

Systolic BP (SBP) ≥140 mmHg or
Diastolic BP (DBP) ≥90 mmHg on two occasions at least 4 hours apart or
SBP ≥160 mmHg or DBP ≥110 mmHg, confirmed within a short interval.

(Note – Automated devices may underestimate BP, Korotkoff phase 5 should be used to determine DBP)

+

Proteinuria

≥300 mg per 24-hour urine collection or
Protein/Creatinine ratio ≥30 mg/mmol or
Dipstick reading of 1+ (only if other quantitative methods unavailable)

Or, New onset of:

2) High blood pressure

Systolic BP (SBP) ≥140 mmHg or
Diastolic BP (DBP) ≥90 mmHg on two occasions at least 4 hours apart or
Systolic BP ≥160 mmHg or diastolic BP ≥110 mmHg, confirmed within a short interval.

+

Any of the following severe features:

Thrombocytopenia: platelet count <100 × 109/litre

Renal insufficiency: serum creatinine >97 mmol/litre or
Two × normal ? serum creatinine concentration in the absence of other renal disease

Impaired liver function: two × normal blood concentrations of liver transaminases and/or severe persistent right upper quadrant or epigastric pain unresponsive to medication and without alternative diagnosis.

Pulmonary oedema

Cerebral/visual symptoms

Utero-placental involvement

Box 1

Risk factors for pre-eclampsia

High-risk factors (aspirin recommended if one or more present)

- History of pre-eclampsia especially when accompanied by adverse outcomes
- Type 1 or 2 diabetes
- Chronic hypertension
- Renal disease
- Auto-immune disease/antiphospholipid antibodies/factor V Leiden

Moderate risk factors (aspirin recommended if two or more present)

- Age >35 years
- First pregnancy
- Obesity
- Family history of pre-eclampsia (mother or sister)
- Pregnancy interval >10 years
- Socio-demographic characteristics (African race)

Box 2

Pathogenesis, aetiology and risk factors

The main risk factors for pre-eclampsia are highlighted in Box 2.[3]

During normal pregnancy, cytotrophoblasts invade the inner third of the myometrium, and spiral arteries lose their endothelium and most of their muscle fibres leading them to become low-resistance vessels. In pre-eclampsia this invasion by trophoblasts is deficient. This leads to inadequate perfusion of the placenta and release of substances such as free radicals, oxidized lipids, prostaglandins, cytokines, and endothelial dysfunction. Inadequate perfusion of placenta also results in a decrease in pro-angiogenic factors, that is, vascular endothelial growth factor (VEGF), placental growth factor (PGF), placental protein 13 (PP-13), pregnancy-associated plasma protein A (PAPP-A) and an increase in anti-angiogenic factors, that is, soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin (sEng) and asymmetric dimethyl arginine (ADMA).[4]

In a prospective multi-centre study of 287 women with suspected pre-eclampsia at less than 35 weeks' gestational age, low PGF (<5th percentile or <100 pg/ml) was found to have high sensitivity and negative predictive value for determining which women are likely to need delivery within 14 days.[5] Some recent studies claim that the sFlt-1/PlGF ratio has the potential to predict early-onset and preterm pre-eclampsia at mid-pregnancy in asymptomatic women.[6]

Multiple theories are postulated for the abnormal placentation seen in pre-eclampsia. Genetic and immunological seem to be the most commonly accepted and are possibly interlinked. Factors favouring genetic theory include a family history of pre-eclampsia on either maternal or paternal side. A meta-analysis in 2013 identified seven relevant gene variants in or near six genes associated with pre-eclampsia. More than 40% of pre-eclamptic women do not respond to traditional anti-hypertensive therapy. This has led to identify genetic polymorphisms of responders and non-responders.

Limited exposure to paternal antigen supporting immunological theory, as is seen in teenage mothers, conception by donor insemination, nulliparity and increased inter-pregnancy interval. Also increased incidence of pre-eclampsia in auto-immune diseases support immunological mechanisms.

Recently it has been suggested that this condition could actually be a reflection of mismatch between the stimulus of fetal