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Severe preeclampsia: what's new in intensive care?

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Introduction

In 2013, the British period drama television series "*Downton Abbey*" portrayed the death of Lady Sybil Branson from postpartum eclampsia, raising public awareness to signs of preeclampsia and instigating debate regarding the potentially lethal outcome of hypertensive disease of pregnancy. Obstetrical complications constitute 0.15 % of hospital deliveries and 1.84 % of intensive care unit (ICU) admissions. Peripartum hemorrhage, the most prevalent cause of maternal death, has a 55 % cause-specific mortality [1]. Early identification of hemorrhage, definitive surgery, transcatheter arterial embolization and correction of coagulopathy are the mainstays of treatment. Hypertensive diseases constitute the second most prevalent cause of maternal death worldwide [2], and are responsible for 36–66 % of ICU admissions and 10 % of maternal deaths in Europe [3]. Women admitted to ICU for pregnancy-related hypertensive complications are increasingly more ill [4].

Diagnosis, causes and epidemiology

The four hypertensive disorders of pregnancy include pre-existing (chronic) hypertension, gestational hypertension, preeclampsia and eclampsia (Table 1). Diagnosis requires two separate measurements of a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg in the same arm [5]. Preeclampsia is confirmed when ≥300 mg protein is also detected in 24 h urine collection. Preeclampsia is reported in 2–8 % of pregnancies. It is associated with an eight-times higher frequency of maternal near-miss than in pregnancies without this condition [6]. Malignant hypertension is defined when maternal hypertension is associated with ischemic organ damage [7].

Preeclampsia has been associated with several cardiovascular diseases. Current knowledge establishes the presence of shared risk factors rather than a causative relationship. Preeclampsia is attributable to a disparity between uteroplacental supply and fetal demands, leading to both maternal and fetal systemic manifestations of inflammation. Severe preeclampsia, defined as preeclampsia accompanied by at least one severe complication, is responsible for 38 % of maternal deaths among obstetrical ICU admissions [3].

HELLP syndrome and thrombotic thrombocytopenic purpura (TTP) are often confounded with preeclampsia. The hallmarks of HELLP are microangiopathic hemolysis (schistocytes in peripheral blood smear and elevated indirect plasma bilirubin), elevated liver enzymes and a platelet count below 100,000 mm^3. Conversely, HELLP syndrome may be accompanied by only mild elevations in blood pressure. Up to 20 % of the cases have no

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Table 1 The four hypertensive disorders of pregnancy

Type of hypertension	Definitions
Hypertension	Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg observed on at least 2 occasions ≥4 h apart, but <7 days apart
Pre-existing hypertension	Hypertension that was present either pre-pregnancy or that develops at <20 weeks gestation
Gestational hypertension	Hypertension that develops for the first time at >20 weeks gestation
Preeclampsia	Gestational hypertension and one or more of the following: New proteinuria, or One/more adverse condition(s) or One/more severe complication(s) Severe preeclampsia: preeclampsia with one or more severe complications
Eclampsia	New onset of grand mal seizure activity and/or unexplained coma during pregnancy, intrapartum or in the early post-partum period

proteinuria [8]. Recent literature suggests there may be a genetic predilection for the syndrome [9]. Acquired TTP, at times triggered by pregnancy, corresponds to disseminated microvascular thrombosis leading to ischemic organ damage and failure [10]. Malignant complications of TTP are prevented with early initiation of plasmapheresis and/or delivery.

Evidence-based management

Interventions reducing maternal mortality from hypertensive diseases of pregnancy include routine calcium supplementation, antiplatelet agents in women at risk of preeclampsia, magnesium sulphate ($MgSO_4$) for treatment of preeclampsia and eclampsia, antihypertensive drugs for the treatment of mild to moderate hypertension [11] and adherence to established guidelines [12]. Despite measurable reductions in the rate of suboptimal care, inadequate management is still reported in 70 % of maternal deaths due to hypertensive disorders, and 50 % of these are avoidable [3]. Prevention of systolic hypertension and bridging support for failing organs are treatment priorities. Systolic arterial hypertension is the most important predictor of stroke in preeclampsia. First line therapy is either intravenous labetalol and oral nifedipine or intravenous nicardipine. High dose diazoxide and sodium nitropusside are recommended for refractory hypertension in the ICU [5]. Hydralazine is no longer considered first line treatment and $MgSO_4$ should not be used as an antihypertensive [5].

$MgSO_4$ blocks neuromuscular transmission, thereby decreasing acetylcholine release and preventing convulsions. The recommended anticonvulsant dose is an intravenous loading dose of 4 g followed by maintenance 1–2 g/h. Steady state is usually achieved within 3–4 h in pregnancy. Caution is advised in the presence of renal impairment since 90 % of the $MgSO_4$ dose is excreted in the urine within 24 h. Antenatal corticosteroids should be considered for preeclampsia presenting at <34 weeks gestation or if delivery is expected within 7 days [5]. The risk of increasing maternal resistance to antihypertensive therapy should be balanced against the probability of respiratory disease of the newborn.

Cardiovascular and fluid management

Gestational age, stage of labor, disease severity, concomitant comorbidities and medications may all affect the hemodynamic condition of the pregnant woman with preeclampsia. Most women will present with high peripheral vascular resistance and a low cardiac index [13]. Left ventricular diastolic dysfunction with preserved ejection fraction and left ventricular hypertrophy are also often observed. Cardiac ultrasound discriminates heart failure with preserved ejection fraction from peripartum cardiomyopathy with reduced ejection fraction. Maternal mortality is strongly associated with pulmonary hypertensive crises and refractory right heart failure [14], thus fluids should be administered with caution. Pulmonary edema occurs in up to 0.5 % of preeclamptic women [13].

Acute renal failure occurs in ~1 % of women with severe preeclampsia. Urine output does not mirror variations in stroke volume in this population because both substantial increases in sympathetic vasoconstrictor activity and/or secondary organic renal injury may be present. Oliguria should prompt assessment of cardiac function and volume status in order to differentiate between prerenal and renal causes. In future, one can expect that biomarkers of kidney injury will facilitate an earlier diagnosis [15].

Fluids should be administered only after prerenal azotemia has been established, since only half of the women with severe preeclampsia and oliguria will respond to fluids [16]. Pulse pressure variation and respiratory variation of inferior vena cava diameter do not predict fluid responsiveness [16]. However, a >12 % increase in the velocity time integral of subaortic blood flow during passive leg raising does predict fluid responsiveness [16], and the presence of B-lines in lung ultrasound correlates with echocardigraphic findings of heart failure and may suggest pulmonary fluid overload in this patient population [17].

Management of delivery

Women with preeclampsia can be expectantly managed up to a gestational age of 34 weeks but should be delivered at term [5]. Manifestations of organ failure should prompt delivery regardless of gestational age. Vaginal delivery is acceptable and cervical ripening should be undertaken if conditions are unfavorable [5]. The third stage of labor should be actively managed with oxytocin [5]. Early insertion of an epidural catheter is recommended for labor pain control if there is no contraindication to neuraxial anesthesia [5]. As they are at increased risk for difficult airway management, spinal anesthesia is recommended for cesarean delivery. The decrease in blood pressure induced by spinal anesthesia in preeclamptic parturients is less severe than that observed in healthy parturients [18]. Reversal of the effects of neuraxial anesthesia may be accompanied by decreased stroke volume and cardiac output. If general anesthesia is required, remifentanil at 1.34 μg/kg attenuates the hypertensive response to tracheal intubation [19].

Summary

Preeclampsia remains an important cause of avoidable maternal morbidity and mortality. Publication of guidelines and monitoring adherence to life-saving therapies should be prioritized. Prediction of fluid responsiveness requires individual hemodynamic investigation. Future studies are required to determine the optimal early warning system and monitoring tools for providing early and non-invasive hemodynamic assessment.

Conflicts of interest The authors have no conflict of interest to disclose in relation with this topic.

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