



## Aetiology, prophylaxis and management of preeclampsia

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### ABSTRACT

Although preeclampsia affects approximately 3%–8% of pregnancies worldwide and is a major contributor to maternal and neonatal mortality and morbidity, the aetiology of preeclampsia is still not fully understood. This review presents the current knowledge on the aetiology of preeclampsia, with a special emphasis on risk factors and their role, and describes recommendations for the prevention and treatment of preeclampsia.

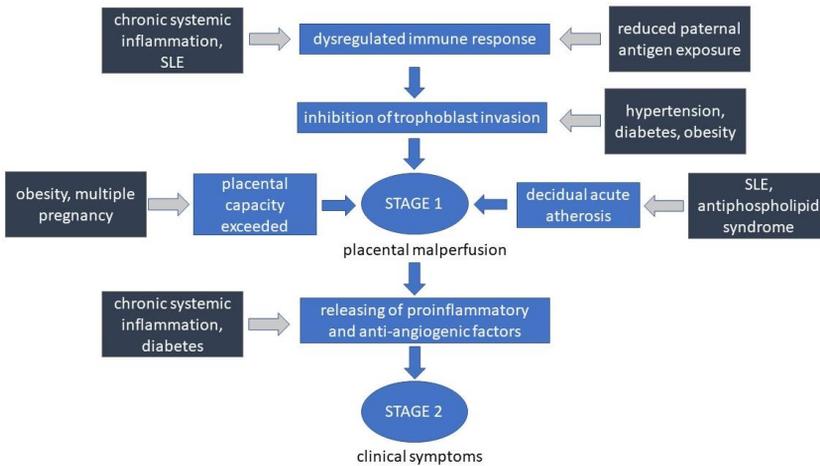
**KEYWORDS:** proteinuria, gestational hypertension, trophoblast invasion, uteroplacental malperfusion, endothelial dysfunction

### Introduction

Preeclampsia (PE) is defined as de novo gestational hypertension after the 20th week of pregnancy ( $>140/90$  mmHg) with new-onset proteinuria ( $>300$  mg/24 h) or at least one other sign of maternal organ dysfunction (haematological complications, kidney and liver dysfunction, neurological complications such as eclampsia) or uteroplacental dysfunction (such as foetal growth restriction) (Braunthal and Brateanu, 2019; Tomimatsu *et al.* 2019). The course progressively worsens, potentially leading to maternal and foetal death. Although the clinical signs of PE resolve after delivery, PE causes persistent disruption of maternal and foetal physiology. PE has long-term effects on both the mother and child, causing increased susceptibility to hypertension

and chronic kidney disease (Turbeville and Sasser; 2020). Women after a pregnancy complicated by PE are more likely to have hypertension, renal dysfunction and cardiovascular and cerebrovascular diseases (Benschop *et al.* 2019).

Although PE affects approximately 3%–8% of pregnancies worldwide (Aouache *et al.* 2018) and is a major contributor to maternal and neonatal mortality and morbidity (Geldenhuys *et al.* 2018), the aetiology of this disorder is still not fully understood. A two-stage model of PE pathogenesis is currently accepted (Figure 1). The first stage, uteroplacental malperfusion, leads to the second stage, in which cycles of ischaemia-reperfusion in the placenta trigger the release of cytokines, anti-angiogenic factors and reactive oxygen



**Figure 1.** The two-stage model of preeclampsia pathogenesis. The risk factors may affect the trophoblast invasion of spiral arteries, conducive to decidual acute atherosclerosis and exceeded placental capacity, which lead to Stage 1. The reduced uteroplacental perfusion induces placental release of proinflammatory and anti-angiogenic factors into the maternal circulation, leading to systemic vascular dysfunction, Stage 2. Pre-existing maternal risk factors such as diabetes and chronic systemic inflammation also predispose to vascular dysfunction. SLE, systemic lupus erythematosus.

species (ROS). When these molecules reach the maternal circulation, they can cause maternal endothelial dysfunction and systemic inflammation. Systemic maternal disease is associated with clinical symptoms of PE and is proposed as a second stage of PE pathogenesis model (Staff 2019).

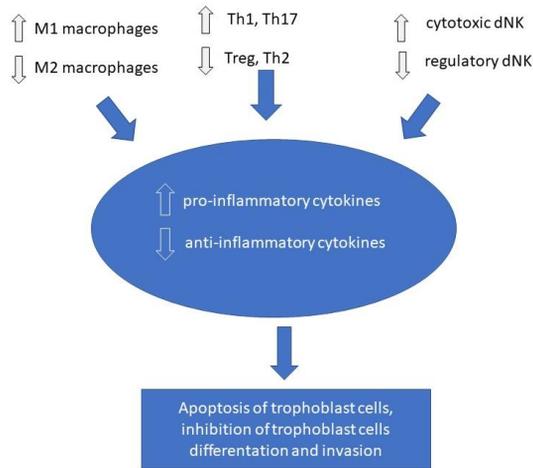
### Stage 1: inhibition of trophoblast invasion

The process of extracellular trophoblast invasion (EVT) that occurs after embryo implantation is essential for normal placental development. After implantation of the embryo into the maternal endometrium, the blastocyst grows into an inner cell mass and an outer trophoblast. The inner cell mass forms the embryo, while the outer cell mass gives rise to the primary, secondary and tertiary villi. These villi form the structural basis of the placenta. Trophoblasts differentiate into two main cell lineages: villous and extravillous. The EVT participate in the process of attach-

ment of the placenta to the uterine wall and in the remodelling of the maternal spiral artery (Li *et al.*, 2021).

There are many risk factors that may affect the trophoblast invasion of the spiral arteries and may lead to the vascular dysfunction observed in PE (Figure 2). Epidemiologic observations regarding the risk of PE include the first pregnancy with a given partner, conception early in a new relationship, contraception using barrier methods and donor egg pregnancies. Moreover, oral exposure to the father's semen can be protective against PE in a subsequent pregnancy (Kenny and Kell, 2017). These risk factors suggest the involvement of reduced paternal antigen exposure in the pathogenesis of PE.

Maternal interactions with paternal alloantigens induce local maternal-foetal immunotolerance. Regulatory T cells (Tregs) have been acknowledged as the most important cells involved in the prevention of immune-mediated rejection of the semiallogenic foetus (Gobert and



**Figure 2.** The dysregulation of the immune system in preeclampsia is associated with an imbalance of pro-inflammatory and anti-inflammatory cytokines. The plethora of pro-inflammatory immune cells promote inflammation. The reduced count of anti-inflammatory cells is not efficient in suppression the activation and proliferation of proinflammatory cells subsets. dNK, decidual natural killer cells; Th, helper T cell; Treg, regulatory T cell.

Lafaille 2012). Transforming growth factor- $\beta$  (TGF- $\beta$ ) and prostaglandin E, constituents of seminal fluid, act as Treg-inducing agents (Kenny and Kell 2017). The fact that over 20% of pregnant women with systemic lupus erythematosus (SLE) have pregnancies complicated by PE confirms the important role of Tregs in pregnancy. SLE is an autoimmune disease that is associated with immune alterations, especially with a reduction in Tregs (Amaral *et al.* 2017). Due to anti-inflammatory properties, Tregs ensure protection against inflammatory injury via suppression of the activation and proliferation of proinflammatory cell subsets (Lu and Hu 2019). The protective role of Tregs has been shown in a reduced uterine perfusion pressure (RUPP) rat model (Cornelius 2018). This model closely mimics the hypertension, systemic and renal vasoconstriction, oxidative stress and immune system dysregulation in the mother, and intrauterine growth restriction in the offspring (Li *et al.* 2012). Transfer of Tregs from normal pregnant rats into

RUPP rats reduced both blood pressure and levels of inflammatory cytokines and attenuated the occurrence of foetal growth restriction. The Treg transfer was associated with increased levels of anti-inflammatory cytokines, reduction of oxidative stress and downregulation of placental vasoconstrictor endothelin 1 (ET-1) (Cornelius 2018). A reduction in the number of Tregs or their function may lead to incorrect trophoblast invasion and unfavourable spiral artery remodelling (Gobert and Lafaille 2012; Staff 2019). Depletion of decidual Tregs resulted in increased trophoblast apoptosis and disturbed the invasion of extravillous trophoblasts into the decidua (Cornelius 2018). Previous pregnancy with the same father generates memory Tregs, a phenomenon that reduces the risk of PE in subsequent pregnancy. However, the level of Tregs seems to decline over time, and thus the protective effect of previous pregnancies disappears when there is long time period between pregnancies (Staff 2019).

There is dysregulation of the immune system in preeclamptic pregnancies. Figure 2 provides a summary of the main components of a dysregulated immune system in PE. Immunological imbalance occurs due to elevation of following subsets of proinflammatory T helper cells: Th17 and Th1 and reduction of Th2 and Treg subsets (Geldenhuys *et al.* 2018). Proinflammatory helper T cell subsets are linked to chronic systemic and local placental inflammation in PE. Activated Th1 and Th17 cells secrete proinflammatory cytokines including tumour necrosis factor  $\alpha$  (TNF- $\alpha$ ) and interleukins (ILs), namely IL-6 and IL-17. TNF- $\alpha$  signalling results in endothelial cell activation, reduction of nitric oxide synthase (NOS) and elevation of vasoconstrictor ET-1. IL-6 has also been shown to mediate the expression of endothelin and it plays a role in endothelial permeability. IL-17 plays a role in the pathophysiology of PE via generation of placental oxidative stress, which stimulates neutrophils, leading to the release of ROS. In addition, IL-17 stimulates B cells to produce agonistic autoantibodies to the angiotensin II type I receptor (AT1-AA) (Cornelius 2018). Activation of the AT1 receptor by AT1-AA results in the inhibition of trophoblast invasiveness (Aouache *et al.* 2018). Stimulation of AT1 is also associated with the release of antiangiogenic factors ET-1 and soluble vascular endothelial growth factor receptor 1 (sFlt1) (Lu and Hu, 2019). In RUPP rats, AT1-AA inhibition reduced blood pressure, improved renal function, and diminished circulating factors associated with PE, such as ET-1 and sFlt1 (Cunningham *et al.* 2019). Excessive secretion of sFlt1 is also associated with several PE risk factors, such as diabetes mellitus and gestational hypertension (Geldenhuys *et al.* 2018; Tomimatsu

*et al.*, 2019). sFlt1 affects normal endothelial function by reducing the available placental growth factor (PIGF) and vascular endothelial growth factor (VEGF) levels; these growth factors are essential for angiogenesis. Excess sFlt-1 leads to inhibition of extravillous trophoblast invasion and differentiation and subsequently contributes to the poor placentation (Staff 2019).

Uterine natural killer (uNK) cells have regulatory functions in addition to the classical killing role of NK cells (recognition and destruction of infected cells and cancer cells). There are two types of uNK cells observed in the uterus. In the nonpregnant uterus, the uNK cells are known as endometrial NK (eNK) cells whereas those in the pregnant uterus are termed decidual NK (dNK) cells. The latter are phenotypically and functionally different from NK cells in the peripheral circulation. They have unique functions such as the production of cytokines, chemokines and growth factors, and they participate in all steps of placentation including trophoblast invasion into the maternal endometrium and vascular remodelling (Jabrane-Ferrat and Siewiera 2014). This is associated with the features of the decidual microenvironment characterised by physiological hypoxia in the placenta and regulation by hormones (progesterone, oestrogen) and trophoblast-derived soluble factors (like soluble HLA-G). The phenotype of dNK cells can be modified by severe inflammation in the uterine microenvironment caused by severe stress, autoimmune diseases and infections. In PE, dNK cells shift from a regulatory to a cytotoxic phenotype. This alteration is associated with elevated production of interferon  $\gamma$  (IFN- $\gamma$ ), causing apoptosis of trophoblasts that invade the developing spiral arteries (Geldenhuys *et al.* 2018). Maternal uNK cells with a regulatory pheno-

type are associated with reduced PE risk in the next gestation. uNK cells may develop trained memory after a first pregnancy, potentially promoting more efficient placentation in subsequent pregnancies. These cells are essential for proper uterospiral artery evolution. Interactions between killer-cell immunoglobulin-like receptor, expressed on the uNK cells, and foetal HLA-C proteins, expressed on invading trophoblasts, are important for the placentation process. It has also been proposed that uNK cells interact with Tregs to facilitate vascular remodelling. In addition, it has been demonstrated using myometrial sections that spiral arteries of parous uteri sustain some of the remodelling patterns that occur during pregnancy, a phenomenon that could explain the reduced risk of PE in parous women and the general increase in birth weights in subsequent pregnancies (Staff 2019).

In the decidua, two types of macrophages are prevalent: M1 macrophages with proinflammatory properties, phagocytic and microbicidal functions, and M2 macrophages with immunosuppressive properties that support maintenance of immunological homeostasis during pregnancy. M2 macrophages regulate inflammation by producing immunosuppressive cytokines (such as IL-10 and TGF- $\beta$ 1), inducing the expression of Tregs and inhibiting the cytotoxic function of dNK cells and phagocytosing apoptotic trophoblasts. Furthermore, M2 cells promote placentation via secretion of factors associated with tissue remodelling and angiogenesis (like VEGF, PlGF). The decreased level of immunosuppressive cytokines observed in PE is associated with a reduced M2 macrophage count (Geldenhuys *et al.* 2018). In PE, lower levels of IL-10 have been observed; this anti-inflammatory cytokine has important functions during

pregnancy. Thanks to its ability to inhibit the secretion of inflammatory cytokines, it provides an important counterbalance for inflammation at the foetal-maternal interface and is responsible for stimulating the differentiation of Tregs from naïve T cells (Cornelius 2018). Augmented inflammation then induces proinflammatory M1 macrophages, which increase apoptosis of cytotrophoblasts (Geldenhuys *et al.* 2018).

### **Stage 2: causes of uteroplacental malperfusion**

Uteroplacental malperfusion can occur without poor placentation, when the placenta outgrows the uterine capacity (placental compression). Women who are obese and have had multiple pregnancies are more likely to have larger placentas, and they also have an increased risk of developing PE. It can cause the terminal villi to be compressed, a factor that impedes intervillous perfusion and causes syncytiotrophoblast hypoxia and oxidative stress. This process triggers a maternal response that is similar to defective uteroplacental artery remodelling and the release of harmful molecules derived from the placenta. Maternal factors (e.g. chronic arterial disease, obesity and some autoimmune diseases) may impact multiple aspects of placentation, placental size and placental function, in addition to amplifying maternal vascular sensitivity to factors shed by the placenta to generate the maternal clinical signs. Maternal autoimmune diseases are associated with excessive decidual inflammation. This process could predispose a woman to develop decidual acute atherosclerosis at any stage of pregnancy (Staff 2019). Acute atherosclerosis is a vascular change of the placenta characterised by lipid-filled foam cell accumulation, lymphocytic infiltration and fibrinoid

and fibrinoid necrosis (similarly to atherosclerosis) (Kim and Kim 2015). It is also associated with spiral artery thrombosis and can worsen placental intervillous perfusion. Decidual acute atherosclerosis has been observed in women with concurrent systemic lupus erythematosus and antiphospholipid syndrome, suggesting that massive pre-pregnancy vascular inflammation observed in autoimmune diseases may be associated with the generation of inflammatory arterial pregnancy lesions (Staff 2019). Antiphospholipid antibodies (aPLs) are able to induce the formation of thrombi in the vasculature and activate cells involved in haemostasis, including platelets, endothelial cells and monocytes. aPLs also inhibit fibrinolysis, which leads to placental thrombosis (Lu and Hu 2019). Pregestational obesity may disrupt the arterial architecture in the placenta and affect the contraction and relaxation capacity of the placenta. Placentas in obese woman generate excessive mitochondrial ROS (due to defective respiratory chain), exacerbating the imbalance between free radicals and antioxidants (Alcala *et al.* 2018).

### **Stage 3: maternal systemic inflammation and vascular endothelial dysfunction**

Persistent episodes of hypoxia-reoxygenation caused by defective placentation can injure the villi and generate oxidative stress (OS) in placental tissue (Staff 2019). The syncytiotrophoblast (the outer layer of the trophoblast) is notably sensitive to ROS because of insufficient concentrations of antioxidative enzymes like manganese superoxide dismutase (Cornelius 2018). Placental malperfusion has also been linked to increased placental endoplasmic reticulum (ER) stress and activation of the unfolded protein response (Staff 2019). During PE, the syncytiotrophoblast experiences

accelerated ageing with upregulation of the apoptotic cascade, necrotic breakdown with release of necrotic debris and an increase in syncytial aggregates. The syncytiotrophoblast cells secrete senescence-associated beta-galactosidase (SA $\beta$ -Gal) and express proapoptotic p53 and cyclin dependent kinases (CDKs) inhibitors at a higher rate, indicating cessation of cell cycle and senescence. It has been proposed that senescence in placental cells can be a result of excessive ROS accumulation and ER stress. The pro-inflammatory senescence-associated secretory phenotype (SASP) is observed with production of SASP proteins, which then activate the cyclooxygenase pathway and enhance the generation of proinflammatory factors (cytokines and chemokines) (Manna *et al.* 2019). Syncytiotrophoblast stress, associated with excessive trophoblast senescence or other causes of trophoblast dysfunction, leads to the release of increased levels of inflammatory factors into the maternal circulation. Even a relatively low degree of syncytiotrophoblast stress could be sufficient to reach stage 2 of PE development, especially in women who are susceptible to excessive inflammatory substances, such as women with prior chronic vascular inflammation, or with pregnancy-related excessive vascular inflammation, such as in gestational diabetes mellitus. The more excessively inflamed the maternal vasculature is, the less inflammatory stimuli from the placenta are needed to reach the clinical stage (Staff 2019).

Defective placentation causes the release of multiple particles from trophoblasts. These placental-derived factors act directly on the maternal vascular endothelium or act indirectly by increasing OS and stimulating the release of pro-inflammatory cytokines and vasoactive compounds (Alcala *et al.* 2018). The placenta as a source of circulating

vasoactive factors causes widespread systemic maternal vascular dysfunction. It is associated with the stimulation of prostaglandin synthesis, activation of the renin-angiotensin system, the release of various anti-angiogenic factors, altered synthesis of gasotransmitters and vasoconstrictors and changes in reactivity to vasoactive factors (Tong and Giussani 2019). The vascular endothelium comprises a single layer of epithelial cells overlaying the interior surface of blood vessels. This layer acts as a semi-selective barrier between the vessel lumen and the more exterior layers of the vessel wall. The cells have paracrine and autocrine functions, allowing them to modulate arterial vasomotility, leucocyte adhesion and extravasation, proliferation and differentiation of smooth muscle building more exterior layer of the vessel wall, and platelet coagulation and fibrinolysis (Aouache *et al.* 2018). The endothelium plays a key role in modulating vascular tone by releasing a variety of endothelium-derived relaxing factors (such as vasodilator prostaglandins, NO) and contracting factors. The direct contact of epithelial cells with the blood flow makes them sensitive to circulating factors. Endothelial dysfunction is characterised by reduced production or action of these relaxing mediators (Godo and Shimo-kawa 2017). Secretion of trophoblast-derived angiogenic factors – for example, sFlt1 and soluble endoglin (sEng) – cause anti-angiogenic imbalance that is characteristic of PE. sFlt1 represents an important link between placental dysfunction (Stage 1) and the maternal symptoms (Stage 2). sFlt1 affects endothelial function by reducing available PIGF and VEGF in placental and maternal cells (by binding to them and blocking their ability to act on the endothelium) (Staff 2019). VEGF enables vasodilation by stimulating the

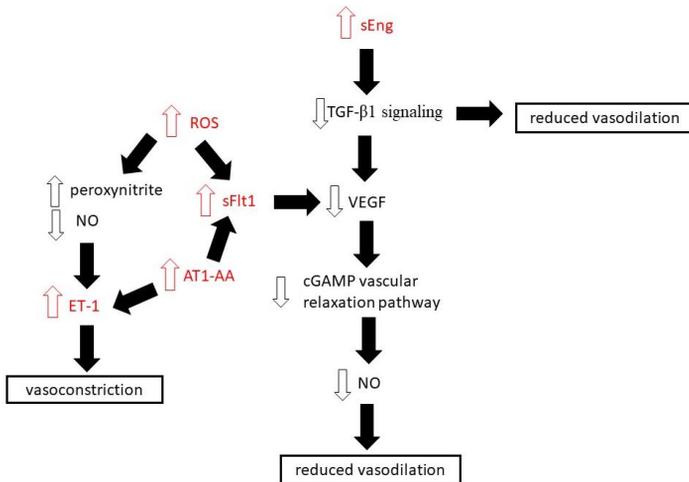
NO-cyclic guanosine monophosphate vascular relaxation pathway and by increasing calcium ion ( $\text{Ca}^{2+}$ ) production.  $\text{Ca}^{2+}$  binds to endothelial nitric oxide synthase (eNOS) and increases eNOS activity, enhancing NO production from L-arginine (Geldenhuys *et al.* 2018). Therefore, due to a reduction in available VEGF, the NO concentration also decreases. NO may also be reduced due to decreased expression of NO-synthesising enzymes or due to NO reactions with free radicals (Tong and Giussani 2019). The systemic inflammatory response in PE results in high amounts of ROS, produced by activated blood cells. The accumulation of ROS produced by blood cells and released from hypoxic placental cells is a reason for systemic oxidative stress with high production of ROS and reactive nitrogen species (RNS). ROS may react with NO, causing a lower bio-availability of NO (Mannaerts *et al.* 2018). The superoxide anion reacts with NO to form peroxynitrite, a powerful oxidising agent that can initiate lipid peroxidation, among other functions (Taravati and Tohidi 2018). In addition, peroxynitrite promotes the production of the vasoconstrictor ET-1 (Aouache *et al.* 2018). Increased sEng contributes to endothelial dysfunction by the inhibition of TGF- $\beta$ 1 signalling. This pathway is involved in angiogenesis by regulating VEGF expression. The inhibition of TGF- $\beta$ 1 signalling will reduce endothelium-dependent vasodilation and increase endothelial cell apoptosis (Geldenhuys *et al.* 2018). TNF- $\alpha$  and other circulating factors present in the plasma of preeclamptic woman can induce oxidative stress in epithelial cells indirectly by upregulating the receptors associated with oxidised low-density lipoprotein (LDL) uptake. AT1-AA can activate the AT1 receptor in arterial epithelial and smooth muscle cells as

well as in renal mesangial cells. In vivo experiments in pregnant rats showed that administration of AT1-AA induces PE symptoms, including hypertension and proteinuria (Aouache *et al.* 2018). The mechanisms leading to endothelial dysfunction and reduced vasodilation are summarised in Figure 3. Disturbances in endothelial homeostasis lead to a pro-inflammatory, vasoconstrictive and prothrombotic tendency of endothelial cells (Mannaerts *et al.* 2018). Clinically, these changes are associated with vascular resistance and increase in arterial blood pressure in preeclamptic woman and proteinuria due to acceleration of glomerular endotheliosis (Manna *et al.* 2019).

### Prophylaxis and management

The National Institute for Health and Clinical Excellence (NICE) has proposed a classification of the risk factors for PE. This grading distinguishes moderate and high risk factors to allow defining the

group of patients for whom the immediate application of prophylactic measures should be applied. The high-risk factors are: hypertensive disorders in previous pregnancies, chronic arterial hypertension, chronic kidney disease, autoimmune diseases and diabetes (type 1 or 2). Moderate risk factors include: primiparity, inter-delivery interval > 10 years, multiple gestations, body mass index (BMI) > 35 kg/m<sup>2</sup>, advanced age (> 40 years old) and a family history of PE. The presence of two moderate risk factors or a single high risk factor indicates that prophylactic measures should be implemented. The American College of Obstetricians and Gynecologists (ACOG) has reported the same risk factors but has classified them all as high risk. The only exception is the BMI factor >30 kg/m<sup>2</sup> (Mayrink *et al.* 2018). To prevent the occurrence of PE, the International Society for the Study of Hypertension in Pregnancy (ISSHP) recommends that women at high risk of



**Figure 3.** Mechanisms leading to endothelial dysfunction and reduced vasodilation in preeclampsia. Placental-derived factors – sEng, sFlt1, AT1-AA and ROS – contribute to a massive systemic endothelial dysfunction and vasoconstriction. AT1-AA, agonistic autoantibodies to the angiotensin II type 1 receptor; cGAMP, cyclic guanosine monophosphate–adenosine monophosphate; ET-1, endothelin 1; ROS, reactive oxygen species; sENG, soluble endoglin; sFlt1, soluble vascular endothelial growth factor receptor-1; TGF-β1, transforming growth factor beta-1; VEGF, vascular endothelial growth factor.

PE should be treated (preferably before 16 weeks but definitely before 20 weeks) with low-dose aspirin. In addition, women considered at increased risk should receive supplemental calcium (1.2–2.5 g/day) if their calcium intake is likely to be low (< 600 mg/day) (Brown *et al.* 2018; Braunthal and Brateanu 2019).

Currently, there is no effective treatment for PE and the only effective management is termination of pregnancy. The aim of clinical management of PE is to prevent maternal and foetal mortality. The most important elements of management are: tight control of maternal and foetal conditions, treatment of hypertensive emergency and prevention of maternal seizures (Amaral *et al.* 2017). Maternal monitoring should include blood pressure monitoring, evaluation for proteinuria (if it is not already present), blood tests for haemoglobin, platelet count, liver transaminases, creatinine and uric acid (Brown *et al.* 2018). If treatment fails to compensate for severe maternal hypertension or if severe complications of pregnancy are present, preterm delivery is recommended. To prevent adverse consequences for the foetus, it is necessary to optimise the time of delivery (Amaral *et al.* 2017). The ISSHP advises that women with PE should be induced to deliver their baby if they have reached 37 weeks of gestation or if they have developed complications such as: severe hypertension resistant to treatment, pulmonary oedema, progressive thrombocytopenia, worsening renal and liver disorders, visual disturbances, convulsions and non-reassuring foetal status (suspected foetal hypoxia) (Brown *et al.* 2018). Corticosteroids (betamethasone, dexamethasone) are recommended if preterm labour is suspected in a woman with PE or if preterm termination of pregnancy is considered. Corticosteroid treatment should be given for 7 days before preterm delivery (Fox *et al.* 2019)

to accelerate structural maturation of the lungs (by stimulating surfactant phospholipid production in alveolar cells). Recognition and management of persistently elevated (> 15 min duration) severe hypertension is necessary to prevent a hypertensive crisis, which is associated with life-threatening complications such as eclampsia. This is accomplished by aggressive treatment of systolic blood pressure (SBP)  $\geq$  160 mmHg and/or diastolic blood pressure (DBP)  $\geq$  105 mmHg. Intravenous labetalol or hydralazine treatment is considered the first-line therapy for an acute hypertensive emergency. Oral nifedipine may also be used as a first-line therapy, especially when intravenous access is not available. Emphasis is put on avoiding excessive lowering of blood pressure because it may further decrease placental perfusion and potentiate negative effects on the foetal condition. The goal of treatment is to lower the maternal blood pressure to a SBP of 140–150 mmHg and a DBP of 90–100 mmHg. Prophylaxis against maternal seizures (eclampsia) is achieved by the use of magnesium sulphate. This anticonvulsant is administered intravenously or intramuscularly (Amaral *et al.* 2017). Magnesium sulphate is also used if preterm termination of pregnancy is planned before 32 weeks of gestation due to its proven neuroprotective effects in neonates (Fox *et al.* 2019). Platelet transfusion is recommended in patients with platelets < 50,000/ $\mu$ l before caesarean section or when the platelet count is  $\leq$  20,000–25,000/ $\mu$ l before vaginal delivery to prevent excessive bleeding during delivery (Lam and Dierking 2017). In the early postpartum period, women with PE should be considered at high risk for preeclamptic complications (eclamptic seizures may develop for the first time in the early postpartum period). The patient's condition should be

monitored at least every 4 h for at least 3 days after delivery (Brown *et al.* 2018).

## Conclusions

Although PE is one of the leading causes of maternal and neonatal morbidity and mortality worldwide, due to limited understanding of its aetiology, there is still no effective therapy for this condition. At present, the only effective treatment is termination of pregnancy. The aim of clinical management of PE is to prevent maternal and foetal mortality. The most important elements of management are the treatment of emergency conditions and the prevention of maternal seizures. Although the clinical symptoms of PE resolve after delivery, PE causes permanent disruption to maternal and foetal physiology. Further research into the pathogenesis of PE is needed to find an effective therapy.

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