

Eclampsia



Eclampsia is a life-threatening complication of pregnancy for both the baby and the mother. It is not precisely known what causes it, but it usually clears up when the baby is born. Research is underway to understand this complex condition and to improve the treatments that are currently used to control it.

What is eclampsia?

Eclampsia is defined as seizure activity unrelated to other cerebral conditions in a pregnant woman with pre-eclampsia. The origin of the word eclampsia is Greek: the preposition “ek” means “out,” and the verb “lampein” signifies “to shine forth” or “to flash.” The combination of the two words describes a state of “flashing out” or, more literally, “a bolt from the blue”.

Pre-eclampsia is an abnormal state of pregnancy characterised by hypertension, fluid retention causing oedemas and albuminuria (excretion of protein via the urine). Most patients with eclampsia have systolic blood pressures higher than 160 mmHg or diastolic blood pressures higher than 110 mmHg. Nearly all cases of eclampsia present in the third trimester of pregnancy or within the first 48 hours following delivery. There are few descriptions of the development of eclampsia without prior pre-eclampsia. Both conditions create a life-threatening disturbance of many organs of the human body, such as the central nervous system, the liver, the kidneys, and the cardiovascular system.

So far, no definitive causes have been identified and there is no set of laboratory determinations which may predict for the mother or baby in women with eclampsia. Research has suggested genetic, immunological, hormonal, and nutritional agents as possible causes. Presumably, the placental and foetal membranes play a role in the development of pre-eclampsia because of the prompt resolution of the pathological symptoms following delivery.

A common pathway thought to be associated with the development of the disease is low blood perfusion of the uterus and the placenta. Dysfunction of the placenta may cause generalised vasoconstriction, platelet aggregation, and a state of hyper-coagulation. Eventually, local ischaemia predisposes to the release of biochemical mediators

that enter the maternal circulation, causing dysfunction of the cells that line the blood vessels, such as constriction of small arteries. Some of the problems caused include generalised spasmodic contraction of blood vessels, increased peripheral vascular resistance, increased blood viscosity, disturbance of blood coagulation, decreased function of the kidneys, damage to liver cells, as well as cerebral oedema and cerebral bleeding.

Who does eclampsia affect?

Approximately five per cent of all pregnancies are complicated by pre-eclampsia. Of these patients, one to two per cent develop eclampsia. The incidence is higher in women of low socioeconomic status. The condition affects women of all ages, but the frequency is increased in women younger than 20 years old who are pregnant for the first time. Also, women older than 40 years old with pre-eclampsia develop eclampsia far more often compared to women in their twenties.

There is no clear racial pattern. Approximately 25 per cent of women with eclampsia have hypertension in subsequent pregnancies. Approximately two per cent of women with eclampsia develop eclampsia in future pregnancies. Other risk factors include pre-existing hypertension or renal disease, poor prenatal care, and a family history of pre-eclampsia and eclampsia. Five per cent of patients with hypertension develop severe pre-eclampsia.

Both pre-eclampsia and eclampsia account for significant maternal and foetal morbidity and mortality. In Europe, maternal mortality rates due to eclampsia have been reduced to less than one per cent with early diagnosis and aggressive management, making it the second leading cause of maternal death. Foetal mortality rate from eclampsia also has been decreased, but still remains at approximately 12 per cent. Worldwide, eclampsia accounts for approximately 50,000 maternal deaths annually.

Present treatments:

The goals of pharmacotherapy are to reduce morbidity, prevent complications, correct eclampsia, and deliver a healthy baby. Eclampsia will resolve after the mother has been stabilised and her baby has been delivered either vaginally or by Caesarean section.

The medicines of choice to prevent further convulsions and terminate clinical seizure activity include anticonvulsants such as intravenous magnesium sulphate and anti-epileptic medications in the phenytoins or benzodiazepines classes. The mechanism of action of magnesium sulphate is that it inhibits the release of acetylcholine (ACh) at the neuronal-muscular junction, the point where nerve cells communicate with muscle cells. The anticonvulsant effect of orally administered phenytoin is due to stabilising neuronal activity by decreasing the ion flux across depolarizing membranes. Benzodiazepines depress all levels of the central nervous system such as the limbic and reticular formation, possibly by increasing activity of gamma-amino-butyric acid (GABA).

Hypertension associated with eclampsia is often controlled adequately by stopping the seizure. If not, high blood pressure is treated with antihypertensive agents like a direct arteriolar vasodilator, beta-blocking compounds with concomitant alpha-adrenergic blocking effects and calcium channel blockers. Also a compound containing nitric oxide may be used occasionally; it causes peripheral vasodilatation by directly acting on venous and arteriolar smooth muscle, reducing peripheral resistance. Care must be taken not to decrease the blood pressure too drastically to avoid abnormal blood supply to the baby and foetal distress.

What's in the development pipeline?

Preventing the development of pre-eclampsia should decrease the risk of eclampsia and its complications later in pregnancy. Acetylsalicylic acid blocks platelet aggregation and vasospasm in pre-eclampsia, and it may be effective in preventing the con-

dition. Recent Phase 3 clinical studies have shown that low-dose aspirin in women at risk contributes to a decreased risk of pre-eclampsia, a reduction in preterm delivery rates, and a reduction in foetal death rates.

In 2003, scientists reported results of a study establishing that complications of pre-eclampsia appear linked to a dysfunction in the endothelial cells – the cells that line the blood vessels – caused by the natural chemical compound asymmetric dimethyl-arginine (ADMA). These findings may help the development of more accurate tests for prediction of the condition and more effective treatment.

High plasma levels of leptin and low levels of gonadotrophin releasing hormone (GnRH) may also play a role in pre-eclampsia. The protein hormone leptin – from the Greek noun "*leptos*", meaning "thin" – has important effects in regulating body weight, metabolism and reproductive function. Its effect on reproduction is due to the secretory enhancement of GnRH, and thus luteinising and follicle-stimulating hormones from the anterior pituitary. Detection of abnormal high and low levels of these two hormones in early pregnancy may be useful for the diagnosis of a pre-eclamptic condition.

The longer term future:

Research groups are studying the implications of altering placental blood flow and protein synthesis in early pregnancy. Monoclonal agents are used to inhibit placental proteins at a critical time in pregnancy and the local and systemic responses are examined. Recent study results hint that pre-eclampsia may be caused by an imbalance of angiogenic factors. Researchers reported that low levels of placental growth factor (PLGF), a pro-angiogenic protein, at mid-gestation predict subsequent development of pre-eclampsia.



When a woman conceives, her immune response has to be modulated to accept the foetus and placenta which both contain foreign proteins from the father's genes. Semen contains agents which prompt the woman's immune system to accept it. One agent identified is transforming growth factor (TrGF)-beta. Scientists are investigating whether men who have fathered pregnancies which ended in pre-eclampsia have had low TrGF-beta levels in their semen. If the theory is confirmed, application of TrGF-beta could help prevent the condition.

It is also held that the widespread activation of the maternal vascular endothelium is due to oxidative stress. Reactive oxygen molecules invoke endothelial cell activation. In a condition like pre-eclampsia, one mechanism could be the activation of nuclear enzyme poly (ADP-ribose) polymerase (PARP), leading to endothelial dysfunction. Inhibiting PARP activity would be another approach for a new therapy. With each new study another piece of the puzzle is found, yielding a better understanding of this complex condition.

DISCLAIMER

EFPIA has made all reasonable efforts to include accurate and up-to-date information in this PDF, but cannot guarantee completeness or accuracy of the information.

You must consult your doctor, or other qualified healthcare professional on any specific problem or matter covered by the information in this PDF.

The "Medicines for Mankind" publications are made available on condition that no part of the publications (including photographs) may be reproduced or abstracted without prior agreement with the European Federation of Pharmaceutical Industries and Associations (EFPIA). Under no circumstance can any of the material included in this PDF be used in promotional material and/or campaigns.

Editing Board: Dr. Robert Geursen (Chief Editor), Peter Heer, Bill Kirkness, Philippe Loewenstein, Steve Mees, Dr. Jean-Marie Muschart, Marie-Claire Pickaert (Coordinator).

Photocredits: ABPI, Allergan, AstraZeneca, EFPIA/Lander Loeckx, Damian Foundation, Galderma, Hilaire Pletinckx, Roche, sanofi-aventis; Design & Production: Megaluna+Triumviraat