

# COMPLEMENTARY MEDICINE STRATEGIES IN THE MANAGEMENT OF PRE-ECLAMPSIA

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## Abstract

Pre-eclampsia is a serious condition that affects 5–10% of all pregnancies in Australia and the USA. This article examines the aetiology, pathophysiology, clinical manifestations and complementary medicine strategies in the management of pre-eclampsia.

## Reference

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## Keywords

Complementary medicine; Pre-eclampsia; Pregnancy disorders.

## Introduction

Pre-eclampsia (PE) is defined as a pregnancy-specific syndrome. It occurs after mid-gestation with a de novo appearance of hypertension and proteinuria. The hypertension is defined as equal to or above 140/90 mm Hg, and the proteinuria is greater than or equal to 300 mg in 24 hours. Oedema was previously included in the PE definition, but has now been excluded on the basis that it is seen in many normotensive pregnant women<sup>(5)</sup>.

PE is a serious condition that affects 5–10% of all pregnancies in Australia and the USA. If untreated, PE can develop into eclampsia, or prove fatal to mother and foetus<sup>(1)</sup>. It is a multisystemic syndrome, the hypertension due to increased vasoconstriction, usually after the twentieth week of pregnancy<sup>(2)</sup>.

Pregnant women who may be suffering from PE will typically present with non-specific symptoms, such as persistent headaches, blurred vision, photophobia and possibly abdominal pain<sup>(3)</sup>. Risk of PE is increased in women with a history of previous PE, and in people with vascular or renal disease, hypertension, diabetes and thrombophilia<sup>(4)</sup>. This article examines the causative factors, pathophysiology, clinical manifestations and complementary medicine strategies in the management of PE.

The focus of this article is on prevention and management of PE with complementary medicine. It is emphasised that PE can progress to become a medical emergency. Medical treatment, when required, must be utilised without hesitation.

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## Causative Factors Of PE

Research into the aetiology or causative factors of PE has revealed no single cause, but rather a number of factors. Some of these factors include genetic predisposition or the presence of certain genetic markers, metabolic syndrome, diabetes, external stressors, depression, endothelial dysfunction, and inflammation with various biochemical changes and markers.

Genetics have been found to play a strong part in PE. Some studies have looked at various populations and have isolated particular haplotypes with a predisposition to PE. A study of 132 women with PE compared to 112 healthy controls showed a significant association of two haplotypes with PE, particularly those individuals who had two copies of the high-risk haplotypes<sup>(13)</sup>. Another study of ten polymorphisms in nine genes found a strong association between a specific angiotensinogen haplotype and genetic susceptibility to PE<sup>(14)</sup>.

Angiotensin II levels are modulated by angiotensin-converting enzyme (ACE). Research has found that the D allele of the insertion/deletion polymorphism of the ACE gene has been associated with higher ACE activity—accounting for 47% of the total phenotypic variance of serum enzyme levels. This has been shown to affect uteroplacental and umbilical flows, and the recurrence of adverse pregnancy outcomes in women with a history of PE<sup>(15)</sup>.

Women with metabolic syndrome, insulin resistance and diabetes are also over-represented in PE. Metabolic syndrome, which features central adiposity, impaired glucose metabolism, high blood pressure and dysregulated cholesterol, causes inflammation and cardiovascular disease. Some women with metabolic syndrome have chronic hypertension prior to conception, which in itself is a strong predisposing factor for PE.

Two review articles, which looked at more than 15 studies, demonstrated a positive correlation between metabolic syndrome and PE, as well as a strong prediction of serious cardiovascular disease for the mother within fifteen years of a PE-affected pregnancy<sup>(16,17)</sup>.

Women with Type 1 diabetes also have a greater chance of developing PE. One study found that the incidence of PE among these clients was at 17% instead of the average 5–10%. The maternal vascular dysfunction present in these women during early pregnancy was an accurate predictor of the condition<sup>(18)</sup>.

Another cause of PE is external stress. A study of 933 healthy Irish normotensive primigravidas (18–24 weeks gestation) women were classified into three groups: working, unemployed, and usually working but not on the day of testing. After adjustment for variables such as age, body mass index, and smoking and drinking habits, a significant independent relationship was found between maternal work and ambulatory blood pressure levels in mid-pregnancy. The rate of subsequent development of PE was higher in working women than in the unemployed<sup>(19)</sup>.

Internal stress is also evident through inflammatory processes causing oxidation. Free radicals from sources such as trans-fatty acids initiate lipid peroxidation, and cause cellular dysfunction and damage to biomolecules. Researchers proposed that this may initiate maternal endothelial vascular dysfunction and leukocyte activation, which are common to PE<sup>(4)</sup>.

Dietary intake of trans-fatty acids is associated with plasma concentrations of biomarkers of systemic inflammation, and in particular, C-reactive protein, interleukin-6, soluble tumour necrosis factor receptor, E-selectin, and soluble intercellular and vascular cell adhesion molecules—even in apparently healthy women<sup>(20)</sup>.

Depression may also be a predictor of subsequent pre-eclampsia. A study of 623 healthy, white, pregnant nulliparous women found that depression was associated with an increased risk of PE. The same study also examined a number of confounding factors including bacterial vaginosis. Bacterial vaginosis with concurrent depression (n=44) was associated with a 5.3-fold increase in risk for PE<sup>(21)</sup>.

### Clinical Manifestations

Eclampsia occurs when PE progresses to a life-threatening convulsive phase, which may happen in mid to late pregnancy, or in the immediate post-partum period. Gestational hypertension is defined as de novo hypertension arising after mid-pregnancy, but without proteinuria.

Pregnant women may also suffer from chronic hypertension, which is an elevated blood pressure that predated the pregnancy. PE is said to be superimposed on the chronic hypertension. When this occurs, it predisposes the woman to PE, preterm delivery, foetal growth restriction or demise, and other serious health conditions<sup>(5)</sup>.

None of these symptoms necessarily indicate that PE is present; however, on examination, elevated blood pressure and protein detected by a urine test will define the condition.

Other symptoms may include the HELLP syndrome ie Haemolysis, Elevated Liver enzyme levels, Low Platelet count, and possibly oedema<sup>(4)</sup>. On investigation, foetal distress may be evident as there is reduced uteroplacental blood flow, which may lead to foetal growth restriction<sup>(2)</sup>. PE may also cause placenta detachment (placental abruption) which can cause problems for newborn babies in their first few days<sup>(6)</sup>.

Reliable methods to predict PE are largely lacking—although a woman diagnosed with chronic hypertension is known to be at risk. Research has also identified cardiovascular oscillations, as measured in pregnant women in the eighteenth to twenty-sixth weeks of pregnancy, as a possible warning sign. The study's parameters found a positive predictive value of 70% with a sensitivity/specificity of 87.5%<sup>(7)</sup>. In other research, Doppler measurement of uterine arteries at 23 weeks gestation was found to identify most women at risk of developing PE<sup>(8)</sup>.

### Pathophysiology Of PE

PE can begin late in the first trimester, when the secondary invasion of maternal spiral arteries is impaired. When maternal spiral arteries remain high resistance vessels, this leads to impaired placental function and, as the foetus develops, hypoxia. Hypoxia induces proliferation of many biochemical changes such as reduced levels of nitric oxide for vasodilation resulting in maternal hypertension, 50% reduction in placental perfusion and reduced maternal plasma volume.

If the condition persists, trophoblastic epithelial cell injury may occur, with foetal cell fragments being carried to the mother's lungs where they are destroyed. This process releases thromboplastins which cause intravascular coagulation and fibrin deposition in the mother's glomeruli, which in turn, further increases vasoconstriction. If not treated, fibrin will build up in the vessels of the central nervous system, causing eclampsia with convulsions<sup>(9)</sup>.

One study showed abnormal placentation as a source of PE, which may result in foetal cell transfusion. The study found that 14 out of 20 women with PE had foetal-maternal transfusion (FMT), as opposed to 3 out of 20 controls, although there appeared to be no correlation between severity of PE and the amount of FMT present<sup>(10)</sup>.

Foetal changes that are consistent with hypoxia include decreased:

- total superoxide dismutase
- mRNA expression
- glutathione peroxidase activity;

and increased:

- lipid hydroperoxide concentrations
- 9-isoprostane production
- malondialdehyde production
- membrane fluidity
- neutrophils<sup>(11)</sup>.

Shed membrane particles from various biochemicals and cytokines are also found in PE. Additionally, leukocyte levels have been shown to be higher in women with PE.

Microparticles derived from leukocytes and platelets were found to induce *ex vivo* vascular hyporeactivity to serotonin in human omental arteries<sup>(12)</sup>. Moreover, biochemical markers and cytokines are involved in PE pathology. Immune markers neopterin and interleukin-2 were increased in women with severe PE, showing that a T-helper 1 immune mechanism may also be present in the condition<sup>(22)</sup>.

PE is interesting because it is exclusively pregnancy-related, but may occur in the absence of a foetus where a hydatidiform mole is present. The mole is primarily trophoblastic, and contains small amounts of foetal tissue. This phenomenon has given rise to the theory that the placenta may be the primary cause of PE<sup>(5,11)</sup>. However, the exact sequence of events is unclear.

### Complementary Medicine Strategies

If pre-conception care is possible, the priority is to work holistically to ensure the client is well-prepared and educated about pregnancy. This would involve helping the client to manage her body weight, and diagnosing and removing any food allergies and sensitivities she may have. It would also encompass advising the client about diet to achieve optimal nutrition, and encouraging her to cease smoking and recreational drug use, and minimise alcohol and stimulants, if necessary.

As well, a holistic approach might encompass exploration of emotional issues with various therapies and supports such as flower essences, affirmations to promote a positive outlook, and assisting the client to find a spiritual space of comfort and connectedness<sup>(23)</sup>.

### Counselling And Lifestyle Modification

As stress is a major PE predictor, talking about problems with a counsellor or therapist may offer relief, validation or solutions that the client can discover for herself. Taking up meditation<sup>(24)</sup>, yoga<sup>(25)</sup>, tai chi or other gentle pastimes that help with stress management would activate her parasympathetic nervous system.

Flower essences could also be used for support. Bach flower essences such as walnut to facilitate the changes faced through pregnancy and birth, as well as current challenges in changing negative life habits; mimulus for fear of known things, including fear of a failed pregnancy or what the future might bring; larch for lack of self-confidence as a mother; and agrimony for anxiety or denial could all provide benefits<sup>(26)</sup>.

Where the client is employed in a job that she does not enjoy, or which negatively affects her health through stress<sup>(19)</sup>, the possibility of resigning or taking extended leave could be investigated, although circumstances may make this difficult or impossible.

As metabolic syndrome is a major risk for PE, a regime of appropriate daily exercise is important for improving the body's muscle:fat ratio, reducing the risk of gestational diabetes<sup>(27)</sup>, improving nitrogen oxide bioactivity<sup>(28)</sup>, preventing depression and lifting mood<sup>(29,30)</sup>, improving general cardiovascular fitness and well-being, and enhancing self-image.

### General Dietary Strategies

Given that hypertension, metabolic syndrome, immune system deficits, and inflammation are common in PE, they can provide useful starting points for treatment.

General naturopathic principles should be implemented such as a daily diet that incorporates a high intake of fresh wholefoods; low levels of sodium chloride (defined as within 460–920 mg/day)<sup>(31)</sup>, sugar, saturated fats and stimulants; together with zero alcohol and trans-fat consumption. Australian Government guidelines recommend 5–6 serves of fresh fruit and steamed or raw vegetables daily<sup>(32)</sup>. These provide dietary fibre, antioxidants and phytonutrients.

The GI level of foods should be examined, with low GI prescribed for overweight women or those who have metabolic syndrome. One meal of oily fish per week will provide omega-3 fatty acids and, although more would be desirable, the threat of heavy metal contamination to the foetus makes supplementation with high-quality fish oils a better option. It is recommended to drink green tea or herb teas with honey, plus 2 L of water per day. If the client's vegan, or whose diet is insufficient in protein, whey-based smoothies with berries could solve this and provide valuable antioxidants.

Assuming there is no serious kidney dysfunction (as individuals with kidney disease do not process potassium in the normal way)<sup>(33)</sup>, including potassium-rich foods such as apricots, avocados, bananas, citrus fruits, dates, herring, milk, nuts, potatoes, raisins, sardines and sunflower seeds in the diet will help reduce hypertension. Potassium is also indicated for adrenal stress and is synergistic with magnesium, calcium and B vitamins<sup>(34)</sup>.

### Hypertension

A magnesium supplement with co-factors (particularly B vitamins) is useful in hypertension, and can be used to improve endothelial dysfunction and reduce blood pressure<sup>(35)</sup>. National guidelines suggest an upper level of 350 mg of magnesium daily<sup>(31)</sup>. The need for magnesium supplementation is particularly potent if diuretics have been prescribed, as they can cause magnesium depletion<sup>(33)</sup>. Magnesium is also important in cell signalling and active transport of ions across cell membranes, both of which are critical in pregnancy<sup>(35)</sup>. Vitamin C assists the immune and cardiovascular systems, and also helps to remove toxins such as lead from the body, thereby supporting the regulation of hypertension<sup>(33)</sup>. Chromium could be useful in regulating blood glucose levels in cases of insulin resistance, and chromium picolinate is indicated for gestational diabetes<sup>(35)</sup>.

### Cardiovascular Disease

Where cardiovascular disease is present or suspected, there may be increased levels of homocysteine<sup>(35)</sup>, so a product that has good levels of B vitamins 6, 9 and 12 would be appropriate to improve methylation. B6 would be particularly helpful, as it influences the nervous system in a manner that leads to a reduction in blood pressure and reduces norepinephrine levels<sup>(33)</sup>. Alpha-lipoic acid is another antioxidant which helps to reduce inflammation and oxidative stress, and which has a role in reducing the excessive production of nitric oxide in uremia<sup>(36)</sup>.

## Bacterial Vaginitis

Where bacterial vaginitis is present, probiotics are indicated. *Lactobacillus acidophilus* helps maintain healthy vaginal microflora, and is particularly important if the client has recently been prescribed antibiotics for any reason. Beta-carotene supplementation up to 50,000 IU will promote mucosal healing. This is preferred over vitamin A which can be teratogenic in doses above 5,000 IU<sup>(37)</sup>.

## Conclusion

PE is a dangerous condition that requires careful monitoring, emotional support and community education in order to prevent it wherever possible. This is all the more imperative as obesity, diabetes and cardiovascular disease—conditions that have the potential to increase the incidence of PE—become more prevalent in Western societies. Complementary medicine has an important role to play in improving and educating the community about healthy life-style and diet.

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