

## New Approach for the Prevention of Preeclampsia

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### Abstract

The etiology of preeclampsia is still unknown; however, many risk factors that compromise cardiovascular and endothelial function have been identified. Therefore, with this new approach it is possible to adopt intervention measures. In this review we have described and analyzed the pathophysiological events leading to endothelial dysfunction related to preeclampsia. In addition, preventive measures are proposed, including diet, healthy lifestyle, medical evaluation, controlled weight gain, calcium intake, low dose acetylsalicylic acid, adequate hydration and reasonable physical activity to complement the prevention plan.

**Keywords:** Prevention, Preeclampsia, Endothelial Dysfunction.

### Introduction

Preeclampsia (PE) is a relatively frequent pathology of pregnancy with a worldwide incidence of 2% and 10% of pregnancies [1]. It represents the most frequent medical complication of pregnancy and is an important cause of perinatal maternal morbidity and mortality [2].

The etiology of preeclampsia is still unknown. However, it is recognized that the pathophysiological basis of PE is in the endothelium of the entire vascular system, especially in the uteroplacental [3]. Several factors can modify the functions of the endothelium and lead to endothelial dysfunction [4].

Endothelial dysfunction can be defined as an imbalance in the bioavailability of active substances of endothelial origin that predisposes to inflammation, vasoconstriction and increased vascular permeability, facilitating the development of arteriosclerosis, platelet aggregation and thrombosis [4,5].

The current scientific development has allowed us to recognize risk factors that compromise the function of the endothelium and, therefore, it is possible to adopt intervention measures to improve endothelial function [6]. This new prevention approach emphasizes the function of the endothelium to allow adequate uteroplacental circulation. Prevention measures could also support the prevention of fetal growth restriction, diabetes, metabolic syndrome, etc. In this review we propose a new approach for the prevention of PE based on intervention measures that improve endothelial function.

## Endothelial Dysfunction and Preeclampsia

Endothelium plays a central role in the regulation of blood flow through continuous modulation of vascular tone [7]. Healthy endothelial cells are essential for the maintenance of vascular homeostasis that involves antioxidant, anti-inflammatory, pro-fibrinolytic, antiadhesive or anticoagulant effects [8]. Ischemia/placental hypoxia, generates profound effects on the cardiovascular system in a sequence of uterine hypoperfusion, oxidative stress, reduction of angiogenic factors and increase in anti-angiogenesis being these aggravating effects of endothelial dysfunction already established [9]. Low density lipoproteins have been implicated in the increase of permeability and cellular adhesion, as well as in the alteration of the production of vasoactive molecules such as nitric oxide and prostacyclin [4,10].

Shear stress is the tangential force of laminar blood flow on the endothelium, protects endothelial cells by inhibiting apoptosis and reducing the release of endothelial microparticles [11-13]. The disturbed flow pattern in branch points and curvatures causes the preferential localization of atherosclerotic lesions [14]. Shear Stress generated by increased blood flow is a powerful stimulus for the production of nitric oxide and by various mechanisms produces flow mediated vasodilation [15-17].

The preeclampsia syndrome is modulated by the previous maternal cardiovascular or metabolic state [18]. This could reflect a common cause for PE and cardiovascular disease [19-23]. In preeclampsia, lipid deposition in walls of the spiral arteries regularly occurs. These vascular lesions resemble early stages of atherosclerosis and are named "acute atherosclerosis" and are thought to regress after delivery. The mechanisms that contribute to acute atherosclerosis in PE are largely unknown, but are related to the impaired vascular remodeling of the spiral arteries in the first half of pregnancy [24,25].

## Early Detection Methods

One of the main objectives of adopting a method of early detection should be the determination of patients at high or low risk of developing PE by detecting those early pathophysiological changes that compromise endothelial and cardiovascular function. This implies carrying out an adequate clinical history in search of risk factors for PE and cardiovascular risk factors such as mean arterial pressure, hemoglobin, decreased flow-mediated vasodilation, atherogenic risk with hyperlipidemia, and intima-media of the common carotid artery > 1 mm. In addition, request laboratory tests and perform Doppler of uterine arteries [26-39].

## Preeclampsia Prevention Measures

PE as a vascular disease is dependent on the previous vascular health status against the physiological and metabolic changes

of pregnancy. Those pregnant women with a history of adverse pregnancy outcome appear to be at increased risk of metabolic and vascular diseases in later life [40]. Likewise, those pregnant women with good vascular health will develop endothelial dysfunction in unfavorable metabolic changes such as dyslipidemia [41]. Therefore, preserving endothelial function and blood flow as a preventive measure could be useful and requires further investigation. These measures should begin before pregnancy and continue after pregnancy, through healthy habits, modifying those unfavorable risk factors such as obesity, smoking, sedentary lifestyle, etc. It is possible that despite adopting such measures we cannot avoid the disease due to non-modifiable factors or the presence of factors still unknown, especially in PE of early onset. Contrarily, it would not be possible to understand PE in pregnant women without risk factors and without vascular, circulatory and hematological compromise.

In this sense, it is necessary to implement preventive measures in pregnant women with only one risk factor from the first trimester of pregnancy and continue with periodic monitoring. In addition, we consider fundamental the evaluation of each case in particular according to the risk of PE and adopt as far as possible in an integral way the following preventive measures:

**Diet and Healthy Lifestyle:** When there are non-modifiable risk factors such as history of PE, maternal age <19 and ≥35 years, the pregnant woman should lead a healthy lifestyle to avoid cardiovascular risk. We can adopt the recommendations of the AHA / ACC of consuming a dietary pattern that emphasizes the intake of vegetables, fruits and grains in general; includes low-fat dairy products, poultry, fish, pulses, vegetable oil, nuts, limit the consumption of sweets, sugary drinks and red meats [42]. Reduce the percentage of calories from saturated fats to no more than 5-6% of the calories in the diet. Adapt this dietary pattern according to the caloric requirements appropriate to personal and cultural preferences and other medical conditions such as diabetes mellitus. The diet of vegetable fruits and grains reduces the inflammatory state [43]. However, protein intake is essential for fetoplacental development.

**Gestational Weight Gain:** It is important to calculate the pregestational body mass index in the pregnant woman to recommend an adequate weekly or monthly gestational weight gain [44,45]. Weight gain due to excessive food intake exposes the cardiovascular system to a prolonged postprandial hyperlipidemia, thus the metabolism of carbohydrates and postprandial lipids produces multiple proatherogenic products and inflammation. Even a transient increase in these factors can worsen vascular function and endothelium-dependent vasodilation [46].

**Medical Evaluation:** Pregnant women with mean arterial pressure above normal values according to the stage of pregnancy

should have a general or specialized medical evaluation in search of atherogenic risk factors and management of those modifiable or partially modifiable factors. We have observed an increase in mean arterial blood pressure with a monthly gestational weight gain above that recommended.

**Calcium, Sodium and Acetyl Salicylic Acid:** According to the WHO report, the strength of the recommendation is strong for the consumption of calcium in the diet with a dose of 1.5 to 2.0 g of elemental calcium per day and the daily administration of acetylsalicylic acid in a dose of 75 mg [47]. The recommendations of AHA/ACC, on sodium intake should not be higher than 2400 mg/day and that if the intake is 1500 mg/day; it is related to the reduction of blood pressure [42]. However, the WHO does not recommend the restriction on sodium intake during pregnancy in order to prevent the development of PE and its complications, the quality of scientific evidence is moderate and the recommendation is weak [47].

**Exercises in Pregnancy:** Many studies have shown the benefits of exercise in normal pregnancy and should strictly follow the recommendations given by the ACOG [48-50]. In relation to exercise and PE there is evidence in support of the protective function of physical exercise, increases cardiac output, promotes blood circulation and increases shear stress [51]. However, the impact of the exercise on reducing the risk of PE is still under debate [52]. Little is known about the mechanisms by which exercise can reduce the risk of PE and has been proposed to promote placental growth and vascular development, reduce oxidative stress and improve endothelial function, as well as immune and inflammatory responses [53]. In the placenta, an organ without autonomic innervations, local control of vascular tone is critical for the maintenance of fetal growth and the mechanisms underlying the response of shear stress induced by blood flow are essential during pregnancy [54].

**Hydration in Pregnancy:** Pregnancy is a physiological condition in which there is a marked increase in body composition and weight for a short period. Body weight increases approximately 12 kg during pregnancy between week 10 and 37 and most of the weight gain is water this increases 7 L or 260 mL per week [55]. Recent findings have suggested that maternal body composition allows differentiating healthy from pre-eclamptic women and longitudinal changes in total body water in pregnant women can predict the deterioration of PE preceded by edema [56-58]. Therefore, adequate hydration is a fundamental condition for the maternal and fetal cardiovascular physiological development. Dehydration states can reduce cardiac output and blood flow by producing hemodynamic changes in the uteroplacental circulation. It has not been possible to establish a single value of water intake that ensures hydration and health. In any case, a total daily water intake of 2.7 L is recommended for the adult woman. These amounts include the water contained in the

food, which contributes approximately 20 to 25% of the total ingested during the day [55].

**Other Prevention Measures:** There are some studies on supplementation with omega 3, zinc, magnesium, antioxidants such as vitamin C and E that are associated with the prevention of PE [59,60]. However, current scientific evidence requires human studies to demonstrate clinical utility [61,62].

These preventive measures are consistent with what was published by Parikh NI, who mentions that lifestyle modification during the preconceptional, pregnancy and postpartum periods would resolve a significant scientific gap and could represent a low-cost and high-performance strategy for prevent and/or attenuate the adverse consequences of preeclampsia in both mothers and their descendants [63].

It is important to point out that excessive weight gain from a hypercaloric diet triggers a dysmetabolism that can lead to endothelial dysfunction and gestational weight gain is a factor that can be controlled, but it is the set of prevention measures that they will give better results. The personal and family history of the pregnant woman is also important and they are related to vascular status and lifestyle, which are non-modifiable or partially modifiable risk factors. Also, remember that risk is a probability and the presence of risk factors does not always lead to the development of the disease. At the beginning of pregnancy, preventive measures will be aimed at early detection and the promotion of endothelial function to avoid or limit the most serious complications depending on the vascular and metabolic status of each patient. Inevitably, gestation will end in the case of PE with signs of seriousness.

## Conclusion

Endothelial dysfunction is considered one of the first manifestations of vascular disease. This link between endothelial dysfunction and vascular diseases is the key point for a potential intervention with preventive measures. Diet, healthy lifestyle, medical evaluation, controlled weight gain, calcium intake, acetylsalicylic acid at low dose, adequate hydration and reasonable physical activity according to gestational age and appropriate to the condition of the pregnant woman completes the prevention plan. These measures improve blood flow and can preserve the endothelial function of the macro and microcirculation.

## Declaration

### Conflict of Interest

The author declared no potential conflicts of interest with respect to the content, authorship, and/or publication of this article.

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