What Is New in Preeclampsia? From Prediction to Precision Therapy Best Articles from the Past Year

O Que Há de Novo na Pré-eclâmpsia? Da Predição à Terapêutica de Precisão Os Melhores Artigos do Último Ano

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Abstract

Preeclampsia remains one of the leading causes of maternal and perinatal morbidity and mortality worldwide. During the past year, several landmark studies have substantially advanced the field, particularly in prediction, prevention and disease-modifying treatment. The PREVENT-PE trial demonstrated that third-trimester risk stratification followed by planned early-term birth significantly reduces the incidence of term preeclampsia without increasing neonatal morbidity. Simultaneously, the first-in-human trial of selective soluble fms-like tyrosine kinase-1 (sFlt-1) removal by targeted apheresis provided proof-of-concept that correcting angiogenic imbalance may prolong pregnancy and improve maternal disease. In parallel, advances in angiogenic biomarkers, artificial intelligence and precision medicine approaches are reshaping clinical management. This review highlights the most influential publications of the past year and discusses their implications for future maternal-fetal medicine.

Keywords: Preeclampsia; Angiogenic biomarkers; sFlt-1; Placental growth factor; Artificial intelligence; Precision medicine.

Resumo

A pré-eclâmpsia continua a ser uma das principais causas de morbilidade e mortalidade materna e perinatal em todo o mundo. Durante o último ano foram publicados estudos de elevado impacto que modificaram substancialmente o conhecimento nesta área, particularmente nos domínios da predição, prevenção e tratamento dirigido da doença. O ensaio PREVENT-PE demonstrou que a estratificação de risco no terceiro trimestre seguida de parto programado reduz significativamente a incidência de pré-eclâmpsia de termo sem aumento da morbilidade neonatal. Paralelamente, o primeiro estudo em humanos de remoção seletiva do fator antiangiogénico sFlt-1 através de aférese dirigida demonstrou o conceito de que a correção do desequilíbrio angiogénico poderá prolongar a gravidez e melhorar a doença materna. Em simultâneo, os avanços nos biomarcadores angiogénicos, na inteligência artificial e nas abordagens de medicina de precisão estão a redefinir a prática clínica. Esta revisão destaca os artigos mais influentes do último ano e discute as suas implicações para o futuro da medicina materno-fetal.

Palavras-chave: Pré-eclâmpsia; Biomarcadores angiogénicos; sFlt-1; Fator de crescimento placentário; Inteligência artificial; Medicina de precisão.

INTRODUCTION

Preeclampsia affects approximately 2-8% of pregnancies worldwide and remains one of the leading causes of maternal and perinatal morbidity and mortality. Despite decades of research, delivery has remained the only definitive treatment. Nevertheless, recent advances have transformed our understanding of disease pathophysiology and opened new opportunities for prediction, prevention and treatment[1].

Among the publications of the past year, four developments stand out for their potential to change clinical practice. First, the consolidation of angiogenic biomarkers within prediction models. Second, the demonstration that personalized timing of birth can reduce the incidence of term preeclampsia. Third, increasing recognition that preeclampsia represents a heterogeneous spectrum of placental disorders. Finally, the first successful attempt to directly target a key pathogenic pathway through selective removal of circulating soluble fms-like tyrosine kinase-1 (sFlt-1)[2,3].

Together, these advances suggest that preeclampsia is entering the era of precision medicine.

WE CAN PREDICT BETTER

Prediction of preeclampsia has evolved substantially over the past decade. The integration of maternal characteristics, mean arterial pressure, uterine artery Doppler indices and biochemical markers has enabled individualized risk assessment with increasingly high predictive performance[4].

Particularly important has been the widespread adoption of angiogenic biomarkers. The sFlt-1/PlGF ratio has evolved from a diagnostic tool to an important instrument for risk stratification, prognostic assessment and clinical decision-making. Increasingly, angiogenic markers are being incorporated into pathways that guide surveillance, hospitalization and timing of delivery[5,6].

An additional development has been the emergence of artificial intelligence-based prediction models capable of integrating large amounts of clinical, biochemical and ultrasound information. Machine-learning algorithms have demonstrated encouraging predictive performance and may further improve individualized risk assessment. Although most remain in validation phases, they illustrate a broader shift toward precision obstetrics and data-driven clinical decision making.

For fetal medicine specialists, the convergence of Doppler velocimetry, placental biomarkers and artificial intelligence is likely to redefine screening strategies over the coming years. The ability to identify women at highest risk with greater accuracy may allow more personalized surveillance and intervention strategies than ever before.

WE CAN PREVENT BETTER: THE PREVENT-PE TRIAL

One of the most important publications of the year was the PREVENT-PE trial, published in *The Lancet*[2].

Although approximately three-quarters of preeclampsia cases occur at term, preventive strategies have traditionally focused on early-onset disease. Aspirin prophylaxis has successfully reduced the incidence of preterm preeclampsia but has shown limited impact on term disease[4].

The PREVENT-PE investigators evaluated a novel strategy based on third-trimester screening using the Fetal Medicine Foundation algorithm at 36 weeks followed by risk-stratified planned birth[2]. More than 8,000 women were randomized to either usual care or individualized timing of delivery according to estimated risk.

The intervention reduced the incidence of preeclampsia from 5.6% to 3.9%, corresponding to an approximately 30% relative reduction. Importantly, this benefit was achieved without increasing emergency Caesarean delivery or neonatal unit admission[2].

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For the first time, a randomized trial demonstrated that personalized timing of birth based on late-pregnancy risk assessment can significantly reduce the incidence of term preeclampsia. Beyond its immediate clinical implications, the study validates the utility of third-trimester prediction models and highlights the growing importance of precision obstetrics.

The implications extend beyond prevention alone. PREVENT-PE provides proof-of-concept that prediction is clinically meaningful only when linked to effective intervention. In this regard, the study represents a milestone in the translation of risk assessment into improved maternal outcomes.

Whether this strategy will be incorporated into future international guidelines remains uncertain, but PREVENT-PE undoubtedly represents a major step forward in the prevention of term disease.

WE UNDERSTAND THE DISEASE BETTER

Historically, preeclampsia has been viewed as a single clinical entity. Increasingly, however, evidence suggests that it represents a heterogeneous group of disorders characterized by different placental and maternal pathways[7].

Recent studies have identified distinct angiogenic, inflammatory and metabolic profiles associated with different disease phenotypes. Early-onset and late-onset preeclampsia appear to differ not only clinically but also biologically. Likewise, pregnancies complicated by fetal growth restriction often display more severe angiogenic imbalance than those presenting predominantly maternal manifestations[7].

This evolving understanding has important therapeutic implications. If preeclampsia encompasses multiple biological subtypes rather than a single disease, future interventions may need to be tailored according to underlying pathophysiology. Such an approach mirrors developments already observed in oncology and other specialties where molecular phenotyping has transformed patient management.

The concept of placental syndromes, once largely theoretical, is becoming increasingly relevant to clinical practice. Biological characterization may soon guide not only prediction and prognosis but also therapeutic selection.

WE MAY FINALLY BE ABLE TO TREAT THE DISEASE ITSELF

The most exciting publication of the year was undoubtedly the *Nature Medicine* report describing selective removal of circulating sFlt-1 through targeted apheresis[3].

More than two decades of experimental and clinical research have identified excess placental production of sFlt-1 as a central mechanism in the pathogenesis of preeclampsia[7]. Elevated circulating concentrations of this antiangiogenic factor promote endothelial dysfunction, hypertension and multisystem disease.

Thadhani and colleagues developed an extracorporeal adsorption system capable of selectively removing circulating sFlt-1[3]. In women with very preterm preeclampsia, treatment was associated with reductions in circulating sFlt-1 levels, lower maternal blood pressure and prolongation of pregnancy by a median of ten days.

Although the study was small and primarily designed to assess safety and tolerability, its conceptual significance is profound. For the first time, a therapeutic intervention directly targeted a central pathogenic mechanism rather than simply controlling the consequences of disease.

The possibility of prolonging pregnancy even by a few days in severe early-onset preeclampsia could translate into substantial neonatal benefit. This is particularly relevant in pregnancies at the threshold of viability, where every additional day in utero may improve neonatal outcomes.

Larger randomized studies are now required to determine whether this strategy can improve maternal and perinatal outcomes. Nevertheless, this study represents one of the most important milestones in preeclampsia research in recent decades and may ultimately be viewed as the beginning of a new therapeutic era.

CONCLUSION

The most important message from the past year is that preeclampsia is no longer viewed solely as a condition to be detected and delivered.

Advances in angiogenic biomarkers and prediction models are improving risk stratification[4-6]. The

PREVENT-PE trial demonstrated that individualized obstetric management can prevent a substantial proportion of term disease[2]. At the same time, molecular phenotyping is redefining our understanding of disease heterogeneity[7]. Most importantly, selective removal of sFlt-1 has provided the first convincing evidence that directly targeting the biological mechanisms of preeclampsia may be feasible[3].

The past year may ultimately be remembered as a turning point in preeclampsia research. For decades, progress was largely confined to improving prediction and optimizing the timing of delivery. Today, the field is moving beyond risk assessment toward biologically informed prevention and targeted intervention. The transition from prediction to precision therapy is underway, and preeclampsia may soon become one of the first placental disorders amenable to mechanism-based treatment.

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AUTHOR CONTRIBUTIONS

Luís Guedes-Martins contributed to the literature review, manuscript drafting, and critical revision of the manuscript. Ana Cunha contributed to the critical revision of the manuscript. Both authors approved the final version of the manuscript.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest related to the preparation and publication of this article.

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