Pre-eclampsia update – Advancements in prediction and management of preeclampsia: The clinical role of the PERT test

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Abstract

Preeclampsia, a hypertensive disorder unique to pregnancy, presents significant risks to maternal and fetal health globally. Despite extensive research, its multifactorial aetiology challenges timely diagnosis and effective management. The Pre-Eclampsia Ratio Test (PERT) emerges as a promising tool for risk prediction, prognosis assessment, and clinical decision-making. This essay explores the pathogenesis of preeclampsia, clinical implications of the PERT test, and its potential to revolutionize obstetric care.

Introduction

Preeclampsia, characterized by hypertension and proteinuria after 20 weeks of gestation, poses substantial risks to maternal and fetal well-being. Its complex aetiology involves placental dysfunction, genetic predisposition, immune dysregulation, and vascular abnormalities. Traditional management relies on symptom monitoring and blood pressure control, but recent advancements in biomarker testing, particularly the PERT test, offer novel insights into disease prediction and management.

Pathogenesis of preeclampsia

Placental dysfunction, stemming from inadequate trophoblast invasion and vascular remodelling, underlies preeclampsia pathogenesis. Genetic, immunological, and environmental factors further modulate susceptibility. Placental ischemia triggers the release of vasoactive factors, contributing to systemic endothelial dysfunction and multi-organ damage. Complications such as eclampsia and HELLP syndrome underscore the urgency of effective management strategies.

The role of PERT test

The PERT test leverages biomarkers like soluble fms-like tyrosine kinase 1 (sFlt-1) and placental growth factor (PlGF) to predict preeclampsia risk. By analysing these markers, PERT enables early identification of high-risk individuals, guiding personalized management.
strategies. Its ability to predict disease progression and differentiate preeclampsia from mimicking conditions enhances clinical decision-making and optimizes maternal and fetal outcomes.

**Molecular basis of PERT test**
The PERT test combines the levels of two proteins in the mother’s blood: soluble fms-like tyrosine kinase 1 (sFlt-1) and placental growth factor (PIGF).

**Procedure and steps**
1. **Sample Collection:** A blood sample is collected from the pregnant woman, typically during a prenatal visit.
2. **Measurement of sFlt-1 and PIGF Levels:** The blood sample is analysed to measure the levels of sFlt-1 and PIGF proteins.
3. **Calculation of the Ratio:** The ratio of sFlt-1 to PIGF is calculated based on the measured levels of these proteins in the blood sample.
4. **Interpretation:** The ratio of sFlt-1 to PIGF is compared to established thresholds. A higher ratio indicates an increased risk of developing preeclampsia.
5. **Clinical Decision Making:** Based on the PERT test results and other clinical factors, healthcare providers can determine the appropriate course of action. This may include closer monitoring, further diagnostic tests, or interventions to manage preeclampsia if it’s already present.

The PERT test is valuable because it can help identify women at high risk of developing pre-eclampsia, allowing for early intervention and management to improve outcomes for both the mother and the baby. However, like any medical test, it could be better, and clinical judgment is also essential in interpreting the results and making decisions about patient care.

**Reliability of PERT test and cut-off values**
Based on the provided information, both the sFlt-1:PIGF ratio and PIGF alone exhibit high reliability in predicting the likelihood of developing preeclampsia, particularly in specific clinical scenarios.

1. **sFlt-1: PIGF Ratio**
   - **Accuracy:** The sFlt-1: PIGF ratio, when below 38, demonstrates a very high negative predictive value (99.3%) in ruling out the likelihood of developing preeclampsia within the next week among women with suspected preeclampsia.
   - **Predictive Value:** While a ratio above 38 modestly predicts the risk of preeclampsia, its positive predictive value is lower (36.7%) compared to the negative predictive value.
   - **Clinical Utility:** This test has the potential to reduce unnecessary admissions for blood pressure monitoring by confidently excluding the likelihood of preeclampsia in women with normal results.

2. **PIGF as the only indicator**
   - **Accuracy:** PIGF alone, especially when below 100pg/ml, exhibits a high sensitivity and negative predictive value (96% and 98%, respectively) in predicting the occurrence of preeclampsia within two weeks among women presenting with suspected preterm preeclampsia.
   - **Clinical Utility:** Incorporating PIGF into clinical decision-making can lead to shortened time to diagnosis and reduced severe maternal adverse outcomes, particularly in cases with an intermediately low PIGF level (12-100pg/ml).

Overall, both biomarkers offer reliable predictive value, with the sFlt-1:PIGF ratio excelling in ruling out the likelihood of preeclampsia within the next week, while PIGF alone demonstrates high accuracy in predicting preeclampsia within a two-week timeframe. These tests provide valuable information to guide clinical management decisions and optimize maternal outcomes in cases of suspected preeclampsia.

**Clinical Scenarios**
Clinical vignettes illustrate the utility of PERT testing in various scenarios, from risk assessment in asymptomatic high-risk women to severity assessment and differential diagnosis. PERT’s role in guiding management strategies, particularly in twin pregnancies and comorbid conditions, underscores its clinical versatility and cost-effectiveness. These clinical scenarios demonstrate the practical application of the Pre-Eclampsia Ratio Test (PERT) in the management of pregnant women at risk of developing preeclampsia.
Case 1

In this scenario, a 28-year-old primigravida with a BMI of 25 presents with increased edema at 34 weeks of gestation. Despite normal urinalysis, her blood pressure is slightly elevated at 135/85 mm Hg. Given the clinical suspicion of preeclampsia (PE), PERT testing reveals a high value of 145. This prompt increased antenatal surveillance with twice-weekly short stay pregnancy day care reviews. Subsequently, preeclampsia is diagnosed at 35 weeks, and delivery is recommended at 36 weeks due to worsening PE indicated by persistently high PERT values. The use of PERT testing aided in early identification and management of preeclampsia, optimizing maternal and fetal outcomes.

Case 2

A 33-year-old multigravida with a BMI of 27 has a history of severe preeclampsia and fetal growth restriction (FGR) in her first pregnancy, leading to significant anxiety in her subsequent pregnancy. As a proactive measure, she is prescribed low-dose aspirin (LDA) from 10 weeks of gestation and undergoes monthly PERT testing from 22 weeks. All PERT values remain below the threshold of 38, alleviating her anxiety and enabling outpatient antenatal care. With reassuring PERT results, she delivers at term without complications, highlighting the role of PERT testing in risk stratification and reducing maternal anxiety.

Case 3

In this case, a 35-year-old primigravida with a BMI of 38 has a complicated pregnancy with gestational diabetes mellitus (GDM) diagnosed at 28 weeks. At 31 weeks and 1 day of gestation, she presents with borderline elevated blood pressure (140/85 mm Hg) and undergoes PERT testing, revealing a markedly elevated value of 902. This prompts an urgent scan, revealing severe fetal growth restriction (FGR) below the 3rd percentile. Immediate admission and corticosteroid therapy are initiated, and delivery occurs at 31 weeks and 3 days. The baby, weighing 1130 g at birth, receives five weeks of neonatal care and is discharged weighing 2274 g. In this case, the elevated PERT value facilitated early detection of severe FGR, guiding timely intervention and improving neonatal outcomes. In summary, these clinical scenarios underscore the value of PERT testing in risk assessment, surveillance, and management of pregnant women at risk of preeclampsia. By providing timely and actionable information, PERT testing enhances clinical decision-making and optimizes maternal and fetal outcomes.

PERT test appraisal

The PERT test represents a paradigm shift in preeclampsia surveillance and management. Its predictive power, reliability, and clinical utility make it indispensable in high-risk pregnancies. From early risk assessment to guiding delivery timing and optimizing resource allocation, PERT transcends barriers, offering a standardized approach to preeclampsia. The utilization of the Placental Growth Factor (PIGF) Endoglin Ratio Test (PERT) in the surveillance and management of preeclampsia represents a significant advancement in obstetric care. This innovative approach leverages the predictive power of PIGF and endoglin, two biomarkers intrinsically linked to the pathophysiology of preeclampsia, to enhance risk assessment, prognosis, and clinical decision-making.

In the context of asymptomatic high-risk women, the early integration of PERT testing offers unparalleled insight into the trajectory of preeclampsia development. By initiating monthly PERT tests from 20 weeks gestation, clinicians can proactively monitor for subtle changes indicative of impending pathology. A PERT result below the threshold of 38 serves as a reassuring indicator, assuaging concerns for both patients and clinicians alike.

The multifaceted utility of PERT extends beyond mere risk assessment, encompassing the crucial role of severity assessment in preeclampsia management. Elevated PERT levels correlate with heightened maternal complications, including acute lung edema, HELLP syndrome, placental abruption, renal failure, and refractory hypertension. Furthermore, PERT serves as a valuable tool in predicting adverse fetal outcomes, such as growth restriction and prematurity, thereby facilitating comprehensive antenatal care.

Of paramount significance is PERT’s capacity to discern the rate of preeclampsia progression, thereby informing timely intervention strategies. A rapid escalation in PERT levels signifies a worsening clinical prognosis, necessitating judicious management strategies tailored to mitigate maternal and fetal risks. However, it is imperative to note that while elevated PERT levels signal disease progression, immediate delivery may not invariably be warranted, necessitating individualized clinical judgment.

The diagnostic prowess of PERT extends to the realm of differential diagnosis, enabling clinicians to delineate preeclampsia from other mimicking conditions.
Notably, conditions such as chronic hypertension, thrombocytopenia, and chronic kidney disease pose diagnostic challenges, which PERT adeptly navigates through its discriminative capabilities\(^2\).

Moreover, in the intricate landscape of high-risk pregnancies riddled with comorbidities, PERT emerges as a beacon of diagnostic precision. By disentangling placental dysfunction from concurrent autoimmune diseases or diabetes, PERT facilitates tailored management strategies optimized for improved maternal and fetal outcomes\(^1\).

In the realm of twin pregnancies fraught with heightened preeclampsia risk, PERT serves as a pivotal prognostic tool. While acknowledging variations in PERT normal ranges between singleton and twin pregnancies, its utility in stratifying risk and guiding clinical management remains unparalleled.

Furthermore, the integration of PERT into clinical practice not only streamlines management planning and delivery timing but also underscores its cost-effectiveness in diverse healthcare settings. From resource-limited environments to sophisticated healthcare facilities\(^3\), PERT transcends barriers, offering a standardized approach to preeclampsia management across diverse healthcare settings.

**Conclusion**

As our understanding of preeclampsia evolves, the PERT test remains a cornerstone of obstetric care, empowering clinicians with the insights needed to navigate the complex landscape of high-risk pregnancies with precision and efficacy. Its integration into clinical practice heralds a new era in preeclampsia prediction and management, promising improved maternal and fetal outcomes worldwide. On the merits of its life saving and cost-effective nature of PERT test use in the latter half of pregnancy has been recommended in the Medicare programme in Australia\(^1\).

**References**

2. https://www.nhs.uk/conditions/pre-eclampsia/diagnosis/