***Conclusion**:* Overall, there was no significant change in the management of pre-eclampsia and outcome rate in the hospital over the time periods studied. However, there were some significant differences in the demographics and signs of the women between the development and temporal data. Therefore, it is important to investigate if and how these changes could affect the fullPIERS model performance on temporal validation.

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Basic science

40 Sepiapterin, a potential therapeutic approach to restore the metabolic phenotype switch induced by sFlt-1 in preeclampsia

Endothelial dysfunction, anti-angiogenic factors

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***Introduction**:* Preeclampsia (PE) is an often fatal cardiovascular complication related to pregnancy with no current effective way of treatment. Evidence of early increased circulating anti-angiogenic factors (AAFs) support the onset of a multi-systemic disorder and widespread maternal endothelial dysfunction in PE. However, the molecular mechanisms are still not well understood.

***Objectives**:* To determine the potential early metabolic perturbations and mitochondrial bioenergetics effects of sFlt-1 in bovine aortic endothelial cells (ECs) and first trimester extravillous trophoblasts (HTR-8/SVneo). Also, to evaluate the potential use of sepiapterin (SE), a precursor of eNOS's cofactor tetrahydrobiopterin (BH4), in abrogating the effects of sFlt-1 in cells.

***Methods**:* Metabolic perturbations and mitochondrial bioenergetics were assessed in ECs and HTR-8/SVneo in an in-vitro model of preeclampsia using exogenous sFlt-1 and serum from preeclamptic women. Mitochondrial bioenergetics was assessed using an XFe24 Extracellular Flux Analyzer. Nitric oxide (NO) was determined by chemiluminescence. Mitochondrial function and metabolism in sFlt-1-treated cells was evaluated also in galactose media. Mitochondrial membrane potential and superoxide was evaluated by JC-1 and Mito-Sox, respectively, by flow cytometry.

***Results**:* We found that treatment with sFlt-1 affected the mitochondrial maximal respiration and spare respiratory capacity in ECs in a dose dependent manner leading to a metabolic phenotype switch to glycolysis. In contrast, HTR-8/SVneo, displayed an unexpected strong glycolytic metabolism. sFlt-1 was found not to disturb the trophoblast mitochondrial metabolic and bioenergetics profile even at relatively high doses. In addition, we found that sFlt-1 treatment caused concentration dependent decreases in mitochondrial membrane potential and diminished NO levels in ECs. Moreover, treatment of ECs with sFlt-1 in galactose strongly impaired cell viability suggesting the role of sFlt-1 as a mitochondrial disruptor. SE, protected ECs and HTR8/SVneo cells from sFlt-1-induced superoxide formation and restored the NO levels and metabolic phenotype switch induced by sFlt-1 and maternal PE serum in ECs.

***Conclusions**:* sFlt-1 disrupts mitochondria bioenergetics and metabolism in both, ECs and HTR-8/SVneo. This evidence could explain the potential detrimental effects of AAFs in the maternal endothelium and the hallmark of hypertension in PE. Hence, we demonstrate that SE, by enhancing BH4/NO bioavailability and diminish mitochondrial superoxide formation, restored the metabolic phenotype switch induced by sFlt-1 and PE serum. Based on this evidence, we postulate the use of SE as a potential therapeutic approach to prevent or treat PE.

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Basic science

41 Placental growth factor and severity of preeclampsia

Biomarkers, prediction of preeclampsia

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***Introduction**:* Many markers have been studied to improve the understanding of preeclampsia (PE) pathophysiology. PlGF stands out as an important marker to predict PE. We hypothesized that PlGF could be associated with the severity of the disease.

***Objectives**:* To analyze PlGF levels in maternal plasma in normotensive and preeclamptic women, in the third trimester of pregnancy, and evaluate severity parameters in PE group with levels of PlGF, and correlate PlGF levels with maternal and fetal variables.

***Methods**:* Case-control study that included 117 pregnant women (50 with PE and 67 in the control group). After consent of the patients, maternal plasma samples were collected and stocked at −80°C until the time of the analysis. The PlGF was quantified using MagPlexTH-C microspheres system and analyzed using ANCOVA adjusted by body mass index, gestational age (GA) and maternal age. PE group was stratified in relation to GA (cut point in 34 wks) and proteinuria levels (proteinuria/creatininuria ratio – P/C, cut point in 0.5). Variables as newborn and placental weight; systolic and diastolic blood pressure were correlated to PlGF levels. To estimate the difference between groups, mean ratio (MR) and confidence interval (CI) of 95% was calculated. Analysis between PlGF levels were made by Pearson correlation. The null hypothesis was rejected when $p < 0.05$.

***Results**:* There was a 62% reduction of PlGF levels in pregnant women with PE (excluding superimposed PE and HELLP Syndrome) in relation to the control group (MR = 0,38; CI 95%: 0.15–0.95; $p = 0.041$). When the PE group was stratified, PlGF levels were significantly lower in the group with PE with GA < 34 wks vs. GA ⩾ 34 wks ($p = 0.018$), and those with P/C ⩾ 0.5 vs. P/C < 0.5 ($p = 0.027$). It was also observed a correlation between PlGF levels and the newborn and placenta weight ($r = 0.510$, $p < 0.001$; $r = 0.331$, $p < 0.001$, respectively) and systolic and diastolic blood pressure ($r = -0.352$, $p < 0.001$; $r = -0.360$, $p < 0.001$, respectively).

***Conclusion**:* It was found that the PlGF levels were significantly reduced in maternal plasma when GA < 34 wks and P/C > 0.5. Also, it was observed a direct correlation between PlGF and weight of placenta and the newborn, and a negative correlation with blood pressure. Thus, in view of the findings presented, the question is if PlGF besides being studied with focus on the prediction of PE, could also be inserted in the context of the disease severity.

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