HYPERGLYCEMIA IMPAIRS CYTOTROPHOBLAST FUNCTION VIA STRESS SIGNALING

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Abs: Gestational diabetes occurs in 3-14% of all pregnancies and has a 3-12 fold increased risk of developing preeclampsia (PreE). The first trimester cytotrophoblast (CTB) cells are involved in the vascular remodeling during placental development and PreE is believed, in part, to be caused by the dysfunction of CTBs. The aim of this study is to determine whether excess glucose induces anti-angiogenic effects in CTBs in vitro. Human extra villous CTB cells (Sw.71), derived from first trimester placenta were treated with 90, 180, 450 and 900 mg/dl glucose for 72 h. Thereafter, the cell lysates were utilized to measure vascular endothelial growth factor (VEGF)-1, angiotensin 1 (AT1) and AT2 receptor, p38 MAPK and peroxisome proliferator-activated receptor γ (PPARγ) expression while the levels of angiogenic and anti-angiogenic factors were measured in the cell culture media. AT2 receptor, p38 MAPK and PPAR-gamma expression was significantly up regulated in ≥ 180 mg/dl glucose-treated CTBs compared to basal; however, the AT1 and VEGFR-1 receptor expression were down regulated at ≥ 450 mg/dl. sFlt-1 and sEnd secretion were increased while VEGF and PlGF were decreased in the culture media of CTB cells treated with ≥ 180 mg/dl glucose. Exposure of CTB cells to glucose causes an induction of anti-angiogenic profile by: (i) up regulating AT2; p38 MAPK; PPARγand (ii) down regulating AT1 and VEGF-1; (iii) increasing secretion of sFlt-1 and sEnd; and (iv) decreasing secretion of VEGF and PlGF.