



O-07 - A NEW ROLE OF THE SUCCINATE-SUCNR1 AXIS IN HUMAN PREGNANCY: ASSESSING THE EFFECTS OF GESTATIONAL DIABETES

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Resumen

Introduction: Traditionally considered an energetic metabolite of the Krebs cycle, succinate has recently emerged as an extracellular signaling metabolite governing local stress, tissue damage and immunologic danger via its cognate receptor SUCNR1. Our group has recently demonstrated that pathological conditions such as obesity and type 2 diabetes are associated with increased levels of circulating succinate and disturbed succinate-SUCNR1 signaling, which are directly related to the chronic inflammatory process observed in those patients due the inability to properly resolve inflammation. **Objectives:** The aim of this work is to explore the potential implication of succinate in normal and gestational diabetes mellitus (GDM)-affected pregnancies, and to investigate the possible alterations in the succinate-SUCNR1 axis in umbilical cord and their consequences for fetal health.

Material and methods: This is a case-control study in which 108 pregnant women (54 with GDM and 54 with normal glucose tolerance) and their offspring were included. Maternal blood was collected at the beginning of third trimester of pregnancy, at delivery and postpartum. Umbilical cord blood and tissue were collected immediately after delivery. Data related to pregnancy evolution was recorded. Circulating succinate concentration and the levels of succinate transporters, SUCNR1 and downstream target genes were determined.

Results: The highest succinate concentration in maternal blood was observed in the peripartum period, with no differences between GDM and normal glucose tolerant women. Similar levels were found in umbilical cord blood. Vaginal delivery was associated with significantly higher maternal and cord blood succinate levels compared with elective caesarean. Circulating succinate levels at the beginning of third trimester were associated with birth weight whereas those from umbilical cord were associated with neonate subscapular fold. The diabetic environment also promotes a higher succinate accumulation and release by umbilical cord explants. Nonetheless, SUCNR1 and its downstream targets PTGS2 and VEGF were downregulated in umbilical cord of GDM women, along with the extracellular succinate transporters SLC13A3 and SLC13A5.

Conclusions: For the first time, our results suggest a potential physiological role of succinate-SUCNR1 at the end of pregnancy. GDM could impair its signaling pathway in umbilical cord which might affect the physiological mechanisms of childbirth and have a direct impact on fetal health.

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