Endothelin/endothelin receptor system is upregulated in preeclampsia with or without fetal growth restriction in contrast to gestational diabetes

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Introduction In addition to its vasoregulative function, in the human placenta endothelin-1 (ET-1) also regulates cell differentiation, proliferation, invasion and apoptosis. ET-1 effects are signaled through two receptor subtypes ETR-A and ETR-B. We tested the hypothesis that the expression of ET-1 and ETRs is altered in preeclampsia (PE), fetal growth restriction (FGR) and in gestational diabetes (GDM) and differs between early (gestational week ≤ 34) and late (GW >34) third trimester pregnancies.

Methods The study included women (GW 28-41) with PE (blood pressure >140/90 mmHg, protein >300mg/24hrs; n=16), with FGR (<10th birthweight centile and pathological umbilical blood flow; n=7) and PE+FGR (n=5) and with GDM (±insulin treatment n=21), as well as age-matched controls (n=20). ET-1, ETR-A and ETR-B mRNA and ETR-A and ETR-B protein were quantified in placental tissues by real-time PCR and immunoblotting.

Results

Table 1: mRNA expression in third trimester pregnancies:

Fold changes versus age-matched controls (p-values)

	GW ≤ 34			**GW > 34**		
	ETR-A	**ETR-B**	**ET-1**	**ETR-A**	**ETR-B**	**ET-1**
PE	2.6 (0.04)	3.0 (0.01)	3.5 (0.01)	0.6 (0.05)	2.0 (0.02)	0.4 (0.05)
PE+FGR	5.1 (0.05)	3.4 (0.04)	6.9 (0.003)	**-**	**-**	**-**
FGR	n.s	n.s.	3.8 (0.02)	0.6 (0.05)	n.s.	n.s.
GDM	**-**	**-**	**-**	0.5 (<0.001)	0.8 (0.05)	0.4 (<0.001)

-: not determined, because no material available, n.s.: not significant

In early third trimester pregnancies ETR-A protein was upregulated (+26%) only in PE. There were no changes in ETR-B protein. In late third trimester pregnancies ETR-A (-17%) and ETR-B protein (-33%) were downregulated in GDM. ETR-B protein was also downregulated in FGR (-23%) and PE (-35%).

Discussion The upregulation of the ET/ETR system in PE is correlated with the severity of the disease: mild-late<severe-early<PE+FGR). The ET/ETR system is downregulated in GDM.

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