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Investigation of base excision repair and oxidative stress in preeclampsia-complicated placentas – a pilot study

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Although the molecular pathways underlying pre-eclampsia (PE) are not entirely elucidated yet, the pathogenesis of PE involves elevated levels of oxidative stress in the placenta. Oxidative stress leads to DNA damage, including 8-oxoguanine (8-oxoG), which can interfere with normal placental development. Fortunately, oxidative stress induced DNA damage is repaired by base excision repair (BER), and a decreased ability to repair DNA may be involved in PE.

Therefore, the current pilot study investigated the correlation between PE and BER activity of the placenta. Additionally, we investigated the relationship between BER and antioxidant activity. We observed a significantly lower BER incision activity in PE-complicated placentas when compared to healthy controls by means of a comet-assay based assessment of DNA repair related incision activity. Furthermore, gene expression of various genes that are involved in the initial steps of BER (including OGG1, APEX1 and NEIL1) was significantly lower in PE (n=9) than in healthy control placentas (n=11). The expression of APEX1 correlated with BER incision activity (r= 0.72, P= 0.0027). Additionally, we observed a positive correlation between mitochondrial copy number and BER incision levels (r= 0.67, P= 0.0192). Higher antioxidant capacity was observed in PE, which was negatively correlated with BER incision capacity.

In conclusion, these data show that antioxidant and DNA repair defenses interact in the response to oxidative stress in the placenta and that decreased BER may play a role in the development of PE.

Keywords:
preeclampsia; oxidative stress; BER; antioxidants; mitochondria;