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Endothelial damage and complement dysregulation in fetuses from preeclamptic mothers

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Objective

Recent studies demonstrated that preeclampsia is associated with endothelial damage and complement dysregulation in mothers, however there are no data about the complement system in fetuses from preeclamptic mothers. The aim of this study is to evaluate endothelial damage and complement biomarkers in fetuses from preeclamptic pregnancies.

Methods

Cord blood samples were obtained from preeclamptic (n=33) and normotensive (n=38) pregnancies at the time of delivery. Circulating plasma biomarkers were analyzed, including vascular and intercellular cell adhesion molecules (VCAM-1, ICAM-1), tumor necrosis factor receptor (TNFR1), von Willebrand factor (VWF) and soluble complement membrane attack complex (sC5b-9). Complement activation was further assessed by analyzing deposits of C5b-9 on cultured endothelial cells exposed to activated plasma (1: 1 mix of patient's citrated plasma and healthy subjects pooled sera). C5b-9 deposits were assessed by immunofluorescence and calculated as the percentage of labeled area with respect to the total area analyzed. Results were expressed as fold increase of deposits (mean±SEM) compared to the deposits obtained with plasma pools from healthy subjects.

Results

VCAM-1, ICAM-1 and TNFR1 were significantly higher in preeclamptic fetuses compared to fetuses from normotensive pregnancies ([519.7±27.2 vs. 360.4±29.8 ng/mL; p<0.001], [164.5±12.2 vs. 120.9±7.2 ng/mL; p=0.002] and [2.55±0.34 vs 1.30±0.26 ng/mL; p=0.003] respectively). These results remained significant after adjusting for differences in gestational age at delivery. No significant differences in VWF and sC5b-9 were observed between the study groups. C5b-9 deposits induced by fetal plasma from preeclamptic pregnancies were significantly lower than those induced by control fetal samples (0.09±0.02 vs. 0.60±0.17; p=0.002).

Conclusion

The high levels of inflammation-related biomarkers (VCAM-1, ICAM-1 and TNFR1) reflect a status of endothelial damage in fetuses from preeclamptic mothers. In addition, the complement system seems to be depleted in fetuses from pregnancies complicated by preeclampsia. Future studies are warranted to investigate underlying mechanisms and potential implications on preeclampsia offspring.