Superoxide-anion production of neutrophil granulocytes in healthy and preeclamptic pregnant women

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SUMMARY

Data on respiratory burst activity of granulocytes from healthy and preeclamptic pregnant women have remained contradictory. To further investigate a possible role of reactive oxygen species in the etiology of preeclampsia we measured the phorbol-12.13-dibutirate- and n-formyl-methionyl-leucyl-phenylalanine induced superoxide-anion generation by granulocytes from non-pregnant, healthy and preeclamptic pregnant women. We also examined the reciprocal effects of heat-inactivated and not-inactivated non-pregnant, normal and preeclamptic pregnant plasma on superoxide production by neutrophils from non-pregnant, healthy and preeclamptic pregnant subjects. Superoxide generation was measured by ferricytochrome c reduction. Both the phorbol-12.13-dibutirate- and N-formyl-methionyl-leucyl-phenylalanine-induced superoxide production was significantly decreased in normal pregnancy compared with non-pregnant and preeclamptic pregnant women. The phorbol-12.13-dibutirate-induced superoxide generation by non-pregnant and preeclamptic neutrophils was significantly inhibited by heat-inactivated and not-inactivated healthy pregnant plasma. The N-formyl-methionyl-leucyl-phenylalanine-stimulated superoxide production by non-pregnant and preeclamptic granulocytes was suppressed only by not-inactivated healthy pregnant plasma. The phorbol-12.13-dibutirate-induced superoxide generation of healthy pregnant neutrophils was significantly increased by inactivated and not-inactivated non-pregnant and preeclamptic plasma. The N-formyl-methionyl-leucyl-phenylalanine-stimulated superoxide production by healthy pregnant granulocytes was significantly enhanced following treatment of the cells with not-inactivated non-pregnant and preeclamptic pregnant plasma. The deficient superoxide generation in normal pregnancy may be caused by maternal immunosuppressive factors. The failure of reduction in superoxide production in preeclampsia may be partly responsible for endothelial dysfunction. Apart from oxidative stress, a possible role of inefficient maternal immunosuppression should also be considered in the pathogenesis of preeclampsia.

In conclusion, $O_2^{-\cdot}$ production by neutrophils is decreased in normal pregnancy hich may be due to a defense mechanism to protect the maternal and fetal cells against the neutrophil-mediated oxidative damage. The deficient $O_2^{-\cdot}$ generation in normal pregnancy may be caused by maternal immunosuppressive circulatory factors. The failure of reduction in $O_2^{-\cdot}$ production in preeclamptic pregnant women may be partly responsible for endothelial injury. Therefore, besides the proposed hypothesis of neutrophil-mediated oxidative stress a possible role of inefficient maternal immunosuppression should also be considered in the pathogenesis of preeclampsia.

Keywords: Preeclampsia; Pregnancy; Oxidative stress; Superoxide-anion; Neutrophil granulocytes; Plasmafactors