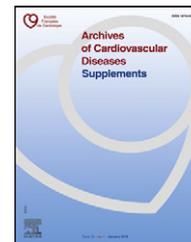




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05 – Hypertension and women

Preeclampsia is associated with changes in the composition and dysfunction of high-density lipoproteins



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Objectives Preeclampsia (PE) is a hypertensive disorder of pregnancy associated with abnormal placentation leading to poor placental perfusion, oxidative stress, and inflammation, which then leads to the dysfunction of the maternal endothelium. High density lipoproteins (HDL) exert protective effects on the vascular endothelium, especially by exerting an antioxidant effect and by stimulating the NO (nitric oxide) production by a mechanism involving sphingosine-1 phosphate (S1P). However, HDL can become dysfunctional and lose these protective properties. An increase in low-density lipoprotein (LDL) oxidation and a decrease in NO production have been described in PE. We hypothesized that HDL become dysfunctional in PE and fail to protect the maternal endothelium with, in particular, a loss of their antioxidant properties, explaining the increase of LDL oxidation and an S1P depletion explaining the decrease in NO production.

Methods We conducted a case-control study in 10 pregnant women with early severe PE matched by age and gestational age to 10 control healthy pregnant women. We isolated HDL from the serum of patients and control women by ultracentrifugation. In order to evaluate the antioxidant effect of HDL, we incubated human endothelial cells with the purified HDL, LDL and CuSO₄ for 6 hours. Then, we measured TBARs (ThioBarbituric Acid Reactive Substances) produced in cell culture supernatants. We have also measured the concentrations of S1P and apoM (apolipoprotein M), the apolipoprotein which binds S1P in HDL, by LC-MS-MS.

Results The TBARs levels in culture supernatants were significantly raised when the endothelial cells were incubated with HDL purified from PE women rather than with HDL purified from control pregnant women (respectively $3.24 \pm 1.25 \mu\text{M}$ versus $2.50 \pm 0.95 \mu\text{M}$, mean \pm SD, $P = 0.02$). These data show that HDL from PE patients have less antioxidant effect than HDL from pregnant control women. S1P and apoM concentrations were significantly lower in HDL purified from PE women compared to HDL purified from control pregnant women, with a strong correlation ($r = 0.75$) between the concentrations of these 2 parameters (respectively, 477 ± 131 versus $659 \pm 120 \text{ nM/L}$ for S1P and 1.5 ± 0.3 versus $2.1 \pm 0.7 \text{ mg/dL}$ for apoM, $P < 0.05$). These results show that HDL from PE patients contains less S1P and apoM than HDL from control pregnant women.

Conclusion We showed that HDL from PE pregnant women lose their antioxidant properties and are depleted in S1P and apoM, which could explain respectively the increase in LDL oxidation and the decrease in NO production by the endothelium previously described in the PE. These dysfunctional HDL, whose composition is modified, may be less protective for the vascular endothelium, a mechanism potentially involved in the pathophysiology of endothelial dysfunction seen in PE.

Disclosure of interest The authors declare that they have no competing interest.

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Proposal for distinctive biological profilings of pre-eclampsia



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Background The interaction between the endothelial cell and plasma biomolecules determine its dysfunction in renal disorders. In order to explore the implication of these interactions in renal failure, we used the pre-eclampsia as a model for studying renal impairment in human pathology.

Purpose Our goal was to determine the weight of each immunopathological hypothesis in the same series of patients and to find the one most associated with renal impairment.

Methods One hundred and twelve plasma samples from normotensive, hypertensive and pre-eclampsia women were analyzed