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Modulations of human placental transfer of lopinavir, ritonavir and enfuvirtide

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Background

Lopinavir boosted by ritonavir is one of the most prescribed HAART during pregnancy. This study used the human cotyledon-perfused model to investigate different elements (albumin concentrations, High-molecular weight antiviral (enfuvirtide, 4491 g/mol) and P-glycoprotein inhibitor drugs (ciclosporin, 1202 g/mol)) that modulate its placental transfer.

Methods

Thirteen human cotyledons were perfused with different concentrations of albumin (10, 20, 30, 40 g/L). Ciclosporin A (n = 11) and enfuvirtide (n = 2) were respectively coperfused at middle time of the perfusion. Clearance index (CI) of lopinavir and ritonavir were compared at different albumin concentrations and between control and ciclosporin or enfuvirtide phases.

Results

The CI of lopinavir was significantly lower at physiologic (30 and 40 g/L) albumin concentrations in control phases ($p < 0.0001$). When adding ciclosporin A at physiological albumin concentrations, the CI of lopinavir increased significantly 10.3 fold ($p = 0.046$) and became positive for ritonavir. The mean CI of lopinavir was 0.184 ± 0.169 in the control phase and 0.253 ± 0.239 following the addition of enfuvirtide, wich is 1.4 times higher but not statistical significant (p= 0.39). There was no placental transfer of ritonavir at baseline and no variation after adding enfuvirtide. Even at supraphysiologic concentration, enfuvirtide did not cross the placenta.

Discussion

This study suggests that the most influent event for placental transfer of highly bound drug like lopinavir during pregnancy is the physiologic variation of serum albumin. P-glycoprotein expression on human placenta has also a role but seems to be slighty. Also the competition with another antiviral highly bound drugs like enfuvirtide (92%) has a little but not significant effect on placental transfer of lopinavir.

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