

Vertical transmission of virus infections-placenta as facilitator or inhibitor

Abstract

Maternal to child transmission (MTCT) of human immunodeficiency virus type 1 (HIV-1) infection has been greatly controlled by administration of anti-retroviral therapy (ART).¹ We have reported that the sulfatide (3-O-galactosylceramide) promotes rescue of hematopoiesis *in vivo*.² Infection of human parainfluenza virus type 3 (hPIV3) has been shown to be inhibited by sulfatide (HSO3-3-galactosylceramide) by other investigators.³ Thus our earlier discussions on the importance of the different isoforms of and the seemingly differing types of biologically occurring sulfatides, lend credence to our proposed necessity of opposing (bi)directional investigations and their extent of beneficial or deleterious roles.⁴ Further such varying functional roles emanating from the placental plasma membranes may well seal the fate of vertical transmission of each type of virus, in the absence of prenatal maternal treatments. This is more so when a temporary or permanent abstinence from sex is not practiced by the parents when aware of the diagnosed infections and thus the nature of virus persistence.

Keywords: Placenta, UBC, Sulfatide, MTCT, Virus

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Opinion

The biologically occurring sulfatides produced in different organs of the human and animal species seem to carry the properties of helping the humans from virus infections by reversing such processes even in MTCT. Presence of sulfatides is evidenced not only in placenta but also in kidney, brain and certain other organs. The counter-active anti-virus-spread action of the sulfatide(s) in the plasma membranes as reported by other investigators supports our earlier contention that the human fetal adnexa may consist of a natural biologically inherent/intrinsic protection against vertical transmission. In the case of HIV, any presence of CD4+ T lymphocytes in umbilical cord blood (UCB) due to inflammatory infiltration, or from differentiation of CD34+ hematopoietic progenitor stem cells, may well be dealt with by sulfatides within the placental plasma membranes by interfering with CCR5/CXCR4 co-receptors of this virus. This hypothesis is reinforced by the reported action of anti-sulfatide monoclonal antibody, GS5, with respect to hPIV3 infection.³

Though as we have found that sulfatide possesses the property of enhancement of rescue of hematopoiesis *in vivo*,² this does not necessarily mean terminal differentiation of the CD34+ progenitor cells present in UCB into CD4+ T lymphocytes and circulation via the cord blood in placenta, but such a rescue most likely prefer just an increased self-renewal of the CD34+ cells in the cord blood. The latter implies that the fetus maintains immunity from the mother and lineage differentiation and acquirement of their phenotypes, of the largely primitive CD34+ cells (for example, long term-culture initiating cells, LT-CICs) in the progeny occurs post-delivery. This is an added advantage to contain MTCT of HIV-1 infection potentially due to lack of fetus' own CD4 receptors since the virus that was able to be transmitted into the fetus, found to be eliminated later in the child due to maternal immunity.⁵

The recent increasingly more potent anti-HIV therapies administered to the virus infected patients⁶ kill most of the CCR3/CCR5-tropic viruses and some of the CXCR4-tropic variants face survival from such newer drug therapies. Such greater resistant virus

variants⁷⁻⁹ could exert increased burden on the sulfatides and “escape” into the child during MTCT. This also increases the time period for clearance or non-detectability of the virus strains from the newborns and also requires more lethal therapeutic regimens against the virus unlike in a previous case apparently without ART.⁵

Thus CD1d-mediated HLA-independent sulfatide-conferring² and cytotoxic T lymphocyte (CTL), CD8-mediated immune responses seem to work against their own functional exhaustion, despite use of increasingly potent ART due to transition from R5 to X4 HIV-1 strains. This compounding effect of immune exhaustion¹⁰ and drug induced severity is not uncommon in non-communicable diseases such as cancer, but may be better controlled in infectious diseases. It is therefore suggested that a balance between detection of maternal HIV infection and type of ART be maintained for optimal benefits during the prenatal, perinatal, and postnatal periods of child birth for absence or clearance of the virus in the newborns, simultaneously avoiding excessive drug related systemic stress and side effects.

Conclusion

Thus placenta by virtue of the presence of sulfatides in their plasma membranes seems to be beneficial for protection from MTCT of virus infections.

Acknowledgments

None.

Conflicts of interest

None.

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