Background

- For reasons that remain unclear, people living with HIV (PLWH) are twice as likely to develop cardiovascular disease (CVD)\(^1\).
- Certain classes of antiretroviral drugs (ARVs) (e.g., abacavir sulphate (ABC) and protease inhibitors) may contribute to increased cardiovascular risk\(^2,3\).
- Endothelial dysfunction has a well-established role in atherosclerosis and CVD\(^4\).
- Endothelial dysfunction can involve cellular activation, pro-coagulant effects and increased cellular crosstalk.

ABC Increases Vascular Endothelial Cell Activation

Endothelial cells interact with circulating blood cells via numerous adhesion molecules, including ICAM-1. We measured ICAM-1 expression to assess the effects of ARVs on endothelial activation. \(n=5, *=p<0.05\)

ABC Enhances Endothelial Pro-Coagulant Properties

The vascular endothelium influences coagulation through expression of TF, which can initiate thrombosis. We examined inflammation-induced TF expression to determine any changes in pro-coagulant properties. \(n=5, *=p<0.05\)

TAF Increases Endothelial Anti-Thrombotic Properties

CD39 and CD73 degrade cell-free ADP, a platelet agonist that drives granule release, platelet aggregation and thrombus formation. We examined CD39 and CD73 expression to assess differences in anti-thrombotic effects. \(n=5, *=p<0.05\)

ABC Increases Microparticle Production and Promotes a ‘Pro-Thrombotic’ Microparticle Phenotype

Microparticles are small vesicles (0.1-1.0μm in size) that are produced by all cells. When activated, cells release more microparticles. Ablatorex microparticle production has been implicated in various inflammatory diseases. We quantified endothelial microparticles and examined adhesion molecule (inflammatory), TF (pro-coagulant) and ectonucleotidase (CD39 and CD73) (anti-thrombotic) levels to determine any modulatory effects of ARVs upon potential platelet crosstalk. \(n=5, *=p<0.05, **=p<0.01\)

Proposed Mechanism

In summary, we found:
- ABC-treated cells had higher levels of endothelial activation and pro-coagulant properties.
- TAF increased endothelial anti-thrombotic properties.
- ABC enhanced pro-thrombotic endothelial microparticle production.
- TAF increased basal anti-thrombotic endothelial microparticle production.

In conclusion, differential impacts of ARVs on endothelial activation may provide potential mechanisms underlying CV risk in PLWH. Patient studies are required to validate our findings within a clinical setting and determine the potential of endothelial dysfunction markers to act as predictive biomarkers of cardiovascular risk and/or therapeutic targets in PLWH.

Abacavir Sulphate and Tenofovir Disoproxil Fumarate or Tenofovir Alafenamide Differentially Regulate Endothelial Dysfunction

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