10.03 Meclizine induces aerobic glycolysis in human macrophages and can enhance the glycolytic response to Mtb infection

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Background: *Mycobacterium tuberculosis* (Mtb)-infected macrophages undergo metabolic shift, with induction of "aerobic glycolysis", which drives anti-TB effects (1). Virulent Mtb strains attenuate this glycolytic response to evade host defences (2). Meclizine is an over-the-counter antihistamine prescribed for motion sickness that can induce aerobic glycolysis in neuronal and fibroblast cells (3, 4). We investigated the impact of meclizine on human macrophage metabolism, and its ability to enhance the glycolytic response to Mtb infection.

Methods: Central carbon metabolism of PMA-treated THP-1 cells or primary human MDM pre- and post-treatment with Meclizine or Vehicle control was interrogated using Agilent Seahorse XFe24 Analyzer. Macrophages were treated with Meclizine or Vehicle control for 3 hours prior to stimulation with LPS or infection with irradiated Mtb (iMtb), and metabolic activity and cytokine production assessed at 24 hours by Seahorse and sandwich ELISA, respectively.

Results and Discussion: Meclizine induced glycolysis and inhibited oxidative phosphorylation in human macrophages, with maximal effects at 180 minutes post treatment. Meclizine enhanced glycolytic reprogramming in iMtb-infected macrophages compared to Vehicle-treated controls. However, no significant difference in TNFα or IL-1β secretion was observed.

Conclusions: Meclizine enhances the macrophage glycolytic response to iMtb infection, however this is not associated with an increased induction of pro-inflammatory cytokines. Further work is underway to investigate the impact of Meclizine-induced metabolic changes on macrophage mitochondrial function and bacillary clearance.

Keywords: Tuberculosis; macrophage; glycolysis; host-directed therapy

Disclosures: The authors declare that they have no conflicts of interest.

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