Ivacaftor alters macrophage and lymphocyte infiltration in the lung following lipopolysaccharide exposure

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Abstract

Background and Purpose: Cystic fibrosis (CF) is associated with a myriad of respiratory complications including increased susceptibility to lung infections and inflammation. Progressive inflammatory insults lead to airway damage and remodelling, resulting in compromised lung function. Treatment with ivacaftor significantly improves respiratory function and reduces the incidence of pulmonary exacerbations; however, its effect on lung inflammation is yet to be fully elucidated. Experimental approach: This study investigates the anti-inflammatory effects of ivacaftor in the lung post lipopolysaccharide (LPS) exposure and compare effects of prophylactic and therapeutic ivacaftor treatment in a C57BL/6 mice model. All groups received intra-tracheal (IT) administration of LPS (10 ug). Prophylactic treatment involved intraperitoneal injections of ivacaftor (40mg/kg) once a day beginning 4 days prior to LPS challenge. The therapeutic group received a single intraperitoneal ivacaftor injection (40mg/kg) directly after LPS. Mice were culled either 24h or 72h post LPS challenge and serum, bronchoalveolar lavage fluid (BALF) and lung tissue samples were collected. The degree of inflammation was assessed through cell infiltration, cytokine expression and histological analysis. Key Results: Ivacaftor did not alter the total number of immune cells within the BALF, however, prophylactic treatment did significantly alter macrophage and lymphocyte infiltration. Prophylactic treatment saw a significant negative correlation between immune cell number and ivacaftor concentrations in BALF, however, no significant changes in cytokine expression nor histological parameters were determined. Conclusion & Implications: Ivacaftor possesses some inherent immunomodulatory effects within the lung following LPS inoculation, however, further analysis of larger sample sizes is required to confirm results.

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