EFFECT OF FLUTICASONE AND SALMETEROL ON HUMAN ALVEOLAR MACROPHAGE CYTOKINE PRODUCTION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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RATIONALE: Macrophage derived cytokines, interleukin-8 (IL-8) & tumour necrosis factor-alpha (TNF-α), have been implicated in the pathogenesis of COPD. Corticosteroids & long-acting β_2-agonists are widely used in the treatment of COPD. **AIM:** We investigated the effects of fluticasone & salmeterol, alone & in combination, on alveolar macrophage cytokine production. **METHODS:** Alveolar macrophages, obtained via lung lavage of 7 patients, were cultured & exposed for 24 hours to varying concentrations of fluticasone (10^{-12} – 10^{-7}M) &/or salmeterol (10^{-7} – 10^{-5}M) plus lipopolysaccharide (LPS), & salmeterol (10^{-12} – 10^{-5}M) without LPS. IL-8 & TNF-α levels were measured by ELISA. **RESULTS:** Salmeterol in the absence of LPS inhibited both IL-8 & TNF-α production in a dose-independent manner & more effectively than fluticasone alone & in combination with salmeterol ($p<0.0001$). Fluticasone alone & fluticasone with salmeterol 10^{-6} & 10^{-5}M, inhibited TNF-α production in a dose-dependent manner. Adding salmeterol 10^{-5}M to fluticasone was more effective than fluticasone alone in reducing TNF-α production ($p=0.006$). Upregulated IL-8 production was reduced in a dose-dependent manner with fluticasone alone & in combination with salmeterol 10^{-7} & 10^{-5}M. Salmeterol 10^{-5}M was more effective than salmeterol 10^{-7}M when combined with fluticasone in reducing IL-8 ($p=0.025$). **CONCLUSION:** Combining fluticasone with salmeterol enhances the anti-inflammatory effect of the corticosteroid on alveolar macrophage cytokine production in patients with COPD.

KEY WORDS: COPD, macrophage, cytokine, fluticasone, salmeterol