

European Respiratory Society Annual Congress 2012

Abstract Number: 7165

Publication Number: P2741

Abstract Group: 10.1. Respiratory Infections

Keyword 1: COPD - exacerbations **Keyword 2:** Infections **Keyword 3:** Treatments

Title: Association of airway bacterial load with inhaled corticosteroid dosage in stable COPD

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Body: Inhaled corticosteroids (ICS) are commonly used in COPD, either alone or in combination with bronchodilators to reduce exacerbation frequency, but may also increase risk of pneumonia (Calverley et al, NEJM, 2007; Wedzicha et al, AJRCCM, 2008) which is not well understood. Lower airway bacterial colonisation is often present in stable COPD and may predispose to pneumonia. We investigated the relationship between airway bacterial load and ICS dose in stable COPD patients. We quantified typical bacterial load using a validated PCR (for *H. influenzae*, *S. pneumoniae*, *M. catarrhalis*) from the sputum of 47 stable COPD patients positive for at least one of these species. Patient characteristics: Mean(SD) age 71.6(8.0) years; Male gender 64%; Current smoker 34%; FEV₁ 49.0(18.4)% predicted. Median (IQR) beclomethasone-equivalent dosage was 2000 (640-2000) µg daily. Higher airway bacterial load was correlated to higher ICS dosage (corrected for beclomethasone equivalence) in a univariate analysis; $r=0.382$; $p=0.008$ (Fig. 1). This relationship remains significant in a multivariate analysis including age, smoking status and FEV₁ % predicted ($p=0.022$). For the first time we have shown that the use of high ICS dose is associated with higher airway bacterial load and may therefore play a part in increasing susceptibility to pneumonia in COPD.