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Title: Pro-surfactant protein B, a promising BAL biomarker of COPD progression in heavy smokers, is increased by budesonide/formoterol short-term therapy

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Body: Rationale & Aim: Reduced levels of surfactants in lung and bronchoalveolar lavage fluid (BAL) generally signal disease progression. The aim of this study was to determine the effects of Symbicort® therapy on the BAL levels of pro-surfactant protein B (pro-SPB) and other biomarkers in heavy smokers with or without COPD. Methods: We recruited 37 heavy smokers (3 current and 34 former; ≥30 pack-years), age 65±6 years (mean±SD), free of exacerbations for ≥ 4 weeks, with FEV1 of 73.1±18.3% predicted and FEV1/FVC ratio 66.3±9.4% (clinical trials.gov: NCT00569712). COPD was defined as FEV1/FVC <70%. BAL was obtained at baseline and after 4 weeks of Symbicort Turbuhaler® 400/12 mcg (budesonide/formoterol) BID therapy. Lung-predominant proteins: pro-SPB, surfactant protein D (SP-D) and Club Cell Secretory Protein (CCSP)-16 were measured in BAL supernatants. Results: Symbicort therapy significantly increased pro-SPB levels in BAL (geometric mean±SD: 322±619 versus 268±394 ng/ml; p=0.0166). The pro-SPB levels (but none of the other BAL biomarkers) were significantly related to lung function expressed by FEV1% of predicted (Spearman rho=0.36; p=0.026) and FEV1/FVC ratio (rho=0.51; p=0.0013), and to the levels of SP-D (rho=0.43; p=0.0073) and CCSP-16 (rho=0.54; p=0.0005), and to body mass index (rho=0.46; p=0.0043). Conclusions: In the current and former heavy smokers, pro-SPB levels in BAL were positively related to lung function and significantly increased by 4 weeks therapy with Symbicort. Pro-SPB is a very promising BAL biomarker to evaluate lung function in heavy smokers and thus disease progression in COPD and other chronic airway diseases.