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Title: First dose response to tiotropium in COPD: Impact on dyspnea, lung hyperinflation and distal airways

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Body: In COPD, response to bronchodilators is not limited to FEV1, distal airways may also be a target of bronchodilators. Our aim was to evaluate the impact of tiotropium 18 µg on lung volumes and airway resistance (plethysmography and forced oscillation). Patients and methods Response to tiotropium after the first dose (at 90 minutes) and 6 weeks later was assessed in 10 patients (mean FEV1: 48±11% pred, aged 61±6 years) by spirometry, plethysmography (including specific conductance (sGaw)), forced oscillation resistance (Rrs) and reactance (Xrs). Rrs and Xrs at 6 Hz preferentially evaluate distal airways. Change in dyspnea was assessed by a visual analog scale (VAS). Results At baseline forced oscillation and lung hyperinflation were related (Rrs6/RV: r=0.63, p=.0001; Xrs6/RV: r=0.72, p<.0001). After the first dose of tiotropium, dyspnea significantely improved (-11±8 mm), FEV1 and FIV1 increased (+19±7%; +18±29%, p<.01). Lung volumes decreased (RV: -13±4%) and sGaw increased (60±61%, p<.01). Low frequency oscillometry also improved, particularly Xrs6 (Rrs6: -20±7%; Xrs6: -43±7%, p<.01) but Rrs 16 Hz did not change. Dyspnea change correlated with ΔFIV1 (r=-0.80, p=.02), which itself correlated with ΔIC (r=0.49, p=.01). These responses increased or were maintained at six weeks of treatment. Conclusion Despite clear limitations (small sample, no comparator), these results suggest that lung volumes and low frequency oscillation parameters (particularly Xrs) are useful to assess the response to long acting bronchodilators, and show significant changes in distal airways at the first dose. FIV1 is also highly related to dyspnea improvement. This study is an Investigator Initiated Study (IIS).