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Title: Interaction between airway calibre and exhaled NO: The allergen challenge model

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Body: Background : High fractionated exhaled nitric oxide (FENO) detected in asthma patients reflects increased airway inflammation. However, FENO may be affected by airway calibre reduction, thus introducing a bias in FENO use for asthma control. Aim: to assess the impact on FENO of changes in both airway calibre and inflammation using the allergen challenge model. Methods: FEV₁ (forced expired volume in one second) and FENO were measured during early (EAR) and late (LAR) responses to a house dust mite challenge in 15 mild allergic asthmatics. Ventilation distribution using single breath washout test with inert gases (He and SF₆) was also performed to identify the sites of airway constriction, since different constriction sites result in different FENO reductions. Results: In EAR, mean FEV, fall was 36.8%, FENO decreased by 22% (p=0.002) and SHe was greater than ΔSSF_6 (+189.4% and +82.2%, p=0.001). In LAR, for a FEV₁ fall of 31.7%, FENO decreased by 28.7% (p=0.002) with the same Δ SHe, Δ SSF₆ pattern (+155.8% vs +76%, p=0.001). 8 hours after EAR, whereas FEV₁ was still lowered (p<0.001) FENO returned to baseline (p=0.085). At 24 hours, when FEV_1 returned to baseline, FENO increased by 38.7% (p=0.04). Conclusion: In mild allergic asthma, changes in airway calibre significantly modulate changes in FENO levels resulting from concomitant changes in airway inflammation. Therefore, correct interpretation of FENO changes in asthma patients may require integration of changes in airway calibre occurring concomitantly. Airway constriction and inflammatory processes after allergen exposure seem to involve similar regions of the bronchial tree, mainly the conductive airways.