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Title: Bronchial hyperresponsiveness to methacholine in relation to asthma control – Results from the MIDAS study

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Body: Bronchial hyperresponsiveness (BHR) is a hallmark of asthma. BHR to methacholine is used for diagnosis, but the role in monitoring treated asthma is not established. In the present study we assessed the relation between BHR to methacholine, airways inflammation, asthma control and symptoms. Methacholine challenge and FeNO measurements were done in 371 asthmatics (aged 10-35 years) with inhaled corticosteroids prescribed. PD₂₀ <0.3 mg defined moderate-severe BHR, 0.3 to 1.0 mg borderline-mild BHR, and >1.0 mg normal response (Schulze et al. Resp Med 2009). Well-controlled asthma (≥20 in Asthma Control Test) was found in 68% of children (<18 years) and 75% of adults (≥18 years). All subjects answered questions on asthma symptoms. Moderate-severe BHR was found in 61% of children and 44% of adults. FeNO increased with more severe BHR in both children and adults, with a higher explanatory value in children (R²=0.15 vs 0.06). Well-controlled asthma was less prevalent in the moderate-severe BHR group than the other two BHR groups in adults (66% vs 83% and 82%, p<0.05), whereas no significant difference was found in children (68% vs 76% vs 63%). Higher prevalence of wheezing and asthma attacks last year was found with higher BHR in both children and adults (p<0.05 both). Dyspnea at rest related to BHR in children (p=0.007), while exercise-induced dyspnea was associated with BHR in adults (p=0.007). In conclusion, bronchial hyperresponsiveness to methacholine was common in this treated asthma population and related both to airways inflammation and clinical aspects of asthma. BHR appears to be stronger related to poorer asthma control and exercise-induced dyspnea in adults than children.