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Title: Increased exhaled nitric oxide levels predict uncontrolled asthma in children – Results from the MIDAS-study

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Body: The fraction of exhaled nitric oxide (FeNO) is a marker of steroid-sensitive airways inflammation and is used in asthma management. The Asthma Control Test (ACT) is one of the most used instruments to assess control in asthmatic subjects. The evidence for a relation between airways inflammation and asthma control is inconclusive so far. The aim of the present study was to assess the relation between FeNO and ACT score in treated, stable asthma children. Within the frame of an industry-academy collaboration on minimally-invasive diagnostics (MIDAS), measurements of FeNO and specific IgE against aeroallergen or food allergen mix were done in 165 asthmatic children (101 boys) aged 10-18 years. Among the children, 129 (79%) were positive against aeroallergens and 61 (40%) tested positive against food allergens. Uncontrolled asthma (ACT score <20) was confirmed in 53 children. FeNO levels in subjects with uncontrolled asthma (n=53) were approximately 30% higher than in subjects with controlled asthma (n=112): 19.8 ppb (15.5, 25.3) vs 15.1 ppb (13.1, 17.4), p=0.04. FeNO was a determinant of asthma control in logistic regression models both before (p=0.01) and after adjustments for gender, age, BMI, FEV1, IgE sensitisation to aero- or food allergens (p=0.04). Furthermore, a significant relation between asthma control and FeNO could be found when using absolute values of the ACT score (r=-0.16, p=0.04). In conclusion, increased FeNO in treated, stable asthmatic children relate to uncontrolled asthma. It has to be further studied if intensified anti-inflammatory therapy in these subjects would lead to improved asthma control.