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Title: Can response to inhaled corticosteroids in preschool children with recurrent wheezing predict asthma at age six years?

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Body: Background: A reliable asthma diagnosis is not possible below the age of 6 years. Asthma is effectively treated by inhaled corticosteroids (ICS), however, ICS efficacy in transient wheezers is questionable. Aims and objectives: Prediction of asthma diagnosis at age 6 years by an ICS response at age 2-4 years in recurrent wheezers. Methods: From the Asthma DEtection and Monitoring (ADEM) study, 160 recurrent wheezers aged 2-4 years (≥ 2 episodes, ISAAC questionnaire) received 200 μ g Beclomethasone for eight weeks. Before and after treatment symptom score (inversely to severity), airway resistance (Rint) before and after 300 μ g Salbutamol, Fractional exhaled Nitric Oxide (FeNO), and exhaled breath condensate markers (pH, interleukin (IL) 1a, IL-2, IL-4, IL-5, IL-8, IL-10, IL-13, IFNg, sICAM, and Eotaxin) were assessed. At the age of 6 years a final diagnose (asthma or transient wheeze) was based on symptoms, lung function, and medication use. Analysis was performed by logistic regression. Results: At the age of 6 the study group consisted of 61 asthmatics and 99 transient wheezers. At the age of 2-4 years symptom score before ($OR_{adjusted}=0.86$ 95%CI=0.79-0.94, $p<0.01$), and after treatment ($OR_{adjusted}=0.88$, 95%CI=0.81-0.96, $p<0.01$), and prebronchodilator Rint after treatment ($OR_{unadjusted}=2.80$ 95%CI=1.07-7.31, $p=0.04$) were significantly associated with asthma at the age of 6 years. However, all parameters tested did not change during treatment. Conclusions: In recurrent wheezing children, asthma at 6 years was associated with more severe symptoms before and after ICS treatment and increased prebronchodilator airway resistance after ICS treatment at 2-4 years of age.