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Title: Fungal sensitisation in children with severe therapy resistant asthma

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Body: Adults with severe asthma with fungal sensitisation (SAFS) have reduced lung function and increased morbidity [Am J Respir Care Med 2009;179:11-8]. We hypothesized that fungal sensitisation in children with severe, therapy-resistant asthma (STRA) is associated with increased morbidity. Methods: All children had STRA having had basic management optimized [Lancet 2010;376:814-25]. There were 166 patients (11.7 years [4-17]; 61% boys). SAFS (n=76) was defined as specific IgE (sIgE) or skin prick test (SPT) positivity to *Aspergillus fumigatus*, *Alternaria alternata* or *Cladosporium herbarum*. Non-sensitised patients (n=90) had negative sIgE and SPT. Age, atopy, symptoms, medication, lung function and airway inflammation were assessed. Results: SAFS children were mainly boys (57/76(75%) vs 43/90(48%), p<0.001), had earlier asthma onset (0.5 years [0-12.5] vs 1.5 [0-12.5], p=0.006), higher total IgE (637 IU/mL [12-6737] vs 177 [1-10881], p=0.002) and sum of inhalant allergen SPT and sIgE (16 mm [0-38] vs 9 [0-36], p<0.001; 78 IU/mL [0-400] vs 19 [0-243], p=0.02). SAFS children had a trend for lower FEV1 (72%Pred [29-121] vs 75.5 [23-125], p=0.18) and FVC (90%Pred [36-138] vs 95 [30-123] p=0.13), more bronchodilator reversibility (59/73 (81%) vs 42/81 (52%), p<0.001), and were more likely prescribed maintenance oral steroids (18/76 (24%) vs 8/88 (9%), p=0.02). Symptoms and airway inflammation (sputum, bronchoalveolar lavage and endobronchial biopsy) were similar. Conclusions: Children with STRA and SAFS had earlier asthma onset, more atopy and bronchodilator reversibility, and were more often given prednisolone. We need a randomised controlled trial of antifungal therapy in paediatric SAFS.