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Title: Inflammatory cytokines in serum from children with severe asthma compared to controlled asthmatics

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Body: Introduction: Care of children with severe asthma remains a clinical challenge, partly due to the heterogeneity of the disease and the lack of definite biomarkers. In this study, we compared levels of inflammatory cytokines in serum from children with severe asthma and controlled asthma. Methods: Children with severe therapy resistant asthma (n=34, mean age 13.3 years) and controlled asthma (n=39, mean age 13.8 years) participated in a nationwide Swedish study. The protocol included Asthma control test, exhaled nitric oxide (FE_{NO}) and blood sampling. Interleukin (IL) 4, IL5, IL12p70, tumor necrosis factor alfa (TNFα) and eotaxin were analysed from serum using multiplex technology and results presented as medians with inter quartile ranges (picogram per millilitre). Results: Severe asthmatic children had inferior asthma control ($p<0.001$) in spite of high doses of inhaled steroids (> 800ug budesonide), compared to children with controlled asthma. FE_{NO} ($p=0.93$) and IgE ($p=0.92$) were comparable in these two patient groups. Children with severe asthma had increased levels of cytokines related to both Th1 inflammation (IL12p70 4.1 (0-22) vs. 0 (0-4.7), $p=0.001$ and TNFα 10.4 (4.6-19) vs. 4 (2.1-7.0), $p< 0.001$)) and to Th2 inflammation (IL4 1.6 (0-29) vs. 0 (0-1.9), $p=0.02$; IL5 0 (0-1.1) vs. 0 (0-0), $p=0.04$ and Eotaxin 97.3 (60-146) vs. 49.2 (42-68), $p<0.001$). Conclusions: Severe asthmatic children have increased serum levels of cytokines related to both Th1 and Th2 inflammation compared to controlled asthmatics. These results indicate a heterogeneous pattern of inflammation, and multivariate statistical analyses to further characterize the inflammatory phenotypes are initiated.