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Title: Sputum cells apoptosis by different asthma phenotypes in children

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Body: Background: Reduced apoptosis is one important mechanism for cell accumulation and maintenance of airway inflammation by asthma. However the role of death factors and their receptors in the regulation of granulocyte apoptosis in childhood asthma is still unclear. The aim was to determine the expression of apoptosis receptors in sputum cells by different asthma phenotypes in children. Methods: Seventy eight asthma children aged 6-12 years and 25 age-matched healthy controls were assessed including skin prick testing (SPT), lung function, total and antigen specific IgE, induced sputum analysis. Expression of pro-apoptotic Apo-1/Fas and Bax and anti-apoptotic Bcl-2 antigens in sputum cells were assessed using immunocytochemistry. Results: Among investigated children 69.2% had atopic asthma with increased total and specific IgE, positive SPT at least to one allergen. These children had mild-to-moderate asthma and sputum eosinophilia. They demonstrated decreased apoptotic ratio(AR) in sputum eosinophils that directly correlated with Apo-1/Fas and Bax expression and inversely with Bcl-2 expression and these parameters were more significant in moderate asthma than those in mild($p<0,001$). In contrast 30.8% children with non-atopic asthma had moderate-to-severe asthma and induced sputum neutrophilia. Their sputum neutrophils showed decreased Apo-1/Fas and Bax and elevated Bcl-2 expression that was more significant in severe asthma group($p<0.001$). Conclusion: Our findings indicated that sputum cell apoptosis vary in different asthma phenotypes in children. The identification of differences in the apoptosis regulation may help to define new medicines that allow specific induction of either eosinophil or neutrophil apoptosis.