

Alveolar Macrophage Phagocytosis Is Impaired in Children With Poorly Controlled Asthma

Fitzpatrick AM, Holguin F, Teague WG, Brown LA.

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PURPOSE OF THE STUDY. Because alveolar macrophages (AMs) are important in innate immunity, evidence was sought that AM phagocytosis might be impaired in poorly controlled asthma.

STUDY POPULATION. Children 5 to 17 years of age underwent bronchoscopy with bronchoalveolar lavage for clinical indications ranging from poor asthma control despite maximal inhaled corticosteroid (ICS) doses to suspected aspiration, suspected atypical infection, or confirmation of habitual cough or vocal cord dysfunction. A control group consisted of healthy, nonsmoking adults. Poorly controlled asthma was defined by $\geq 12\%$ forced expiratory volume in 1 second reversibility with bronchodilator and daily asthma symptoms requiring bronchodilator use on ≥ 5 of 7 days. Severe disease was defined by baseline forced expiratory volume in 1 second $< 80\%$ of predicted and asthma-related hospitalization within the past year. Pediatric subjects had received ≥ 8 weeks of ICS treatment.

METHODS. Bronchoalveolar lavage fluid AMs were isolated from 12 children with moderately severe asthma, 16 children with severe asthma, 10 children without asthma treated with ICS for chronic cough, and 10 healthy adults. AMs were stimulated with lipopolysaccharide and exposed to fluorescein isothiocyanate-conjugated inactivated *Staphylococcus aureus*. Phagocytosis was quantified by using a phagocytic index (PI) calculated from the percentage of phagocytic cells multiplied by the relative fluorescence units (RFU) of *S aureus* per cell. Apoptosis was determined from the percentage of cells positive for poly(adenosine diphosphate-ribose) polymerase.

RESULTS. Phagocytosis, as measured by unstimulated PI, was decreased in children with asthma (healthy control: 9330 ± 3992 RFU; chronic cough: 9042 ± 5976 RFU; moderate asthma: 4361 ± 2536 RFU; severe asthma: 3153 ± 1886 RFU; $P < .001$). PI was unchanged in all groups with lipopolysaccharide stimulation. Children with severe asthma also had increased apoptosis in both unstimulated and stimulated states ($P < .001$), which correlated with PI. The degree of corticosteroid treatment did not correlate with PI.

CONCLUSIONS. AM function is compromised in children with poorly controlled asthma, as characterized by decreased phagocytosis and increased apoptosis, and might account for the aberrant response to respiratory infection commonly seen in this population.

REVIEWERS COMMENTS. The most-severe impairment in phagocytosis occurred in the children with the most-severe

asthma. In practice, clinicians treating children experiencing exacerbations of already severe asthma are usually left with the question: is it all asthma, or is there lower respiratory infection to monitor and/or to treat? Although this study used a bacterial microbial stimulus, it is well known that innate AM activation is also important for clearance of respiratory viruses. Various studies suggested that the respiratory burst of AMs might be impaired in patients with asthma, resulting in decreased microbe killing. Additional study regarding the dynamic relationships between the respiratory burst and phagocytosis in the population with asthma is needed.

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β_2 -Adrenergic Receptor Polymorphisms Affect Response to Treatment in Children With Severe Asthma Exacerbations

Carroll CL, Stoltz P, Schramm CM, Zucker AR. *Chest.* 2009;135(5):1186–1192

PURPOSE OF THE STUDY. The purpose of this study was to explore the hypothesis that genotypic differences of the β_2 -adrenergic receptor (β_2 -AR) affect patient responses to short-term β_2 -AR agonist treatment for children who experience severe exacerbations of asthma.

STUDY POPULATION. Children between 2 and 18 years of age with physician-diagnosed asthma admitted to the ICU at a Connecticut medical center during a 4-year period ($N = 37$).

METHODS. A modified pulmonary index score (MPIS) was used to assess the severity of asthma exacerbation. β_2 -AR therapy was titrated on the basis of hourly MPISs. Children who did not respond to high-dose nebulized therapy were treated with intravenously administered terbutaline. Children also received intravenously administered methylprednisolone at 4 mg/kg per day. Genetic samples were obtained from saliva. Genotyping of the adjacent Arg16Gly and Gln27Glu was performed to determine the frequency of the 4 most common haplotypes. Clinical data were retrospectively extracted from the medical record.

RESULTS. At baseline, children with the Gly/Gly genotype at amino acid position 16 of the β_2 -AR were more likely to have intermittent asthma exacerbations than were those with either the Arg/Arg or Arg/Gly genotype. Otherwise, there were no statistical differences in the demographic features, baseline characteristics, or medical histories between these 2 patient groups. No differences were found in admission MPISs among the study groups; however, children with the Gly/Gly genotype

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