Paweł Majak

Department of Internal Medicine, Asthma and Allergy, Medical University of Lodz

Tumor necrosis factor alpha as an asthma biomarker in early childhood

The authors declare no financial disclosure

Pneumonol Alergol Pol 2016; 84: 143–144

Research on biomarkers of asthma in early childhood could be explained by at least three reasons. First, asthma diagnosis in young children is often full of doubts and demands long-term observation of patients. Second, decision on chronic inhaled corticosteroids (ICS) treatment in many cases is questionable, since a common pattern of illness in early life is recurrent episodes of wheezing separated in time by periods of asymptomatic wellness. Third, the heterogeneity and seasonality of asthma symptoms in young children impede implementation of GINA guidelines in real life practice.

Diagnosis of asthma in early childhood is based mainly on carefully taken medical history. Such an approach utilizes the best available tool such as asthma predictive index (API) with various modification. Unfortunately, the positive predictive value (PPV) for the API is modest and significant proportion of children with positive API won't develop asthma in the future [1]. It has been shown previously, that the addition of exhaled biomarkers and the expression of inflammatory genes in peripheral blood in preschoolers with recurrent wheeze improved the predictive capacity of the API. Complex model including API status, volatile organic compounds, and gene expression of toll-like receptor-4, catalase, and tumor necrosis factor-alfa (TNF-α) was highly predictive of asthma (PPV 90%, NPV 89%) [2]. One more thing should be pointed out in this context. Non–phenotype-directed antagonism of TNF-α in general population of adults with moderate-to-severe asthma has failed to improve asthma outcomes [3]. However, increased expression of TNF-α in patients with severe asthma has been clearly demonstrated [4, 5]. What is more, distinct phenotype of a high TNF-α in children with moderate-to-severe asthma has been described recently [6]. Asthma, also severe, starts usually very early in childhood, when clinical manifestation might not justify chronic ICS treatment. Therefore, measurements of biomarkers, including TNF-α, may be the best approach to prevent delay in the final diagnosis and treatment with all clinical consequences.

In the current issue of the journal Chkhaidze *et al.* present the results of the study aimed to determine whether plasma cytokine levels during the acute wheezing illness in infants are associated with the subsequent development of persistent-recurrent wheezing [7]. Observation period in this study corresponded with critical window for asthma development. What is more authors focused on inflammatory response during wheezing episodes, currently recognized as crucial issue in natural history of asthma. They concluded that TNF-α was strongly associated with the risk of persistent-recurrent wheezing and could serve as asthma biomarker in children under 3 years of age. Such a conclusion is limited by the study sample size. Odds ratios

Address for correspondence: Paweł Majak, Department of Internal Medicine, Asthma and Allergy, Medical University of Lodz, e-mail: majakp@wp.pl
10.5603/PiAP.2016.0015
Received: 22.04.2016

ISSN 0867–7077

are probably overestimated due to relatively low number of observations. Also multivariate logistic regression analysis, which allow to conclude on the independence of associations, usually demands significantly higher sample size. Given all the limitations, clinical studies are needed to determine the role of TNF-α in childhood asthma development and its utility in clinical practice.

Conflict of interest

The authors declare no conflict of interest.

References:

1. Bacharier LB. The recurrently wheezing preschool child-benign or asthma in the making? Ann Allergy Asthma Immunol 2015; 115: 463–470. doi: 10.1016/j.anai.2015.09.019.
2. Klaassen EM, van de Kant KD, Jobsis Q et al. Exhaled biomarkers and gene expression at preschool age improve asthma prediction at 6 years of age. Am J Respir Crit Care Med 2015; 191: 201–207. doi: 10.1164/rccm.201408-1537OC.
3. Holgate ST, Noonan M, Chanez P et al. Efficacy and safety of etanercept in moderate-to-severe asthma: a randomised, controlled trial. Eur Respir J 2011; 37: 1352–1359. doi: 10.1183/09031936.00063510.
4. Berry MA, Hargadon B, Shelley M et al. Evidence of a role of tumor necrosis factor alpha in refractory asthma. N Engl J Med 2006; 354: 697–708.
5. Howarth PH, Babu KS, Arshad HS et al. Tumour necrosis factor (TNFalpha) as a novel therapeutic target in symptomatic corticosteroid dependent asthma. Thorax 2005; 60: 1012–1018.
6. Brown SD, Brown LA, Stephenson S et al. Characterization of a high TNF-α phenotype in children with moderate-to-severe asthma. J Allergy Clin Immunol 2015; 135: 1651–1654. doi: 10.1016/j.jaci.2014.08.054.
7. Chkhaidze I, Zirakishvili D, Shavshvishvili N, Barnabishvili N. Prognostic value of TH1/TH2 cytokines in infants with wheezing in a three year follow-up study. Pneumonol Alergol Pol 2016; 145–150.