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Review Article

Eosinophilic Cationic Protein in Bronchial Asthma - current concepts

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Introduction:
Bronchial asthma is a chronic, inflammatory disease of large, small and medium sized airways with typical symptoms (cough, wheezing, breathlessness, chest tightness) and airway narrowing that is partially or completely reversible either spontaneously or by treatment, associated with increased airways responsiveness to a variety of stimuli1. On the basis of pathogenesis, asthma can be grouped into allergic, inflammatory, neurogenic and physical mechanisms with current evidence in favour a combination of allergic and inflammatory processes [2].

Asthma is characterized by a 50 fold increase in the number of eosinophil in relation to neutrophil in the bronchial mucosa[3]. After allergic sensitization, regulatory Th2 cell releases IL-5 [4]. This IL-5 is responsible for differentiation and maturation of eosinophil[5]. On re-exposure, activation and degranulation of eosinophil occur. Which causes release of several proteins like; Major basic protein (MBP), Eosinophil cationic protein (ECP), Eosinophil peroxidase (EPO) and Eosinophil derived neurotoxin (EDN) that are capable to induce pulmonary tissue damage and dysfunction [6].

Properties, characteristics and genetics of ECP:
ECP is heterogeneous in nature both molecular characteristics and functions. It is the best known of the proteins, assessed and used extensively as a marker in asthma and other inflammatory diseases. It was first purified from human myeloid cell in 1971 and identified as eosinophil granule protein in 1975. The protein is a single chain, zinc containing peptide of 133amino acid with a molecular weight of 16-22 KDa depending on the level of glycosylation [7].

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Distribution of ECP in the body fluids:
Eosinophil cationic protein is present in different body fluids such as serum, plasma, sputum, saliva, nasal lavage fluid, broncho-alveolar lavage fluid, tear, synovial fluids and urine[8]. ECP is a ribonuclease which has been attributed with cytotoxic, neurotoxic, and immune-regulatory functions. ECP regulates mucosal and immune cells and may directly act against helminthes, bacterial and viral infections [7].

Role of ECP in pathogenesis of bronchial asthma:
ECP concentration in plasma and other body fluids increases during Eosinophilic inflammatory reactions because only activated Eosinophil releases their granular contents [9]. The role of ECP in the pathogenesis of the bronchial asthma has been analyzed in several assays related to the presence of the eosinophil in the airways and allergy. ECP creates pores in the membrane of the target cells allowing entry of cytotoxic molecules into the cells. Thus, damage bronchial structure and increase bronchial hyper responsiveness. It also inhibits proliferation of T cells, suppress antibody production by B cells and induce histamine release by mast cells and basophil [10].

Diagnostic importance of ECP:
Serum ECP levels are significantly increased in patients with allergic disease compared with normal subjects, even when the number of circulating eosinophil count is within the normal range [11]. Serum ECP appears to correlate better with the severity of asthma than does the eosinophil count[12]. Therefore, the determination of serum ECP concentration is considerably more specific indicator than eosinophil count. Serum ECP has been promoted as a direct marker of eosinophilic inflammation of the bronchi, especially helpful in patient with asymptomatic asthma and better correlated with patients symptoms score than lung function tests especially in children with mild and moderate asthma[13]. It also correlates with other indicators of clinical asthma such as PEF measurments, airway hyperresponsiveness, number of inhaler puff needed, symptom onset, seasonal asthma attack, disease activity throughout the year[14]. Subject sensitized to perennial allergens had significantly higher serum ECP level

than subject with seasonal allergy, where as subject with seasonal allergy ECP levels are significantly increase during pollen season only. Persistent natural exposure to a sensitizing allergen is responsible for a measurable increase in serum ECP levels in patients with allergy[11]. The serum ECP levels are significantly elevated in asthmatic patients as compared to healthy controls and higher levels are found in symptomatic asthma patients than asymptomatic patients. The mean serum ECP level is significantly higher in severe asthma attacks compared those with mild and moderate attacks[15]. Serum ECP level is significantly high in persistent asthma rather than intermittent asthma. Moreover, diagnosis of asthma in children is difficult due to its heterogenous presentation. In addition, very young children cannot perform the pulmonary function tests required for the diagnosis. Situation like this make difficult to regulate long term inhaled anti-inflammatory therapy solely on clinical suspicion and illustrate the importance of having available tools like serum ECP to support a suspected diagnosis of childhood asthma[16].

Prognostic importance of ECP in bronchial asthma:

Asthma therapy consists of suppressing chronic and persistent airway inflammation. It is, therefore, important to find a marker of disease activity, which can be used to see the treatment prognosis. As serum ECP is significantly elevated in asthma patients compared to healthy individual, higher levels are found in symptomatic than asymptomatic patients and mean serum ECP level is significantly higher in severe asthma attacks compared to those with mild and moderate attacks[15]. So, it can be used as marker for monitoring the treatment. Serum ECP significantly reduced within 4 weeks of treatment but eosinophil count does not change significantly with this treatment, suggesting that serum ECP is not dependent on total eosinophil count[12]. It is a guide to tailing down inhaled corticosteroid therapy and assessment of compliance to most forms of anti-inflammatory therapies in asthma and in guiding the tapering of inhaled-corticosteroid (ICS) therapy in stabilized asthmatics[17]. After withdrawal of corticosteroid, levels of ECP in serum increased at first visit and become significantly higher than those in the continuous treatment group. Thus, low levels of ECP can help to estimate the short term prognosis and the need for corticosteroid treatment over a limited time[18]. Symptoms often deteriorate in well controlled asthmatics after a step down in inhaled beclomethasone dipropionate therapy (iBDP) if the serum concentration of ECP is high. High ECP in well controlled asthma may indicate the necessity for a higher iBDP dose over a long period than when the ECP concentration is not high[19]. So, serum ECP may be a useful parameter in monitoring disease activity and estimating anti inflammatory treatment efficacy in patients with asthma.

Conclusion:

These conclusions suggest that the serum ECP level may be a helpfull marker in the diagnosis of bronchial asthma and correlate with recording of lung function especially in patients without typical clinical manifestations of bronchial asthma. It has a special importance in pediatric practice because lung function tests are less easily performed in young children and it is preferable to keep steroid doses as low as possible. The use of ECP to observe and monitor allergic inflammation is finding its place in clinical practice.

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