

Histamine release from blood cells and serum ECP in patients with asthma, during and after a mild pollen season

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Introduction

Asthma is a chronic inflammatory disease with characteristic symptoms caused by variable airway constriction. Secreted products from activated eosinophils (eosinophil cationic protein, ECP) and mast cells (histamine) are thought to play a crucial role in the development of allergic symptoms and their release may be triggered by stimuli such as raised levels of airborne pollen [1]. Such activated cells are found in increased amounts in the bronchial mucosa of patients with allergic asthma. Increased release of ECP from cells localised in airway mucosa has been said to occur in parallel with raised levels of ECP in the serum, secreted by primed circulating cells. Serum levels of ECP have thus been considered useful to monitor fluctuations in clinical asthma [2]. The aim of the present study was to evaluate whether histamine release from circulating mixed blood-cells and/or ECP in serum respond to seasonal changes in airborne birch pollen. The ability of these tests to correctly diagnose variations in asthmatic respiratory constriction was also compared.

Material and methods

Twenty-two patients with a history of mild asthma appeared for testing during a period of moderately increased airborne pollen and again four months later. The studied pollen season only caused mild symptoms in all participants. Twelve of the patients were under treatment with low fixed doses of inhaled glucocorticosteroids (800 mg/day or less). Approval from the Ethics Research Committee, Faculty of Health, University of Linköping, Sweden was obtained and each individual gave informed consent prior to inclusion in the study.

Whole blood was collected and after approximately 60 min at room temperature, serum was separated and kept frozen until analysis for ECP by radioimmunoassay (Pharmacia Diagnostica, Sweden). Another sample of blood was collected in heparinized tubes and used for analysis of histamine release from circulating leukocytes. A commercially available kit (Supplementary Kit for Histamine Release in heparinized Whole Blood, IBL, Hamburg, Germany) was used and *in vitro* release of histamine was stimulated by anti-IgE, supplied by the manufacturer and diluted 1:2. Histamine was then measured by ELISA immunoassay (IBL, Germany).

Lung function tests including forced expirations during one second (FEV₁) and measurements of airway dead-space according to Bohr [3] were performed at each visit.

Paired and unpaired non-parametric statistical tests and analyses of receiver operated curves (ROC) were performed using a computer program (Medcalc Statistical Software, MSS, Mariakerke, Belgium). Median values (lower – upper quartiles) are given.

Results and discussion

The amount of released histamine from anti-IgE stimulated circulating whole-blood cells was significantly higher during a period of raised airborne pollen compared to four months later (40.4 [21.2–73.8] µg/L vs. 25.4 [16.5–53.1] µg/L, *p* = 0.03). Levels of ECP in serum (13.5 [9.2–20] µg/L vs. 5.9 [4.5–6.6] µg/L, *p* = 0.002) and volumes of airway deadspace (179 [159–246] mL vs. 172 [142–196] mL, *p* = 0.02) were also higher compared to the non-pollen-period. No such differences could be demonstrated for FEV₁ (3.2 [2.7–3.7] L vs. 3.2 [2.7–3.7] L. This ‘lack of response’ in FEV₁ is in accordance with previous recordings of lung function tests in patients with asthma, since a deep inspiration, such as precedes the forced expiration in FEV₁-measurements, tends to dilate bronchi in some patients with mild asthma [4]. FEV₁ tends not to be sensitive enough to monitor minor changes in lung function. Measurements of airway deadspace may be more sensitive for mildly affected patients and therefore the clinical relevance of this measurement is higher in this type of study.

The optimal cut-off level for changes in airway deadspace was calculated by MSS (comparison of ROC curves) and found to be 14%. The capacity to correctly diagnose a ‘responder’ i.e. a patient with changes in airway dead-space > 14% was evaluated by ROC analysis using MSS. The sensitivities using histamine release or serum ECP were identical (80%). The specificity of histamine release was lower (33%) than that of serum ECP (56%) in this study. However, analysis of areas under the ROC-curves (Fig. 1), reflecting an overall estimation of specificity and sensitivity, showed no statistically significant differences comparing IgE stimulated histamine-release and serum ECP (*p* > 0.05).

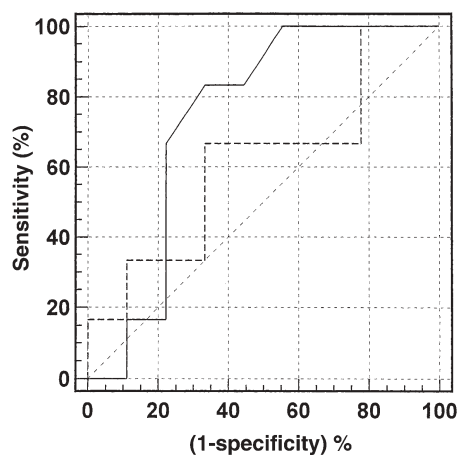


Fig. 1. ROC curves of serum levels of eosinophil cationic protein [ECP] (solid line) and in vitro histamine release (dotted line).

Conclusion

We conclude that the release of histamine from whole-blood cells and levels of serum-ECP had equivalent capacity to correctly diagnose minor changes in airway function, which results from airborne birch-pollen exposure in patients with asthma.

References

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