



Factor VIIa – antithrombin complex concentrations are increased in asthma: relation to exacerbation-prone asthma phenotype

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Introduction

Asthma is associated with a prothrombotic state and fibrinolysis impairment related to a higher exacerbation rate. Since tissue factor (TF) initiates the extrinsic coagulation pathway, we hypothesized that elevated factor VIIa-antithrombin complex concentrations (FVIIa-AT), which reflect TF operation, are elevated in asthma in relation to the disease severity.

Material and methods

In 159 clinically stable adult asthma patients and 62 age-matched controls, we determined FVIIa-AT in plasma and analyzed their relation to inflammatory and prothrombotic markers, including thrombin generation profile and global fibrinolysis (clot lysis time, CLT). We recorded clinical outcomes, including asthma exacerbations, during a 3-year follow-up.

Results

Asthma patients were characterized by 38% higher FVIIa-AT ($p < 0.001$), related to bronchial obstruction, asthma severity, and duration compared to controls. FVIIa-AT showed weak positive associations with C-reactive protein, fibrinogen, and CLT but not with thrombin



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generation parameters. In the follow-up, we documented 151 (47 per year) severe asthma exacerbations in 51 (34%) patients, including 33 (22%) with ≥ 2 such complications. Exacerbation-prone asthma phenotype was related to 13% higher FVIIa-AT ($p=0.01$), along with asthma severity and control ($p<0.01$, both) but also peak thrombin generation in classification and regression tree. High FVIIa-AT (≥ 100.1 pmol/l) was linked to exacerbation-prone asthma phenotype and a shorter time to first exacerbation.

Conclusions

This study is the first to show that FVIIa-AT complex concentrations are higher in asthma in relation to its severity and may help identify individuals at risk of exacerbation-prone asthma phenotype, suggesting a role of TF-mediated coagulation.

Authors declare no conflict of interest.