Effects of topical dosed anti-coagulant on LPS-induced exacerbation in asthma model mice

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RNA virus and bacterial infections induce exacerbation and steroid insensitive airway inflammation in patients with asthma. We have previously demonstrated that dabigatran inhibited steroid insensitive airway inflammation. The aim of this study is to evaluate the effects of anti-coagulant on LPS-induced steroid insensitive airway inflammation in asthma model mice. OVA-sensitized A/J mice were exposed to OVA every other day, then were exposed with LPS intranasally twice daily for 3 days. Fluticasone propionate (FP), dabigatran (Dabi; thrombin inhibitor) and edoxaban (Edo; factor Xa inhibitor) were administered intranasally at 2h before each LPS exposure. BALF was collected at 24 h after the last LPS exposure and eosinophils and neutrophils were quantified by FACS analysis. The level of CXCL1, TNF-α (inflammatory cytokine) and D-dimer, PAI-1 (blood coagulation/fibrinolysis system associated factors) in BALF were measured by ELISA. LPS exposure showed significant increase in eosinophils and neutrophils in BALF. Neither FP nor Edo inhibited inflammatory cells, while Dabi was inhibited in LPS-exposed asthma model mice. In addition, Dabi inhibited increased production of CXCL1, TNF-α, D-dimer and PAI-1 in BALF induced by LPS exposure. This profile provides new insights into steroid insensitive airway inflammation and future treatment.