

Evaluating the sensitivity and specificity of active neutrophil elastase as a biomarker for bacterial infection in subjects with COPD.

Samantha J Thulborn¹, Nigeen Akram², Vijay Mistry³, Christopher E Brightling³, Kelly Moffitt⁴, David Ribeiro⁴, Mona Bafadhel¹

¹Respiratory Medicine Unit, Nuffield Department of Medicine, University of Oxford; ²Department of Biological and Medical Sciences, Oxford Brookes University, Oxford, UK ³Institute of Lung Health, University of Leicester; ⁴ProAxis Ltd, Belfast, UK.

Introduction

COPD is a neutrophilic disease, with the majority of subjects having a sputum neutrophil percentage of >60%. Neutrophil elastase (NE) is a serine proteinase, secreted by neutrophils and macrophages during inflammation and has a role in the destruction of bacteria within the host. New advancements now allow accurate assessment of active protease levels in complex biological samples. We sought to investigate if active NE could be used as a biomarker for bacterial infection in subjects with COPD.

Methods

NE was quantified using ProteaseTag™ active NE Immunoassay (ProAxis, Belfast) from cell-free sputum supernatant from 31 COPD subjects (20 Males; mean age 65, range 45 to 81) at stable state and during an exacerbation. Bacterial infection was defined as $\geq 10^7$ CFU/mL in sputum. Subject demographics, sputum cell differential counts and polymerase chain reaction (PCR) for respiratory pathogens were measured.

Results

*Active NE was higher during an exacerbation compared to stable state (fold difference (95%CI) 0.50 (0.22 to 0.78), $p=0.001$) (Fig.1). NE correlated with total sputum neutrophils ($p<0.0001$, $r=0.48$) and total bacterial load measured by CFU/mL ($p<0.01$, $r=0.39$) and qPCR ($p<0.05$, $r=0.33$). When looking at the main respiratory pathogens no correlations were seen between *H. influenzae* ($p=0.43$, $r=-0.11$), *S. aureus* ($p=0.34$, $r=-0.14$) or *S. pneumoniae* ($p=0.11$, $r=0.23$); however a correlation was seen between NE and *M. catarrhalis* ($p=0.01$, $r=0.36$). NE has an area under the receiver operator curve of 0.72 [0.58 to 0.85] to identify a bacterial infection with a sensitivity and specificity of 67.74% and 67.86% at a NE cut off of 2335ng/mL.*

Conclusion

Active NE is elevated during a COPD exacerbation compared to baseline. Active NE is associated with neutrophilic inflammation and bacteria; and may be a viable biomarker for bacterial infection in COPD.

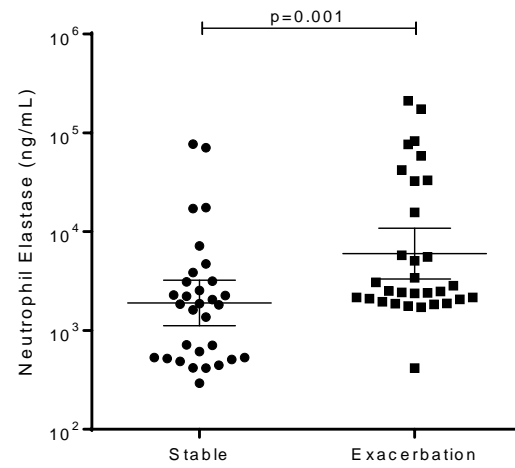


Fig.1. Sputum active NE levels at stable and exacerbation state from 31 paired COPD subjects. Mean and 95%CI