Time course of Infective and Inflammatory Changes at Exacerbation of COPD

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Any remaining errors are entirely my own responsibility.

Contributions

I confirm that the work contained within this thesis is my own original endeavour, with contributions from the following individuals, in the specific areas described:

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Abstract

Chronic obstructive pulmonary disease (COPD) is associated with recurrent episodes of exacerbations that lead to increased morbidity and mortality. Exacerbations are associated with increased airway and systemic inflammation. This thesis examines the relationship between the infective and inflammatory changes at exacerbation of COPD and clinical non-recovery and recurrence of exacerbations.

Patients were recruited from the London COPD cohort and sampled prospectively in the stable state, at exacerbation and after 7, 14 and 35 days. Clinical indices, airway and systemic inflammation and lower airway bacteria were analysed at each visit. Airway inflammation was assessed by sputum interleukin (IL)-6 and IL-8 levels, systemic inflammation was assessed by circulating leucocytes, serum C-reactive protein (CRP) and IL-6. Sputum bacteria were assessed by standard cultures and quantitative real time polymerase chain reaction (qr-PCR).

The key findings were: 1) the persistence of heightened airway and systemic inflammation was associated with clinical non-recovery at exacerbation, 2) a higher level of serum CRP 14 days after an exacerbation was associated with a recurrent exacerbation within 50 days, 3) frequent exacerbators have reduced response to therapy and persistently high systemic inflammation compared to infrequent exacerbators, 4) the presence of a significant relationship between the lower airway bacterial load and circulating leucocytes in stable COPD and 6) the detection of a potentially pathogenic micro-organism from sputum samples is higher by qr-PCR than by standard cultures.

These new findings could form the basis of future therapeutic interventions and strategies for prevention of recurrent exacerbations. Further studies into the mechanisms explaining the differences observed between frequent and infrequent exacerbators may help reduce the high burden due to the disease. Finally refining the qr-PCR assay may help elucidate the complex links between lower airway bacteria and inflammation in COPD.

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Preamble