

C-Reactive Protein Levels in Association with Chronic Obstructive Pulmonary Disease Exacerbation and its Guidance for Antimicrobial Prescription

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Globally, chronic obstructive pulmonary disease (COPD) is the major cause of morbidity and mortality. COPD results in 1.68 years of living with disability (YLD) per 1,000 population, approximately is 1.8% of all YLD, contributing to the fourth leading cause of death, with greater burden in men (1.93%) than women (1.42%). Tobacco smoking is globally the most commonly encountered risk factor. In stable COPD, there is increase of various biomarkers of oxidative stress and systemic inflammation. Increased blood levels of various inflammatory proteins, such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor- α (TNF- α) are identified in systemic circulation of in patients with COPD. Increased blood levels of CRP are associated with major COPD outcomes, such as decreased pulmonary function, hospitalization, and mortality that are assessed by using blood CRP levels increase up to 10,000 fold in response to inflammation and stimuli. Blood CRP levels have been demonstrated to be elevated in patients with stable COPD as a biomarker of persistent low-grade systemic inflammation, which seems to increase with increasing severity of COPD. Blood CRP levels are not necessarily a biomarker of bacterial infection whereas it is a biomarker for COPD exacerbation. These features made blood CRP levels useful as an clinical biomarker for systemic inflammation. A recent study among 653 COPD patients underwent randomization (blood CRP < 20 mg/L, antimicrobial was discouraged; blood CRP 20 - 40 mg/L, antimicrobial was possibly helpful; and blood CRP > 40 mg/L, antimicrobial was encouraged) demonstrated that a lower percentage of COPD patients in the CRP-guided group than in the usual-care group received an antimicrobial prescription at the initial consultation (47.7% versus 69.7%, for a difference of 22.0 percentage points; adjusted odds ratio, 0.31; 95% Confidential Interval, 0.21 to 0.45) and during the first 4 weeks of follow-up (59.1% versus 79.7%, for a difference of 20.6 percentage points; adjusted odds ratio, 0.30; Confidential Interval, 0.20 to 0.46) whereas two patients in the usual-care group died within 4 weeks after randomized from causes considered by the investigators to be not associated with trial participation. A previous study revealed that blood CRP reached the highest levels in exacerbation due to *Streptococcus pneumoniae* (74.1, Interquartile Range (IQR) 42.0 - 220.7) and *Hemophilus influenza* (74.5, IQR 23.9 - 167.9) in comparison with episodes associated with *Pseudomonas aeruginosa* (45.2, IQR 11.1 - 70.1) of viral infections (37.3, IQR 18.6 - 79.1). Blood CRP levels were not associated with bacterial load except for *Streptococcus pneumoniae*. Blood CRP > 100 mg/L was related to the probability of hospital admission rose more than fourfold.

In conclusion, serial blood CRP measurement (CRP-guided prescribing of antimicrobials for COPD exacerbations) results in a lower percentage of patients with reported antimicrobial use and who received antimicrobial prescriptions from clinicians, with no evidence of harm. Blood CRP measurement is useful as early biomarker of COPD exacerbation and also beneficial in assessing treatment efficacy.

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