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Editorial

Pneumonia Complicating COPD: Are Corticosteroids a Help or a Hindrance?

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Abbreviations: chronic obstructive pulmonary disease, **COPD**; community-acquired pneumonia, **CAP**; acute exacerbations of COPD, **AECOPD**; inhaled corticosteroids, **ICSs**; intensive care unit, **ICU**

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Introduction

Patients with chronic obstructive pulmonary disease (COPD) are at increased risk for developing community-acquired pneumonia (CAP) compared to non-COPD patients, and pneumonia itself may lead to a worse outcome of an exacerbation than a simple bronchitic worsening.¹ However, the distinction between pneumonic and non-pneumonic exacerbations is not so simple, particularly since recent data have shown that many hospitalized patients with acute lower respiratory tract infection symptoms, but with no radiographic pneumonia, may actually have an infiltrate if computed tomography scanning or lung ultrasound are performed.² Since both conditions are usually treated with antibiotics, determining if pneumonia is present may not be so essential. However, there is still uncertainty about the use of corticosteroids in hospitalized COPD patients with both an exacerbation and CAP, while the

consensus is that systemic corticosteroids are of value for hospitalized non-pneumonic COPD exacerbation patients.³

In patients who are hospitalized with CAP, the routine use of corticosteroid therapy is not recommended. Although corticosteroids can reduce inflammation and possibly prevent the development of more severe illness, there is also a risk of making the infection worse, particularly if an organism such as *Pseudomonas aeruginosa* is present. In addition, for patients with CAP and influenza, corticosteroid therapy may increase mortality.⁴ In a meta-analysis of corticosteroid therapy in CAP, the authors found no benefit for patients with mild pneumonia, but a slight mortality reduction in those with more severe illness, although relatively few COPD patients were studied.⁵ In spite of these data, the routine use of corticosteroids in all patients with severe CAP may not be ideal, and in one recent study, this therapy was limited to patients with severe CAP who also had high levels of systemic inflammation, as indicated by an elevated C-reactive protein on admission.⁶ In this well-defined population, corticosteroid therapy was valuable, and reduced treatment failure and late radiographic progression.

In patients with exacerbations of COPD who are hospitalized, it is likely that corticosteroid therapy will be used. Should this also be the case if there is also radiographic evidence of CAP? Here the data are less clear, and we have very little information to guide us. Huerta and colleagues compared 116 patients with CAP and COPD to 133 patients with acute exacerbations of COPD (AECOPD) without pneumonia.⁷ They found that the CAP patients had higher levels of systemic

inflammation than those with AECOPD as reflected by serum C-reactive protein, procalcitonin, tumor necrosis factor alpha and interleukin-6. Although outpatient inhaled corticosteroid therapy did not affect these findings, the authors did not explore the impact of systemic corticosteroid therapy after admission. Liapakou et al compared the disease severity and course of 212 admitted patients with CAP and COPD to 1167 admitted CAP patients without COPD.⁸ Thirty-day mortality was not higher in the COPD versus non-COPD pneumonia population. However, 65% of the COPD CAP patients were on inhaled corticosteroids (ICSs) and 13% were on oral corticosteroids prior to admission. In a univariate analysis both oral and inhaled corticosteroids were associated with a reduced rate of pulmonary complications, but the use of systemic corticosteroids in the hospital was associated with a higher 30-day mortality risk on univariate, but not multivariate analysis. Lieberman and associates compared 23 patients with COPD and CAP to 217 with AECOPD and found a higher mortality in the CAP patients, in spite of the fact that all patients in both groups received systemic corticosteroid therapy.⁹ Polverino et al evaluated 3257 hospitalized CAP patients, of whom 260 received corticosteroids, many for chronic respiratory disease, and found no harm when this therapy was used for reasons other than pneumonia.¹⁰ Although the corticosteroid-treated patients were more severely ill, mortality and time to clinical stability were similar to those with CAP and no corticosteroid therapy, although the length of hospital stay was longer in the corticosteroid-treated group. In a large Danish data base, pneumonia complicated 36.1% of first time COPD exacerbations, and was associated with a 12.1% mortality at 30 days, compared to an 8.3% mortality in first-time, non-pneumonic exacerbations.¹¹ The impact of corticosteroids was unclear, but oral corticosteroid therapy was more common in the non-pneumonic exacerbations, raising the possibility that this therapy contributed to a reduction in mortality.

To best assess the impact of corticosteroid therapy on COPD patients with pneumonia, a randomized controlled trial is needed. Unfortunately, many such randomized trials of corticosteroid therapy in CAP have excluded COPD patients or have included only a small proportion of COPD patients in their data set. For example, Fernandez-Serrano et al excluded patients requiring corticosteroid therapy for COPD from their trial, while Snijders et al excluded patients using this

therapy prior to admission (but still included 43 COPD patients in their group of 213 patients), and also eliminated patients who received corticosteroids for COPD exacerbation, which could have overridden the randomization of patients to the placebo group.^{12,13} The study by Blum et al which included 784 patients with CAP, did randomize 133 with COPD, and found that for the group as a whole, corticosteroid therapy reduced the time to clinical stability, and that the same benefit was present in the COPD subgroup.¹⁴ In all of these studies, the dose and duration of corticosteroid therapy was not standardized, and we also need to determine whether patients with CAP and COPD need different doses than patients with CAP alone.

It is in this context, that an [article by Scholl and colleagues](#), in the current issue of this journal, is of great interest.¹⁵ In their study, Scholl et al retrospectively evaluated 138 hospitalized patients with radiographic CAP and an exacerbation of COPD. A total of 89 received systemic corticosteroids, while 49 did not, and since this was not a randomized study, there is no clear understanding about why some patients received corticosteroids, while others did not. Although both groups seemed clinically comparable, more who received corticosteroids were directly admitted to the intensive care unit (ICU) (24% versus 10%), and no data were reported about corticosteroid use prior to admission. In addition, the authors did not report bacteriologic data or the percentage of patients receiving appropriate antibiotic therapy, although both groups received guideline-compatible antibiotics at similar rates. Most importantly, no data are reported about how many patients had infections that could theoretically be worsened by corticosteroid therapy, such as influenza, opportunistic fungal infection, and Pseudomonas pneumonia. There is also no discussion about the dose or the duration of corticosteroid therapy that was used in the patients who were studied. These investigators found that corticosteroid therapy was not associated with any measurable benefit in length of stay, treatment failure, 30-day readmission rate, or 30-day mortality. In the patients with more severe CAP (as defined by the Pneumonia Severity Score, and not by the need for ICU admission), there was a significantly longer length of stay with corticosteroid therapy. However, treatment failure rate was low for patients needing ICU admission, and was similar with and without corticosteroid therapy.

These findings are interesting, but emphasize why we need a randomized trial to definitively answer whether

corticosteroid therapy should be used in patients with CAP and COPD exacerbation, and if so, at what doses, and for how long. Although it is possible that the presence of CAP negates the benefit of corticosteroids in patients with COPD exacerbation, the available data suggest that this therapy is safe for CAP patients with COPD. However, if steroids are used for COPD patients with CAP, caution is needed to avoid this therapy in

patients with influenza, opportunistic fungal infection (as a consequence of outpatient corticosteroid therapy) and possibly pseudomonal infection. Although, in general, we will likely restrict corticosteroid therapy to CAP patients with both severe illness and high levels of inflammation, based on the current data, I see no reason to withhold corticosteroids in patients with COPD exacerbations who also have CAP.

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