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EC PULMONOLOGY AND RESPIRATORY MEDICINE

Research Article

The Impact of Systemic Corticosteroids in Patients with an Exacerbation of COPD Complicating with Pneumonia

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Received: November 15, 2018; **Published:** December 06, 2018

Abstract

Background: Exacerbations account for most of the morbidity, mortality and cost associated with COPD and infections play an important in their ethology. Pneumonia leading cause of death from infectious diseases in the worldwide and patients with COPD is at increased risk of pneumonia because of impaired lung defenses and possible inhaled corticosteroid use. We hypothesized that the use of systemic corticosteroids (SC) would be statistically significant difference in length of hospital stay, ICU admission and ventilator support and mortality rate between patients with an acute exacerbations of COPD (AECOPD) and CAP who receive off course of SC and who did not.

Objective: The purpose of our study was to evaluated the use of SC in patients with an AECOPD complicated with community-acquired pneumonia (CAP).

Methods: This was retrospective evaluation of 439 patients 42 - 85 years of age admitted to the pulmonary medicine department of clinic hospital of medical university. Patients during their hospital stay with a diagnosis of either COPD with exacerbation and an admission diagnosis of pneumonia were examined for inclusion. Patients who received a treatment course of SC (oral prednisolone and IV methylprednisolone) during their hospital stay were compared to patients who did not receive SC.

Results: A total of 439 patients were enrolled in this study based on inclusion and exclusion criteria. Four hundred seven (76.8%) patients have received systemic steroids and 102 (23.2%) patients did not received steroids. All patients enrolled to three groups were similar with no significant difference in key characteristics. Length of hospital stay was significantly highest in patients with AECOPD + CAP receiving SC ($p = 0.04$) and there was no difference 30 day mortality rate depending on SC use, in all three groups patients the 30 day mortality rate was similar ($p = 0.15$). In-hospital treatment failure was higher in patients with AECOPD + CAP who was in the treatment with SC ($p = 0.03$). ICU admission with found with higher rate in patients with AECOPD + CAP who had received SC ($p = 0.04$) and also the rate of administration of mechanical ventilation was higher in patients with AECOPD + CAP who had received SC ($p = 0.04$).

Conclusion: Among patients with AECOPD and CAP the length of hospital stay was significantly longer in the steroid group compared to the non-steroid group. The use of CS in patients with AECOPD and CAP significantly increased in hospital treatment failure, requiring mechanical ventilation and the rate of 30 day readmission for AECOPD and an admission diagnosis of pneumonia were examined for inclusion. Patients who received a treatment course of SC (oral prednisolone and IV methylprednisolone) during their hospital stay were compared to patients who did not receive SC.

Keywords: *Systemic Corticosteroids; Exacerbation of COPD; Pneumonia*

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of mortality and mortality in the worldwide. Globally, COPD is the 4th leading cause of death with an estimated 3 million deaths annually [1,2]. Exacerbations account for most of the morbidity, mortality and cost associated with COPD and infections play an important in their etiology [3,4]. Pneumonia leading cause of death from infections disease in the worldwide. Patient with COPD is at increased risk of pneumonia because of impaired lung defenses and possibly inhaled corticosteroid use [5,6].

A population based cohort study in Denmark showed that approximately 36% of patient hospitalized for a first time COPD exacerbation also received a pneumonia diagnosis [7]. Patient hospitalized for COPD exacerbation and pneumonia have worse outcome with increased health case utilization, longer length of hospital stay and a higher mortality [7].

Systemic corticosteroids (SC) are standard and of care in the management of an acute exacerbation of COPD (AE COPD) [8]. Studies have shown that their use improves short- term lung function and reduces treatment failure rates, 30 day relapse, and length of hospital stay [8,9].

However, studies examining the effectiveness of SC therapy in AE COPD have universally excluded patient with pneumonia [9,10]. The uses of corticosteroid in community-acquired pneumonia (CAP) has been controversial with some studies showing a faster improvement in clinical stability shorter length of hospital stay, and decreased mortality, while other have shown no benefit with an increase in side effects (especially hyperglycemia) [11,12]. Studies examining the use of SC inpatients with CAP have included only small numbers of patient with COPD. Therefore, the benefits of SC use in patient with AE COPD and CAP remains unknown [13,14].

Purpose of the Study

The purpose of this study was to evaluated the use of systemic corticosteroids in patient with an AE COPD complication with CAP. We hypothesized that these would be statistically significant difference in length of hospital stay, ICU admission and ventilatory support and mortality rate between patients with an AE COPD and CAP who receive a course of SC and who did not.

Methods

Study Design

This was retrospective evaluation of 439 patient 42 - 85 years of age admitted to the Pulmonary Medicine Department of Therapeutic and Education Clinic (a 400 bed urban academic medical center) of Azerbaijan Medical University between October 01, 2012 and November 30, 2017 with an AE COPD and CAP. Depends on presence of CAP all patients with AE COPD were divided into three groups:

1) 219 patients with an AE COPD who had used SC;
2) 118 patients with an AE COPD and diagnosis CAP who had used Cs;
3) 102 Patients with an AE COPD and diagnosis CAP who did not receive CS.

Patients during this period with a diagnosis of either COPD with exacerbation on their hospital diagnosis list and an admission diagnosis of pneumonia were examined for inclusion. Patients were excluded if they had a diagnosis of hospital- acquired pneumonia, no radiographic evidence of pneumonia an immunocompromised condition (human immunodeficiency virus, solid organ or bone marrow transplant or receiving immunosuppressive therapy) asthma or other lung disease received oral or IV corticosteroids within 30 days of admission. All data were extracted from the electronic health record.

Patients who received a treatment course of SC (oral prednisolone or IV methylprednisolone) during their hospital stay were compared to patients who did not receive SC.

Outcomes

The primary outcomes were length of hospital stay and 30 days mortality. Our main secondary outcome was in-hospital treatment failure which was defined as intensive care unit (ICU) admission or mechanical or non-invasive ventilation and developed septic shock with the need for vasopressors as a result of treatment failure. We assessed each of these components individually for all three group patients. ICU admission, ventilation and developed septic shock with the need for vasopressors were attributed to treatment failure if they occurred 6 hours or more after the first dose of steroid or 6 hours or more after hospital admission.

For comparisons among the 3 groups the Fisher's exact test was used for categorical variables and continuous variable were evaluated using a student t-test for non-matched samples with unequal variance. All tests were 2-tailed and a p- valve < 0.05 was considered significant All continuous variables are reported as a mean ± standard deviation.

Result

A total of 439 patients were enrolled in this study based on inclusion and exclusion criteria. Four hundred seven (76.8%) patient have received systemic steroids and 102 (23.2%) patient did not received steroids. All patient enrolled to three groups were similar with no significant difference in key characteristic (Table 1).

The mean daily dose of prednisolone was 88.5 ± 25.8 mg. Forty two percent of patients received at least 1 dose of IV methylprednisolone. The mean total duration of steroid therapy was ± 3.9 days with 62% of patients receiving ≤ 7 days total.

	AECOPD n = 219	AECOPD + Pneumonia		
		Steroid group (n = 118)	Non- steroid group (n = 102)	P-value
Age (years) mean ± SD	65.2 ± 12.5	65.4 ± 11.6	65.9 ± 12.2	0.85
Male, n (%)	184 (86.3)	101 (85.5)	89 (87.2)	0.76
Smoking status				
Current smoker n (%)	125 (57.1)	67 (56.7)	60 (58.8)	0.84
Past smoker n (%)	94 (42.9)	51 (43.3)	42 (41.2)	0.98
Pack years of smoking, means -+SD	49.8 ± 22.2	51.5 ± 19.8	50.9 ± 24.6	0.65
Clinical severity				
PSI score at admission ± SD	87.9 ± 24.4	88.5 ± 25.2	86.9 ± 23.8	0.62
Severe Pneumonia (PSI score IV or V), n (%)	-	56 (47.4)	52 (50.9)	0.57
Respiratory failure	114 (52.1)	88 (69.4)*	70 (68.6)*	<0.05
Bacteremia	-	14 (11.9)	10 (10.7)	0.74
Maintenance COPD therapy Prior to Admission				
Combination – LABA/ICS, n (%)	109 (49.7)	79 (66.9)*	57 (65.7)*	0.04
LAMA, n (%)	39 (16.4)	12 (10.9)	18 (17.6)	0.14
LABA, n (%)	10 (4.5)	-	-	-
LAMA+LABA n (%)	43 (19.6)	21 (17.7)	19 (18.6)	0.29
None, n (%)	18 (8.2)	6 (5.1)	9 (8.8)	0.34
Oxygene n (%)	67 (30.5)	58 (49.1)*	49 (48.0)*	< 0.05
Comorbidities				
Chronic kidney disease	12 (5.4)	9 (6.7)	5 (4.9)	0.80
Type 2 DM, n (%)	49 (22.3)	32 (27.1)	26 (25.4)	0.19
Heart failure	34 (15.5)	19 (16.1)	16 (15.7)	0.98
CRP mg/dl	28.5 ± 14.5	86.4 ± 21.8*	90.5 ± 20.2*	0.011

Table 1: *Baseline characteristic of the study population.*

PSİ: Pneumonia Severity Index; COPD: Chronic Obstructive Pulmonary Disease; İCS: Inhaled Corticosteroid; LABA: Long-Acting Beta2 Agonist; LAMA: Long-Acting Muscarinic Antagonist the p-valve between COPD and COPD +CAP Groups.

	AECOPD n = 219	AECOPD+CAP		
		Steroid n = 118	Non-steroid n = 102	p-value
Primary outcomes				
Length of hospital stay (days), mean ±	5.6 ± 2.8	8.8 ± 3/1*	6.2 ± 2.6	0.04
30 days mortality, n/n (%)	14/219 (6.4)	17/118 (144)*	9 (8.8)	0.15
Secondary Outcomes				
In-hospital treatment failure, n (%)	36 (16.4)	37 (31.4)*	20 (19.6)	0.03
ICU admission, n (%)	22 (10.0)	31 (26.2)*	14 (13.7)	0.04
Non-invasive Ventilation, n (%)	35 (18.4)	26 (22.0)	21 (20.5)	0.24
Mechanical ventilation, n (%)	9 (4.1)	19 (16.1)*	8 (7.8)	0.04
Septic shock n (%)		11 (9.3)	8 (7.8)	0.68
30 days readmission for AECOPD or Pneumonia n/n (%)	39/219 (14.2)	36/118 (30.5)*	20/102 (19.6)	0.05

Table 2: *Outcomes according to steroid administration.*

ICU: Intensive Care Unit; AECOPD: Acute Exacerbation of Chronic Obstructive Pulmonary Disease.

**: Mean difference AECOPD + CAP receiving SC and other two groups patients.*

Length of hospital stay was significantly highest in patients with AECOPD+CAP receiving SC (p = 0.04) 30 day mortality rate in patient with AECOPD + CAP receiving SC was similar compared with other two groups (14.4% vs 6.4% and 8.8%; p = 0.15), in-hospital treatment failure was higher in patient with AECOPD + CAP who was in treatment with SC (31.4% vs 16.4% and 19.6% respectively: p = 0.03). ICU admission also was found with higher rate in patients with AECOPD + CAP who had received SC (26.2% vs 10.0% and 13.7% respectively); p = 0.04). There was no difference among patients according to non-invasive ventilation administration (p = 0.24). The rate of administration of mechanical ventilation was higher in patients with AECOPD + CAP who had received SC (16.1% vs 4.1% and 7.8% respectively; p = 0.04) there was also no difference in case of 30-day readmission For AECOPD or Pneumonia between patient with CAP who had received SC and who did not receive it (p = 0.68).

30 days readmission rate for AECOPD or Pneumonia was also higher in patients with AECOPD + CAP who had received corticosteroids (30.5% vs 14.2% and 19.6% respectively; p = 0.04).

Among patients with severe pneumonia, there was no difference in mean age or mean PS/score between the steroid and non-steroid groups (Table 3).

	Steroid group n = 56	Non-steroid group n = 52	P value
Background			
Age in years, mean ± SD	68.8 ± 10.4	68.9 ± 11.7	0.86
PSI score, mean ± SD	116.4 ± 15.0	109.5 ± 15.4	0.31
Outcomes			
Length of hospital stay, mean ± SD	8.9 ± 3.0	6.1+/-1.4	0.04
In-hospital treatment failure n (%)	15/56 (27%)	5/52 (10%)	0.04
30 day readmission for AECOPD or Pneumonia n/n (%)	17/56 (30%)	12/52 (23%)	0.68
30 day mortality, n/n (%)	9/56 (16%)	6/52 (11.5%)	0.45

Table 3: *Subgroup Analysis of all patient with severe pneumonia.*

However, in-hospital treatment failure was higher among patients with severe pneumonia who had receive SC (15/56 [26%] vs 5/52 [10%]; p < 0.05). There was no difference in the frequency of 30 day readmissions and 30 day mortality rate among patients with severe pneumonia associated with COPD who had received SC or who had received SC (17/56 [30%] vs 12/52 [23%]; p = 0.68).

Length of hospital stay was significantly higher in steroid group with AECOPD associated with severe pneumonia compared with patients with severe pneumonia who did not receive steroids (9/56 [16%] vs 6/52 [11.5%]: p = 0.45).

Discussion

In this study to evaluate the impact of systemic corticosteroids in patients with AECOPD without CAP and in patient with AECOPD with CAP Systemic corticosteroids were commonly prescribed in this population with 76% of patients receiving steroids. However, the use of systemic steroids in population with AECOPD with CAP did not result in a shorter length of hospital stay or a lower rate of in hospital treatment failure. Among patients with AECOPD and CAP, length of hospital stay was significantly longer in the steroid group compared to the non-steroid group, despite a similar mean age and PSI score. The use of systemic corticosteroids did not impact to the 30-day mortality rate, however, in-hospital treatment failure rate was higher in steroid group patients. There was no difference the need to use of non-invasive ventilation however, the use of systemic corticosteroids significantly increased the rate of ICU administration. In steroid group patients the number of patients requiring mechanical ventilation was higher compared with patients with patients non-steroids group and AECOPD without CAP. The number of patients requiring mechanical ventilation was similar in patients with AECOPD with CAP who did not use steroids and in patients with AECOPD who use steroids. There was no difference according to readmission rate for AECOPD and pneumonia between patients group AECOPD with CAP without steroids treatment and AECOPD without CAP with steroids treatment. However, use of steroids in patients with AECOPD and pneumonia significantly increased 30-day readmission rate for AECOPD and pneumonia.

Our study has been shown that the impact of systemic steroids in patients with AECOPD and pneumonia was differ compared with patients AECOPD without pneumonia was and we did not notice the beneficial effect of systemic corticosteroids in such group patients which might be significantly beneficial in patients with AECOPD without pneumonia.

In patients with severe pneumonia with high inflammatory response the use of systemic corticosteroids significantly decreased the rate of treatment failure [15]. However, in our study we did not observe this tendency. In all our patients with AECOPD with CAP were noticed high inflammatory response (accordingly definition of high level of CAP) however in patients with severe pneumonia associated with AECOPD the use of steroids significantly increased the number of treatment failure. Our subgroup analysis among patient with severe pneumonia show that, the use of steroids markedly increased the length of hospital stay and this may be directly related with in hospital treatment failure after 72 hours of hospital admission.

The greatest limitation of our study was the retrospective design. A total of 337 received SC, while 102 did not and since was not a randomized study, there is no clear understanding about why some patients received corticosteroids, while others did not. Although both groups with CAP seemed clinically comparable, more who received corticosteroids were directly admitted to the intensive care unit (ICU) (20% versus 13%) and no data were reported about corticosteroid use prior to admission. However, in both groups patients with pneumonia the number of patient who had received ICS was higher compared with patients without CAP (66% versus 49%).

Most importantly in our study no data are reported about how many patients had infection that could theoretically be worsened by corticosteroid therapy, such as Pseudomanal pneumonia. Our data suggest that the use of SC in patients with AECOPD and severe pneumonia as defined by the PSI score, significantly increased length of hospital day and in-hospital treatment failure. We believed that the results of our study will open the new window for further research into use of steroids in patients with pneumonia complicating AECOPD.

Conclusion

Our study suggested that the use of SC in patients with AECOPD and CAP significantly increased the length of hospital stay however, the use of corticosteroids did not impact of to the 30-day mortality rate and among patients who had received and who did not receive these medications this data was similar. There was no difference among patients who had received SC and who did not according to use of non- invasive mechanical ventilation and in both group patients was similar data. However, the use of SC significantly impact to the rate of requiring of mechanical ventilation, requiring mechanical was found in higher in patients with AECOPD and CAP who had received steroids. SC markedly increased the occurrence of the 30-day readmission rate for AECOPD and CAP. Our subgroup analysis shown that the use of SC in patients with AECOPD and severe CAP as defined by the PSI score, significantly increased length of hospital stay and in-hospital treatment failure. However, our data suggested that in patients with AECOPD and severe pneumonia the use of SC did not impact to the 30-day mortality rate. We believed that the results of our study will open new window for further research into use of steroids in patients with pneumonia complicating AECOPD.

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Volume 8 Issue 1 January 2019