Effect of low-dose systemic steroid therapy on the management of severe community-acquired pneumonia

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Introduction The rationale behind the study is that as severe pneumonia is associated with local and systemic inflammatory response, the systemic steroid with its anti-inflammatory effect may affect the outcome and prognosis in severe pneumonia.

Objective The aim was to assess the effect of systemic steroid on the course and outcomes of severe community-acquired pneumonia (CAP).

Patients and methods This study was a prospective, randomized, controlled study conducted on 60 patients, hospitalized with severe CAP. The patients were divided into two groups: a case group undergone usual antibiotic regimen for CAP according to the guidelines plus systemic steroid therapy with prednisolone 0.5 mg/kg daily for 1 week and a control group without any systemic steroids. The primary outcome was the treatment success and duration of hospitalization.

Results The treatment was more successful in the case group compared with the control group (93.3 vs. 70.0%, respectively) with statistically significant difference. The mean days of hospitalization, the mean levels of C-reactive protein after treatment, and the mean decline of C-reactive protein levels were significantly lower among the case group. However, there was no significant difference between the two groups as regards mortality.

Conclusion Low-dose systemic steroids significantly increase the success of treatment in severe CAP with less days of hospitalization.

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Introduction

Community-acquired pneumonia (CAP) is one of the most leading causes of morbidity and mortality worldwide [1]. Additional drug therapy along with usual antibiotics may lead to improve the outcome in patients with CAP. Corticosteroids have been evaluated in the past decades for the treatment of sepsis and septic shock. Using the current definitions of sepsis many studies have shown a survival benefit when corticosteroids were administered at a low dose as an adjuvant therapy in CAP [2].

Patients and methods

This study was a prospective, randomized, controlled study conducted on 60 patients with severe CAP from November 2016 till April 2018 in Al-Hussein University Hospital.

Inclusion criteria

(1) Patients diagnosed as pneumonia clinically (cough, fever, and chest pain) and radiologically.
(2) CURB65 (c: confusion, u: urea(BUN>7 mmol/L), R: respiratory rate:>30. B: blood pressure less than 90/60, 65: age > 65 year) score of more than 2 (3 and 4).
(3) C-reactive protein (CRP) of more than 150 mg/l.
(4) Age more than 18 years.

Exclusion criteria

(1) Patients already on systemic steroid therapy for other indications.
(2) Contraindication to systemic steroid therapy, for example, active hepatitis c virus or HIV, uncontrolled diabetes mellitus.
(3) Bronchogenic carcinoma.
(4) CURB65 score (0, 1, and 2).
(5) Hospital-acquired pneumonia.

An informed written consent was taken from all patients or from first-degree relatives.

The patients were divided in two groups: a case group and a control group.

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The case group has undergone usual antibiotic regimen for CAP according to the guidelines plus systemic steroid therapy with prednisolone 40 mg daily for 1 week, while the control group did not take systemic steroid but usual antibiotic regimen.

All patients were assessed by the CURB65 score, chest radiography, routine lab, blood glucose level, and CRP at day 1 and day 7. Initial and follow-up chest radiography were done to all patients to detect any progression of radiological abnormality.

The primary outcome of this study was the assessment of treatment success and duration of hospitalization.

Treatment success is defined by improved symptoms and signs of pneumonia with a temperature of less than 37.5 for 24 h, decreased CRP, and total leukocyte count toward the normal values.

At the opposite, treatment failure is defined as persistence or progression of symptoms and signs related to pneumonia, deterioration in radiological shadows, or death.

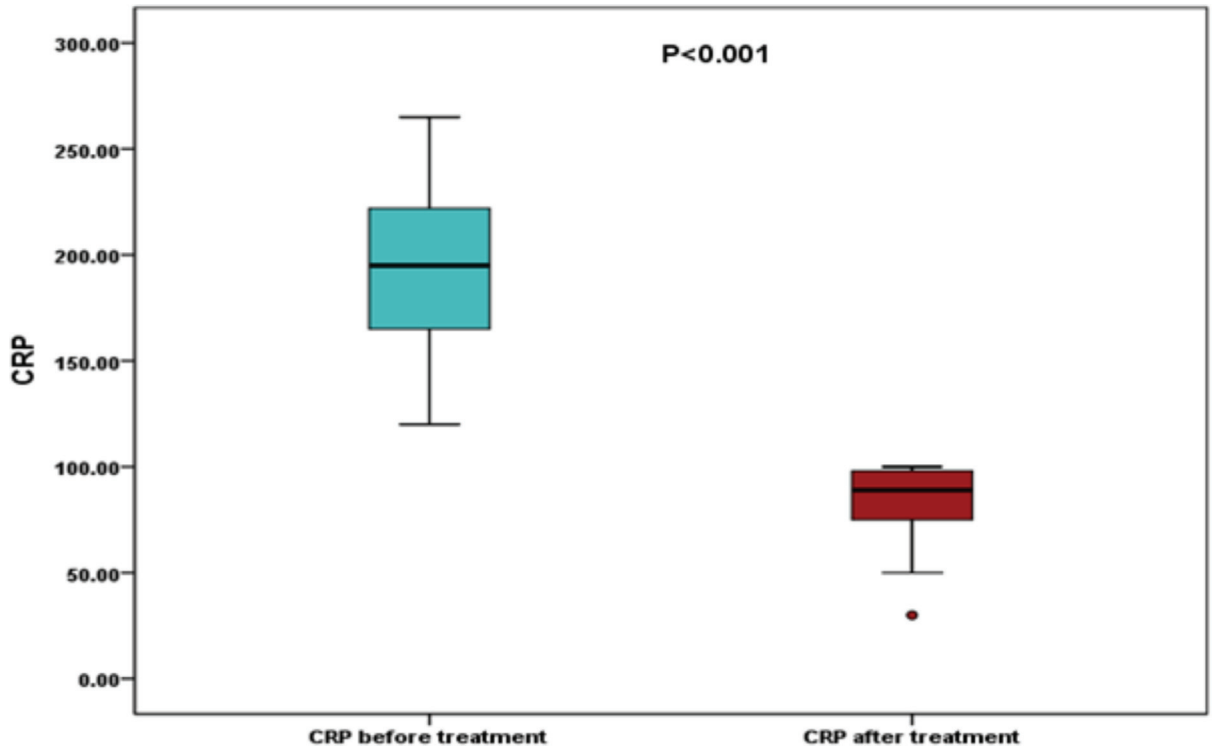
In the control group, patients with obstructive airway disease were administered inhaled steroids with a maximum dose of 1 mg twice daily instead of the systemic steroid. If no adequate response, then systemic steroid is added and the patient is excluded from the study.

Table 1 General characteristics of the studied sample

General characteristics	Case group (*n*=30)	Control group (*n*=30)	*P* value
Age (years)			
Mean±SD	51.03±10.98	52.1±10.23	0.699
Sex			
Male	22 (73.3)	21 (70.0)	0.500
Female	8 (26.7)	9 (30.0)	
Smoking			
Smoker	19 (63.3)	17 (56.7)	0.792
Nonsmoker	11 (36.7)	13 (43.3)	
Comorbidity[a]			
Bronchiectasis	1 (3.3)	1 (3.3)	0.754
DM	9 (30.0)	6 (20.0)	
Asthma	4 (13.3)	5 (16.7)	
Addiction	3 (10.0)	3 (10.0)	
Hepatic	0 (0.0)	3 (10.0)	
COPD	7 (23.3)	4 (13.3)	
IHD	1 (3.3)	1 (3.3)	
COPD, IHD	2 (6.7)	2 (6.7)	
No	3 (10.0)	5 (16.7)	

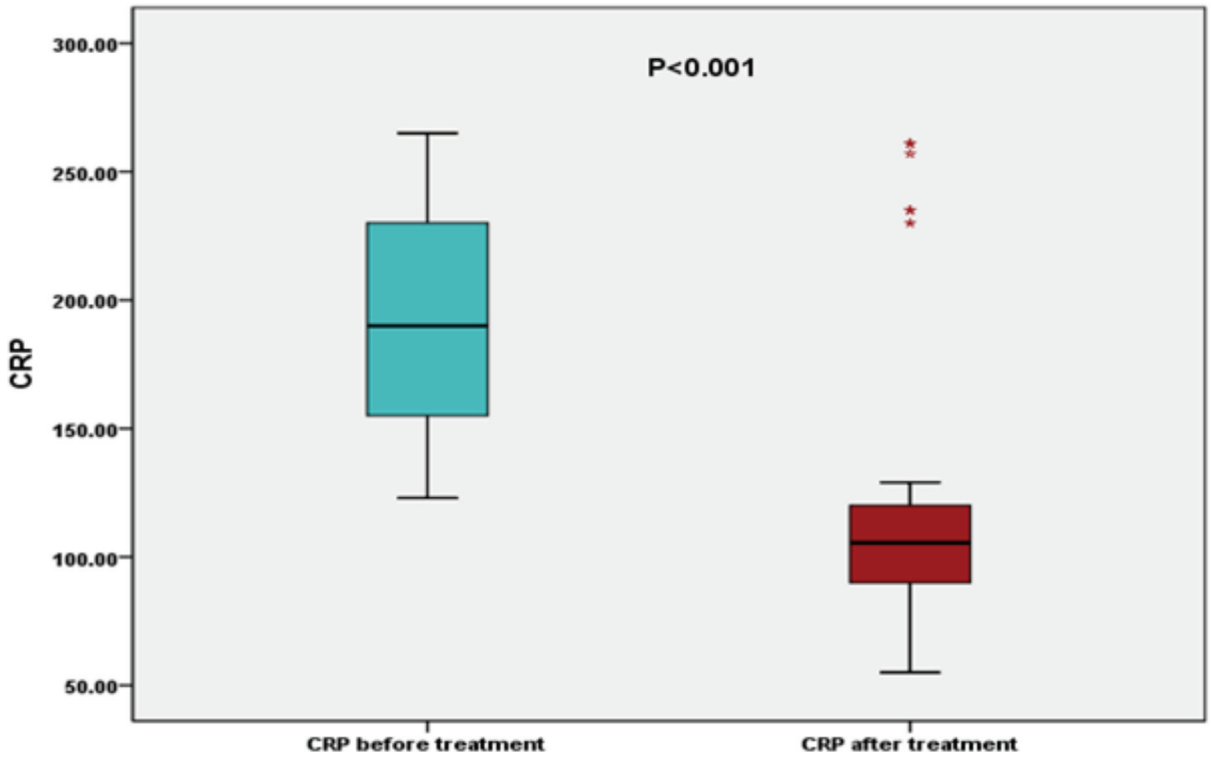
Values present as number and percentage were analyzed by Fisher's exact test. Values present as mean±SD were analyzed by independent samples *t*-test. COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; IHD, ischemic heart disease.
[a]Values present as number and percentage were analyzed by χ^2-test.

Figure 1



Difference in C-reactive protein levels before and after treatment in the case group.

Figure 2



Difference in C-reactive protein levels before and after treatment in the control group.

Results

The study included 60 hospitalized patients with severe CAP who were further divided into two groups: a case group (n=30) that had undergone usual antibiotic regimen for CAP according to the guidelines plus systemic steroid therapy and a control group (n=30) that did not take the systemic steroid. There were no statistically significant differences between both groups regarding their ages, sex, smoking habits, or presence of comorbidity.

The treatment was successful in 93.3% of the case group compared with 70.0% of the control group with statistically significant difference and two (6.7%) patients died in each group. The mean days of hospitalization, the mean levels of CRP after treatment, and the mean decline of CRP levels were significantly lower among the case group (P=0.044, 0.001, <0.001, respectively) (Table 1).

Within each group, the mean CRP levels decreased significantly after treatment; 195.06±37.7 versus 82.56 ±18.86, P value less than 0.001 in the case group and 192.96±39.48 versus 126.4±63.68, P value less than 0.001 in the control group (Figs 1 and 2).

All the studied demographic and clinical characteristics did not significantly affect the success rate of treatment between both groups except for the significant decrease in the mean CRP levels after treatment among the case group (P=0.011) (Table 2 and Fig. 3).

In both groups, duration of hospitalization was significantly increased among patients who were male, smokers, with comorbid conditions, mechanically ventilated and with a PaO_2/FIO_2 of less than 300 (P<0.05) (Table 3) and showed significant positive correlations with age, white blood cells, CURB65 score, and CRP levels before and after treatment (P<0.001) (Tables 4 and 5).

Discussion

This study was a randomized, controlled study conducted in Al-Hussein University Hospital in the period from November 2016 to April 2018.

There were no statistically significant differences between both groups regarding their ages, gender, smoking habits, presence of comorbidity, CURB65 score, or death rate (Tables 1 and 2).

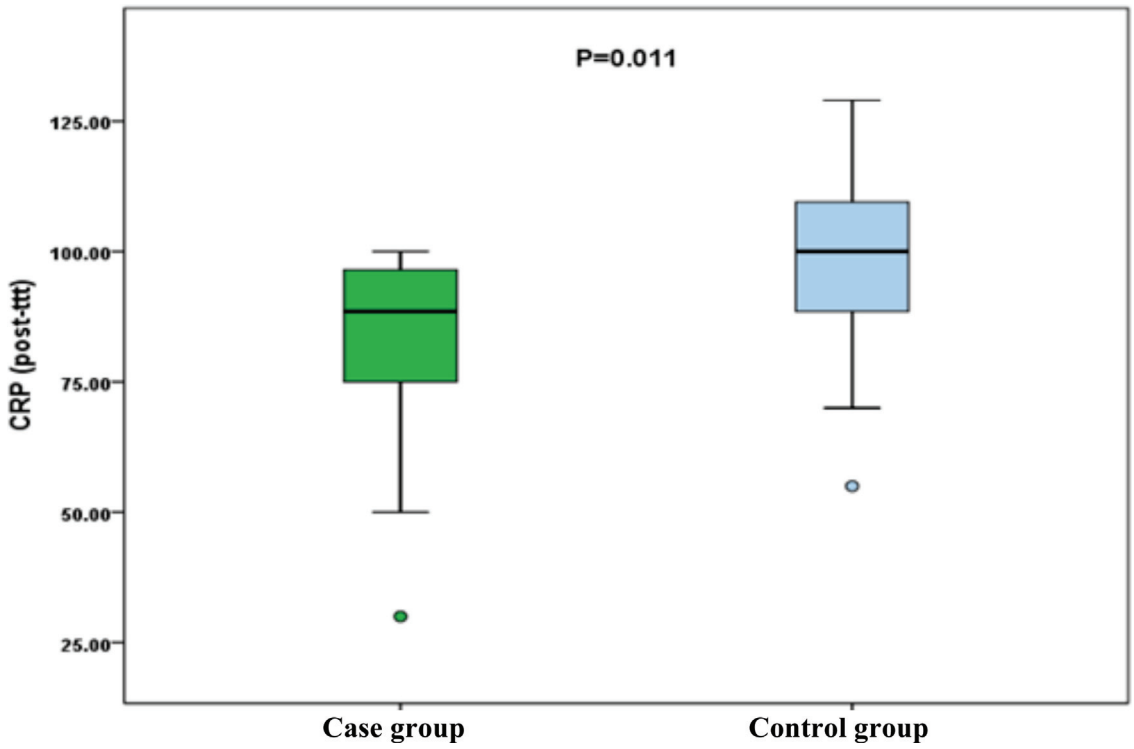
Among the two groups the patients who received a low-dose systemic steroid therapy show a lower incidence of treatment failure and lower post-treatment level of CRP (Table 2).

Table 2 Laboratory and clinical characteristics of the studied sample

Laboratory and clinical characteristics	Case group (*n*=30)	Control group (*n*=30)	*P* value
CRP (pretreatment)			
Mean±SD	195.06±37.7	192.96±39.48	0.834
WBC			
Mean±SD	16.4±3.38	17.05±4.35	0.521
MV			
Yes	5 (16.7)	7 (23.3)	0.748
No	25 (83.3)	23 (76.7)	
CURB65 score			
Mean±SD	3.87±0.82	3.8±0.8	0.752
Hospital stay (days)			
Mean±SD	7.23±3.21	9.03±3.55	0.044*
PaO_2/FiO_2			
<300	19 (63.3)	18 (60.0)	1.000
>300	11 (36.7)	12 (40.0)	
CRP (post-treatment)			
Mean±SD	82.56±18.86	126.4±63.68	**0.001***
CRP decline			
Mean±SD	112.5±24.73	66.57±45.41	<0.001*
Treatment failure			
Yes	2 (6.7)	9 (30.0)	0.042*
No	28 (93.3)	21 (70.0)	
Death			
Yes	2 (6.7)	2 (6.7)	1.000
No	28 (93.3)	28 (93.3)	

Values presented as number and percentage were analyzed by Fisher's exact test. Values presented as mean SD were analyzed by independent samples *t*-test. CRP, C-reactive protein; MV, mechanical ventilation; WBC, white blood cells. *Significant.

Figure 3



Comparisons between treatment success and C-reactive protein levels after treatment among the studied sample.

Many studies conducted on severe pneumonia demonstrated an increase in serum levels of cytokines such as interleukin (IL)-6, IL-8, and IL-10 [3,4].

Corticosteroids being the most effective widely used anti-inflammatory drugs, experimental studies have shown the benefit of corticosteroids administration

in the reduction of inflammatory cytokines in patients with severe pneumonia [5,6]. The concurrent use of methyl prednisolone and antibiotics in severe pneumonia may also decrease the bacterial burden better than antibiotics alone [5].

So, the targeted populations for this study were patients with both severe CAP and a high initial systemic inflammatory response who were diagnosed by clinical and laboratory findings.

Table 3 Comparisons between treatment outcome and different variables among the studied sample

Characteristics	Treatment success		*P* value
	Case group (*n*=28)	Control group (*n*=21)	
Age (years)			
Mean±SD	49.96±10.57	48.91±9.49	0.713
Sex			
Male	20 (71.4)	12 (57.1)	0.370
Female	8 (28.6)	9 (42.9)	
Smoking			
Smoker	17 (60.7)	10 (47.6)	0.398
Nonsmoker	11 (39.9)	11 (52.4)	
Comorbidity			
Yes	25 (89.3)	18 (85.7)	1.000
No	3 (10.7)	3 (14.3)	
CRP (pretreatment)			
Mean±SD	193.28±38.4	180.61±36.38	0.236
WBC			
Mean±SD	16.35±3.49	15.93±4.13	0.694
MV			
Yes	3 (10.7)	2 (9.5)	1.000
No	25 (89.3)	19 (90.5)	
CURB65 score			
Mean±SD	3.78±0.78	3.56±0.73	0.308
Hospital stay (days)			
Mean±SD	6.75±2.73	7.83±2.69	0.165
PaO_2/FiO_2			
<300	17 (60.7)	11 (52.4)	0.576
>300	11 (39.3)	10 (47.6)	
CRP (post-treatment)			
Mean±SD	81.32±18.93	95.35±18.8	0.011*

Values presented as number and percentage were analyzed by Fisher's exact test. Values presented as mean SD were analyzed by independent samples *t*-test. CRP, C-reactive protein; MV, mechanical ventilation; WBC, white blood cells. *Significant.

The rate of treatment failure in the control group was 30%, which is consistent with other studies [7,8] that reported a treatment failure rate of 35% and 31% in patients with severe CAP. Treatment failure was reduced to 6.7% in patients treated with low-dose systemic steroids (Table 2).

The final CRP level was significantly lower in the case group (82.5±18.8) in comparison with the control group (126.4±63.6) with a marked decline from the initial CRP level (Table 2).

However, some studies have found no difference in treatment failure between the two groups [9] in spite of agreement in the decrease of post-treatment level of CRP. The previous study included nonsevere pneumonic patients with initial low levels of CRP.

Table 4 Comparisons between duration of hospitalization and different variables among the studied sample

Characteristics	Duration of hospitalization	
	Case group (*n*=30)	Control group (*n*=30)
Sex		
Male	8.23±3.21	10.38±3.43
Female	4.5±0.53	5.89±0.6
P value	0.001*	<0.001*
Smoking		
Smoker	8.58±3.27	11.12±3.37
Nonsmoker	4.91±1.14	6.31±1.03
P value	<0.001*	<0.001*
Comorbidity		
Yes	7.59±3.19	9.56±3.66
No	4.0±0.0	6.4±0.55
P value	0.008*	0.046*
MV		
Yes	13.2±1.09	14.43±2.51
No	6.04±1.84	7.39±1.67
P value	<0.001*	<0.001*
PaO_2/FiO_2		
<300	8.63±3.2	10.83±3.43
>300	4.82±1.17	6.33±1.3
P value	<0.001*	<0.001*

Values presented as mean±SD were analyzed by Mann–Whitney *U*-test. *Significant. MV, mechanical ventilation.

Table 5 Correlation between duration of hospitalization and different variables among the studied sample

Hospital stay (days)	Age (years)	CRP (pretreatment)	WBC	CURB65 score	CRP (post-treatment)
Case group					
r	0.8	0.8	0.71	0.78	0.62
P value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
Control group					
r	0.75	0.84	0.75	0.7	0.67
P value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

CRP, C-reactive protein; *r*, Pearson's correlation coefficient; WBC, white blood cells. *Significant.

In contrast to our study, we exclude pneumonic patients without profound initial high level of CRP as inflammatory markers who do not benefit from adding systemic steroid to the usual antibiotic regimen.

In our study, the use of low-dose systemic steroids was not associated with superinfection or other adverse events as uncontrolled hyperglycemia. Previous studies of CAP did not find higher rates of superinfection or other potentially adverse events in patients treated with corticosteroids [8–11], except for mild hyperglycemia [11,12]. These findings are consistent with the data in our study. According to that study and others in the literature, the immunosuppression caused by corticosteroids was probably not relevant when administered acutely, in contrast to chronic treatment. In addition, high dosages are not the same as the relatively low dosages used in our study.

Among the predictors of treatment failure diabetes mellitus was the most common comorbidity in both groups, despite the occurrence of uncontrolled hypoglycemia was not reported in this study (Table 1).

The median length of hospital stay was lower in the steroid group (7.2 days) compared with the control group (9 days) which is consistent with other studies [11] where the median length of stay was 6.5 days in the steroid group compared with 7.5 days in the placebo group.

In both groups, duration of hospitalization was significantly increased among patients who were male, smokers, with comorbid conditions, mechanically ventilated, and with a PaO_2/FIO_2 of less than 300 ($P<0.05$) (Table 4).

Conclusion

Low-dose systemic steroids significantly increase the success of treatment in severe CAP with less days of hospitalization with no significant steroid-related adverse effects being reported

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Nil.

Conflicts of interest

There are no conflicts of interest.

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