ISSN: 2577 - 8005

Research Article

Medical & Clinical Research

Efficacy of Systemic and Inhaled Corticosteroid Therapy for Patients with Community-Acquired Pneumonia: An Evidence-Based Case Report

Fahreza Akbar Siregar[1] and Gurmeet Singh[2]

[1]*Faculty of Medicine, University of Indonesia, Jakarta*

[2]*Division of Pulmonology and Respiratory Medicine, Department of Internal Medicine, Dr. Cipto Mangunkusumo National General Hospital, Jakarta*

***Corresponding author**
Fahreza Akbar Siregar, Faculty of Medicine, University of Indonesia, Jakarta.
E-mail: fahreza_akbar@hotmail.com

Submitted: 27 Aug 2019; **Accepted**: 07 Sep 2019; **Published**: 30 Oct 2019

Abstract

Background: *Community-acquired pneumonia (CAP) is one of the top leading causes of morbidity and mortality worldwide. CAP also becomes the sixth most prevalent cause of overall mortality in adults. Corticosteroids are known to be the most potent anti-inflammatory drugs and have physiologic rationale for their use in patients with infection. Its efficacy in the treatment of CAP is still debatable.*

Objective: *This study aims to evaluate the efficacy and clinical outcomes of systemic and inhaled steroid therapy for patients with community-acquired pneumonia.*

Methods: *We used four databases for literature searching process, Pubmed, EBSCO, ProQuest, and Science Direct, which selected articles are those therapeutic studies with relevant clinical question and met the inclusion-exclusion criteria. Critical appraisal was performed by assessed its validity, importance, and applicability based on Oxford Center of Evidenced-Based Medicine 2011.*

Results: *Three retrieved articles feature cohort studies. Two studies conducted systemic steroid therapy research which other conducted inhaled steroid. Two of three articles show steroid therapy was associated with lower mortality and shorter clinical stability.*

Conclusion: *We suggested that steroid therapy, both systemic and inhaled steroids help hasten clinical recovery, prevent pneumonia-related complication, lower mortality, and reduction in the duration of mechanical ventilation and length of hospital stay.*

Keywords: Community-Acquired Pneumonia, Steroid, Inhalation, Therapeutics, Clinical Outcomes

Introduction

Community-acquired pneumonia (CAP) is one of the important causes of morbidity and mortality worldwide [1]. In developing countries, CAP becomes the sixth most prevalent cause of overall mortality in adults. In 2004, approximately 10% adult mortality in Southeast Asia is caused by respiratory tract infection, mostly by lower respiratory tract infection [2]. In Indonesia, CAP is the number one cause of mortality in children and the sixth mortality in adults. Based on Riskesdas (Indonesian Basic Health Research) in 2013, both incidence and prevalence of pneumonia in Indonesia are 1.8% and 4.5% [3].

Despite remarkable advances in etiological investigation, antimicrobial therapy, and supportive measurement, the mortality of those patients still remains at 30-50% [2,4]. Therefore, additional potential approaches are needed for better outcomes in severe CAP. Recent studies found that the level of pro-inflammatory cytokines such as interleukin (IL)-6, IL-8, IL-10, IL-1β, tumor necrosis factor alpha, and interferon gamma were significantly increased in patients with severe CAP and correlated with the severities and outcomes of CAP. Corticosteroids are known to be the most potent inflammatory inhibitors. They inhibit expression of pro-inflammatory cytokines. The immunomodulating and anti-inflammatory pharmacodynamics profile is the physiologic rationale for their use in patients with CAP.

Corticosteroid therapy is usually used as chronic obstructive pulmonary disease (COPD) treatment. Its role in the treatment of CAP remains controversial. In some clinical trials, corticosteroid therapy in patients with CAP is knowingly effective to reduce time to clinical stability and reduce duration of length of stay in hospital. Other trials showed that steroid therapy is correlated with lower mortality rate in patients with severe CAP because it may reduce the excessive inflammatory response in the airway [2,5]. However, a large observational study found that corticosteroids had a possible survival advantage in patients with septic shock, complicating CAP [5]. Thus, findings showing that corticosteroids reduce mortality may be due to the over inclusion of patients with septic shock or with other conditions known to benefit from corticosteroid treatment,

including COPD and asthma [6]. Furthermore, this study is aimed to evaluate the efficacy and clinical outcomes of corticosteroid therapy, both systemic and inhaled, in patients with community-acquired pneumonia.

Material and Methods

Literature searching process was conducted in April 14th 2018 on four databases, such as Pubmed, EBSCO, ProQuest, and Science Direct, to identify relevant literatures. Keywords were inputted in the right order, then used Boolean operation. Searching on the data bases was not filtered. Selected articles are those therapeutic studies with relevant clinical question and met the inclusion-exclusion criteria. Critical appraisal was performed by assessed its validity, importance, and applicability based on Oxford Center of Evidenced-Based Medicine 2011.

Article selection process was managed in several steps, such as selection based on title and abstract, similar articles selection, and full-text selection. Articles were enrolled in this study according to the inclusion criteria (therapy approach study (RCT, meta-analysis, or systematic review), relevant content, and in English) and exclusion criteria (irrelevant study, matched clinical outcome, incomplete text, and similar articles). From the following criteria, we found 3 articles, such as Polverinoet al, Nafaeet al, and Yamauchi et al.

Table 1: Searching Strategy

Data Basis	Searching Strategy	Hits	Title/Abstract Screening
Pubmed	((((((community acquired pneumonia[Title/Abstract]) AND pneumonia[Title/Abstract]) AND steroids[Title/Abstract]) OR inhaled steroids[Title/Abstract]) OR budesonide) AND inhalation administration) AND treatment outcomes	206	11
EBSCO	community acquired pneumonia AND inhaled steroids OR bronchodilator AND therapeutics AND clinical outcomes	149	14
Proquest	(community acquired pneumonia) AND (inhaled steroids) AND bronchodilator AND (therapeutics) AND (clinical outcomes)	233	2
Science Direct	Community Acquired Pneumonia AND Inhaled Steroids OR Bronchodilators AND Clinical Outcomes AND Therapeutics	272	5

Result

Polverinoet al (2012)

This study investigated the clinical conditions associated with corticosteroids prescription in CAP and analyzed their impact on CAP outcomes. It was performed as prospective observational study on adult patients admitted to the Hospital Clinic, Barcelona, Spain with CAP between June 1997 and January 2008. A total number of 4549 patients with CAP were seen in the hospital during the study period, 3257 were included in the analysis according to inclusion/exclusion criteria. Systemic corticosteroids were administered in 260 patients (8% of total) in addition to standard antimicrobial therapy. The mean daily dose of methylprednisolone or equivalents was of 45 (30) mg (median, 36 mg/day; IQR, 27-51 mg) during the first 7 days.

Patients receiving corticosteroids were more frequently hospitalized (90% vs 76%; $P< 0.01$) and received more mechanical ventilation (MV), but had a similar rate of admission to intensive care unit, duration of MV, 30-day mortality to those in the non-steroid group.

This study was separately analyzed the patients in high PSI risk classes (IV-V) in order to evaluate a potentially different impact of systemic corticosteroids on outcome in patients with more severe pneumonia. From the total of 1592 patients (steroid group 198 (12%); non-steroid group, 1394 (88%)). it was not observed any differences in intensive care unit admission rates (steroid group, 12 (6%); non-steroid group, 100 (7%), $P = 0.14$) or mortality (steroid group, 17 (9%); non-steroid group, 135 (11%); $P = 0.41$) or days to clinical stability (steroid group, 4.5 (3-8) days; non-steroid group, 5 (3-8) days; $P = 0.49$) between the two groups. In addition, as with the overall population, patients from the steroid group had longer LOS (steroid group, 10 (6-15) days; non-steroid group, 7(5-11); $P< 0.01$).

Yamauchi et al (2016)

This study aimed to examine the association between inhaled corticosteroid (ICS) and mortality from pneumonia in patients with COPD by comparing in-hospital mortality between those who received ICS with IBD and those who received IBD alone. Data was collected retrospectively from 1,165 hospitals in Japan on patients with COPD who received outpatient inhalation therapy and were admitted with pneumonia. The IBD administered included tiotropium, glycopyrronium, acridinium, umeclidinium, salmaterol, formoterol, indacaterol, and vilanterol. The ICS administered included fluticasone, budesonide, mometasone, and beclomethasone. Patients who received any ICS with any IBD Patients who received one or more IBD but did not receive any ICS were defined as the IBD alone group. To evaluate the severity of pneumonia, it was used A-DROP scoring system. The primary outcome of this study was all-cause in-hospital mortality. The secondary outcomes were length of stay, length of intensive care unit stay, requirement for intubation/mechanical ventilation, duration of mechanical ventilation, and mortality in patients who underwent mechanical ventilation during their hospital stay.

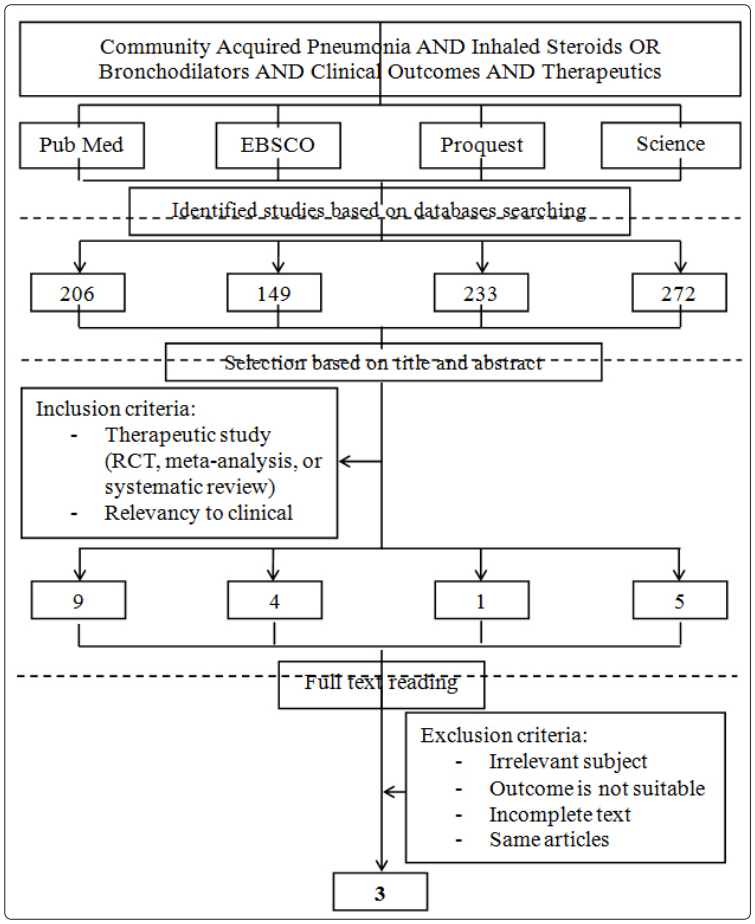

Figure 1: Flowchart of Literature Searching and Article Selection

From 7,033 patients with COPD (aged ≥40 years) who were treated with outpatient inhaled therapy and were admitted to the hospital with pneumonia. Of them, 3,702 patients were treated with ICS and IBD, and 3,331 patients were treated with IBD alone. All-cause in-hospital mortality in the ICS and IBD group was 8.1%, which was significantly lower than that in the IBD alone group (13.2%). Length of stay in the ICS and IBD group was shorter than that in the IBD alone group. The difference in the results for intensive care unit admission or requirement for mechanical ventilation was not significant between the groups. In-hospital mortality in patients who required mechanical ventilation was significantly lower in the ICS and IBD group (31.9%, n=100/313) than in the IBD alone group (39.7%, n=129/325).

Discussion

Polverinoet al. could not find any association of steroid administration with lower mortality or shorter time to clinical stability. In contrast, it was associated with prolonged length of stay (>7 days). Moreover, patients who received steroids for longer time (> 7 days) showed worse clinical course (LOS, clinical stability, mechanical ventilation) and more systemic complications (shock, cardiac arrhythmia). These results remained similar when they were analyzed the more severe patients (elevated PSI) separately, and independently of cumulative corticosteroid doses.

In contrast, Nafaeet al. study, after 7 days follow up of both hydrocortisone and placebo groups, pneumonia complications (septic shock, ARDS); were less in the hydrocortisone group when compared with the placebo. As regards the most common side effects that occur with the steroid therapy, there was non-significant difference in both gastrointestinal tract bleeding and uncontrolled diabetes mellitus, while there was a significant difference in hypokalemia which was more in the hydrocortisone group (58.3%) which was a correctable side effect and this was attributed to the mineralocorticoid action of the hydrocortisone. This study confirmed that the use of hydrocortisone in a low dose for a short period had a protective effect against pneumonia complications with less steroid side effects. Corticosteroids are very potent inhibitors of inflammation. They switch off genes that encode proinflammatory cytokines and switch on genes that encode anti-inflammatory cytokines. Treatment with low dose corticosteroids down regulates proinflammatory cytokine transcription, which prevents an extended cytokine response and might accelerate the resolution of systemic and pulmonary inflammation in the early phase of community-acquired pneumonia.

Moreover, there was non-significant difference in the need of mechanical ventilation in both hydrocortisone and placebo groups (matching in both groups), while there was a significant difference between weaning success which was more in the hydrocortisone group (87.5%) than the placebo group (20%). Regarding the duration of mechanical ventilation, the mean duration of mechanical ventilation was significantly shorter in the hydrocortisone group (1.2 ± 3.75 days) in comparison to the placebo group (4.3 ± 7.83 days).

As regards the clinical and laboratory variables of the follow up that was done at the 7th day of the study; there were highly significant differences in the improvement of conscious level, CRP, ESR, Na level, RR ($P< 0.001$) which improved more in the hydrocortisone group. Hydrocortisone group also showed more improvement in pulmonary oxygenation parameters following the treatment course as compared with placebo group. As regards other improvement parameters, there was a significant difference in CXR resolution, pneumonia and drug complications, both ICU and ward length of stay and hospital outcome (number of deaths and number of improved cases) in the both hydrocortisone and the placebo groups, also there was a highly significant difference ($P< 0.001$) in the total length of stay and duration of mechanical ventilation in both groups (being less in the hydrocortisone group).

However, there are a few points that are arguable in Polverinoet al study. The most possible cause of the different result is because in Polverino et al study, they used low dose of methylprednisolone or equivalents was of 45 (30) mg once daily, which the administered dose was not adequate to be effective in the circulation system within 24 hours. Moreover, patients receiving steroids had an elevated PSI, this could be explained by the fact that patients receiving corticosteroids had received ICS therapy more frequently and this may play an undetermined influence on modulation of local inflammatory response or microbial growth.

Yamauchi et al. study confirmed that the outpatient usage of ICS was associated with lower mortality than no usage of ICS, even after adjusting for several confounders, including pneumonia severity. This indicates that treatment with ICS has protective effects against pneumonia-related mortality. Their study also demonstrated that A-DROP scores in patients receiving outpatient ICS treatment were lower than those not receiving ICS. A previous study demonstrated that the use of ICS was associated with a lower degree of pleural inflammatory effusion, suggesting that ICS has a protective effect against the progression of pneumonia and related complications [7]. Because ICS has been reported to reduce bacterial invasion into the airway epithelium in an experimental model and has the potential to reduce inflammation, prior use of ICS may lead to less severe pneumonia [8]. Their study demonstrated that the percentage of patients requiring mechanical ventilation was lower in the ICS and IBD group, although this result was not significant. These results also suggest that ICS may have protective effects against pneumonia and pneumonia-related mortality.

Conclusion

Adjunctive 7 days course of low-dose systemic corticosteroid in patients with CAP fastens recovery, prevents the development of sepsis-related complications with a significant reduction in the duration of mechanical ventilation, duration of IV antibiotic treatment and length of hospital stay with improvement of hospital outcome and weaning success from mechanical ventilation. Outpatient inhaled corticosteroid was also associated with lower mortality from pneumonia. ICS may have protective effects against pneumonia and help prevent-related mortality.

References

1. Cheng M, Pan Z, Yang J, Gao Y (2013) Corticosteroid Therapy for Severe Community-Acquired Pneumonia: A Meta-Analysis. Respiratory Care 59: 557-563.
2. Bi J, Yang J, Wang Y, Yao C, Mei J, et al. (2016) Efficacy and Safety of Adjunctive Corticosteroids Therapy for Severe Community-Acquired Pneumonia in Adults: An Updated Systematic Review and Meta-Analysis. PLOS ONE 11: e0165942.
3. Basic Health Research (2013) RI Ministry of Health Research and Development Agency. Jakarta: Ministry of Health Republic of Indonesia.
4. Nafae R, Ragab M, Amany F, Rashed S (2013) Adjuvant role of corticosteroids in the treatment of community-acquired pneumonia. Egyptian Journal of Chest Diseases and Tuberculosis 62: 439-445.
5. Yamauchi Y, Yasunaga H, Hasegawa W, Sakamoto Y, et al. (2016) Effect of outpatient therapy with inhaled corticosteroids on decreasing in-hospital mortality from pneumonia in patients with COPD. International Journal of Chronic Obstructive Pulmonary Disease. 11: 1403-1411.
6. Almirall J, Bolíbar I, Serra-Prat M, Palomera E, Roig J, et al. (2013) Relationship between the Use of Inhaled Steroids for Chronic Respiratory Diseases and Early Outcomes in Community-Acquired Pneumonia. PLoS ONE 8: e73271.
7. Sellares J, López-Giraldo A, Lucena C, Cilloniz C, Amaro R, et al. (2013) Influence of Previous Use of Inhaled Corticoids on the Development of Pleural Effusion in Community-acquired Pneumonia. American Journal of Respiratory and Critical Care Medicine 187: 1241-1248.
8. Barbier M, Agusti A, Alberti S (2008) Fluticasone propionate reduces bacterial airway epithelial invasion. European Respiratory Journal 32:1283-1288.

Citation: *Fahreza Akbar Siregar, Gurmeet Singh (2019) Efficacy of Systemic and Inhaled Corticosteroid Therapy for Patients with Community-Acquired Pneumonia: An Evidence-Based Case Report. Med Clin Res 4(10): 1-4.*