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CORTICOSTEROID THERAPY FOR PATIENTS HOSPITALIZED WITH COMMUNITY-ACQUIRED PNEUMONIA : A SYSTEMATIC REVIEW

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Abstract

Introduction: *Pneumonia is an inflammation of the lung parenchyma in the distal terminal bronchioles, which includes the respiratory bronchioles and alveoli. Corticosteroids are routinely used for severe pneumonia symptoms. Numerous studies on adjuvant corticosteroids for community-acquired pneumonia (CAP) have yielded equivocal results. Several systematic reviews and meta-analyses have studied the efficacy of corticosteroids in treating CAP.*

The aim: *This article showed about corticosteroid therapy for patients hospitalized with community-acquired pneumonia (CAP).*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *The PubMed database yielded a total of 423 articles in response to our search query, while the search conducted on SagePub retrieved 491 articles. The search run for the last year of 2013 generated a total of 223 articles from PubMed and 212 articles from SagePub. Ultimately, a cumulative sum of 21 scholarly articles was assembled, with 15 originating from the PubMed database and the other six sourced from SagePub. We have incorporated four studies that satisfied the specified criteria.*

Conclusion: *Administration of steroids as early as possible in patients with severe CAP who are treated to benefit, where they do not experience therapy failure. Slower administration and inadequate doses do not provide any benefit.*

Keyword: *Community-acquired pneumonia; Corticosteroid; Inflammation*

INTRODUCTION

Pneumonia is an inflammation that affects the lung parenchyma which is part of the distal terminal bronchioles which includes the respiratory bronchioles and alveoli, and causes consolidation of lung tissue and impaired local gas exchange.[1] Severe community-acquired pneumonia (sCAP) is a prominent factor contributing to hospitalization rates and can lead to substantial morbidity and mortality, particularly among susceptible populations like the elderly, immunocompromised individuals, and individuals with chronic medical conditions.[2] Approximately 7-20% of community-acquired pneumonias are secondary to atypical bacterial microorganisms.[3,4]

They cannot be seen on gram stain and are difficult to culture because of their intra-cellular nature, so the true number of cases is unknown.[3] Community-acquired pneumonia (CAP) is a major cause of hospitalization and death worldwide. The estimated annual burden of CAP in the United States accounts for >1.5 million hospitalized adults and one-third of hospitalized patients who die within 1 year.[4,5] Epidemiological assessment of CAP-associated pathogens is essential to target appropriate empiric therapy. Treatment of bacterial pneumonia consists of antibiotics and supportive/non-medical treatment.[6]

Administration of antibiotics to patients with pneumonia should be based on microorganism data and the results of the sensitivity test, but for several reasons, namely: Severe disease can be life-threatening; Pathogenic bacteria that have been isolated are not necessarily the cause of pneumonia; and bacterial culture results take a long time causing pneumonia patients to be given empirical therapy. Non-medical management for pneumonia patients includes breathing assistance, humidification, chest physiotherapy and fluid management.[7–9]

Corticosteroids are widely used in the symptomatic treatment of severe pneumonia.[8] Numerous randomized controlled trials (RCTs) have been conducted to examine the efficacy of adjuvant corticosteroids in the treatment of sCAP, resulting in inconclusive outcomes.[9] Moreover, a number of systematic reviews and meta-analyses have examined the effectiveness of corticosteroids in managing patients with CAP. It is worth noting, however, that not all research incorporated in these meta-analyses specifically targeted sCAP, and there is a lack of consistent findings throughout these studies.[10–12]

Based on the results of this study, the utilization of corticosteroid therapy among individuals admitted to the hospital with community-acquired pneumonia has been examined.

METHODS

In In keeping with the guidelines specified in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the researcher of this study implemented procedures to ensure rigorous compliance with these criteria. The use of this strategy is intended to ensure the accuracy of the results obtained from the investigation. The primary aim of this literature review was to provide a comprehensive analysis of the efficacy and potential benefits of corticosteroid therapy in the management of patients who have been admitted to the hospital with community-acquired pneumonia. The primary objective of this work is to demonstrate the importance of the aforementioned challenges discussed inside the text.

In order to meet the eligibility requirements for participation in the study, researchers were required to satisfy the following criteria: The composition of the article should be in the English language and its focus should revolve on the topic of corticosteroid therapy for patients who are admitted to the hospital with community-acquired pneumonia. In order to meet the requirements for publishing, the paper must fulfill both of these criteria. A number of the examined articles were published throughout the period spanning from 2013 to the pre-established timeframe deemed pertinent for this systematic review. The following are considered prohibited: editorials, submissions without a Digital Object Identifier (DOI), review articles that have already been published, and entries that are essentially duplicates of previously published journal papers.

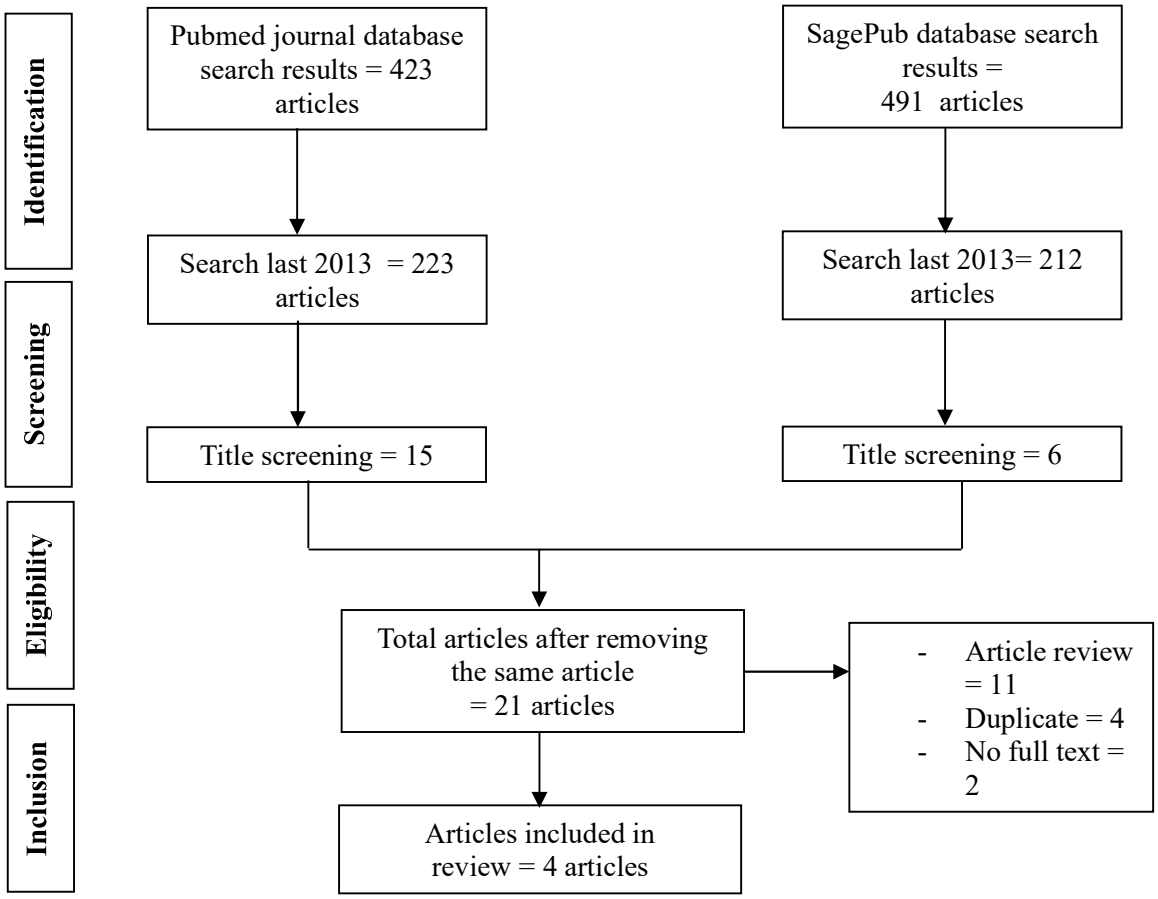

Figure 1. Article search flowchart

We used "corticosteroid therapy" and "community-acquired pneumonia" as keywords.The search for studies to be included in the systematic review was carried out from August, 8th 2023 using the PubMed and SagePub databases by inputting the words: *("adrenal cortex hormones"[Supplementary Concept] OR "adrenal cortex hormones"[All Fields] OR "corticosteroid"[All Fields] OR "adrenal cortex hormones"[MeSH Terms] OR ("adrenal"[All Fields] AND "cortex"[All Fields] AND "hormones"[All Fields]) OR "corticosteroids"[All Fields] OR "corticosteroidal"[All Fields] OR "corticosteroide"[All Fields] OR "corticosteroides"[All Fields]) AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "therapy s"[All Fields] OR "therapys"[All Fields]) AND "community-acquired"[All Fields] AND ("pneumonia"[MeSH Terms] OR "pneumonia"[All Fields] OR "pneumonias"[All Fields] OR "pneumoniae"[All Fields] OR "pneumoniae s"[All Fields])* used in searching the literature.

After reviewing the abstract and title of each study, the authors determined whether or not it met the inclusion criteria. The authors then determined which prior studies would serve as the article's sources and selected those studies. Examining a variety of studies that all appeared to indicate the same trend led to this conclusion. All submissions must be written in English and have never been published before. Only publications that satisfied all inclusion criteria were considered for the systematic review. This restricts the search results to those which are germane to your query. We do not consider the results of any study that does not meet our criteria. The research findings will then be thoroughly analyzed. The following information was uncovered as a result of the research conducted for this study: names, authors, publication dates, location, study activities, and parameters.

Before deciding which publications to investigate further, each author conducted independent research on the research included in the publication's title and abstract. The subsequent step is to evaluate all of the articles that satisfy the inclusion criteria for the review. Then, we will choose which articles to include in the review based on the findings. This criterion is employed to select documents for additional evaluation. To facilitate as much as possible the selection of papers for evaluation. This section discusses which prior studies were conducted and what aspects of those studies made their inclusion in the review appropriate.

RESULT

In the PubMed database, the results of our search brought up 423 articles, whereas the results of our search on SagePub brought up 491 articles. The results of the search conducted for the last year of 2013 yielded a total 223 articles for PubMed and 212 articles for SagePub. In the end, we compiled a total of 21 papers, 15 of which came from PubMed and six of which came from SagePub. We included four research that met the criteria.

Dequin, et al (2023)[12] randomization had been done on a total of 800 patients when the study was stopped after the second planned analysis. The information from 795 cases was looked at. By day 28, 25 of the 400 patients in the cortisol group (6.2%; 95% confidence interval [CI] = 3.9–8.6) had died, while 47 of the 395 patients in the placebo group (11.9%) had died (absolute difference = -5.6 percentage points; 95% CI = -9.6–1.7; P = 0.006). Endotracheal intubation was done on 40 of 222 patients in the hydrocortisone group (18.0%) and on 65 of 220 patients in the placebo group (29.5%; hazard ratio [HR] = 0.59) who were not getting mechanical breathing at the start of the study. Patients who weren't getting vasopressors at the start of the study were given them by day 28 in 55 of 359 (15.3%) of the hydrocortisone group and 86 of 344 (25.0%) of the saline group (HR = 0.59; 95% CI = 0.43–0.82). Both groups had about the same number of hospital-acquired infections and GI bleeding, but patients in the hydrocortisone group got more insulin each day during the first week of treatment.

Meduri, et al (2022)[13] showed condcuted a study with 586 patients originating from 42 Veterans Affairs Medical Centers were subjected to randomization. However, it is worth noting that the sample size fell short of the intended objective of 1,420 due to challenges encountered during the recruitment process. There was no statistically significant disparity observed in the 60-day death rates between the groups receiving methylprednisolone and placebo (16% vs. 18%; adjusted odds ratio (OR) = 0.90, 95% confidence interval [CI] = 0.57–1.40). No statistically significant changes were observed in secondary outcomes or complications.

Odeyemi, et al (2020)[14] showed the utilization of steroids in ICU demonstrated biomarker concordance in 88 patients, accounting for 52% of the total, whereas biomarker discordance was observed in 81 patients, representing 48% of the cohort. The use of biomarker-concordant steroids was found to be associated with a faster resolution of lung injury. Specifically, there was a significant difference in the median fraction of inspired oxygen on day 3 (0.4 [0.3, 0.5] vs 0.3 [0.21, 0.4], P=.005), day 4 (0.35 [0.3, 0.5] vs 0.28 [0.21, 0.38], P=<.001), and day 5 (0.30 [0.24, 0.45] vs 0.28 [0.21, 0.40], P=.03). Additionally, the use of biomarker-concordant steroids was associated with an increase in ICU (3.5; 95% CI = 0.5 to 6.4, P = 0.02) and hospital-free days (3.6; 95% CI = 0.4 to 6.8, P = 0.03) according to multivariate analysis.

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Intervention	Result
Dequin, 2023[12]	France	Randomized clinical trial	800 severe community-acquired pneumonia patients	Intravenous hydrocortisone (200 mg daily for either 4 or 7 days as determined by clinical improvement, followed by tapering for a total of 8 or 14 days) or placebo	In the cohort of individuals diagnosed with severe community-acquired pneumonia and undergoing intensive care unit (ICU) treatment, it was shown that the administration of hydrocortisone resulted in a reduced likelihood of mortality by the 28th day compared to individuals who were administered a placebo.
Meduri, 2022[13]	United State of America	Randomized clinical trial	586 patients with CAP	Intravenous 40 mg loading bolus was followed by 40 mg/day through day 7 and progressive tapering during the 20-day treatment course	The administration of extended low-dose methylprednisolone therapy did not yield a statistically meaningful reduction in the mortality rate within a 60-day period among individuals diagnosed with severe community-acquired pneumonia (CAP). The administration of treatment did not exhibit a correlation with a higher incidence of problems.
Odeyemi, 2020[14]	United State of America	Single-center retrospective cohort study	3,481 ICU admissions with community-acquired pneumonia	No describe	The utilization of steroids in patients who are critically ill with community-acquired pneumonia is infrequently guided by biomarkers and frequently does not align with the levels of inflammatory biomarkers. The utilization of steroids that align with biomarkers was found to be correlated with a more rapid resolution of hypoxemia and an increase in the number of days spent free from intensive care unit (ICU) admission and hospitalization.
Torres, 2015[15]	Spain	Randomized clinical trial	120 patients with CAP	Intravenous bolus of 0.5 mg/kg per 12 hours of methylprednisolone (n = 61) or placebo (n = 59) for 5 days started within 36 hours of hospital admission	In the cohort of individuals diagnosed with severe community-acquired pneumonia and exhibiting a pronounced first inflammatory response, the administration of methylprednisolone in the acute phase demonstrated a significant reduction in treatment failure when compared to the administration of a placebo.

Torres, et al (2015)[15] showed incidence of treatment failure was lower in the methylprednisolone group (13%) compared to the placebo group (31%) (P = 0.02), indicating a significant difference between the two groups of 18% (95% confidence interval [CI] = 3-32%). The administration of corticosteroid medication resulted in a decreased likelihood of treatment failure, as indicated by an odds ratio (OR) = 0.34 (95% CI = 0.14-0.87; p = 0.02). There was no significant difference in in-hospital mortality between the two groups. In the methylprednisolone group, 10% died, compared to 15% in placebo group (P = 0.37). The between-group difference was 5% (95% CI = -6% to 17%). Eleven patients (18%) in the methylprednisolone group and seven patients (12%) in the placebo group experienced hyperglycemia, with no statistically significant difference between the two groups (P = 0.34).

DISCUSSION

Corticosteroids, hormone mediators produced by the adrenal cortex, include glucocorticoids (cortisol is the main one) and mineralocorticoids (aldosterone is the main one), as well as androgenic sex hormones. Glucocorticoids, which are physically and pharmacologically identical to cortisol, have anti-inflammatory, immunosuppressive, antiproliferative, and vasoconstrictive actions.[16] Glucocorticoids play an important role in the maintenance and regulation of immune and circulatory function. The hypothalamic-pituitary (HPA) axis regulates adrenal glucocorticoid release.[17]

The hypothalamic release of corticotropin-releasing hormone (CRH) stimulates the pituitary gland to produce adrenocorticotropin hormone (ACTH) which acts on the adrenal cortex to stimulate the release and synthesis of cortisol, thereby completing the cycle by exerting a negative feedback loop for the release of CRH and ACTH.[18,19] Short, medium, and long-acting corticosteroids are classified by duration. Short-acting drugs have a biological half-life under 12 hours. Medium-working preparations last 12–36 hours biologically. Long-acting drugs last beyond 36 hours. Cortisol is the body's main corticosteroid.[20–23]

The effectiveness of glucocorticoid treatment may be influenced by the extent of dysregulated systemic inflammation.[14,15,24] A randomized controlled trial (RCT) was conducted to investigate the effects of methylprednisolone on treatment failure in patients diagnosed with severe CAP and exhibiting elevated levels of C-reactive protein (CRP) over 150 mg/L.[15] In a retrospective cohort study conducted on patients with severe CAP who were admitted to ICU and received glucocorticoid treatment, it was shown that the subgroup of patients with CRP levels >150 mg/L exhibited a more rapid resolution of hypoxemia and had a greater number of days free from ICU and hospitalization.[14]

The aforementioned findings indicate that the utilization of biologic indicators may be instrumental in identifying individuals who are most likely to experience positive outcomes from glucocorticoid treatment. The blood samples obtained in the ESCAPe study will enable investigation into the correlation between clinical outcomes and indicators of systemic inflammation over a period of time. This analysis has the potential to lay the foundation for the formulation of individualized glucocorticoid therapy approaches.[25]

Clinicians should exercise caution regarding the potential adverse effects associated with systemic corticosteroids when considering their therapeutic use in the treatment of sCAP. These potential hazards encompass hyperglycemia, myopathy, superinfection, osteopenia, gastrointestinal bleeding, weight gain, and cutaneous bruising.[26] The relationship between systemic steroids and osteoporosis is well known and widely recognized. Glucocorticoids affect bone in a number of ways, where they reduce the lifespan of osteoblasts and osteoclasts by inducing apoptosis as well as reducing the recruitment of these cells from progenitor cells. Glucocorticoids promote hepatic gluconeogenesis and glucagon release, causing hyperglycemia. Reduce liver glucose absorption and adipocyte insulin binding.[27,28] Immunocompromised is a condition characterized by quantitative or qualitative defects in the cellular, humoral, or a combination of the two immune systems. Immunocompromised hosts are at increased risk of infection for various reasons.[29]

CONCLUSION

Administration of steroids as early as possible in patients with severe CAP who are treated to benefit, where they do not experience therapy failure. Slower administration and inadequate doses do not provide any benefit.

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