Original Article

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Comparison of Oral (Prednisolone) Versus Intravenous (Hydrocortisone) Steroids in Acute Exacerbation of Bronchial Asthma in Hospitalized Patients

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Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, [4,6]Active participation in active methodology, [2,3]analysis, or interpretation of data for the work, [5]Drafting the work or revising it critically for important intellectual content, [3]Final approval of the study to be published

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ABSTRACT

Objective: To compare the efficacy of oral versus intravenous corticosteroids in improving peak expiratory flow (PEF) in patients admitted with acute exacerbation of asthma.

Methodology: This randomized controlled trial was conducted from October 17, 2018, to April 16, 2019, at the Department of Pulmonology, PIMS, Islamabad. A total of 166 patients (18–65 years, both genders) with a documented history of bronchial asthma presenting with acute exacerbation were enrolled. Patients were randomly assigned to Group A (intravenous hydrocortisone 100 mg every 8 hours for 72 hours) or Group B (oral prednisolone 60 mg once daily for 72 hours). Both groups received standard bronchodilator therapy with nebulized salbutamol 2.5 mg/2.5 ml four times daily and as needed. PEF was measured before and after salbutamol at baseline, every 6 hours for 72 hours, and twice daily until discharge. The percentage change in PEF from baseline was assessed at 72 hours and compared using an independent sample t-test.

Results: At baseline, mean PEF was 409.3 ± 65.4 L/min in Group A and 408.7 ± 69.2 L/min in Group B (p=0.956). After 72 hours, PEF improved to 545.3 ± 64.4 L/min in Group A and 539.7 ± 67.2 L/min in Group B (p=0.594). The mean percentage change in PEF was 34.2% ± 6.4 in Group A and 33.1% ± 6.5 in Group B (p=0.274).

Conclusion: Oral corticosteroids were found to be equally effective as intravenous corticosteroids in treating acute asthma exacerbations. Given their cost-effectiveness, ease of administration, and patient comfort, oral corticosteroids should be preferred whenever possible.

Keywords: Acute exacerbation of asthma, intravenous steroids, oral steroids.

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Introduction

Asthma is a common chronic disease worldwide and its prevalence shows global variations.[1] Prevalence rates for current asthma increased in the United States from 2001 to 2009 (8.7 to 9.7 %) and then plateaued. In Pakistan the overall prevalence of asthma reported in different population subgroups was in the range of 5-20%.[2,3,4] The concomitant inflammation of airways, intermittent obstruction in airflow and hyper-responsiveness of bronchioles make the pathophysiology of asthma complex and multi-faceted. Sign and symptoms of asthma may include cough, wheezing, dyspnea, and tightness of chest.[5,6] With the use of inhaled long acting β2 agonists and inhaled corticosteroids (ICSs), significant improvements have been observed in overall asthma control rate. Nonetheless, considerable variations have been observed in asthma control rate. A minor proportion

of asthma patients (5%–10%) continue to experience symptoms despite receiving optimal treatment. Before recent therapeutic advancements, these individuals faced a significant deterioration in quality of life.[7] According to the American Thoracic Society, the management of severe asthma involves high-dose inhaled corticosteroids in combination with a second asthma controller, which may include systemic corticosteroids.[8] Treatment response, intensity of symptom and asthma prognosis are all diverse in nature and among them the most critical one is the acute exacerbation (AE) of asthma (AE).[9] In addition, the heterogeneity in exacerbations related to severity, frequency, predisposing factors and duration of exacerbations are the major cause of frustration among both the patients and treating physicians. As for instance, some individuals experience exacerbations of mild to moderate severity at few occasions, whereas others experience severe exacerbations so frequently that lead to their visits to the department of emergency. These exacerbations are the major cause of morbidity and incur a high cost to healthcare system. It is, therefore, very important to manage asthma exacerbations promptly.[10]

Prompt management is also essential as exacerbations are associated with progressive loss of functional capacity of lungs.[11] A significant associations have been found between acute exacerbation and certain demographic and clinical factors. These include, gender, race, environmental factors (air pollution, smoking, viral infections) and compliance to treatment protocols.[12]

Acute exacerbations are most frequently triggered by viral infections of respiratory tract, especially with human rhinovirus.[13] Corticosteroids have strong anti-inflammatory actions, and are the most effective anti-inflammatory agents in the treatment of asthma.[14,15] The European Respiratory Society/American Thoracic Society (ERS/ATS) and the Global Initiative for Asthma (GINA) guidelines provide pragmatic approaches to treatment strategy for severe asthma based on patient stratification and expert opinion.[16] The treatment of asthma has d been revolutionize after the introduction of corticosteroids(both systemic and inhaled) in the therapy. Several studies have shown that systemic steroids in combination with bronchodilator therapy are the mainstay of treatment in asthma exacerbations and preventing hospital admissions, decreasing relapse rate and speedy recovery[17] however the optimum route of administration for patients requiring hospitalization is unclear. Intravenous (IV) corticosteroids are preferred in practice, but there is no clear evidence that intravenous steroids are superior to oral. Oral steroids are easily available and convenient to administer even in health care setups of under privileged and remote areas. In severe exacerbation of acute asthma it is important that the steroids and bronchodilator therapy should be started as early as possible as any delay may lead to serious consequences. We therefore hypothesized that there is no difference in the effectiveness of oral and intravenous corticosteroids in acute exacerbation of asthma

Comparing the effectiveness of oral with intravenous steroids in adult patients hospitalized with AE of asthma has been shown to be equal in a previous study [18]

The objective of this study is to compare the efficacy of oral versus intravenous corticosteroids in improving peak expiratory flow (PEF) in patients admitted with acute exacerbation of asthma.

Methodology

This comparative study was conducted in the Department of Pulmonology, PIMS, Islamabad, from 17-10-2018 to 16-04-2019 vide letter no F.2-11/szabmu/AS&RB-50/2018. A total of 166 patients aged 18-65 years with a documented history of bronchial asthma, presenting with acute exacerbation, were enrolled using non-probability consecutive sampling. Acute exacerbation was defined as a worsening of asthma symptoms, including shortness of breath, cough, wheezing, or chest tightness, leading to emergency visits or hospital admission. The sample size was calculated using the WHO calculator (version 7.4b) with a power of 80% and a significance level of 5%, resulting in 83 patients per group. Patients with pneumonia, COPD, unstable diabetes, ischemic heart disease, malignancy, hepatic or renal failure, or requiring endotracheal intubation were excluded.

Baseline investigations, including CBC, LFT, RFT, serum electrolytes, chest X-ray (PA view), and spirometry, were performed. Patients were randomly assigned to two groups using the lottery method. Group A received intravenous hydrocortisone 100 mg every eight hours for 72 hours, and Group B received oral prednisolone 60 mg once daily for the same duration. Thereafter, both groups received prednisolone 30 mg for two days, followed by dose tapering in decrements of 5 mg every two days until discontinuation. All patients received identical bronchodilator therapy with nebulized salbutamol 2.5 mg/2.5 ml four times daily and as needed, along with inhaled corticosteroids.

Peak expiratory flow (PEF), measured in L/min using a handheld peak flow meter (Cipla), was recorded before and after salbutamol administration at baseline, every six hours for the first 72 hours, and subsequently twice daily until discharge. The primary outcome was the percentage improvement in PEF at 72 hours. Patients were monitored for adverse drug reactions, including gastrointestinal disturbances and hyperglycemia, with blood glucose levels recorded at baseline and 72 hours post-admission.

Data were analyzed using SPSS version 20. Continuous variables, such as age and PEF, were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The independent sample t-test was applied to compare the percentage change in PEF at 72 hours between the two groups, with a p-value ≤ 0.05 considered statistically significant. Stratification for age, gender, and baseline PEF was performed to control for effect modifiers.

Results

A total of 166 patients with acute exacerbation of bronchial asthma were enrolled and randomly assigned to two groups: Group A (intravenous steroids) and Group B (oral steroids). Baseline demographics, peak expiratory flow (PEF) measurements, and treatment outcomes were assessed.

The study included both male and female participants, with a mean age of 47.7 ± 12.3 years in Group A and 47.5 ± 12.1 years in Group B. Age distribution is shown in Figure 1, while gender distribution is represented in Figure 2.

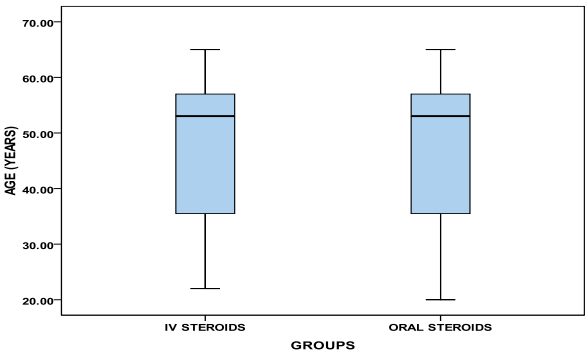

Figure 1: Age distribution of study participants.

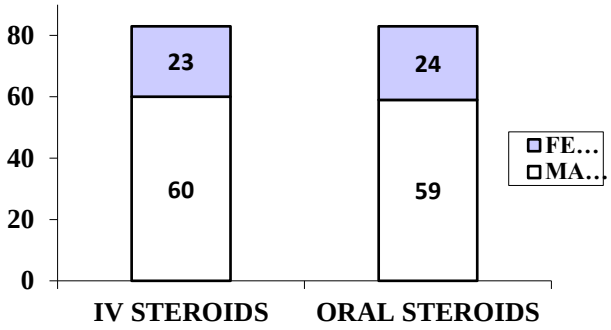

Figure 2: Gender distribution of study participants.

At baseline, the mean PEF was 409.3 ± 65.4 L/min in Group A and 408.7 ± 69.2 L/min in Group B (p = 0.956). After 72 hours of treatment, the mean PEF improved to 545.3 ± 64.4 L/min in Group A and 539.7 ± 67.2 L/min in Group B (p = 0.594), showing no statistically significant difference between the groups. The percentage change in PEF from baseline was 34.2% ± 6.4 in Group A and 33.1% ± 6.5 in Group B (p = 0.274). These values are detailed in Table I.

Table I: Peak Expiratory Flow (PEF) at Baseline and 72 Hours.

Variables	Group A (IV Steroids)	Group B (Oral Steroids)	p-value
	Mean±SD		
PEF Baseline (L/min)	409.3 ± 65.4	408.7 ± 69.2	0.956
PEF at 72 Hours (L/min)	545.3 ± 64.4	539.7 ± 67.2	0.594
Percentage Change (%)	34.2 ± 6.4	33.1 ± 6.5	0.274

When stratified by gender, males in Group A had a mean percentage PEF improvement of 30.5% ± 1.6, while those in Group B had 29.2% ± 1.5 (p = 0.121). Among females, the mean percentage improvement was 43.9% ± 3.3 in Group A and 42.9% ± 2.8 in Group B (p = 0.219), as shown in Table II.

Table II: Percentage Change in PEF Stratified by Gender.

Gender	Group A (IV Steroids)	Group B (Oral Steroids)	p-value
	Mean±SD		
Males	30.5 ± 1.6	29.2 ± 1.5	0.121
Females	43.9 ± 3.3	42.9 ± 2.8	0.219

Similarly, when stratified by age, patients aged 18-40 years showed a mean percentage PEF improvement of 32.1% ± 5.2 in Group A and 29.9% ± 4.7 in Group B (p = 0.117). Among patients aged 41-65 years, the improvement was 35.4% ± 6.8 in Group A and 34.8% ± 6.7 in Group B (p = 0.609), as summarized in Table III.

Table III: Percentage Change in PEF Stratified by Age.

Age Group	Group A (IV Steroids)	Group B (Oral Steroids)	p-value
	Mean±SD		
18-40 Years	32.1 ± 5.2	29.9 ± 4.7	0.117
41-65 Years	35.4 ± 6.8	34.8 ± 6.7	0.609

The percentage change in PEF for both groups is visually represented in Figure 3, highlighting similar improvements across treatment modalities.

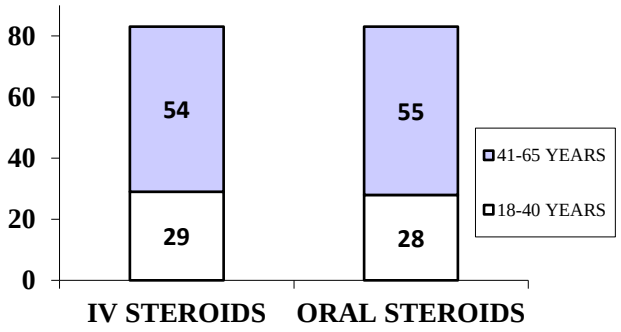

Figure 3. Percentage change in PEF in both groups.

Discussion

The results of this study show that 72 hours after start of treatment there is no significant difference in PEFR in the group treated with intravenous versus oral corticosteroids. Oral and IV administered glucocorticoids show similar effects when comparable doses are used. In patients with acute asthma exacerbation, who are not responding to inhaled bronchodilators, treatment with systemic glucocorticoid is recommended as obstruction to airflow persists due to inflammation of airways and mucus plugging. [19]Current guidelines recommend early initiation of systemic glucocorticoids in these situations:[19,20] The importance of early glucocorticoid administration has been highlighted in a systematic review analyzing 12 studies with 863 participants. The findings demonstrated that initiating glucocorticoid therapy within the first hour significantly reduced the risk of hospitalization compared to delayed administration. Additionally, a short course of systemic corticosteroids has been shown to lower relapse rates and decrease the likelihood of hospitalization after an asthma exacerbation.[18]

Oral and IV administered glucocorticoids show similar efficacy when comparable doses are used. Oral prednisone and methyl-prednisolone are absorbed rapidly after ingestion with virtually complete bioavailability and comparable efficacy with IV methylprednisolone. Prednisone is rapidly converted to prednisolone in the liver.

The results of our study are comparable to previous studies comparing intravenous and oral routes for steroids . Dembla G et al. (2011) compared the effectiveness of oral with intravenous steroids in adult patients who were admitted with AE of asthma. They divided the enrolled patients into 2 groups. One group received prednisolone 100 mg OD (oral) and other group received intravenous hydrocortisone 100 mg QID for 72 hours after the admission. Concurrently, all the enrolled patients received inhaled bronchodilators and corticosteroids. Investigators compared improvement in peak expiratory flow (PEF) at 72 hours from the baseline values among both the treatment groups and demonstrated that both the groups showed similar improvement in PEF at 72 hours).[18] In another study Cunnington D et al. (2005) compared the effectiveness of oral versus IV steroids in the treatment of AE of asthma.. One group received oral prednisolone 100 mg OD and other group received hydrocortisone 100 mg intravenous . 6 hourly for 72 hours After 72 hours both groups had improvement in PEF with no significant difference (27%)between the two groups, P>0.05).[19]

In our study we administered lower doses; IV hydrocortisone 100 mg three time a day ,oral Prednisolone 60 mg once daily for 72 hours after hospital admission. We achieved similar results as that of Dembla et al and Cunnington et al. Mean percentage change in PEF from baseline was 34.2% ± 6.4 SD in IV steroid group and it was 33.1% ± 6.5 SD in oral steroid group (p=0.274) .In a retrospective study Fulco PP et al. (2002) compared oral and intravenous corticosteroids for an acute asthma exacerbation by reviewing the medical records of 53 patients .. Their analysis revealed that no significant difference was observed in peak expiratory flow rate at discharge. They concluded that both the oral and intravenous corticosteroids demonstrated similar efficacy in the treatment of acute asthma exacerbation.[20]

The optimum dose of steroids for acute asthma exacerbation is not clear . The equivalent of prednisone 40-60 mg (methylprednisolone 32 to 48 mg) daily in single or divided doses is usually administered. [21] For life-threatening asthma exacerbations, higher corticosteroid doses are sometimes administered. This practice is largely based on clinical expertise and concerns about the adequacy of lower doses in critically ill patients, rather than strong evidence-based recommendations..[22] Several studies attempted to address

the issue of optimal dosing of steroids and revealed no remarkable additional advantage from systemic corticosteroids administered at doses >60-80 mg/day or 2 mg/kg/day in terms of improvement in pulmonary function, reducing the length of stay in the hospital and rate of readmission. Manser et al. (2001) conducted a systematic review of RCTs on adults with AE of asthma and aimed to compare different corticosteroids doses with a minimum follow-up of 24 h. Investigators had divided the included trials on the basis of different doses. Three groups were identified one with low dose (≤80 mg), second with medium dose (81-360 mg) and third with high dose (>360 mg). A total of 9 trials comprising of 344 adult patients were analyzed. Their analysis revealed no significant difference between different doses.[22]

Regarding the preferred route , intravenous (IV) glucocorticoids are recommended for patients experiencing impending or actual respiratory failure or those who are not able to take or tolerate oral corticosteroids.[23] If both IV and oral administration are not feasible, intramuscular glucocorticoids may be used as an alternative; however, their onset of action is slower, taking up to 24 hours. Due to this delay, intramuscular steroids are generally not preferred for patients presenting to the emergency department with acute asthma exacerbation. Some studies have suggested that in mild to moderate asthma, high-dose inhaled glucocorticoids may offer similar efficacy to oral or IV steroids, but findings remain inconclusive.[24,25] However, a large randomized controlled trial by Harrison TW et al did not support this finding .[26]

In our country we have two peak seasons of allergic asthma , spring with high pollen counts and dry winters with dust and grass pollens. With an overburdened healthcare system and a tendency for poor compliance to treatment by patients the large urban hospital receive a very high number of patients with severe asthma in these seasons . Encouraging the use of oral steroids for acute exacerbation will facilitate the management in the peripheral healthcare setups .It is the timely administration of systemic steroids oral or intravenous which can make a difference in the management of acute exacerbation. There are several advantages of corticosteroids when administered orally over intravenous administration. They are easily available even in the peripheral and remote areas, cost-effective, easy to administer. We suggest that wherever possible, oral corticosteroids should be used initially for the treatment of acute exacerbation of asthma. In the present study we used only lower doses of both oral and IV steroids as compared to what other investigators have used. We suggest further studies comparing different doses on larger sample size.

Conclusion

Oral corticosteroids are as effective as intravenous, in treating acute exacerbations of asthma in adult patients.

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