Oral Versus Intravenous Steroids in Acute Exacerbation of Asthma – Randomized Controlled Study

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Abstract

**Background:** Use of corticosteroids in asthma is a must however the route of administration of steroid in acute exacerbation is a matter of debate. Intravenous steroids used very frequently in clinical practice may not offer any advantage over oral steroids.

**Aim:** To compare to the efficacy of oral vs intravenous steroids in adults admitted with acute exacerbation of bronchial asthma.

**Methods:** Adults admitted to hospital with acute exacerbation of asthma were randomized to receive oral prednisolone 100 mg once daily or hydrocortisone 100 mg IV 6 hourly for 72 hrs following admission. All patients concurrently received inhaled corticosteroids and bronchodilators. Improvements in peak expiratory flow rate (PEF) from baseline were compared for 72 hrs.

**Results:** A total of 65 patients were randomized, 34 received oral prednisolone and 31 received intravenous hydrocortisone. Both groups were matched at baseline for age (40±13.11 vs 44±16.23, p 0.27) and percentage prediction both pre (20.11%±6.17 vs 20.58%±4.78, p 0.73) and post bronchodilator (24.35%±5.43 vs 25.38%±5.01, p 0.43). After 72hrs both groups had improvement in PEF which was statistically insignificant (53.23%±9.54 vs 55.87%±10.34, p 0.28)

**Conclusion:** Corticosteroids administered orally and IV had similar efficacy in the treatment of adults hospitalized with acute exacerbation of bronchial asthma.

Introduction

With the advent of newer investigative techniques like bronchoscopy and bronchoalveolar lavage there has been a radical change in the previously held view regarding the pathogenesis of bronchial asthma. Thus, the emphasis has now shifted from smooth muscle contraction to airway inflammation. It has now been proved beyond doubt that the airway obstruction in asthma is caused by airway inflammation leading to mucosal infiltration and edema with mucus hypersecretion combined with smooth muscle hypertrophy and bronchial hyper reactivity. It is therefore, logical that in a disease where inflammation plays a major role in the pathogenesis, corticosteroids by the virtue of their potent anti-inflammatory effects would help in the relief of the symptoms. Both inhaled and systemic corticosteroids have revolutionized the treatment of asthma. Currently systemic corticosteroids added to bronchodilator therapy are the cornerstones of management of significant asthma exacerbations. Several studies have shown the efficacy of systemic corticosteroid therapy in combination with bronchodilator treatments in preventing hospital admission, reducing relapse rate and hastening recovery. Systemic corticosteroids also facilitate improvement of asthma symptoms and lung function and reduced need for beta-agonist therapy. Oral corticosteroids are convenient to administer and potentially safer as compared to high dose intra venous corticosteroids. Although oral corticosteroids take longer to reach therapeutic levels in blood than intravenous corticosteroids do, it does not appear to be clinically significant.

Materials and Methods

**Study design**

This study was a randomized, parallel comparison of oral prednisolone versus intravenous hydrocortisone for 72 hrs in the treatment of adults admitted to hospital with acute exacerbation of asthma. The study was conducted in a community based, teaching hospital, NKPSIMS and Lata Mangeshkar Hospital, Nagpur from June 2007 to November 2009. The study was approved by the Institute Ethics Committee. A written informed consent was taken from all the study participants. Patients were enrolled if they met the eligibility criteria. All patients eligible and willing to participate in the study were enrolled and randomized to either of the study group according to a computer generated randomization table. Patients were randomly assigned to receive IV hydrocortisone 100 mg 6 hourly or prednisolone 100 mg orally daily for the first 72 h after admission to hospital. After 72 hours, patients in both groups received oral prednisolone 50 mg daily for 2 days. The dose of prednisolone was then reduced to zero in 5 mg decrements every second day.

All asthma treatment apart from route of administration of corticosteroids was kept the same to reduce the confounding effect of other treatments. All patients received bronchodilator therapy with nebulised Salbutamol 2.5 mg/2.5 ml four times a day and as required. All patients also received inhaled corticosteroids throughout the study. If patients were taking inhaled corticosteroids prior to randomization they...
were continued on the same, otherwise patients were given budesonide 500 mcg/2ml twice daily.

Antibiotics were only administered if patients had lower respiratory tract infection, and patients considered to have pneumonia were excluded from the study. Treatment failures were defined as deterioration in the first 48 hours, requiring endotracheal intubation, administration of a higher dose of corticosteroids than given in the protocol. Side effects: Patients were monitored for vomiting, abdominal pain and sleep disturbances during the study period. Blood sugar level was done at baseline and after 72 hours of admission and hyperglycemia was defined as random blood sugar level > 200 mg/dl.

**Patients**

Patients admitted to hospital with acute asthma were enrolled if they met the eligibility criteria during the study period. To be included in study patients age should be between 18 to 70 yrs, there was a documented history of bronchial asthma, patients should have a short term reversibility in peak expiratory flow > 20%. All patients having changes on chest X-Ray consistent with pneumonia were excluded from the study, also patients with asthma requiring endotracheal intubation during hospital stay, history of significant chronic obstructive pulmonary disease (COPD), patients having significant other disease like unstable diabetes, ischemic heart disease, malignancy, hepatic or renal failure and patients who had received more than a total of 70 mg prednisolone in one week prior to admission were excluded from the study.

**Measurements**

In all the patients, Peak Expiratory Flow (PEF) was measured using hand-held PEF meters (Peak Flow Master; Cipla) before and after salbutamol in the emergency department, OPD/IPD. Once admitted to the ward all patients had their PEF measured 6 hourly, before and 10 min after nebulisation with salbutamol and after salbutamol in the emergency department, oPD/IPD. Using hand-held PEF meters (Peak Flow Master; cipla) before and after salbutamol in the emergency department, O/P/D.

**Sample Size calculation**

A mean improvement in PEF of 50 L/min between the two groups after 72 hrs of treatment was defined as clinically significant. To detect this difference after 72 hours of treatment, with an α of 0.05 and power of 80% an estimated sample size of 68 patients (34 in each study group) was calculated.

**Results**

During the study period from June 2007 to November 2009, 68 patients were enrolled, however 3 subjects were withdrawn from the study following randomization, one person was unable to perform the peak expiratory flow while other two were withdrawn after the first dose of hydrocortisone as they were felt to have radiographic changes consistent with pneumonia. The remaining 65 patients were successfully studied as per the protocol. Of these 34 patients received oral prednisolone while 31 patients received intravenous hydrocortisone. The two groups were well matched at baseline, with respect to age, sex, height and baseline PEF. The p value was found to be not significant with respect to age, sex and height (Table 1). The PEF (post bronchodilator) improved from 108.53±27.32 at zero hr to 235±37.26 at 72 hr in oral prednisolone group versus 116.77±29.26 at zero hr to 257.74±66.72 at 72 hr in hydrocortisone group (Fig. 1). The percentage improvement in PEF with oral prednisolone was from 24.35±5.43% to 53.23±9.54% by day three (p<0.0001) and in the hydrocortisone group from 25.38±5.01 to 55.87±10.34% (p<0.0001). After 24, 48 or 72 hrs there was no significant difference in percent predicted PEF between the two groups (Fig. 2). The mean length of hospitalization in days was nearly equal in both groups; 4.44±0.66 in group A verses 4.58±0.92 in group B (p= 0.47). The patients were monitored for side effects such as hyperglycemia (RBS > 200 mg/dl), pain in abdomen, vomiting and sleep disturbances. Most of the patients did not have any difficulty in tolerating the treatment.

**Discussion**

This study was undertaken to compare the role of oral and intravenous steroids in acute exacerbation of bronchial asthma by measuring the peak expiratory flow rate. This is in support of the hypothesis that airway narrowing in asthma is primarily due to inflammatory changes in the airway wall and therefore...
shorter and have less peak expiratory flow rates. Indians as compared to western population are constitutionally admitting criteria in this study were similar for the two groups, confounding effect of unequal dosing.

A striking observation in our study is that patients had a low PEF at presentation as compared to any of the studies done previously highlighting that Indians have low PEF as compared to western population which may be due to climatic conditions, nutritional and genetic factors leading to decreased lung and chest cage size; therefore the magnitude of improvement in PEF seen in our study population is likely to be less than that seen in any other studies, as they start from a higher baseline at presentation. This also establishes the fact that oral steroids are as effective as intravenous even if the PEF is as low as 80-100 L/min. Although current consensus guidelines for the management of asthma recognize that it is appropriate to use oral corticosteroids in acute asthma there has been no Indian study to validate this. Indians as compared to western population are constitutionally shorter and have less peak expiratory flow rates.

The mean length of hospital stay in patients of acute exacerbation of asthma is almost equal with the use of oral or intravenous steroids.

The strength of our study is that it is a randomized, parallel design. This reduces the likelihood of bias in the results obtained and is a methodologically sound way of conducting a comparative study between the efficacies of different drugs. A further strength is the relatively low dose of corticosteroids used and the use of inhaled corticosteroids as concomitant asthma treatment, as these reflect current clinical practice making the results more relevant and more generalized to adults admitted to hospital with acute asthma. The dose of corticosteroids used in this study was based upon the commonly used intravenous dose of hydrocortisone 100 mg 6 hourly and oral dose was then set as prednisolone 100 mg daily, a dose with equivalent glucocorticoid and mineralocorticoid properties to 400 mg of hydrocortisone, or 80 mg methylprednisolone. Although the dose of prednisolone is higher than commonly used and recommended in clinical practice, we felt it was important to use the dose of corticosteroids that was the same given IV and orally so that this study compares route of administration without the confounding effect of unequal dosing.

Although a double-blind study is preferable, a randomized, nonblind study can be valid when the data are objective. The admitting criteria in this study were similar for the two groups, as was their treatment, other than the dosage of steroids. Despite using lower doses of systemic corticosteroids and concomitant medications our results are consistent with the studies done previously.

The major weakness of our study is that we were unable to exclude a small difference in PEF improvement between groups due to the large variability in response seen between individuals and the relatively small number of patients studied. Another drawback in this study is that after matching for age, sex and height the PEF measurement was higher in hydrocortisone group as compared to patients in prednisolone group at the time of admission which suggested that the patients in hydrocortisone group were less severe as compared to prednisolone group. However the overall magnitude of improvement seen in the prednisolone group was not different to that seen in less severe hydrocortisone group and there were no treatment failures in prednisolone group.

In this study oral corticosteroids were effective in the treatment of acute asthma in adults, and appeared to be at least as effective as corticosteroids administered intravenously even when the basal PEF was found to be low. Given that oral administration of corticosteroids has advantages over intravenous administration in terms of cost, ease of administration, and patient comfort; the use of oral corticosteroids for acute exacerbation of bronchial asthma is recommended wherever possible especially in resource limited settings. However since this study was carried on a small subset of population and we could not achieve the target sample size so we cannot exclude a small difference in effectiveness between oral and IV corticosteroids on lung function in adults 72 h after admission to hospital for acute asthma; therefore further studies on a larger scale and on different subsets of Indian population are required.

References