ORIGINAL ARTICLES

EFFECT OF A SHORT COURSE OF PREDNISOLONE (RESCUE PREDNISOLONE) IN THE PREVENTION OF EARLY RELAPSE AFTER EMERGENCY TREATMENT OF ACUTE ASTHMA

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Summary

Relapse after the treatment of acute asthma is common & is not accurately predicted by any available measurements. This study was conducted to see the usefulness of Prednisolone in reducing this high rate of relapse. Two hundred & twenty three patients treated in the Asthma Centre for acute exacerbations of asthma were assigned in randomized, single blind fashion to receive Prednisolone for 10 days or matching traditional treatment without oral steroid. Eighty eight patients were included in primary analysis, a comparison of relapse rates over the 14 days period were done. Relapse was defined as an unscheduled medical visits occasioned by the patient's perceived need for further asthma treatment. The overall risk of relapse was significantly lower in the Prednisolone group (group-A) (P <0.01), as compared with group without steroid (group-B) (5 of 46 in group - A as compared with 16 of 42, in the group -B). Patient came back with partially controlled asthma significantly higher in group -B than group-A (P<0.01) i.e. 10 of 46 in group - A compared with 22 of 22 group -B. Additional needs of steroid over 14 days significantly lower in group-A than group-B (P <0.05) (3 of 46 in group-A, compared with 9 of 42 in group-B) So, a short course of Prednisolone reduces early relapse rate after the treatment of acute asthma.

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Introduction

Relapse after management of acute asthma is common[1]. Twenty five percent to thirty percent will have a relapse within 10 days of acute management. Physicians who treat patients with acute asthmatic attacks can base their therapeutic decisions on numerous experiences directed specifically to the care of such patients in the emergency department[2,3]. If hospitalization is required, there is also an extensive body of literature that addresses early in hospital and intensive care management[4]. The decision to admit these patients or discharge them from the emergency room is more problematic. There are no reliable indicators to ensure that patients with asthma who are considered to be well enough to go home from the emergency room will remain well[5,6]. Instructions for follow-up are provided infrequently, and it is unclear what those instructions should be in this critical period[7].

In acute severe asthma, parenteral corticosteroids administered in a hospital setting can be lifesaving[8]. For the management of stable asthma in ambulatory patients, oral or inhaled corticosteroids are clearly effective[9,10]. It would appear reasonable, then to administer oral coriticosteroids during the critical period following the management of asthma in the emergency room. Nonetheless, this potentially useful therapeutic approach has not yet been validated objectively.

We become happy when we see that after a few dose of nebulizer therapy, patient becomes all right. Usually we give less attention regarding patients treatment plan after control of acute attack[3]. Our thinking is that how might relapse of recently managed patients with acute asthma be prevented ? We conducted a single blind

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randomized trial of a short course oral Prednisolone in the prevention of relapse in the first 14 days after a visit to the Asthma Center for the management of acute asthma.

Materials and Method

This was a 12 months, prospective, randomized, single blind study started from 1st June, 1995 to 31st May, 1996, done as an out patient basis at the Asthma Centre, Institute of Diseases of the Chest and Hospital (IDCH). Patients with acute asthma attended to Asthma Centre who were not steroid dependent, were randomized into 2 groups. The patients receiving steroid with Adult-Step III (N.A.C Protocol)10 were categorized as group-A & those patients receiving Adult-Step III without steroid were categorized as group-B. At first they were evaluated by a chest physician. Spirometric evidence of moderate to severe obstruction & improvement of FEV1 ≥ 200 ml & / or PEF > 60 L/min. Half an hour after 200 µg Sulbutamol &/or evidence of imporvement of PEF by anti-asthma medication over one month at least 60 L/min was taken as a diagnostic criteria of Bronchial Asthma. At least 4 weeks had to have elapsed since the last course of oral corticosteroids.

Inclusion Criteria

- Age ≥ 18 years
- Fulfilling our diagnostic criteria[11] i.e.

1. Past and/or present history of paroxysmal attack of cough/dyspnoea/chest tightness
2. Sputum Eosinophil - present
3. PEFR evidence of obstruction & at least 60L/min improvement after nebulizer therapy.

Exclusion criteria

Patient with acute asthma with following criteria were excluded from the study

- ECG showed features of IHD or arrhythmia
- Associated with other major illness e.g. Hypertension, Diabetes Mellitus
- Pregnancy or breast feedings
- Already taken corticosteroids
- Failed to improve PEFR ≥ 70% of predicted by 3 doses of nebulizer therapy.

Treatment Protocol

All patients with acute asthma after assessment a recommended treatment was given.

Recommended therapy consisted of

- O_2 inhalation 4 L/min through nasal canula
- Nebulize with Terbutaline (Bricanyl) nebulizer sol. 5 mg to 10 mg + 2 cc Normal saline inhalation through a Turboneb nebulizer machine stat and 5 mg terbutaline + 2 cc Normal saline 20-30 min interval 2 doses, if PEFR < 70% of predicted.

Patients showed sign of improvement with PEFR > 70% were included in the trial in a randomized single blind fashion to receive 10 days tapering course of oral Prednisolone 40 mg/day with adult Step III management or only adult Step III management without rescue steroid.

In Adult Step III[10] - we were giving

- Inhaler Beclomethasone - 400-800µg/day
- Tab. Aminophylline - 100 mg thrice daily
- Inhaler Salbutamol - 200 µg as per need.

The patients were instructed to record need of salbutamol/day frequency of asthma symptoms/day. We defined[10,11] asthma symptoms as–

1. Cough or congestion
2. Wheezing
3. Tightness in the chest
4. Shortness of breath
5. Sleeping difficulties (due to cough. wheeze or shortness of breath)

We advised the patient to take 2 puffs of Salbutamol if any of the above symptoms appeared.

The patients were advised to attend our centre after 14 days if their asthma remained controlled & if any problem to control symptoms i.e. needs salbutamol > 6 puffs/day, persistent nocturnal symptoms which disturb sleep etc. attend to our centre at any time. The patients were asked whether they had sought further treatment of their asthma & if they had the details of the visit were recorded.

We defined relapse means an unscheduled visit to a physician's chamber or any emergency department or in asthma centre with a feeling of patients of worsening or unresponsive asthma. Relapse within 2 weeks was designated as early relapse.

Pulmonary function was monitored objectively by flow-volume spirometry at the time of discharge & after 1 month. Spirometric measurements at follow up were made by one trained physician using a Cosmed spirometer that was calibrated weekly. Variables were recorded from the best of three maximum respiratory manoeuvers as determined by ATS[11] criteria with a print out of graphic & numerical data retained in the computer for subsequent analysis. Flow-volume loops were rejected as sub-optimal unless the two best results of FEV_1 & FVC different up to 5% or less. Peak flow was then measured before spirometry test by a separate expiratory manoeuver with a peak flow meter.

The patients receiving steroid with Adult Step III were categorized as group-A & those patients receiving only adult Step III without steroid were categorized as group B.

Analysis of Data

Results were expressed as mean ± S.D. / S.E. Means were compared between group - A & group - B by unpaired t-tests. Frequency of symptoms, hospital visits etc. qualitative data were compared by the Chi-square tests. Results were considered to indicate significance at a P-value of less than 0.05.

Results

Two hundred twenty three patients with acute asthma were assessed at the asthma centre. Of these 112 patients did not begin the trial, – 92 because they were subsequently admitted to the hospital from the centre after acute management, 9 because they were discovered not to meet inclusion criteria & 11 because they were considered to have life threatening condition & received at least one bolus of IV Hydrocortisone at the direction of physician. Of the remaining 111 patients 23 patients did not come back for follow-up after 14 days. The remaining 88 patients (46 in group-A & 42 in group-B) participated in primary analysis, a comparison of relapse rates over the 14 days period.

The characteristics of the patients in the prednisolone and without prednisolone groups are shown in Table-I.

Table-I

Characteristics of the Patient in the Prednisolone (Group-A) group and group without Prednisolone (Group-B)

Characteristics	Group-A (n=46)	Group-B (n=42)	P-value
Mean (±SD) age (years)	28.7±8.4)	32.1±10.5	N.S.
Sex (M/F)	(25/21)	(24/18)	N.S.
Mean (±SD) duration of Asthma	13.1±12.2	13.6±11.9	N.S.
Somking Status			
Current	5(10.9%)	7(16.6%)	N.S.
Former	22(47.8%)	15(35.7%)	
Never	19(41.3%)	20(47.6%)	
Previous Use of Oral Steroids for Exacerbation			
Yes	21.(45.7%)	18(42.9%)	N.S.
No	25(54.3%)	24(57.1%)	
Previous Hospitalizations for Asthma			
Never	34 (73.9%)	28(66.7%)	N.S.
1 - 3	8(17.4%)	11(26.2%)	
More than 3	4 (8.7%%)	3(7.1%)	
Usual Maintenance Medications on Arrival			
Oral Salbutamol	42(91.3%)	39(92.9%)	N.S.
Oral Aminophylline	16(34.8%)	15(35.7%)	N.S.
Reliever Inhaler	5(10.7%)	5(11.9%)	N.S.
Inhaled Steroid	2(4.3%)	1(2.4%)	N.S.
Na-Chromoglycate	0	0	N.S.
Ipratropium	0	0	N.S.

Characteristics of response of treatment was studied. The relapse rate was significantly less in predinsolone treated group. PEFR results also significantly better in prednisolone treated group but other spirometric results were not significantly different between the 2 groups.

Discussion

This is a common question whether short course of rescue oral Prednisolone after acute management of asthma should be recommended for all patients or not. Some studies showed that in children asthma improved more rapidly after emergency therapy when treated with short course oral steroid1[3]. Another study reported that in adults a decrease in the relapse rate from 21% to 6% in patients given a tapering dose of steroid[14]. As maintenance therapy their patients received only an inhaled bronchodilator for intermittent "rescue" therapy, and follow-up consisted fo a single telephone call, with no documentation of pulmonary function changes or follow-up beyond 10 days. The rates of relapse, which in the control group were comparable to those reported in the literature[9,15] were reduced significantly in the group receiving steroids but no significant different pattern of spirometric response to therapy emerged as early as the 14 days after the administration of oral steroids except PEFR.

We chose to add aminophylline to the treatment regimen of all patients after discharge (when tolerated) for two reasons. First, we thought that it was ethical to ensure that the patients given placebo received some form of supplemental maintenance therapy, given the reported rates of relapse in this high-risk group. Second, we wished to emulate a common clinical practice, thereby enhancing the general applicability of our result.In one sense, the direction of this chance difference between the prednisolone and without prednisolone groups was fortunate; one would expect that adding aminophylline more often in the placebo group would bias the trial against finding an advantage for prednisolone treatment. We suspect, therefore, that the true benefits of prednisolone treatment may be even greater than suggested by the present data. We cannot rule out entirely the possibility that aminophylline somehow contributed to the higher rate of relapse among the patients given placebo, but we consider this unlikely. Aminophylline is of demonstrable benefit in the maintenance treatment of asthma, and its side effect, troublesome to a minority of patients, are unlikely to have provoked a relapse, since patients received aminophylline only if they reported previous tolerance of the agent[5,16]. Our data suggest indirectly that aminophylline therapy is of minimal benefit as compared with oral steroids in reducing the fate of relapse after acute attacks of asthma.

Our study may not reflect optimal steroid use for all or even the majority of patients with asthma. The duration of the oral-seroid course chosen might be too short and the dosage too low for some patients.

Tapering of the dosage, although it reduces the likelihood of a sudden flare-up of asthma during steroid withdrawal, may also complicate the regimen unnecessarily. From this study it is obvious that short course steroid reduces the likelihood of a sudden flare-up of asthma after acute management by nebulizer therapy. Nc serious side effects or toxicity was noted from short term use of Prednisolone.

Conclusion

All patient with acute asthma should receive a short course of corticosteroids as a rescue therapy.

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