A comparison of ‘abruptly stopping’ with ‘tailing off’ oral corticosteroids in acute asthma


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Systemic corticosteroids are almost universally used in the treatment of severe acute asthma but the optimum length of treatment with corticosteroids following recovery from an acute attack of asthma is not established. Thirty-five patients admitted with acute asthma and treated with oral prednisolone 40 mg daily in addition to bronchodilator therapy until full recovery, with stable peak expiratory flow recordings (PEF) within 15% of their previous best PEF or predicted PEF were studied. They were all discharged home on regular inhaled corticosteroids and regular or as required use of bronchodilators and randomized to receive either prednisolone 40 mg daily or placebo for the first 14 days. Median PEF values increased from 31% predicted on admission to hospital to 71% predicted on discharge from hospital in the active treatment group (19 patients) and from 32–73% in the placebo group (16 patients). There was no difference between the two groups in the median values of the forced expiratory volume in one second, forced vital capacity, total lung capacity or diurnal variation in PEF either at the time of discharge from hospital or at 14 and 28 days after discharge from hospital. This study suggests that there is no need to reduce prednisolone gradually following recovery from an exacerbation of asthma, provided systemic corticosteroid treatment is continued until a satisfactory and stable PEF is achieved.

Introduction

There is a general agreement about the need to use relatively high dose systemic corticosteroid treatment in acute asthma. This is usually started at the earliest opportunity and continued until symptoms and pulmonary function improves to a satisfactory level. Although the dose response characteristics of prednisolone in acute asthma are well documented (1), there is little published work on the length of treatment required following clinical recovery from an acute exacerbation of asthma. Advice generally varies from continuing corticosteroids for 7–14 days following discharge from hospital with an abrupt cessation of corticosteroid treatment or a gradual ‘tailing off’ of treatment (2,3).

This double-blind placebo controlled study was designed to compare an abrupt cessation of prednisolone treatment with a gradual ‘tailing off’ of treatment in patients admitted with an acute exacerbation of asthma once their asthma had improved and remained stable for 48 h in hospital.

Methods

Patients aged 16–80 years admitted with an acute attack of asthma were studied. Treatment of these patients was not standardized except that all patients received prednisolone 40 mg a day from the date of admission. Those on long term oral corticosteroids and those who required ventilatory support during the admission were excluded from the study. Patients included were required to have achieved at least a doubling of their admission peak expiratory flow rate (PEF) prior to discharge from hospital and to have achieved a PEF at the time of discharge which was within 15% of the previous pre-admission best recorded PEF values or within 15% of predicted. They were also required to have achieved a stable PEF over 48 h; this was defined as <15% variability in PEF measured at the same time of day. The study was approved by the local medical ethics committee and informed consent was obtained from all patients.

All patients were discharged on inhaled corticosteroid treatment (daily dose range of budesonide or beclomethasone was 400–2000 µg) and bronchodilators. They were randomized to receive a 14 day course of prednisolone or placebo. The dose of prednisolone was reduced by 5 mg every second day. An emergency supply of prednisolone was given to all patients together with an appropriate self management plan. Patients were asked to keep twice daily PEF recordings (taken before inhalers) with a mini-Wright peak flow meter. FEV₁ and FVC were...
measured using a dry bellows spirometer (Vitalograph) and lung volumes were measured using a constant volume body plethysmograph (PK Morgan, U.K.) on day 1 (day of discharge) and on days 14 and 28.

Analysis

Of the 40 patients entered into the study (21 active treatment and 19 placebo), five (two active, three placebo) defaulted from the study for social reasons and were excluded from the study. Following discharge from hospital each patient required treatment with prednisolone for an exacerbation of asthma; two of these patients in each group required treatment in the first 14 days. Because exclusion of the results of these eight subjects would have introduced bias, non-parametric methods were used to compare the active and placebo treated groups to enable all subjects recruited to the study (excluding social defaulters) to be included in the analysis (4,5). Subjects who required prednisolone treatment were assumed to have deteriorated and allocated worst group values from the time they were treated with prednisolone.

PEF, FEV₁, FVC and TLC values were expressed as % predicted for analysis and diurnal variation in PEF was calculated as amplitude % mean (100 × [difference between PEF am and PEF pm]/mean PEF). The values obtained at 14 and 28 days (mean over 7–14 days and 21–28 days in the case of PEF) were compared with the baseline values at discharge in each group using Wilcoxon's rank-sum test to determine if there had been a significant change in these values following hospital discharge. In addition the baseline values obtained on the day of discharge from hospital (the mean over the last 2 days before discharge in the case of PEF) and the change from baseline in these values at 14 and 28 days (mean over 7–14 days and over 21–28 days in the case of PEF) were compared between the two groups by the Wilcoxon rank-sum test.

Results

Nineteen patients in the active treatment group (median age 30 years) and 16 patients in the placebo group (median age 45 years) were analysed. There was no difference between the two groups for length of stay in hospital (median 6 days for both groups). PEF increased in the active treatment group from a median of 31% predicted on admission to 71% at discharge (P<0.0001); corresponding figures for the placebo group were 32% and 73%, respectively.

Discussion

We have studied a selected group of asthmatic patients who responded quickly following an exacerbation of asthma with a standardized dose of 40 mg prednisolone. There was no difference in lung
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Fig. 2 Change in FVC (a) and FEV₁ (b) during admission and following discharge from hospital with abrupt cessation of oral prednisolone at the time of discharge (+) and tailing-off of prednisolone after discharge (■).

function over the 4 weeks following discharge from hospital between the patients who stopped prednisolone abruptly and those who 'tailed off' the prednisolone gradually over 2 weeks.

It is important to note that patients in our study were continued on 40 mg prednisolone until they achieved a satisfactory and stable PEF for 48 h before they were discharged from hospital with a gradual reduction or sudden cessation of prednisolone treatment. It is likely that premature cessation of systemic corticosteroid therapy would result in a worsening of asthma. All our patients were continued on inhaled corticosteroid treatment and it is likely that this prevented the deterioration in lung function in some patients.

British Thoracic Society Guidelines recommend that all patients admitted to hospital with acute severe asthma should continue prednisolone for 1–3 weeks following discharge from hospital. This is justified on the grounds that it may take up to 2 weeks for maximum improvement in pulmonary function to be achieved (1). There is at present no agreement on the length of corticosteroid treatment required. The practice of a gradual reduction in systemic corticosteroid treatment was introduced in the mid 1950s (7). This was aimed at preventing a rebound worsening of asthma and allowing a recovery of the hypothalamic-pituitary-adrenal axis following corticosteroid induced suppression. Recovery in adrenal function following short courses of prednisolone up to 3 weeks appears to be rapid (8) however and does not justify a gradual 'tailing off' of oral corticosteroid treatment. Our study does not show a rebound worsening in asthma following sudden cessation of prednisolone. There does not therefore appear to be a need to reduce prednisolone gradually following recovery from an acute exacerbation of asthma provided prednisolone treatment is continued until a satisfactory and stable PEF is achieved.

References


