

PAPERS AND ORIGINALS

High-dose corticosteroids in severe acute asthma

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Summary

Twenty-six patients admitted to hospital for treatment of severe exacerbations of asthma unresponsive to bronchodilators were assigned to high-, medium-, or low-dose corticosteroid treatment regimens. The rates of recovery were assessed by changes in pulse rate, peak expiratory flow rate, and spirometric measurements and were not related to the dose of corticosteroids given. Very high systemic doses of corticosteroids do not offer significant advantages in treating severe exacerbations of asthma.

Introduction

A recent study of patients presenting with severe exacerbations of asthma showed that most patients had been ill for days or

weeks.¹ For such patients treatment with systemic corticosteroids is usually considered necessary, and, since widespread plugging of airways is usually present, not surprisingly recovery may be slow. Several days' treatment with corticosteroids is generally advocated, and there has been a recent trend towards giving larger doses.² We gave three groups of patients with severe asthma different corticosteroid regimens to see if the rate of recovery was affected by the dose given.

Patients and methods

Twenty-six patients were studied after admission to hospital for severe asthma lasting more than 24 hours. All had proved resistant to their usual medication and showed no clinical or spirometric improvement after receiving 10 mg of salbutamol by intermittent positive pressure-breathing (IPPB). All were given continuous oxygen (35% Ventimask) and intravenous aminophylline 1 g per 24 hours for the first two days. They also received salbutamol three times daily by IPPB until recovery was well established. The patients were divided into three groups and they received corticosteroids as follows: (a) 10 patients received an initial intravenous injection of hydrocortisone hemisuccinate followed by oral prednisolone, the dose being reduced after the fifth day (low-dose group); (b) 10 patients received a loading dose of intravenous hydrocortisone hemisuccinate and intermittent injections for 48 hours, followed by oral prednisolone, the dose being reduced after the seventh day (medium-dose group). This regimen has been reported^{3,4}; (c) six patients received a loading dose of methylprednisolone and a continuous intravenous infusion for two days. From the third day these patients received intramuscular injections, reducing in dose to zero by the ninth day (high-dose group). Methylprednisolone was chosen as the most suitable preparation for

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TABLE 1—Treatment schedules

Group	Loading dose	Daily dose	Day										Total dose over 10 days*
			1	2	3	4	5	6	7	8	9	10	
Low-dose	Intravenous hydrocortisone 280 mg	Oral prednisolone (mg)	80	80	80	80	80	60	40	30	20	10	36.2 mg
Medium-dose	Intravenous hydrocortisone 4 mg/kg body weight	Intravenous hydrocortisone (mg/kg)	12	12									61.2 mg
		Oral prednisolone (mg)			80	80	80	80	80	60	60	60	
High-dose	Methylprednisolone 1 mg/kg body weight	Methylprednisolone	10 mg/kg IV	10 mg/kg IV	500 mg IM	250 mg IM	125 mg IM	40 mg IM	40 mg IM	20 mg IM			175.5 mg

*Total dose of corticosteroids expressed as equivalents of hydrocortisone mg/kg body weight.

TABLE II—Initial assessment of severity of asthma in three groups. Values are expressed as group means \pm SE

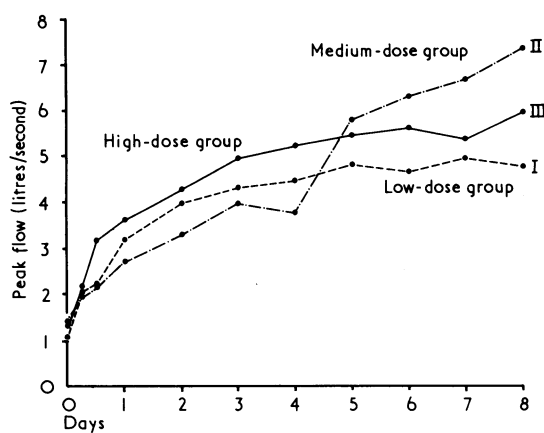
Group	No of patients	Pulse	Peak flow (l/s)	Peak flow (%)	FEV ₁ (l)	FVC (l)	H ⁺ ion (nmol/l)	Po ₂ * (kPa)	Pco ₂ (kPa)	Age (years)
Low-dose	10 (6 M; 4 F)	118	1.08 \pm 0.33	9.3 \pm 5.4	0.45 \pm 0.15	1.08 \pm 0.80	43 \pm 1.6	8.83 \pm 0.78	4.69 \pm 0.24	36.6 \pm 4.0
Medium-dose	10 (5 M; 5 F)	133	1.43 \pm 0.42	14.7 \pm 7.4	0.46 \pm 0.13	0.90 \pm 0.38	46 \pm 3.4	7.06 \pm 0.27	5.71 \pm 0.77	30.9 \pm 4.5
High-dose	6 (4 M; 2 F)	134	1.32 \pm 0.38	14.0 \pm 5.0	0.35 \pm 0.13	0.91 \pm 0.59	39 \pm 4.6	9.10 \pm 0.59	4.60 \pm 0.42	29.1 \pm 4.4

*Significance of differences between group means for arterial oxygen tension: Medium dose *v* low dose: $P < 0.02$; medium dose *v* high dose: $P < 0.005$.
Conversion: SI to traditional units—Blood gases: 1 kPa \approx 7.5 mm Hg.

complete dose administration in such large doses. Schedules are shown in table I. Patients were assessed on entry to the study by clinical examination and measurements of peak expiratory flow rate (PEFR), measured with a Wright peak flow meter, and forced expired volume in one second (FEV₁) and forced vital capacity (FVC), measured with a Vitalograph spirometer. Arterial blood was obtained by puncture for measurements of hydrogen ion concentration and tensions of oxygen and carbon dioxide. The responses to treatment were assessed by comparing measurements of pulse rate, PEFR, FEV₁, and FVC taken six, 12, and 24 hours after the start of treatment and thereafter three times daily to discharge. Single factor analysis of variance was performed on the group means to determine the significance of the differences between the groups.

Results

In the initial assessment (table II) the only statistically significant difference between the groups was in the mean arterial oxygen tension: that of the medium-dose group was lower than the mean values for the other two groups. The rates of recovery were assessed by comparing the group mean values for pulse rate, PEFR, and FEV₁ at each time interval. The patterns of recovery of the three groups for PEFR are shown in the figure. Similar patterns were observed for FEV₁ and



Patterns of recovery of the three groups for PEFR.

percentage of predicted peak flow. Throughout most of the study there were no significant differences between the group means for peak flow, FVC, and pulse rate. Those differences that did reach significance are shown in table III. The rate of recovery in the first 72 hours was also assessed by calculating the slope of the regression line for PEFR against time for each patient and deriving a mean and standard error of the mean for the regression for each group. When these group values

TABLE III—Analysis of variance showing significance of differences between group means

	Groups	P value
	"., Predicted peak flow	
Day 7	Low-dose <i>v</i> medium-dose	<0.05
Day 8	Low-dose <i>v</i> medium-dose	<0.01
	FEV ₁	
Day 1	Medium-dose <i>v</i> high-dose	<0.05
Day 5	Low-dose <i>v</i> medium-dose	<0.01

were compared no significant differences were observed between the groups.

Discussion

Little is known of the factors that influence the response to treatment of patients with severe asthma. But it seems reasonable to expect that recovery may be influenced by the cause of deterioration, the various mechanisms contributing to the airways obstruction, and the duration of the exacerbation. Thus comparisons between individual patients or between groups of patients may be misleading. Nevertheless, some attempt must be made to evaluate different treatments if rational advances are to be made.

In our study the patients in the high-dose group were marginally quicker to respond to treatment in the first 72 hours, but significant differences from the other regimens were not achieved. The large doses of corticosteroids used increased the likelihood of complications. One patient in this group developed severe leucopenia that recovered when the corticosteroids were withdrawn, while another had a recurrence of symptoms from a duodenal ulcer. The patients in the medium-dose group were the slowest to recover initially but they seemed to be more ill in terms of arterial hypoxaemia. This group, however, subsequently showed the best response to treatment by the end of the study.

We conclude that there is no significant advantage in using a very high dose of corticosteroids for treating severe exacerbations of asthma.

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