THE EFFECT OF A NEW STEROID AEROSOL—BECLOMETHASONE DIPROPIONATE (BECOTIDE) IN CHRONIC ASTHMA

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SYNOPSIS

This paper reports the results of the use of beclomethasone dipropionate aerosol in the treatment of 13 asthmatic patients. 4 patients were on standard bronchodilator therapy when the steroid aerosol was initiated, while 9 others who were steroid-dependent, were transferred from oral prednisolone to aerosol therapy. In both groups of patients inhaled beclomethasone produced significantly higher mean peak expiratory flow rates. Patient acceptability was high and there were no noticeable systemic effects. Steroid withdrawal symptoms were also not observed. It would thus appear that this steroid aerosol is preferable to oral prednisolone and should be considered in the control of chronic asthma requiring long term steroid therapy.

Severe chronic bronchial asthma is a potentially serious condition with a high morbidity. It is difficult to manage and frequently requires long-term oral corticosteroid therapy which may produce undesirable and dangerous side effects including suppression of the hypothalamo/pituitary/adrenal response. To avoid this, steroid aerosols in smaller doses have been used in the past, but with disappointing results. Hydrocortisone hemisuccinate administered by aerosol produced no objective improvement (Langlands and McNeill, 1960), while dexamethasone-sodium-21 phosphate by aerosol although giving good symptomatic control of the asthma (Arbesman *et al*, 1963) showed significant systemic absorption and therefore had little or no advantage over oral steroids. Recently, beclomethasone dipropionate has been introduced as a new corticosteroid with powerful topical activity (Caldwell *et al*, 1968) but poor systemic absorption with little or no effect on pituitary-adrenal function (Raffle and Frain-Bell, 1967). Using this drug as a pressurised aerosol good clinical results have been reported in asthmatic patients (Morrow Brown *et al*, 1972; Clark, 1972; and Lal *et al*, 1972) without depressing plasma cortisol levels in the recommended doses (Lal *et al*, 1972; Chatterjee *et al*, 1972; and Gaddie *et al*, 1973).

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The objectives of this study were:—

(i) To assess the efficacy of beclomethasone in the treatment of mild asthmatics as well as those with severe steroid-dependent asthma.

(ii) To determine the acceptability of beclomethasone to patients and to observe the incidence and severity of any clinical side-effects.

MATERIAL AND METHODS

Thirteen asthmatic outpatients (five men and eight women) were studied. Their mean age was 33 years (range 13—49 years). All had a long history of attacks of paroxysmal breathlessness relieved either spontaneously or by bronchodilator therapy and a wide variation in the reversibility of airways obstruction. Nine patients were dependent on oral steroids (up to 10 mg. prednisolone/day) and had been so for varying periods of time (1—5 years). Previous attempts at steroid withdrawal were unsuccessful. Four patients were maintained satisfactorily on bronchodilators only.

Each patient was seen on entry to the trial and every week thereafter. The patients attended at 9 a.m. on each occasion to exclude the effect of diurnal variation. At each visit the best of 3 measurements of the peak expiratory flow rate (PEFR) was recorded using a Wright's Peak Flow Meter (Wright and McKerrow, 1959). The nine patients who were steroid-dependent on entry to the trial were kept on their usual maintenance dosage of prednisolone and bronchodilators for the first 4 weeks. Thereafter, prednisolone was withdrawn and they were placed on beclomethasone dipropionate 100 mg. four times a day by aerosol for 4 weeks. This was then followed

TABLE I

WEEKLY PEFR READINGS IN THE NINE STEROID-DEPENDENT ASTHMATICS WHILE ON FOUR-WEEK PERIODS OF PREDNISOLONE, BECLOMETHASONE DIPROPIONATE AND WITHOUT EITHER OF THE DRUGS

Case No.	Daily Prednisolone Dosage (MG)	Weekly PEFR Readings L/min											
		Prednisolone				Beclomethasone				Control Period			
		1st	2nd	3rd	4th	1st	2nd	3rd	4th	1st	2nd	3rd	4th
1	10	350	385	365	390	320	320	350	380	295	—	—	—
2	10	355	330	350	310	470	360	280	435	140	—	—	—
3	5	380	340	380	390	400	380	390	390	310	300	—	—
4	5	230	270	280	320	300	270	300	290	—	—	—	—
5	5	360	400	390	360	415	425	415	445	430	420	425	400
6	5	540	540	565	550	570	590	585	660	560	480	510	500
7	7·5	360	320	320	330	460	430	425	395	—	—	—	—
8	5	375	370	400	400	435	425	420	420	400	400	400	400
9	10	380	390	370	230	360	370	360	360	300	310	330	310

— =Trial discontinued

TABLE II

WEEKLY PEFR READINGS IN THE FOUR PATIENTS NOT ON ORAL STEROIDS WITH AND WITHOUT BECLOMETHASONE THERAPY

Case	Weekly PEFR Readings (L/min)							
	Control Period (Weeks)				Beclomethasone (Weeks)			
	1st	2nd	3rd	4th	1st	2nd	3rd	4th
10	450	460	455	450	450	475	470	475
11	360	320	320	330	355	400	400	405
12	425	400	440	400	390	420	430	420
13	355	340	400	400	390	380	400	430

by a control period of 4 weeks during which both beclomethasone dipropionate and prednisolone were withheld but bronchodilator therapy administered as required. Five of these patients, however, were unable to complete this control period because of increasing severity of the asthma.

The four patients who were not on steroids had a control period of 4 weeks on their usual medication followed by another four-week period during which beclomethasone dipropionate 100 mg. four times a day was administered.

All patients were instructed in the correct use of the pressurised aerosol and were observed to be proficient in firing the aerosol at the beginning of inspiration.

RESULTS

The weekly PEFR values and their distribution over the whole period of the trial for the 13 patients in this study are shown in Tables I and II.

Five of the steroid-dependent patients were unable to complete the 4-week control period because of increasing severity of the asthma (Table I).

The mean PEFR for patients on inhaled beclomethasone therapy was significantly greater ($p<0{\cdot}002$) than that observed for the patients on either oral prednisolone or during the control period, respectively (Table III).

TABLE III

COMPARISON OF THE MEAN PEFR READINGS IN THE ASTHMATIC PATIENTS DURING TREATMENT WITH ORAL PREDNISOLONE AND BECLOMETHASONE, AND DURING A CONTROL PERIOD AND BECLOMETHASONE, RESPECTIVELY

Treatment	PEFR L/min		p Value
	Mean	± S.D.	
Oral Prednisolone	372·0*	75·0	
Versus			<0·002
Inhaled Beclomethasone	403·9*	83·3	
Control	402·5+	43·7	
Versus			<0·001
Inhaled Beclomethasone	434·1+	66·6	

* Each mean was calculated from 36 single readings (9 patients)

\+ Each mean was calculated from 32 single readings (8 patients)

No significant side-effects were noted while patients were on inhaled beclomethasone. In particular, patients did not complain of any throat irritation after inhalation of beclomethasone. Change-over from oral steroids to beclomethasone was carried out without tailing off the steroid dosage and no untoward effects were observed.

DISCUSSION

The results of this study show that inhaled beclomethasone is effective in the management of severe chronic asthma and that replacement of oral steroid therapy may be undertaken without symptomatic deterioration when daily prednisolone maintenance dosage is under 10 mg. A higher maintenance dosage (>10 mg. Prednisolone/day) may necessitate a short period of concurrent administration of oral steroid with a higher daily dosage (800—1000 mg.) of inhaled beclomethasone followed by a more gradual withdrawal of the oral steroid. Alternatively, a smaller maintenance dosage of steroid may be used together with inhaled beclomethasone (a dosage of 400 mg./day from the start has been shown to produce no systemic effects) (Morrow Brown *et al*, 1972; Lal *et al*, 1972; and Chatterjee *et al*, 1972). It may thus be possible to decrease unwanted systemic effects by concurrent low-dosage administration of each steroid.

No adverse side-effects attributable to inhaled beclomethasone were noted in this study and patient acceptance was excellent. Steroid withdrawal symptoms were not a problem as observed in other studies (Morrow Brown *et al*, 1972; and Chatterjee *et al*, 1972). However, patients in this study did not initially have other allergic disorders nor were they on a high maintenance dosage of steroids.

Finally, it needs to be emphasized that in status asthmaticus or with severe intercurrent respiratory infection, initial oral steroid therapy in high dosage is mandatory as the aerosol may not be able to overcome the barrier posed by the contribution of excessive mucus, pus and bronchospasm. When the acute condition has been overcome beclomethasone therapy may then be initiated in usual dosage and oral steroids tailed down and discontinued if possible.

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