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BECLOMETHASONE DIPROPIONATE AEROSOL IN TREATMENT OF PERENNIAL AND SEASONAL RHINITIS: A REVIEW OF FIVE YEARS' EXPERIENCE

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1 Five years' experience in the use of beclomethasone dipropionate aerosol (BDA) in the treatment of 315 patients with upper respiratory tract allergy is reviewed.

2 A total of 223 patients with perennial rhinitis was treated. In 23, where the nasal allergy had recurred after oral corticosteroid therapy for asthma was withdrawn, BDA was effective in 69% of cases. A similar success rate (68%) was recorded in 169 patients suffering from perennial allergic rhinitis alone, but a satisfactory response was observed in only 45% of 31 patients with nasal polypi.

3 In 92 patients with seasonal allergic rhinitis freedom from symptoms was achieved in 80%.

4 A total of approximately 534 patient-years of treatment has been recorded without any evidence of side-effects either clinically or on nasal biopsy.

Introduction

Allergic rhinitis is often a minor disorder, more a nuisance than a disability, but the perennial type (PAR) can lead to complications such as sinusitis, eustachian blockage, otitis media and polypi. It is frequently associated with allergic asthma or precedes its development by many years. During our original clinical trial of beclomethasone dipropionate aerosol (BDA) in allergic asthma in adults and children (Brown *et al.*, 1972), some corticosteroid-dependent asthmatics with PAR, who were successfully transferred to BDA, complained bitterly of symptoms of PAR which had previously been suppressed by oral corticosteroids. We treated the nasal allergy in these cases with BDA, and the excellent results we obtained prompted us to embark on a clinical trial at the end of 1970. The results of nasal BDA therapy in seasonal allergic rhinitis (SAR) have already been reported (Brown & Storey, 1974; Mygind, 1973; Blair & Butler, 1976; Lofkvist & Svensson, 1975). We now report on the long-term administration of BDA in the treatment of 223 patients with PAR and 92 with SAR.

Methods

All patients with PAR had a history of sneezing, rhinorrhea, nasal congestion and blockage of over one year's duration, with characteristic findings on rhinoscopy and excessive numbers of eosinophil cells in the nasal mucus, using our wet smear technique (Brown, 1958). A comprehensive allergy investigation (Brown, 1970) was undertaken in all cases, and 50 patients had been unsuccessfully treated by hyposensitization. All patients kept our specially designed allergy symptoms and treatment charts, and treatment was not begun until records had been satisfactorily kept for at least 2 weeks. Treatment with BDA was then started, using one metered dose of 50 μg into each nostril four times daily. Antihistamine or other therapy was continued for the first week, but patients were then instructed to phase out these treatments if their symptoms improved, and by the next visit 3 weeks later most of them had had at least 1 week on BDA alone. At first, a special nasal adaptor for BDA was used, but in 1972 a specially designed aerosol (Beconase) was introduced, delivering the same dose with less propellant and less force.

No aerosol can be effective if the nose is blocked, so that in severe PAR and in patients with nasal polypi a short course of oral corticosteroid was an essential preliminary treatment. When the nasal airway was clear, BDA was introduced, oral corticosteroids were phased out, and BDA therapy was continued.

Four main groups emerged as the trial progressed:

97 with PAR alone, 72 with both PAR and asthma, 23 ex-corticosteroid-dependent asthmatics transferred to BDA whose PAR had recurred, and 31 with nasal polypi. In nine of the last group the development of nasal polypi seemed to be related to the unmasking of nasal allergy on corticosteroid withdrawal. All 92 patients with SAR had classical hay fever, with positive nasal tests for grass pollen.

Results

Perennial allergic rhinitis

Results were assessed on the symptoms charts, rhinoscopy, patency of nasal airways and on whether antihistamines or other treatment could be stopped without relapse. It had been intended to use symptom scores for assessment, but this was found to be unnecessary, because the response was so obvious when the treatment was successful that there were practically no symptoms to record. It was therefore decided to classify the results as 'obviously successful', 'moderately successful', in which symptoms were reduced by half, and 'failures' (Table 1).

In 23 patients with perennial asthma, in whom PAR was a 'side-effect' following transfer from oral to inhaled corticosteroids, the nasal symptoms were completely controlled in 16 (69%). Only three were able to reduce the standard dose, and all have continued to require BDA for both nasal and bronchial allergy, seven for more than 5 yr.

Of the 169 patients with PAR only, 115 (68%) were able to discontinue all other treatment and remain symptom-free. BDA was withdrawn in 40 without relapse. Seventy-seven others (35%) were able to reduce BDA to four or two metered does of 50 μg daily, and 15 recovered their sense of smell, which had been absent for years (Table 2).

In the 31 patients with nasal polypi the success rate was not so high (45%), but in six of the 14 cases who were on the waiting list for a polypectomy the operation was found to be no longer necessary on reassessment by the surgeon. In eight cases polypectomy had been required every 6–12 months on up to five or six occasions, suggesting that BDA was having a substantial effect, but in three surgery was eventually required after 2 yr. The remainder benefitted moderately, but in nine no improvement was obtained.

Fourteen patients with PAR were treated continuously with BDA for 5 yr, 34 for 4 yr, 48 for 3 yr, 57 for 2 yr and 70 for 1 yr—a total of 534 patient-years of treatment. The duration of PAR before treatment, when a clear history was obtainable, showed that the success rate of 68% was the same whether the PAR had been present for 1 or 20 yr. In no case were any local side-effects observed, bacterial infection was not enhanced, and there was no evidence of *Candida albicans* infection. Occasional slight nasal bleeding was the only side-effect, as also noted by Mygind (1975).

Biopsy was carried out on the anterior end of the inferior turbinate in six patients with PAR who had inhaled eight metered doses of BDA 50 μg daily for 2.5–3.5 yr. Oedema and cellular infiltration were decreased, the basement membrane was thickened (as in the bronchi of asthmatics), the lamina propria was intact, and there was no loss of collagen. No evidence of damage to the mucosa was found. These studies are continuing, and will be reported elsewhere in detail.

Seasonal allergic rhinitis

We have already reported in detail on the use of BDA in 47 cases of SAR (Brown & Storey, 1974), but can now update our experience (Table 3).

There were two groups, one of 28 patients who had seasonal as well as PAR, and the other of 64 who had SAR only. Our previous comments regarding the importance of regular daily dosage, greater success in milder cases, and breakthrough on peaks of the pollen count are still valid. Most of the patients (80%) have now had summers free from hay fever for four successive years.

Table 1 BDA treatment of PAR (overall results in 223 cases)

	Total cases	*Failures*	*%*	*Moderate success*	*%*	*Obvious success*	*%*
PAR 'unmasked' by corticosteroid withdrawal	23	2	9	5	22	16	69
'Primary' nasal polypi	169	30	18	24	14	115	68
Nasal polypi	31	9	29	8	26	14	45
Totals	223	41	18	37	17	145	65

Discussion

Several other clinical trials, both double-blind and open, have established the efficacy of BDA in SAR and PAR (Gibson *et al.*, 1974; Hansen & Mygind, 1974; Smith *et al.*, 1975) and for nasal polypi (Mygind *et al.*, 1975). All the results have been very similar to ours, but we can now confirm by long-term observation in large numbers of patients that no side-effects have been found even when treatment has been given daily for up to 5 yr. In view of the report (Harris *et al.*, 1974) that up to 20 metered doses of intranasal BDA 50 μg daily did not suppress adrenal function, and was less likely to do so than bronchial inhalation, we did not consider that tests of pituitary and adrenal function were necessary.

Nasal biopsies have shown no evidence of mucosal damage, but further studies are required. The report by Mygind *et al.* (1976) that scanning electron microscopy revealed no change in surface structure after continuous treatment for a year with BDA is in accordance with our findings. It seems likely that the respiratory epithelium is regenerated much more easily and quickly than, for example, the skin, where side-effects due to corticosteroid are a common sequel of topical application for long periods.

Clinically, it was obvious in our series that the best response to treatment with BDA was in the milder cases. Many patients commented most favourably on the improvement in well-being after ceasing antihistamine therapy, which they had been taking for so long that they were no longer conscious of the depressive effects of these drugs. A surprising finding, just as in asthmatic patients (Brown *et al.*, 1977), was that an appreciable number could stop treatment without relapse. It would seem that if the nasal mucosa can be brought back to something approaching its normal state, clinical relapse often does not occur even if the allergic process is still present in a latent form.

The results with intranasal BDA closely resemble those reported by Brostoff & Czarny (1968, 1969) using betamethasone 17-valerate, a corticosteroid with similar properties, in PAR and SAR. In one report this corticosteroid aerosol was compared, using a 'double-dummy' technique, with intranasal sodium cromoglycate, and showed a clear advantage in favour of the corticosteroid preparation (Frankland & Walker, 1975).

It seems reasonable to conclude that BDA is of considerable therapeutic value in the long-term treatment of all types of nasal allergy, provided that the nasal airway is sufficiently patent to permit effective topical application to the nasal mucous membrane. There seem to be no contraindications to the use of BDA in PAR or SAR. The optimum daily dose can only be established individually, but often does not exceed four metered doses of 50 μg.

Table 2 BDA treatment of PAR (maintenance dosages)

Daily dosage	*Number of cases*	*%*
400 μg	104	47
200 μg	61	27
100 μg or less	18	8
Ceased after desensitization or avoidance of allergens	13	6
Stopped without relapse for no known reason	27	12

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Table 3 BDA treatment of SAR (results by number of seasons treated)

Type of case	*Total cases*	*Total seasons*	*Failed control*		*Good control*	
			Number	*%*	*Number*	*%*
Seasonal only	64	110	22	20	88	80
Seasonal and perennial	28	47	10	21	37	79
Totals	92	157	32	20	125	80

All patients had kept good records in previous years, had positive nasal tests for grass pollen or other summer allergens, and had no densitization therapy.

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