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Beclomethasone dipropionate aerosol in treatment of hay fever in children

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Prahl, P., Wilken-Jensen, K., and Mygind, N. (1975). *Archives of Disease in Childhood*, **50**, 875. **Beclomethasone dipropionate aerosol in treatment of hay fever in children.** Eighteen children suffering from hay fever were treated with intra-nasal beclomethasone dipropionate (400 μg/day) and an identical placebo aerosol in a double-blind cross-over trial. 17 of the children preferred the intranasal beclomethasone dipropionate, one had no preference, none preferred the placebo. The effect on the nasal symptoms was impressive. Symptom scores decreased, on average, to 12% and the number of antihistamine tablets taken to 18% of the pre-treatment amount. Some beneficial effect on eye symptoms was also discernible, possibly due to an indirect influence from the nasal mucosa via the nasolacrimal reflex. Adrenal function was not affected. It was concluded that 400 μg beclomethasone dipropionate given intranasally daily for some weeks is an effective and safe treatment for hay fever in children.

Glucocorticoids such as dexamethasone phosphate applied locally exert a pronounced effect in adult hay fever patients (Norman and Winkenwerder, 1965). A depot steroid injection gives similar results (Ganderton, Brostoff, and Frankland, 1969). However, since corticosteroids so administered affect adrenal function their use in children for such a minor disorder as hay fever is usually unjustifiable. Recently it has been shown that the local application of beclomethasone dipropionate is an efficient treatment of nasal symptoms in adults with hay fever (Mygind, 1973), perennial rhinitis (Hansen and Mygind, 1974; Gibson *et al.*, 1974), and nasal polyps (Mygind *et al.*, 1975). As the daily dose used in these trials has been shown not to suppress adrenal function we felt justified in using the drug intranasally in children suffering from hay fever

Patients and methods

Eighteen children with a history of hay fever symptoms for at least two seasons entered the trial. Positive sensitivity in all cases to Timothy grass pollen was shown beforehand by a positive skin prick test and by nasal challenge. 4 patients were also allergic to birch or mugwort pollen. None of the children suffered from either asthma or perennial rhinitis and none had at any time received hyposensitization treatment. 13 patients were boys and 5 were girls. Their ages ranged from 8 to 16 years (mean 12 years). The duration of symptoms ranged from 2 to 10 seasons with a mean of 5.

The nasal aerosol spray used was the commercially available preparation Beconase, which delivers 50 μg beclomethasone dipropionate with each spray. The dose was one spray into each nostril four times a day. One nasal aerosol spray was given to every patient for each 2-week period. By assessing the number of sprays contained in 10 aerosols the mean was found to be 231 with a range of 212 to 237. The children and their parents were carefully instructed in the correct use of the aerosol emphasizing that only the prescribed dose should be used each day. One discharge of the aerosol into the air was allowed to ensure that it functioned correctly.

The children were allocated at random in a double-blind fashion to two groups, one of which initially received the active drug and the other the placebo. After 2 weeks the treatments were crossed over for a further 2 weeks. The trial started on 6 June, the onset of the grass hay fever season in Denmark. The patients were given a supply of antihistamine tablets (dexchlorpheniramine maleate 2 mg) to be taken if required and eye drops (diphenhydramine methyl bromide) for eye symptoms. They were instructed not to use eye drops and antihistamine tablets concurrently. A note of drug usage was kept and patients completed daily diary cards in which the occurrence of nasal blockage, nasal

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secretion, sneezing, and itching of the eyes was evaluated on a semiquantitative basis on a scale of 0 to 3 (0=nil, 1=mild, 2=moderate, 3=severe). After the trial the patients were asked to state which of the two aerosol nasal sprays they preferred.

Urinary 17-oxogenic steroid concentrations were estimated in 12 of the children at the end of treatment with both active drug and placebo. Beclomethasone dipropionate has been shown to exert a negligible effect on urinary 17-oxogenic steroid levels, because only a small proportion of the drug is excreted as polar metabolites which would be determined as 17-oxogenic steroids (Martin, Harrison, and Tanner, 1975).

Results

Because the weather was cold and rainy during the trial the hay fever symptoms were mild. Nevertheless each patient had enough symptoms for a reliable evaluation of the cross-over treatments to be made.

Of the 18 children, 17 preferred the active drug, none preferred the placebo, and one had no preference. The symptom scores from the diary cards showed that the active aerosol nasal spray had had a pronounced beneficial effect on blocked nose, nasal secretion, and sneezing. The mean total daily scores for nasal and eye symptoms for both 2-week periods are shown in Table I. During the second week of treatment the total of nasal scores when the patients were receiving active drug was only 12% of those when they were using the placebo. The corresponding figure for the eye scores was 53%.

The total number of antihistamine tablets taken by patients using active drug during the last week of the trial was 26 compared with 145 taken by those using placebo—a difference of 82%. This difference is highly significant ($P<0\cdot0001$). The corresponding figures for the use of eye drops were 41 and 104, a difference of 61%, which does not, however, reach the level of significance ($P>0\cdot05$).

Beclomethasone dipropionate did not act immediately but, as may be seen from the Fig. exerted a significant effect on the second day. The active drug was effective for some days after it had been discontinued, thus protecting the children from their usual early morning sneezing attacks. The only side effect noted was sneezing after using the aerosol. This was reported by 5 children when they used both the active and placebo aerosols. In no case was treatment stopped because of it. Beclomethasone dipropionate administered intranasally may therefore be said to be well tolerated by children.

The mean urinary 17-oxogenic steroid level was 23·9% lower during the active drug treatment period than during the placebo period (Table II). However, this difference is not significant ($P>0\cdot1$).

Assessment of the number of sprays left in the aerosols showed that 3 children had probably taken active drug and placebo in excess of the prescribed dose (Table III). The calculated daily doses of beclomethasone dipropionate for these children were 735, 825, and 825 μg, respectively. 6 children had taken a daily dose ranging from 155 to 360 μg. These figures are the maximum since any discharges of the aerosol into the air are not included in the

TABLE I

Total daily symptom scores for the second week of each 2-week period of treatment

Case no.	Nasal symptoms		Eye symptoms	
	Placebo	Beclomethasone dipropionate	Placebo	Beclomethasone dipropionate
1	6	0	2	7
3	22	0	5	2
4	31	0	8	0
5	16	1	7	0
6	14	4	2	0
7	42	21	14	8
8	12	0	0	6
9	32	0	9	4
10	27	2	4	5
11	29	0	16	0
12	35	0	13	10
13	39	18	19	4
14	36	2	3	8
15	60	2	20	7
16	1	0	1	2
17	36	5	3	3
18	17	0	0	1

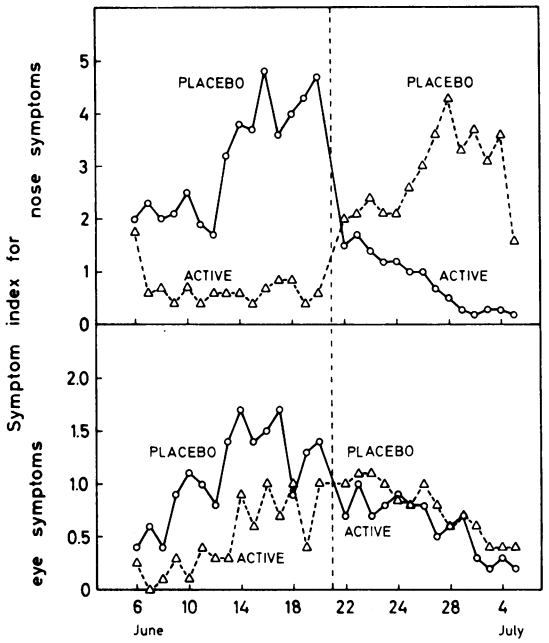

FIG.—*Average daily symptom scores from 18 diary cards.*

calculations. No significant correlation between the calculated doses, the 17-oxogenic steroid level, and the reduction in symptom scores was found. However, the 3 patients with the smallest reduction in nasal symptom scores were in the group taking too low a dose of the drug.

TABLE II

Urinary excretion of 17-oxogenic steroids in 12 children at the end of treatment periods

Case no.	Placebo aerosol (μmol/24 h)	Beclomethasone dipropionate aerosol (μmol/24 h)
1	22	17
3	8	8
4	18	8
5	17	18
6	14	7
7	16	13
10	9	4
12	11	12
13	15	14
14	21	14
17	30	15
18	14	19
Mean	16·3	12·4

Discussion

The effect of the treatment in children with hay fever was even more pronounced than in adults (Mygind, 1973). As the children's nasal symptoms were strikingly diminished and their use of antihistamine tablets was also greatly reduced we found intranasal beclomethasone dipropionate to be the most effective drug we have used for treating

TABLE III

Correlation between calculated daily dose of beclomethasone dipropionate, effect on nasal symptoms, and urinary levels of 17-oxogenic steroids

Case no.	Calculated maximum daily dose of beclomethasone dipropionate (μg)	Nasal symptom scores during active treatment in percentage of scores during placebo treatment	Urinary levels of 17-oxogenic steroids during active treatment in percentage of levels during placebo treatment
1	825	0	77
6	825	29	50
16	735	0	—
15	570	3	—
18	555	0	136
12	520	0	109
10	505	7	44
11	505	0	—
14	470	6	67
17	445	14	50
8	420	0	—
7	360	50	81
5	340	6	106
3	330	0	—
4	280	0	44
2	255	40	—
13	155	50	93
Mean	476	12·1	77·9

hay fever in children. No side effects of any significance were noted. The apparently beneficial effect of intranasal beclomethasone dipropionate on the eye symptoms, though not achieving statistical significance, is interesting and could be explained either by a nasolacrimal reflex or by the difficulty children may have in distinguishing between the different symptoms. The intranasal steroid had no effect on eye symptoms in adult hay fever patients (Mygind, 1973).

In this trial the drug was shown to have local rather than systemic activity, as indicated by the lack of significant fall in the urinary excretion of 17-oxogenic steroids. This correlates well with our findings in adult hay fever patients when treated intranasally with similar doses (Mygind, 1973). Many trials have shown that a daily dose of 300 to 400 μg does not suppress adrenal function, as indicated by plasma cortisol estimation, in adult asthmatics (Lal *et al.*, 1972; Chatterjee *et al.*, 1972–1973, Maberly, Gibson, and Butler, 1973; Buisseret, 1973). and the same applies to children (Brown and Storey, 1973; Wilken-Jensen, 1975).

The daily dose used in this trial was possibly too high for some children since nasal symptoms were reduced by 90% in many of them and far fewer antihistamine tablets were taken. A dose-response investigation has indicated, however, that the daily starting dose should be 400 μg in all hay fever patients (Andersen, Halberg, and Mygind, 1975). Gibson *et al.* (1974) have shown that intranasal beclomethasone dipropionate 200 μg daily over a 3-week period improved the symptoms of adults suffering from perennial rhinitis without any evidence of adrenal suppression. Godfrey and König (1974) showed that inhaled beclomethasone dipropionate at doses varying from 100 to 600 μg/day during their trials and for a maximum of 8 months' follow-up showed no evidence of suppressing either adrenal function or growth. Harris *et al.* (1974) have shown that when the drug is both inhaled and taken intranasally there is no clear evidence of adrenal suppression when the combined dose is less than 5 mg/day. It seems, therefore, that in severe cases of perennial rhinitis in children a trial of the drug is justified. In children with hay fever 400 μg/day beclomethasone dipropionate intranasally provides an efficient and safe treatment. The resulting reduction in antihistamine drug dosage is advantageous as many children suffer from their soporific side effectis.

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