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Inhaled Budesonide Aerosols in Treatment of Childhood Asthma

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SUMMARY **Twenty-six children with chronic bronchial asthma, 19 boys and 7 girls, aged between 6 and 16 years with duration of asthma ranging from 1-12 years, were studied by a control, oral prednisolone 5 mg twice a day and inhaled budesonide 200 μg twice daily, each for 3 weeks. The clinical efficacy assessed daily by day and night symptom scores of cough, wheeze, sleep disturbance, limitation of activity, symptomatic inhaled terbutaline usage, daily morning and afternoon Peak Expiratory Flow Rate (PEFR), and weekly PEFR and Forced Expiratory Volume in 1 second (FEV_1) in percent of predict, showed statistically significant improvement during the inhaled budesonide aerosol and oral prednisolone treatment periods in comparison with the control. No side effect was observed during any study periods.**

Inhalation of topical corticosteroid for the treatment of bronchial asthma in adults [1-5] and in children [6-8] has been shown to be both effective and safe. It's therapeutic benefit is as good as orally administered corticosteroids with less or negligible undesirable severe adverse effect, [5-8] particularly following long-term administration. However, despite the obvious clinical advantages the search for better and longer-lasting topical steroids continues. Budesonide, [9-11] a non-halogenated glucocorticoid with high topical anti-inflammatory potency, low bio-availability, and which is less metabolized in the lung, represents a new generation of inhaled steroids. It is the objective of this study to evaluate the clinical efficacy of this drug in Thai chronic asthmatic children.

MATERIALS AND METHODS

Twenty-six Thai asthmatic children, 19 boys and 7 girls, age 6-16 years, (10.5 ± 2.85, mean $\pm$ SD) with duration of bronchial asthma 1-12 years (5.88 ± 3.17), were selected from the patients attending the Pediatric Allergy Clinic, Ramathibodi Hospital, Bangkok. Bronchial asthma was diagnosed on the basis of clinical history of recurrent wheezing and evidence of reversible bronchial obstruction on physical examination through the use of bronchodilator drugs. Since spirometry is an important objective measurement of airway reversibility, all patients selected for this study (except patient No. 23 in Table 1), demonstrated at least a 20% reversibility in Forced Expiratory Volume in one second (FEV_1) with 0.25 mg terbutaline inhalation.

All patients had moderate bronchial asthma defined as requiring continuous daily oral bronchodilator drugs (β_2 agonist and theophylline) for at least the previous 6 months. The control of their symptoms of bronchial asthma occasionally needed addition of oral steroids. Demographic data are shown in Table 1.

The study was begun with a three week run-in period during which existing therapy was continued unchanged. This was followed by three weeks each of prednisolone 5 mg twice a day and inhaled budesonide 200 μg twice daily. Throughout the study periods, the patients were asked to keep daily records of morning and evening Peak Expiratory Flow Rate (PEFR) done at home, using

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Table 1. Demographic data of the patients.

No.	Age (yr)	Sex	Weight (kg)	Height (cm)	Duration of Asthma (yr)	Beta–2 Reversibility (% change in FEV_1)
1	13	M	37.5	136	10	33.3
2	9	M	42.0	137	2	26.5
3	7	F	20.0	121	2	46.0
4	13	M	36.7	150	7	47.8
5	13	F	48.0	156	1	37.2
6	8	M	23.0	122	3	25.0
7	7	M	18.4	115	1	26.6
8	10	M	24.5	131	9	73.3
9	9	M	33.0	130	4	26.1
10	13	F	41.5	145	7	35.7
11	9	M	36.5	133	5	76.0
12	6	M	20.0	116	4	22.0
13	12	F	27.5	143	2	29.9
14	12	M	33.5	146	10	23.5
15	6	F	17.0	115	3	110.0
16	16	F	51.0	154	12	67.7
17	10	M	32.5	145	9	80.0
18	12	M	31.7	145	7	30.4
19	10	M	30.0	137	4	54.5
20	9	M	22.5	128	8	33.3
21	15	M	52.0	160	6	20.3
22	15	F	55.0	162	7	27.2
23	13	M	42.5	157	11	13.3
24	10	M	27.5	140	8	25.0
25	10	M	29.2	127	6	31.0
26	6	M	19.0	115	5	69.2
$\bar{X} \pm 2$ SD	10.5 ± 5.7	–	32.8 ± 21.7	137.2 ± 28.7	5.9 ± 6.3	42.0 ± 46.4

a mini Wright peak flow meter. The highest of the three PEFR measurements was used for analysis. Daily symptom scores were recorded, using a modified scoring system previously developed by the Drug Committee of the American Academy of Allergy.[12] The scale ranged from 0 for symptom free, to 3 for the most severe for limitation of activity, cough, wheeze or breathlessness or chest tightness and sleep disturbance. Symptomatic terbutaline inhaler usage was also recorded on a daily basis. Pulmonary function measurements using electronic spirometer (Microspiro HI-298, Chest Corporation, Japan) were performed weekly during the clinic visits throughout the three periods of study. Oral and throat examinations for candidiasis were evaluated weekly before, during, and at the end of each study period.

Statistical analysis of the data in the study was made by using the paired *t* test.

All parents were informed of the nature of the study and written informed consents were obtained before initiation into the study.

RESULTS

The efficacy of treatments assessed by symptom scores during three weeks each of inhaled budesonide, oral prednisolone and control period as weekly mean symptom scores are shown in Fig. 1. The budesonide treatment produced significant improvement in asthma response indices of cough ($P < 0.05$), wheeze ($P < 0.001$) and sleep disturbance ($P < 0.01$) but non-significant alteration of the limitation of activity in comparison with the control. Improvement was also observed during the oral prednisolone treatment period in the same parameters with statistical significance ($P < 0.05$, < 0.01 and < 0.01, respectively). No significant difference between the period of oral prednisolone and inhaled budesonide was observed.

Symptomatic terbutaline inhaler usages with $\bar{X} \pm SD$ of 5.2 ± 7.1, 1.42 ± 2.6 and 0.92 ± 1.7 during control, oral prednisolone and inhaled budesonide periods, respectively, were observed with statistical significance between the control and the budesonide period ($P < 0.01$) and the control and the oral prednisolone period ($P < 0.025$) but non-significant differences between the oral prednisolone and the budesonide period.

Mean daily PEFR in AM and

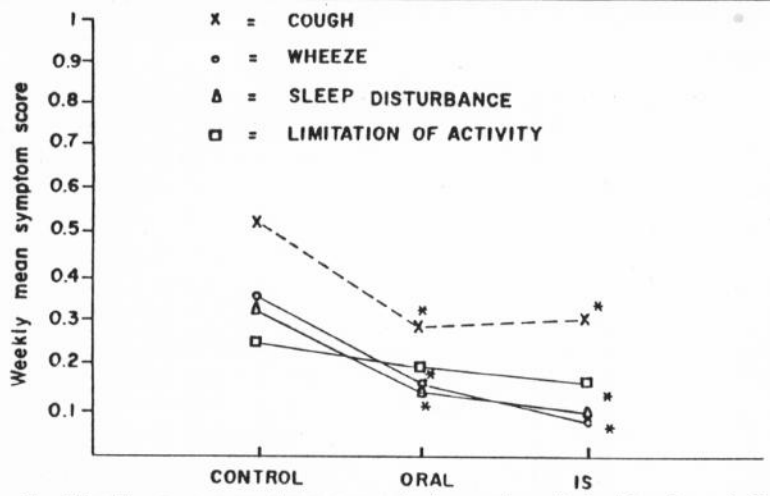

Fig. 1 Weekly mean symptom scores during each period of treatment. Oral = oral prednisolone; IS = inhaled budesonide. Points marked (*) show statistically significant differences compared with the control.

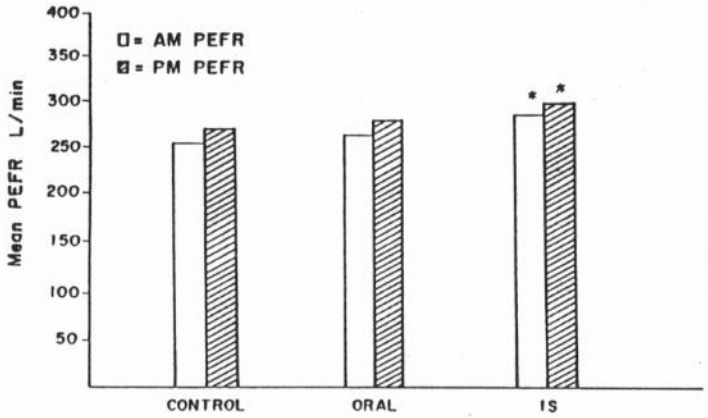

Fig. 2 Mean AM and PM Peak Expiratory Flow Rates (PEFR) during each period of treatment. Oral = oral prednisolone; IS = inhaled budesonide. Marked values (*) show statistically significant differences compared to control and oral prednisolone periods.

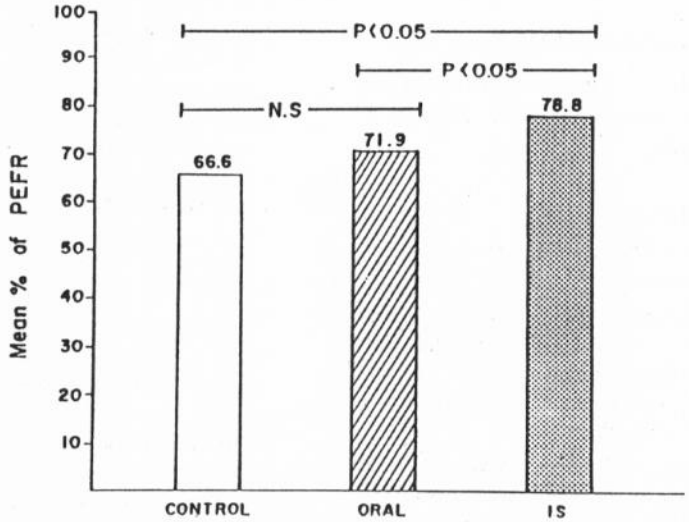

Fig. 3 Mean PEFR in percent during each period of treatment. Oral = oral prednisolone; IS = inhaled budesonide.

PM during each treatment period are shown in Fig. 2, with statistically significant differences between the control and the inhaled budesonide period ($P < 0.001$ for AM, $P < 0.005$ for PM), the oral prednisolone and the inhaled budesonide ($P < 0.005$ for both AM and PM) and non-significant differences between the control and the oral prednisolone period.

Mean PEFR in percent of predict at the clinic visits during each treatment period are shown in Fig. 3. There were statistically significant differences between the control and the inhaled budesonide period ($P < 0.05$) and the oral prednisolone and the inhaled budesonide period ($P < 0.05$) but non-significant differences between the control and the oral prednisolone period.

Mean FEV_1 in percent of predict at the clinic visit during each treat ment period are shown in Fig. 4. Statistically significant differences were found between the control and the oral prednisolone period ($P < 0.05$), the control and the inhaled budesonide period ($P < 0.0005$) and the oral prednisolone and the inhaled budesonide period ($P < 0.025$).

No oral or pharyngeal thrush was observed in any period of the study.

DISCUSSION

Inhaled budesonide in this study has an additive effect to bronchodilators in the control of bronchial asthma, in accord with the results of several other clinical studies in adults [13-16] and children. [17,18] Statistically significant improvement of asthmatic symptoms assessed by symptom scores, symptomatic terbutaline inhaler usages, weekly pulmonary function, and daily AM and PM PEFR were observed.

The inhaled budesonide when administered in a higher dose of 200 μg twice daily in this study in comparison to our previous study [19]

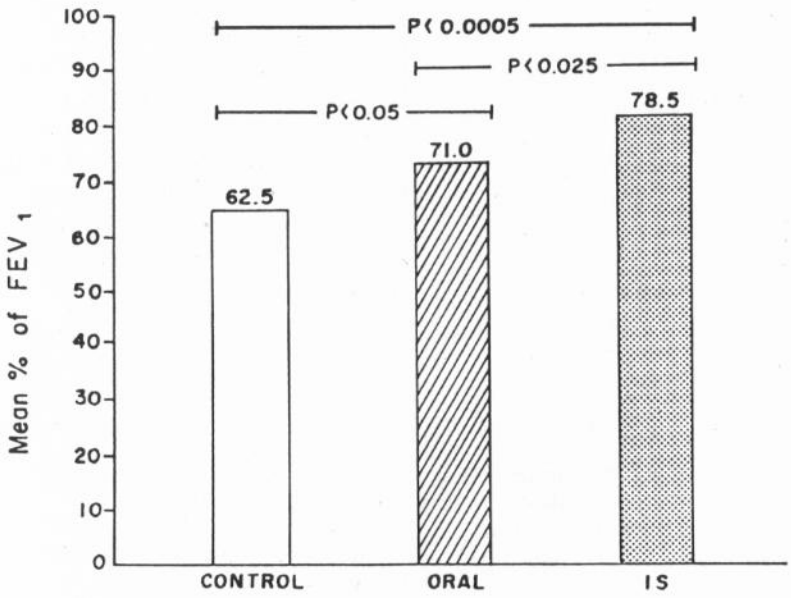

Fig. 4 Mean Forced Expiratory Volume in 1 min (FEV_1) in percent during each treatment period. Oral = oral prednisolone; IS = inhaled budesonide.

of 100 μg twice a day, resulted in a more favorable out-come with statistical significance in the parameters measured. This might be explained by the effects of the potent local activity of this drug which has been shown to suppress the underlying airway inflammation resulting from several kinds of allergic mediators especially ones that have a late response reaction.

Pediatricians concerned with treating childhood asthma are naturally apprehensive about giving steroids to them because growth and adrenal suppression have been observed with systemic or daily oral steroids.[20-22] The topical administration of budesonide has distinct advantages over the oral intake steroid, especially the long lasting local action and a minimum of systemic side effects.[10,23] Doses up to 800 μg have no suppression of normal plasma cortisol levels in adults.[10]

This study has shown that inhaled budesonide was highly effective in treatment of bronchial asthma in children and no serious side effects were noted. If this initial response is maintained and more studies of systemic side effects in long term administration in children are confirmed, this drug may well become the treatment of choice for asthmatic children requiring steroids and in those children who do not respond to conventional bronchodilator therapy.

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