

Intranasal Budesonide for the Treatment of Perennial Rhinitis in Thai Patients

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Topical glucocortico-steroids have proved beneficial in the treatment of seasonal allergic rhinitis as well as perennial rhinitis.¹ Most antihistamines are also effective but their use has been limited due to their unwanted sedative effects. Recently, a new potent non-halogenated corticosteroid, budesonide, has been developed for topical administration.² It possesses a greater anti-inflammatory activity than beclomethasone dipropionate and has been shown to exert minimal systemic effects.³ Several studies have demonstrated that intranasal administration of budesonide is effective and well-tolerated in patients with allergic and non-allergic rhinitis.⁴⁻⁶ The long-term safety of intranasal budesonide has recently been documented in a 5.5 year follow-up study.⁷

The budesonide nasal spray (Rhinocort®, Astra, Sweden) is now available in Asia but there has been little experience of this preparation in Asian patients. It was therefore the aim of this study to assess the efficacy and tolerability of budesonide in Thai patients suffering from perennial rhinitis.

SUMMARY The efficacy and tolerability of a new intranasal glucocorticosteroid, budesonide, was evaluated in 28 Thai adult patients with perennial rhinitis. After one week pre-treatment observation period, the nasal spray was given as two puffs into each nostril twice daily (400 µg/day) for four weeks. The severity of all nasal symptoms decreased significantly after 1 week treatment reaching a minimal level after 2 weeks. The amounts of antihistamine tablets taken by the patients were also significantly reduced during the treatment with budesonide. Three patients reported adverse effects which were mild and easily tolerated. Morning plasma cortisol levels measured before and after four-week treatment in 15 patients revealed no significant changes. This study suggests that intranasal budesonide is an effective and well-tolerated treatment for perennial rhinitis.

PATIENTS AND METHODS

Patients attending the ENT Allergy clinic of the Siriraj Hospital, Bangkok Metropolis were selected for the study. Eligible patients were those aged 16 and above and who had had typical symptoms of perennial rhinitis through at least 2 years. At entry, all patients should have at least 2 of the most common symptoms, namely, blocked nose, runny nose, itching nose and sneezing. Patients were excluded if they were pregnant or lactating or had received corticosteroid therapy during the preceding 4 weeks. Patients were also excluded if they had received hyposensitisation treatment in the preceding 1 year or had respiratory tract infection during the preceding 4 weeks. The study was conducted

according to the declaration of Helsinki and informed consent was obtained from all patients.

The study was of an open non-comparative design. All patients entered a 1-week run-in period during which they were provided with chlorpheniramine maleate 4 mg tablets with instructions to take the tablets only when symptoms persist and treatment was necessary. Patients were asked to record on a

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diary card the severity of symptoms and the use of antihistamine tablets. The severity of the symptoms were rated on a four-point scale ranging from absent (0) to severe (3) for runny nose, blocked nose, itching nose and sneezing, as well as itching and runny eyes. After the run-in period, all patients were given budesonide nasal spray for the subsequent 4 weeks. The spray was given as two puffs into each nostril morning and evening (400 µg/day), each actuation delivered 50 µg of budesonide. All patients returned to the clinic after 2 and 4 weeks of treatment with budesonide. At each follow-up visit, nasal symptoms and signs were recorded, any adverse events were noted and patients were asked to make a global assessment of the overall efficacy of the treatment received using a rating scale of 0 to 3 (0 = ineffective, 1 = slightly effective, 2 = moderately effective and 3 = extremely effective). Throughout the study, the patients kept daily records of nasal and eye symptoms and the number of antihistamine tablets taken. Patients were asked to return the spray and unused antihistamine tablets to the clinic; the canisters were weighed and tablets were counted to assess the patient compliance.

Before initiation of the treatment with budesonide, intracutaneous tests were performed on each patient. A standard panel of 12 common allergen extracts including house dust, house-dust mite, pollens, molds and household insects were used and any positive reactions recorded. Blood samples were also collected in the morning (08.00-09.00 hr) in 15 patients for determination of cortisol before and after treatment with budesonide. Serum cortisol concentrations were determined using a direct RIA method described by Ruder.⁸ The cortisol RIA kit (Magic®) used in the study was available from Ciba Corning Diagnostics, Hong Kong.

Nasal scraping for basophil

count was performed before and after the treatment with budesonide in some patients.

RESULTS

Twenty nine patients were included in the study. One patient defaulted the study and 28 patients (9 males and 19 females), aged 16-52 years (mean 31 years) completed the study and provided diary card data for analysis. All but three patients had positive results to the intracutaneous tests with various allergens.

The mean scores for nasal symptoms observed by the doctor during clinic visits are summarised in Table 1. Significant reduction in all nasal symptoms was observed at 2 weeks after the budesonide treatment as compared to the baseline observations made after the run-in period. A further reduction in severity of symptoms although statistically insignificant was seen after a further treatment period of 2 weeks. At the final clinic visit 12 of the 28 patients were symptom-free. Eight patients complained of eye symptoms (runny and/or sore eyes) before the treatment with budesonide. All but one patient were symptom-free or had their eye symptoms reduced after the budesonide treatment.

The mean daily scores were calculated for each symptom over each week and the results are shown in Fig. 1. For all the nasal symptoms, the severity decreased to a minimal

level in the second week of the budesonide treatment; the effect was sustained for the rest of the study period. The reduction in symptoms was shown to be statistically significant ($P < 0.005$) as compared to the run-in period. In the diary cards, thirteen patients registered runny eyes and eight with sore eyes. The mean daily scores of the eye symptoms for these patients over each week are shown in Fig 2. A slight reduction in the severity of the eye symptoms was observed but the severity of symptoms was not statistically different throughout the study.

The mean daily usage of antihistamine during the run-in was 0.52 tablet per patient and this was significantly reduced to 0.15 tablet during the budesonide treatment period ($P < 0.01$).

The global assessment of the efficacy of the budesonide treatment is shown in Table 2. All patients classified the treatment effective. Sixteen (57%) of them claimed that the treatment was extremely effective at the end of the 4 week treatment period.

The plasma cortisol levels were determined in 15 patients. The mean levels (\pm SEM) before and after the budesonide treatment were 8.52 (± 0.67) µg/dl and 7.44 (± 0.50) µg/dl respectively, which were not statistically different.

Among the patients who had undergone nasal scraping before

Table 1. Mean daily score (\pm SEM) of nasal symptoms recorded at clinic visits

Symptoms	Mean Symptom Score (\pm SEM)		
	Baseline	2 week follow-up	4 week follow-up
Blocked nose	1.21 \pm 0.16	0.57 \pm 0.14*	0.36 \pm 0.12**
Runny nose	1.43 \pm 0.19	0.64 \pm 0.15*	0.57 \pm 0.14*
Itching nose	1.11 \pm 0.16	0.43 \pm 0.11**	0.29 \pm 0.08**
Sneezing	1.32 \pm 0.18	0.39 \pm 0.13**	0.29 \pm 0.08**

* $P < 0.01$, ** $P < 0.001$ vs baseline scores

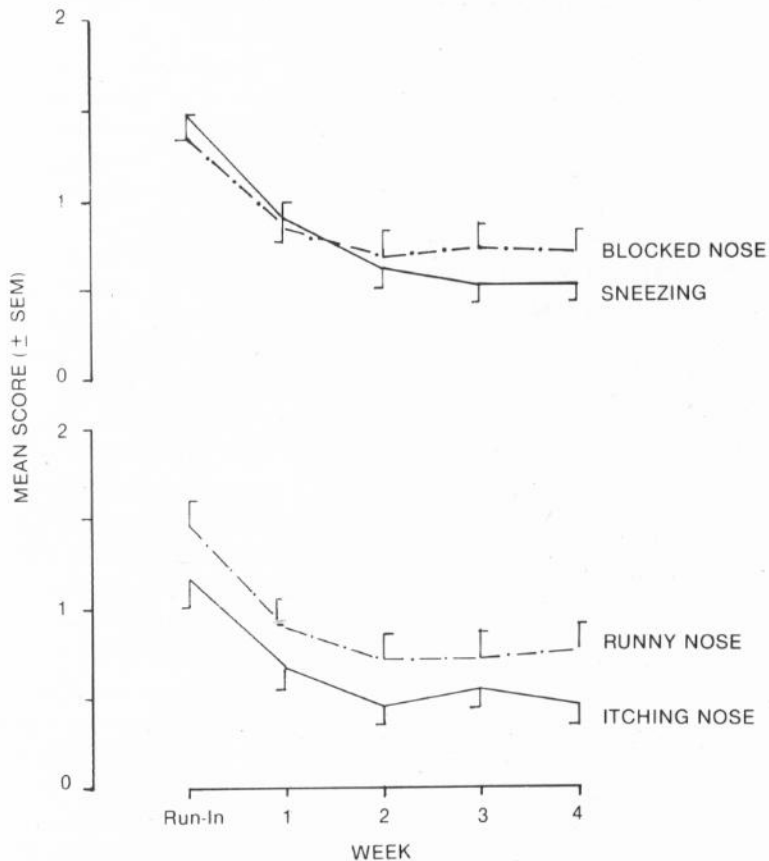


Fig. 1 Mean daily scores for nasal symptoms during run-in and treatment periods.

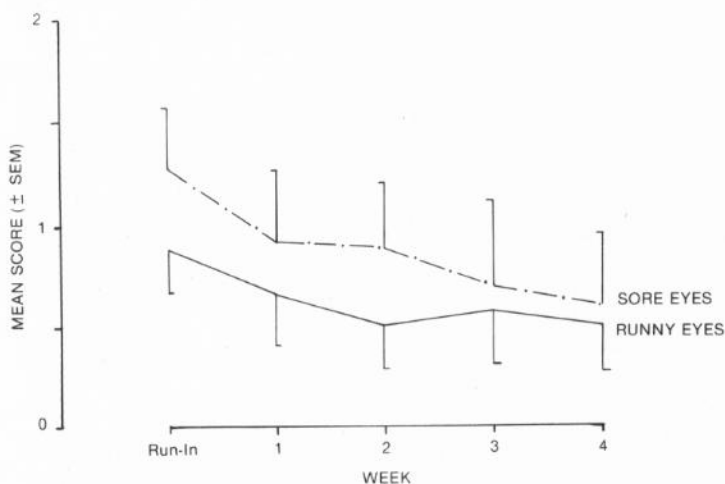


Fig. 2 Mean daily scores for eye symptoms during run-in and treatment periods.

and after treatment, 7 patients had basophils in their nasal scrapings before the budesonide treatment. The number of basophils decreased in 6 patients after treatment. This finding, although observed in a small group of patients, was in accordance with those reported by Okuda⁹ in patients after using beclomethasone nasal spray.

The efficacy of budesonide in the 3 non-allergic patients was judged by both the patient and by the attending physician as moderately effective (1 patient) and extremely effective (2 patients).

Adverse events were reported in three patients. One patient experienced dizziness for a few minutes after the first dose of the spray. Another patient reported a slight burning sensation after each administration for 4 days. One patient had slight burning sensation and a few sneezes after every puff. All these side effects were mild and easily tolerated.

DISCUSSION

The development of topical glucocortico-steroids is considered a great progress in the pharmacological intervention of allergic respiratory diseases. They offer excellent control of nasal symptoms in perennial rhinitis with negligible side effects. In Thailand, the first topical glucocortico-steroid which was shown to be effective and well-tolerated in chronic rhinitis patients was beclomethasone dipropionate (BDP).¹⁰ In a more recent study, another steroid, flunisolide, was compared with BDP in Thai patients with perennial allergic rhinitis. In that study, most patients preferred BDP,¹¹ possibly due to its pressurised aerosol form as compared to the pump spray of flunisolide. BDP remained the only intranasal corticosteroid available in Thailand until recently when budesonide was introduced.

Table 2. Global assessment of efficacy of the budesonide treatment by the patients

Control of Symptoms	Number of patients (%)	
	2 weeks	4 weeks
Ineffective	0	0
Slightly effective	3 (10.7%)	2 (7.1%)
Moderately effective	14 (50.0%)	10 (35.7%)
Extremely effective	11 (39.3%)	16 (57.1%)

The results of this study showed good efficacy as well as tolerability of budesonide in the treatment of perennial rhinitis in Thai patients. Another interesting finding was that budesonide also reduced the eye symptoms in our patients. The effect of budesonide on the eye symptoms was not observed by Steensen and Lindqvist.⁵ A possible explanation of the different results may be that their subjects were grass pollen-induced hay fever patients who might have more severe eye symptoms than those included in this study. The exact mechanism by which intranasal budesonide would reduce eye symptoms is however not clear.

In studies performed elsewhere, budesonide has been compared with BDP in seasonal allergic rhinitis^{12,13} and perennial rhinitis.^{14,15} These studies have shown that both budesonide and BDP had beneficial therapeutic effect but budesonide yielded higher efficacy. In a comparative study with an antihistamine tablet commonly prescribed for symptomatic relief in allergic patients, dexchlorpheniramine maleate sustained-release tablet, the superiority of budesonide to relief nasal blockage was demonstrated, and furthermore, more patients preferred the topical treatment.¹⁶ Another advantage of budesonide over the older aerosol preparations such as BDP is in its convenient dosage. Unlike BDP which is given 4 times daily, budesonide is effective when given twice

daily, which will ensure good compliance.

A recent 12-month study on the safety and efficacy of budesonide, revealed three interesting findings.¹⁷ Firstly, budesonide was shown to be effective in non-allergic as well as allergic perennial rhinitis patients. It is worthy of note that in our study although only 3 patients were classified as non-allergic, all three patients responded very well to the budesonide treatment. The second finding was that there was no influence of budesonide on the hypothalamic pituitary adrenal axis even after such a long term treatment. Thirdly, no tachyphylaxis was observed in the patients.

The satisfactory result from this study led us to conclude that budesonide intranasal aerosol is a safe and effective alternative for the treatment of perennial rhinitis.

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