Clinical Assessment of Levocetirizine and Budesonide in Treatment of Persistent Allergic Rhinitis Regarding to Symptom Severity

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Objective: *To compare effectiveness of levocetirizine and budesonide in treatment of persistent allergic rhinitis (PER) in patients with high and low total symptom scores (TSS).*
Material and Method: *Randomized, parallel-group study. Patients with PER were randomized to receive levocetirizine 5 mg (n = 50) or budesonide 256 μg (n = 50) daily for 4 week and were followed-up for another 4 weeks post-treatment. TSS combining itching, sneezing, rhinorrhea, daytime and nighttime nasal congestion was recorded daily during and after treatment for an entire period of 8 weeks. Efficacy variables included area under curves depicting reduction and increase in TSSs over time relative to baselines and time to response and symptom relapses.*
Results: *Symptoms were categorized as high and low using a median TSS of 8 as cutoff. Levocetirizine was as effective in control of high and low symptoms except for time to achieve maximum effect (2 days versus 1 week, respectively, p = 0.002) but was more effective in preventing relapses of high symptoms (p = 0.001). Budesonide was more effective against high than low symptoms (p < 0.001) but showed no difference in preventing relapses. Typical response rate of levocetirizine and budesonide were demonstrated in treatment of high symptoms. Levocetirizine achieved its full effectiveness in 2 days while budesonide required 2 weeks. Budesonide at full effect (after 2 weeks) was superior to levocetirizine (p = 0.004) but comparable for the entire treatment of 4 weeks (p =.059) and was inferior to in preventing relapses (p = 0.001). No such difference could be observed between these drugs in control of low symptoms.*
Conclusion: *The effectiveness of the drug treatment in the present study is dependent of symptom severity. Levocetirizine bases on its rate of response and relapse was superior to budesonide in treatment of the high symptom group and is comparable in the low symptom group.*

Keywords: *Persistent allergic rhinitis, Symptom severity, Levocetirizine, Budesonide*

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Allergic rhinitis (AR) is a common inflammatory condition of the nasal mucosa affecting 10-40% of the world's population[1]. In Thailand, AR continues to rise as evidenced by the increase in AR prevalence in children at a rate of 37.9% surveyed in 1995 up to 50.6% in 2001[2]. The disease mainly affects atopic individuals who have inherited genetic predispositions to synthesize specific immunoglobulin E (IgE) to environmental allergens[3]. Allergic rhinitis, which is characterized by symptoms of sneezing, itching, rhinorrhea, and nasal congestion, is not a life-threatening condition but the cumulative symptoms can impair daily activities, social functions, and disturb sleep patterns[2,4]. House dust mites, house dust, and cockroaches are the most common allergens that are present all year round and have been implicated the etiology of PER in Thailand[2].

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Antihistamines and intranasal corticosteroids are effective medications for allergic rhinitis. Oral H_1-antihistamines can rapidly control sneezing, itching, rhinorrhea but are less effective against nasal congestion. Intranasal corticosteroids are the most effective medications for allergic rhinitis particularly when nasal obstruction predominates. Nevertheless, the drugs are slow to act and require up to 2 weeks for maximum efficacy[5]. This influences patients' perception of treatment efficiency and may lead to discontinuation of the treatment and switch medication[5]. PER is a condition that requires long-term treatment for disease control. Medication with rapid-onset and long-lasting symptom control without side effect is the high expectation of patients from the treatment[5]. Rinne et al[6] conducted a study on the effect of budesonide compared to cetirizine in a 1-year treatment of perennial allergic rhinitis. Budesonide was observed to be superior to cetirizine in relieving nasal symptoms, improving nasal peak expiratory flow and preventing symptom relapses after treatment discontinuation. The median relapse time of 62 days and 20 days were determined for budesonide and cetirizine respectively. The finding suggests that the periodic treatment may be a promising treatment strategy for perennial rhinitis[6].

Levocetirizine, an active R-enantiomer of cetirizine, has twice the affinity for H_1-histamine receptor compared with cetirizine[7]. In addition to its antihistamine/anti-allergic properties, levocetirizine possesses anti-inflammatory effects[7]. Clinical efficacy of levocetirizine has been previously demonstrated in short-term treatments of seasonal (2-week study)[8] and perennial allergic rhinitis (6-week study)[9] and currently in the long-term treatment (6-months) of PER[10] Nasal congestion, a difficult-to-treat symptom, is well controlled by levocetirizine compared with placebo[9,10]. The effectiveness of levocetirizine in relief of nasal congestion is due to its anti-inflammatory effects[7]. Despite the effectiveness of levocetirizine in controlling symptoms of allergic rhinitis, no study to date has compared the clinical efficacy of levocetirizine with budesonide. Presently, guidelines in management of PER have been suggested on the basis of symptom severity[11], that is antihistamines are medications of choice for mild persistent rhinitis while intranasal corticosteroids for moderate to severe persistent rhinitis[11]. The aim of the present study was to compare the clinical efficacy of levocetirizine with budesonide in a 4-week treatment of PER in patients with high and low symptoms.

Material and Method

Study design

This was a 4-week randomized, parallel-group study in which patients received levocetirizine tablets or budesonide nasal sprays. The study conducted at the Department of Otolaryngology, Ramathibodi Hospital was divided into three phases: screening (-3 to 0 day), treatment (1-28 days) and follow-up (29-56 days) phases (Fig. 1). The present study protocol was approved by Ramathibodi Hospital ethic committee. All patients gave written informed consent to participate in the present study.

Patients and study sequence

One hundred patients were enrolled the present study. The inclusion criteria were patients $\geq$ 18 years of age with a documented history of allergic rhinitis of more than 1 year. Patients had persistent allergic symptoms[11], *i.e.* rhinitis lasting $\geq$ 4 days per week for $\geq$ 4 consecutive weeks per year, and were sensitized to house dust mites, cockroaches, pollens, molds, etc confirmed by skin prick test. The exclusion criteria were allergic bronchial asthma, non-allergic rhinitis (infection or drug-induced, etc), structural abnormality of the nose (deviation of nasal septum, obstructive nasal polyps), known cardiac disease, renal or hepatic dysfunction and pregnant or breast-feeding women. Excluded medications were other antihistamines and corticosteroids, leukotriene inhibitors, decongestants and immunotherapies. Patients who received prohibited medications or treatments in the last 6 weeks were not eligible for the present study.

Before treatment, each patient was evaluated for severity of nasal symptoms including itching, sneezing, rhinorrhea, daytime and nighttime nasal congestion. Each symptom was scored on a 4-point scale: 0 = symptom-free, 1 = mild (symptom present but not bothersome), 2 = moderate (symptom was bothersome but not intolerable), 3 = severe (symptom was bothersome and intolerable requiring treatment to relieve). The sum of all symptom scores gave a total

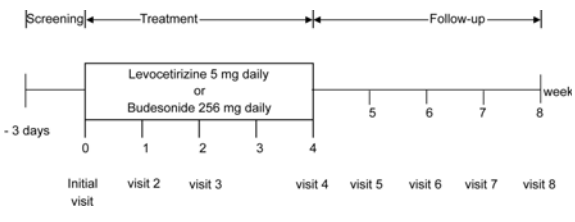

Fig. 1 Schematic diagram of the study sequence

symptom score (TSS), which could yield a theoretical maximum of 15. Patients were then randomized to receive 5 mg levocetirizine tablet or 256 mg budesonide nasal spray (two spays into each nostril, 64 mg per spray) daily. Both medications were taken every morning for 4 weeks. At the end of the treatment, another 4-week follow-up was planned for the study of symptom relapses. Three visits (at 1, 2, and 4 weeks) were scheduled for response evaluation and four weekly visits for the follow-up phase (Fig. 1). Diary cards were provided for symptom rating. Over a period of eight weeks, patients were instructed to rate their symptoms daily before bed time and the next morning for nighttime nasal congestion.

Outcome measures and assessments

During treatment and follow-up visits, patients' diaries were reviewed and validated by physical examination of the ear, nose, and throat for any outward signs (mouth breathing, nose rubbing, transverse nasal crease, infra-orbital blood pooling, frequent sniffing, and throat clearing). TSS was extracted from the patient's diary. Clinical efficacy was assessed on basis of area under curve (AUC), which illustrated the reduction of TSS over time with respect to pre-treatment baseline during the treatment or the increase in TSS over time with respect to end-of-treatment TSS after treatment discontinuation[12]. Averaged TSSs at different time points were used for AUC calculation. Response and relapse times were determined for individual patients. AUCs for response- and relapse-time curves were calculated by the trapezoid equation[12].

$$AUC_n = \frac{1}{2}\sum_{i=1}^{n-1} (t_{i+1} - t_i)(Y_{i+1} + Y_i)$$

where Y_i and Y_{i+1} were $TSSi/TSS_{baseline}$ and $TSS_{i+1}/TSS_{baseline}$ at two consecutive times t_i and t_{i+1}, respectively. Response time was defined as the time to reach a favorable endpoint, *i.e.* TSS $\leq$ 4. On the contrary, the relapse time was the time for symptom relapse after treatment discontinuation to a TSS of 6, which was the lowest score of patients seeking medical treatment. Similar definitions for response and relapse time were also suggested by Rinne et al[6].

Statistics and analysis

Baseline characteristics of the treatment groups were described by descriptive statistics. Difference between sample means was analyzed by Student's t test. Subjects were categorized as high and low symptom groups using the median TSS of 8 derived from the total samples (n = 100). Non-parametric tests, Mann-Whitney U test, χ^2 contingency test and Fisher's Exact test, were employed to test for difference between medians and frequency distributions. Mean AUCs with unequal variances were analyzed for their differences by Welch's t-test. All statistical tests were two-tailed and $p \leq 0.05$ was considered statistically significant.

Results

Baseline characteristics of the treatment groups

The present study enrolled 100 patients, 74 females and 26 males, aged 35.72 (SD10.96) years with a history of allergic rhinitis for 7.67 (SD 2.61) years. Concerning the demographic and baseline clinical characteristics, there were no significant differences between the two treatment groups (Table 1). Regarding symptom severity, the symptom could be graded as follows: grade 0 = symptom free, grade 1 = mild (symptom present but not bothersome), grade 2 = moderate (symptom was bothersome but tolerable), grade 3 = severe (symptom was intolerable and required treatment to relieve). Patients with high TSS had more grade 3 than grade 1 symptoms. The reverse was observed in the low symptom group.

Response to drug treatment

Reduction of treatment TSS over time

Reduction in treatment TSS relative to pre-treatment baseline was observed over time. Fig. 2

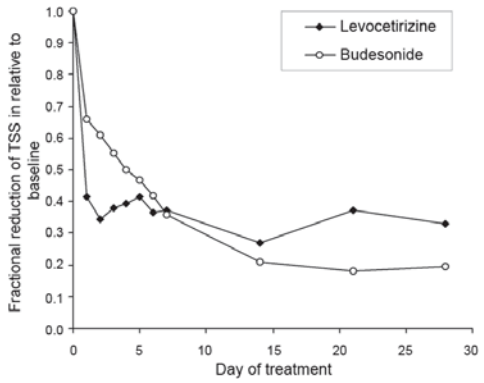

Fig. 2 Reduction of TSS during treatment in relative to pre-treatment baseline in high symptom group. The curves were constructed by plotting the ratio of treatment TSS and pre-treatment TSS at different points of time. TSS = total symptom scores

Table 1. Patient demographic and clinical characteristics at baseline

Demographics	Levocetirizine (n = 50)	Budesonide (n = 50)	p-value
Age (years)			
Mean (SD)	36.10 (10.21)	35.34 (11.71)	>0.5
Range	19-58	19-66	
Gender			
Male	15 (30%)	11 (22%)	0.392
Female	35 (70%)	39 (78%)	
Duration of allergic rhinitis (years)			
Mean (SD)	7.42 (2.66)	7.92 (2.55)	0.282
Median (range)	8 (2-13)	8.5 (3-13)	
Total symptom scores			
Whole group (n)	50	50	
Mean (SD)	7.96 (1.85)	8.50 (2.03)	0.173
Median (range)	8 (6-13)	8 (6-13)	
High symptom group (n)	13	20	
Mean (SD)	10.54 (1.39)	10.60 (1.35)	>0.5
Median (range)	10 (9-13)	11 (9-13)	
Low symptom group (n)	37	30	
Mean (SD)	7.05 (0.88)	7.10 (0.85)	>0.5
Median (range)	7 (6-8)	7 (6-8)	
Symptom severity			
High symptom group (n)	13	20	
Percent nasal symptoms with*			
Score 0	0 (0)	1 (4.47)	0.443
Score 1	24.62 (16.64)	16 (13.32)	0.122
Score 2	40 (29.44)	52 (24.62)	0.22
Score 3	32.62 (24.81)	31 (22.92)	>0.5
Low Symptom group (n)	37	30	
Percent nasal symptoms with*			
Score 0	5.41 (9)	4.67 (8.6)	>0.5
Score 1	50.81 (19.20)	52.67 (17.8)	>0.5
Score 2	40 (16.33)	36.2 (18.87)	0.4
Score 3	3.24 (7.47)	4.67 (10.08)	>0.5

* Percent of a total five nasal symptoms including inching, sneezing, rhinorrhea, day-time and night-time nasal congestion. Data are mean (SD)

represents typical response time curves for levocetirizine and budesonide. AUCs at different time spans, 1-7 days, 8-14 days, 15-28 days and 1-28 days, were calculated (Table 2). Regarding symptom severity, levocetirizine was equally effective, based on AUC (1-28d), in control of high and low symptoms except for time to reach full treatment effect which was much shorter for high symptoms (2 days versus 1 week, $p = 0.002$). In budesonide treatment, significant difference in AUC (1-28d) ($p < 0.001$) suggested a greater efficacy for high than low symptoms. Comparison of levocetirizine and budesonide in treating subjects with high symptoms, levocetirizine achieved the maximum effect in 2 days in contrast to 2 weeks for budesonide (Fig. 2). AUC analysis indicated that levocetirizine was more effective than budesonide during the first week ($p = 0.002$), equally effective in the second and less effective from the third week onwards ($p = 0.004$). In overall, levocetirizine was slightly but not significantly less effective than budesonide ($p = 0.059$). In treatment of low symptoms, levocetirizine was more effective than budesonide in the first week due to its rapid response but no significant difference in AUCs could be confirmed thereafter.

Response time

Response time was the time for the drop in TSS to a value of ≤ 4. In the high symptom group,

Table 2. Area under curve (AUC) to measure the magnitude of fractional reduction in TSS over time during treatment with respect to pre-treatment baseline

Variable	Baseline TSS	AUC (1-7d)	p-value	AUC (8-14d)	p-value	AUC (15-28d)	p-value	AUC (1-28d)	p-value
Levocetirizine									
High TSS (n =13)	10.54	2.29	0.002	2.25	>0.5	4.70	>0.5	9.24	0.40
	(1.39)	(0.52)		(1.32)		(1.93)		(2.40)	
Low TSS (n = 37)	7.05	2.90		2.60		4.42		9.93	
	(0.88)	(0.47)		(1.27)		(1.71)		(2.18)	
Budesonide									
High TSS (n = 20)	10.60	3.06	0.081	1.98	0.03	2.66	0.003	7.70	<0.001
	(1.35)	(0.43)		(0.99)		(1.27)		(1.67)	
Low TSS (n = 30)	7.10	3.32		2.78		4.08		10.15	
	(0.85)	(0.59)		(1.49)		(1.90)		(2.49)	
High TSS									
Levocetirizine (n = 13)	10.54	2.29	0.002	2.25	>0.5	4.70	0.004	9.24	0.059
	(1.39)	(0.52)		(1.32)		(1.93)		(2.40)	
Budesonide (n = 20)	10.60	3.06		1.98		2.66		7.70	
	(1.35)	(0.43)		(0.99)		(1.27)		(1.67)	
Low TSS									
Levocetirizine (n = 37)	7.05	2.90	0.003	2.60	>0.5	4.42	0.459	9.93	>0.5
	(0.88)	(0.47)		(1.27)		(1.71)		(2.18)	
Budesonide (n = 30)	7.10	3.32		2.78		4.08		10.15	
	(0.85)	(0.59)		(1.49)		(1.90)		(2.49)	

Data are mean (SD)

there were 75% of subjects whose symptoms were successfully controlled within 2 days by levocetirizine compared to the 15% by budesonide ($p < 0.001$). The median response times of 1 and 8 days were obtained for levocetirizine and budesonide, respectively ($p = 0.017$). In the low symptom group, difference in percentage of subjects who responded satisfactorily within 1 week was 94.59% for levocetirizine in contrast to 79.31% for budesonide ($p = 0.037$). However, their median response times were comparable (1 versus 2 days, $p > 0.5$).

Regarding the response time in subjects with different symptom severity, patents with high and low TSSs who were treated with levocetirizine, had equal median response time of 1 day. This did not indicate the same rate of response. In fact, a higher rate of response in the high symptom than low symptom group was suggested by AUC analysis (Table 2, $p = 0.002$). In addition, percentage of subjects who responded in 1-2 days and 3-6 days were 75% and 0% for high symptom group and 59.46% versus 35.13% for the low symptom group ($p = 0.05$). Difference in baseline TSS (10.54 versus 7.05) was counter-balanced by different rate of response to render equal median response times. On the contrary, rate of response for budesonide was the same for both high and low symptom groups, but the median response time in the low symptom group was much shorter (2 days versus 8 days, respectively $p < 0.0005$). This was due to the lower baseline TSS of 7.10 of the low symptom group compared to 10.6 of the high symptom group.

Outcome after treatment discontinuation

Increase of post–treatment TSS over time

Increase in post-treatment TSS with respect to end-of-treatment baseline was observed over time. Fig. 3 illustrates typical relapse-time curves for levocetirizine and budesonide. AUCs were calculated for 1-14 days, 15-28 days and 1-28 days (Table 3). Increase of AUC with time was a measure of symptom return. In terms of symptom severity, levocetirizine could prevent symptom relapses in patients with high-grade symptoms far better than the low-grade symptoms ($p \leq 0.05$). No such difference could be recognized in the budesonide-treated groups. Comparing levocetirizine and budesonide in prolonging treatment effects in the high symptom group, levocetirizine was superior to budesonide based

Table 3. Area under curve (AUC) to measure the multiple increase in TSS over time post-treatment with respect to end-of-treatment baseline

Variable	Baseline TSS	AUC (1-14d)	p-value	AUC (15-28d)	p-value	AUC (1-28d)	p-value
Levocetirizine							
High TSS (n =13)	3.46 (2.6)	20.19 (7.98)	0.05	26.70 (11.95)	0.005	46.88 (14.37)	0.001
Low TSS (n = 37)	1.81 (1.87)	26.65 (13.86)		41.57 (23.49)		68.22 (27.28)	
Budesonide							
High TSS (n = 20)	2.08 (1.99)	27.65 (14.66)	>0.50	50.71 (26.57)	>0.5	78.35 (30.35)	>0.5
Low TSS (n = 30)	1.77 (2.18)	28.06 (17.57)		46.70 (29.9)		74.76 (34.68)	
High TSS							
Levocetirizine (n = 13)	3.46 (2.6)	20.19 (7.98)	0.073	26.70 (11.95)	0.002	46.88 (14.37)	<0.001
Budesonide (n = 20)	2.08 (1.99)	27.65 (14.66)		50.71 (26.57)		78.35 (30.35)	
Low TSS							
Levocetirizine (n = 37)	1.81 (1.87)	26.65 (13.86)	>0.5	41.57 (23.49)	0.457	68.22 (27.28)	0.42
Budesonide (n = 30)	1.77 (2.18)	28.06 (17.57)		46.70 (29.9)		74.76 (34.68)	

Data are mean (SD)

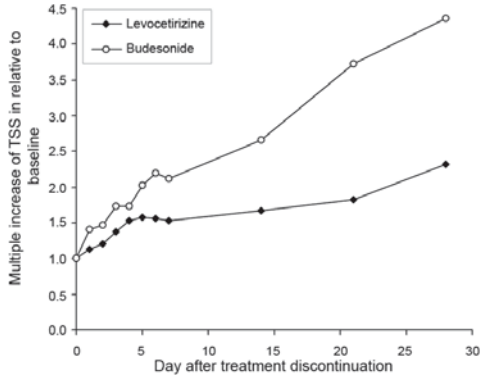

Fig. 3 Increase of TSS after treatment discontinuation in relative to end-of-treatment baseline in high symptom group. The curves were constructed by plotting the ratio of post-treatment TSS and end-of-treatment TSS at different points of time. TSS = total symptom scores

on a smaller AUC (1-28d) (46.88 for levocetirizine and 78.35 for budesonide, $p < 0.001$). The difference in preventing symptom relapses started to become evident after 2 weeks post-treatment ($p = 0.002$). Such a difference could not be observed in treatment of the low symptom group.

Relapse time

Relapse time was the time for the symptom relapse after treatment discontinuation to a TSS of 6. The median relapse times were determined for the levocetirizine-treated group (19.5 days for high symptoms versus 18 days for low symptoms) as well as the budesonide-treated group (11 days for high symptoms versus 14 days for low symptoms). No statistically significant difference could be confirmed for these findings. Considering the distribution of relapse time, a higher percentage of subjects with high symptoms treated by budesonide (85%) compared with levocetirizine (50%) relapsed within 3 weeks ($p = 0.043$).

Discussion

Total symptom score (TSS) is an indicator for disease severity and has been shown to be correlated with degree of impairment in quality of life[13]. In the present study, clinical efficacy of levocetirizine was compared with budesonide in patients with high TSS of 10.57 (SD 1.37) and low TSS of 7.08(SD 0.87). The high symptom group might well represent subjects with moderate to severe symptoms for 80% of them having grade 2 and 3 symptoms, while the low TSS group had relatively mild symptoms because percentage of subjects with grade 3, 2, and 0-1 were 4.81%, 32.09%, and 66.79%, respectively.

Clinical efficacy was assessed on bases of magnitude of symptom control over the entire period of treatment and the prolongation of treatment effect after treatment discontinuation. Efficacy of both drugs appeared to be related to symptom severity. Effect of levocetirizine in control of high and low symptoms differed only in time for development of full effects, *i.e.* 2 days for high symptoms and 1 week for low symptoms. The difference might be explained on the

basis of receptor occupancy (RO), an indicator for clinical efficacy of H_1-antihistamines[14]. RO for levocetirizine is found to be pH dependent and that RO at neutral pH is lower than that at acidic pH[14]. Acidosis, a feature of inflammatory process as seen in allergic rhinitis[15], might be linked to the rapid action of levocetirizine in the high symptom group. Budesonide was more effective in relieving high symptoms than low symptoms. The difference took effect from the second week onwards. This finding was not unexpected since budesonide is known for its capacity in inhibiting the late-inflammatory responses[16], a major process involves the development of severe symptom like nasal obstruction. The low symptoms might be related to more of the histamine-induced allergic reaction.

Levocetirizine, when compared to budesonide in treating subjects with high symptoms, was found to be more effective during the first week of treatment and became less effective when budesonide achieved its full effect after the second week. However, the effectiveness of budesonide over a period of 4 weeks was slightly but not significantly greater than levocetirizine. Again, no significant difference could be observed between the two drugs in treating the low symptom group except for the first week of treatment when levocetirizine displayed a more rapid response. Despite the slow action of budesonide, the rate of symptom relief in the low symptom group was still faster than the rate in the high symptom group. Day et al[17] reported a rapid onset, *i.e*. 7 hours, for budesonide in treating seasonal rhinitis induced by a controlled pollen challenge system. Their pre-treatment baseline TSS was 6, which was comparable to TSS of the low symptom group in the present study.

When the 4-week treatment ended, treatment effects persisted for a few weeks. Approximately 70% and 50% of subjects remained symptom-free-to-mild at the first and second week post-treatment, respectively. Symptom relapse was evaluated based on the area under relapse-time curve and subjects' individual relapse times. In the high symptom group, budesonide was inferior to levocetirizine in preventing symptom relapses based on AUC analysis. Median relapse times for budesonide and levocetirizine were 11 and 19.5 days respectively. With a long-term treatment of 1 year, the relapse time of 62 days was observed for budesonide and 20 days for cetirizine, a parent compound of levocetirizine[6]. No statistically significant difference between these relapse times could be confirmed in the previous[6] and the present study. However, analysis of relapse time distribution revealed a greater percentage of subjects treated with budesonide (85%) than those treated with levocetirizine (50%) relapsed within 3 weeks. Concerning the symptom severity, the capacity of levocetirizine in preventing symptom relapses was better for high than for low symptoms based on the AUC of relapse-time curve. Nearly equal median relapse times, 19.5 versus 18 days for high and low symptoms, could be argued on the difference in end-of-treatment TSS, *i.e.* 3.46 versus 1.81 for high and low symptoms, together with the unequal capability in prolonging the treatment effects making the median relapse time equal.

What factor facilitates a 2-3 week prolongation of the treatment effects observed for the drugs used in the present study is an interesting question for future research on treatment and prevention of allergic rhinitis. Recent reviews have addressed the potential of levocetirizine[18] and budesonide[16] in immuno-modulation. Two recent research publications have generated evidences to support this view[19,20]. Significant increase in $CD4^+CD25^+$ cells constituting the regulator T cell (Treg), a type of T cell recognized for its key role in prevention of allergic rhinitis[21] was observed in patients treated with levocetirizine[19] and budesonide[20]. In addition, a positive correlation of nasal congestion score and percentages $CD4^+CD25^+$ cells was noted at baseline[18]. This would imply that the nasal symptom served as a signal to alert the naturally occurring host-defense in which Treg was increased to down-regulate the inflammatory process and that low symptoms might be less effective than high symptoms in triggering the immune system for protective responses[19]. As pointed out by Akdis et al[21] $CD4^+CD25^+$ Treg cell not only inhibits allergen specific effecter cells but also involves in switching IgE production to IgG_4 hence desensitizes the allergic reaction. This novel concept may partly explain why the levocetirizine-treated low symptom group was more readily relapsed than the high symptom group possibly for their difference in degree of allergic desensitization.

In conclusion, the present study has shown that the efficacy of the drug treatment is dependent of symptom severity. Levocetirizine is equally effective in control of high and low symptoms but is less effective in preventing relapses of low symptoms. Budesonide is more effective against high than low symptoms but shows no difference in preventing symptom relapses. Typical clinical efficacy of budesonide and levocetirizine can be demonstrated in treatment of subjects with high symptoms, levocetirizine achieves

its full effectiveness in two days while budesonide requires two weeks. Budesonide at full effectiveness is superior to levocetiriztine in symptom control. Despite this superiority, budesonide falls short of its capacity in preventing symptom relapses when compared to levocetirizine. The present study provides information for further treatment of relapses, which can be re-categorized as low symptoms and for treatment individualization on the basis of pre-treatment symptom score.

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การประเมินผลทางคลินิกของเลโวเซ็ททิริซีนและบูเดสโซไนด์ในการรักษาโรคจมูกอักเสบภูมิแพ้ตลอดปีตามระดับความรุนแรงของอาการ

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***วัตถุประสงค์**: เพื่อเปรียบเทียบผลของยาเลโวเซ็ททิริซีนและบูเดสโซไนด์ ในการรักษาโรคจมูกอักเสบภูมิแพ้ตลอดปีในผู้ป่วยที่มีอาการรุนแรงและไม่รุนแรง*

***วัสดุและวิธีการ**: เป็นการศึกษาเปรียบเทียบแบบคู่ขนาน โดยสุ่มให้ยาเม็ดเลโวเซ็ททิริซีน ขนาด 5 มิลลิกรัม หรือยาพ่นจมูกบูเดสโซไนด์ ขนาด 256 ไมโครกรัม ต่อวันเป็นเวลานาน 4 สัปดาห์ แก่ผู้ป่วยจำนวน 100 ราย ผู้ป่วยบันทึกระดับคะแนนบ่งชี้ความรุนแรงของอาการต่าง ๆ ได้แก่ คันจมูก จาม มีน้ำมูกใสไหล คัดแน่นจมูก ทั้งในช่วงเวลากลางวันและกลางคืนตลอดระยะเวลา 8 สัปดาห์ ของการศึกษา คะแนนรวมของระดับความรุนแรงของอาการทั้งหมด เรียกว่า total symptom score (TSS) ตัวแปรบ่งชี้ประสิทธิผลของยา และการเกิดโรคกลับ เมื่อหยุดยาคือ พื้นที่ใต้กราฟแสดงความสัมพันธ์ของการลดหรือเพิ่มของ TSS ตามเวลาโดยเปรียบเทียบกับค่า TSS พื้นฐานรวมถึงเวลาการตอบสนองต่อการรักษา และการเป็นโรคกลับเมื่อหยุดยา*

***ผลการศึกษา**: ระดับความรุนแรงของอาการโรคจมูกอักเสบภูมิแพ้ จะจำแนกเป็นรุนแรงและไม่รุนแรง โดยใช้ median TSS เท่ากับ 8 เป็นดัชนีจำแนกเลโวเซ็ททิริซีนสามารถลดอาการของโรค ในผู้ป่วยที่มีอาการรุนแรง และไม่รุนแรงด้วยประสิทธิผลเท่ากัน ต่างกันที่อัตราเร็วในการออกฤทธิ์ คือ 2 วัน ในผู้ที่มีอาการรุนแรง และ 1 สัปดาห์ สำหรับผู้ที่มีอาการไม่รุนแรง ($p = 0.002$) เมื่อหยุดยาการเกิดโรคกลับ ในกลุ่มรุนแรงจะเกิดช้ากว่าในกลุ่มไม่รุนแรง ($p = 0.001$) ประสิทธิผลของยาพ่นจมูกบูเดสโซไนด์ในการควบคุมอาการของกลุ่มรุนแรงจะดีกว่าในกลุ่มไม่รุนแรง ($p < 0.001$) แต่การเป็นโรคกลับเมื่อหยุดยาจะเกิดพร้อมกัน เมื่อเปรียบเทียบเลโวเซ็ททิริซีนและบูเดสโซไนด์ ในการรักษาผู้ป่วยที่มีอาการรุนแรงพบว่า เลโวเซ็ททิริซีน ออกฤทธิ์เร็วกว่าบูเดสโซไนด์ คือ 2 วันและ 2 สัปดาห์ ตามลำดับ ในขณะที่ยาออกฤทธิ์เต็มที่ บูเดสโซไนด์จะมีประสิทธิผลของการรักษาสูงกว่าเลโวเซ็ททิริซีน ($p = 0.004$) แต่ประสิทธิผลการรักษาโดยรวมตลอด 4 สัปดาห์ของตัวยาทั้ง 2 จะใกล้เคียงกัน ($p = 0.059$) ในการป้องกันการเป็นโรคกลับภายหลังการหยุดยาพบว่า บูเดสโซไนด์จะมีประสิทธิ์ผลด้อยกว่า เลโวเซ็ททิริซีน ($p = 0.001$) อย่างไรก็ตามไม่พบความแตกต่างดังกล่าวในการรักษาผู้ป่วยที่มีอาการไม่รุนแรง*

***สรุป**: ประสิทธิผลของยาที่ใช้ในงานวิจัยนี้จะขึ้นอยู่กับ ระดับความรุนแรงของอาการโรคจมูกอักเสบภูมิแพ้ เลโวเซ็ททิริซีนมีประสิทธิผลในการรักษา และการป้องกันการเกิดโรคกลับเหนือกว่า บูเดสโซไนด์ ในกลุ่มผู้ป่วยที่มีอาการรุนแรงและเหมือนกันในกลุ่มผู้ป่วยที่มีอาการไม่รุนแรง*