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Original Article* / *Çalışma - Araştırma

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Desloratadin monoterapisi veya desloratadin artı montelukast kombinasyonu ile tedavi edilen inatçı alerjik rinit hastalarının yaşam kalitesi

Banu Atalay Erdoğan, M.D., Arif Şanlı, M.D., Mustafa Paksoy, M.D., Gökhan Altın, M.D., Sedat Aydın, M.D.

Department of Otolaryngology, Dr. Lütfi Kırdar Kartal Training and Research Hospital, İstanbul, Turkey

Objectives: This study aims to compare the effectiveness of desloratadine monotherapy and desloratadine plus montelukast combination therapy on quality of life in patients with persistent allergic rhinitis.

Patients and Methods: This study consists of 40 patients (28 females, 12 males, mean age 29.8 years; range 17 to 44 years) referred to ear, nose, and throat outpatient clinic between May 2010 and September 2010. A six-week randomized, double-blind, cross-sectional study was performed in two arms: In group 1, 20 patients received desloratadine (5 mg/d) alone; in group 2, 20 patients received desloratadine (5 mg) plus montelukast (10 mg) combination therapy. Quality of life was assessed on the day before starting treatment and on the last day of each treatment period using the Rhinoconjunctivitis Quality of Life Questionnaire and Nighttime Symptom Scores.

Results: In group 1, the mean quality of life scores before and after treatment were 3.17 and 2.43, respectively. In group 2, the mean quality of life scores before and after treatment were 2.94 and 1.73, respectively.

Conclusion: Desloratadine plus montelukast combination therapy may have a positive impact on quality of life, sleep symptoms in particular.

Keywords: Desloratadine; montelukast; persistent allergic rhinitis; quality of life.

Amaç: Bu çalışmada inatçı alerjik rinit hastalarında desloratadin monoterapisi ve desloratadin artı montelukast kombinasyon tedavisinin yaşam kalitesi üzerine etkinliği karşılaştırıldı.

Hastalar ve Yöntemler: Mayıs 2010 - Eylül 2010 tarihleri arasında kulak, burun, boğaz polikliniğine sevk edilen 40 hasta (28 kadın, 12 erkek, ort. yaş 29.8 yıl; dağılım 17-44 yıl) çalışmaya alındı. Altı haftalık randomize, çift kör, kesitsel çalışma iki koldan gerçekleştirildi: Grup 1'deki 20 hastaya yalnızca desloratadin (5 mg/gün); grup 2'deki 20 hastaya ise desloratadin (5 mg/gün) artı montelukast (10 mg/gün) kombinasyon tedavisi verildi. Yaşam kalitesi tedaviye başlamadan önceki gün ve tedavinin son günü Rinokonjonktivit Yaşam Kalitesi Anketi ve Gece Semptom Skoru ile değerlendirildi.

Bulgular: Grup 1'de tedavi öncesi ve sonrası ortalama yaşam kalitesi skoru, sırasıyla 3.17 ve 2.43 idi. Grup 2'de ise, tedavi öncesi ve sonrası ortalama yaşam kalitesi skoru, sırasıyla 2.94 ve 1.73 idi.

Sonuç: Desloratadin artı montelukast kombinasyon tedavisinin, özellikle uyku semptomları olmak üzere, yaşam kalitesi üzerine olumlu bir etkisi olabilir.

Anahtar Sözcükler: Desloratadin; montelukast; inatçı allerjik rinit; yaşam kalitesi.

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Correspondence / İletişim adresi: Banu Atalay Erdoğan, M.D. Dr. Lütfi Kırdar Kartal Eğitim ve Araştırma Hastanesi Kulak Burun Boğaz Hastalıkları Kliniği, 34890 Cevizli, Kartal, İstanbul, Turkey.

Tel: +90 506 - 248 04 66 e-mail *(e-posta):* banuatalay81@gmail.com

Allergic rhinitis (AR) is the most common atopic disorder affecting some 20 to 40 million people annually in the United States, including 10 to 30% of adults and up to 40% of children.[1] Allergic rhinitis is a chronic inflammatory disease of the airways that can diminish quality of life. Allergic rhinitis is a type 1 hypersensitivity reaction of primarily nasal mucosa to allergens.[2] It is an inflammatory disease of rhino-ocular mucosa mediated by immunoglobulin E (IgE). Apart from classical known symptoms such as runny nose, post nasal drip, sneezing and nasal congestion, patients may also suffer from daytime fatigue, poor concentration, cognitive impairment, daytime sleepiness and sleep disturbance.[3] If severe, problems may include paranasal sinus pressure and pain or eustachian tube dysfunction described as ear popping and fullness.[1] According to the Allergic Rhinitis and its Impact on Asthma (ARIA) document, AR should be classified by chronicity (intermittent or persistent), and severity which is based on symptoms and quality of life (mild, or moderate/severe).[4] The terms "seasonal" and "perennial" AR previously categorized AR by the clinically significant mediators which are responsible for recruitment, activation, and perpetuation of cellular infiltrate resulting in continued chronic nasal congestion during the late phase.[5] The latest-generation potent antihistamines such as desloratadine and levocetirizine have shown improved quality of life in allergic rhinitis studies.[6,7] Montelukast, a leukotriene receptor antagonist, significantly improves daytime and nighttime symptoms in patients with allergic rhinitis and is now an approved therapy for allergic rhinitis.[8] This study compares desloratadine monotherapy and combination montelukast with desloratadine on quality of life in allergic rhinitis.

PATIENTS AND METHODS

The sample consisted of 40 patients referred to our polyclinic between May 2010 and September 2010. This study was approved by the Ethics Committee of Kartal Dr. Lutfi Kirdar Education and Research Hospital, and all participants signed an informed consent form.

Forty eligible patients (28 females, 12 males, mean age 29.8 years) were selected on the basis of age (17-44 years), a minimum two-year history of persistent allergic rhinitis, positive skin prick test to perennial allergens (grass, weed pollen and trees) and anterior rhinoscopy findings consistent with allergic rhinitis. Pregnant or lactating patients, smokers, patients with asthma requiring daily treatment and patients sensitized to seasonal allergens were excluded. Other exclusion criteria were upper respiratory tract infection during the six-week period preceding the study, severe illnesses, septal deviation, nasal polyps, acute or chronic rhinosinusitis, and any other condition that might affect nasal breathing or nocturnal sleep pattern. A six-week randomized, double-blind, cross- sectional study was designed:

A. Patients receiving desloratadine (5 mg), (n=20).

B. Patients receiving desloratadine (5 mg) montelukast (10 mg) combination therapy (n=20).

In group 1 and 2, the medication was administered once a day in the evening. Data was collected using the Allergic Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). Health-related quality of life was assessed using the RQLQ adapted for the Turkish population and filled by researchers via interviewing patients. This questionnaire contains 28 items in seven domains (activity limitation, sleep problems, nose symptoms, eye symptoms, non-nose non-eye symptoms, practical problems and emotional function). Each item was scored from 0 (not troubling) to 6 (extremely troubling).[9,10] Before and after the six week treatment the RQLQ was filled by researchers by interviewing patients. The responses of group 1 individuals were compared with group 2. Participants recorded their nighttime symptom scores before and after the treatment period. Results are presented for six-week treatment periods as a mean value of three individual scores, each rated from 0 to 3. The scores were as follows: difficulty falling asleep (0= not at all, 1= a little, 2= moderate, 3= very); nighttime awakening (0= not at all, 1= once, 2= more than once, 3= all night) and nasal congestion on awakening (0= none, 1= mild, noticeable but not troublesome, 2= moderate, noticeable and troublesome some of the time, 3= severe, troublesome most of the time/very troublesome some of the time).[9]

Statistical analysis

Data were analyzed by the Wilcoxon signed rank test, sign test and marginal homogeneity

test using IBM SPSS for Windows 19.0 version software program (IBM Corporation, Armonk, NY, USA). Alpha value greater than 0.05 was considered statistically significant.

RESULTS

In group 1 the mean RQLQ score was 3.17 before visit and 2.43 after six week treatment. In group 2 the mean RQLQ score was 2.94 before visit and 1.73 after six weeks treatment (Table 1 and 2). In other words, in group 1 and 2 mean RQLQ scores before visit were 3.17 and 2.94, whereas after treatment, they were 2.43 and 1.73, respectively. When patient groups 1 and 2 were compared, there was a significant decrease in scores after treatment in group 2

Table 1. Mean Rhinoconjunctivitis Quality of Life Questionnaire scores in patients treated for six weeks with desloratadine alone (n=20)

	Before treatment	After treatment	*p*
Activity limitation			
1	3.6	2.8	0.007
2	3.3	2.5	0.000
3	2.8	2.4	0.023
Sleep symptoms			
Difficulty getting to sleep	3.1	2.5	0.046
Wake up during the night	2.7	2.1	0.032
Lack of a good night's sleep	3.5	2.7	0.007
Non eye/nose symptoms			
Fatigue	3.2	2.4	0.000
Thirst	2.4	2.2	0.248
Reduced productivity	3.3	2.8	0.031
Tiredness	3.3	2.8	0.107
Poor concentration	2.6	2.5	0.358
Headache	3.6	2.7	0.019
Worn out	3.9	3.3	0.074
Practical problems			
Inconvenience of having to carry tissues or handkerchief	3.4	2.2	0.000
Need to rub nose/eyes	3.4	2.4	0.001
Need to blow nose repeatly	4.7	3.3	0.000
Nose symptoms			
Stuffy/blocked	3.7	2.9	0.001
Runny	4.4	2.8	0.000
Sneezing	2.2	1.3	0.000
Post-nasal drip	3	2.1	0.002
Eye symptoms			
Itchy eyes	3.3	2.3	0.000
Watery eyes	3.6	2.3	0.000
Sore eyes	2.1	1.2	0.000
Swollen eyes	1.9	1.2	0.026
Emotional function			
Frustrated	1.5	1.2	0.107
Impatient or restless	2	1.9	0.660
Irritable	3.7	3.3	0.143
Embarrassed by your symptoms	3.6	3	0.018

(α=0.05). In group 1 there was no statistically significant difference in fatigue, thirst, reduced productivity, tiredness, poor concentration, headache, difficulty falling asleep, waking up during night and emotional symptoms. In group 2 although there was no difference in thirst, tiredness, poor concentration, headache, worn out, frustrated and impatient symptoms, there was a statistically significant difference in sleep related symptoms. Statistically significant improvement in eye and nasal symptoms, practical problems and activities were observed in both groups. The sleep impairment evaluation, assessed with a 0-3 point scale before and after the six-week treatment period. The montelukast and deloratadine combination therapy significantly improved nighttime symptom scores in group 2 (Figure 1).

Table 2. Mean Rhinoconjunctivitis Quality of Life Questionnaire scores in patients treated for six weeks with desloratadine plus montelukast combination therapy (n=20)

	Before treatment	After treatment	*p*
Activity limitation			
1	3.75	2.5	0.002
2	3.7	2.6	0.001
3	3.6	2.45	0.002
Sleep symptoms			
Difficulty getting to sleep	2.2	1.6	0.006
Wake up during the night	2	1.15	0.006
Lack of a good night's sleep	3.5	2.3	0.002
Non eye/nose symptoms			
Fatigue	2.55	2.1	0.039
Thirst	1.8	0.8	0.007
Reduced productivity	2.45	1.6	0.004
Tiredness	3.05	1.55	0.000
Poor concentration	2.85	2.05	0.004
Headache	4	3.05	0.014
Worn out	3	3	1.000
Practical problems			
Inconvenience of having to carry tissues or handkerchief	3.6	1.05	0.000
Need to rub nose/eyes	3.35	1.05	0.000
Need to blow nose repeatly	4.35	1.4	0.000
Nose symptoms			
Stuffy/blocked	3.65	2.15	0.002
Runny	3.8	1.95	0.000
Sneezing	3.5	1.2	0.000
Post nasal drip	3.05	1.6	0.000
Eye symptoms			
Itchy eyes	2.7	0.9	0.000
Watery eyes	3.05	0.95	0.000
Sore eyes	1.5	0.3	0.006
Swollen eyes	1.55	0.8	0.002
Emotional function			
Frustrated	1.95	1.55	0.113
Impatient or restless	1.75	1.55	0.414
Irritable	2.65	2.85	0.557
Embarrassed by your symptoms	4.15	1.95	0.000

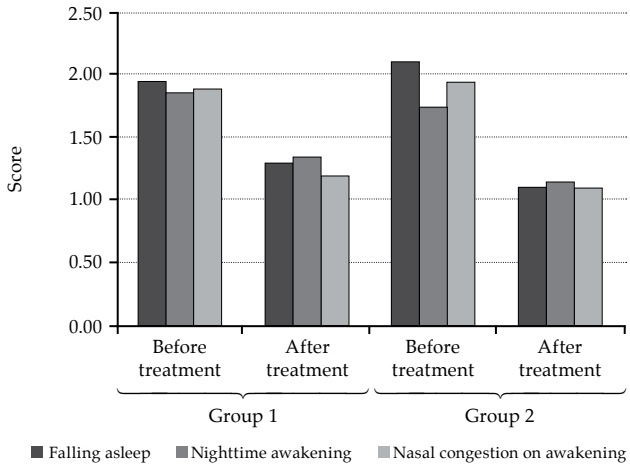

Figure 1. *Night time symptom scores in patients treated for six weeks with desloratadine (group 1) and desloratadine plus montelukast combination therapy (group 2).*

DISCUSSION

Allergic rhinitis is the most common form of allergic disease, estimated to affect up to 20% of the population worldwide.[11] Persistent allergic rhinitis is an allergic inflammation of the upper respiratory tract due to a year-round encounter with allergens.[12] The pathophysiologic mechanism of allergic rhinitis is characterized by inflammation of the nasal mucous membranes as a result of a complex response to nasal allergen exposure. These include the high numbers of inflammatory cells such as mast cells and eosinophils in the airway; when activated on exposure to airborne allergens they undergo degranulation and release inflammatory substances, including cysteinyl leukotrienes, histamine, prostaglandin D2, and kinins.[13]

Although, the symptoms of perennial allergic rhinitis which include nasal congestion, rhinorrhea, pruritis, are not life-threatening, breathing through the mouth may cause difficulties in falling asleep, nighttime awakening, snoring, somnolence, impaired mood, poor memory and decreased productivity at school and work.

The management of allergic rhinitis includes environmental control measures and pharmacotherapy.

Pharmacotherapy includes oral and intranasal H1 antihistamines, intranasal corticosteroids, oral and intranasal decongestants, intranasal anticholinergics, intranasal cromolyn and leukotriene receptor antagonists. None of the guidelines recommend oral first-generation antihistamines as part of treatment for AR. Second generation H1 antihistamines are in general recommended for mild to moderate disease as first line therapy, but not when treating nasal congestion. Oral decongestants are indicated in combination with oral antihistamines for nasal congestion, but patients should be monitored for serious side effects.[14] Topically applied intranasal decongestants should be limited in use to less than 10 days because of rhinitis medicamentosa, which is rebound swelling of the nasal membranes or drug induced rhinitis.[15,16]

Intranasal corticosteroids are often required in moderate to severe disease and are effective in reducing all symptoms of allergic rhinitis in addition to eye symptoms associated with allergic conjunctivitis.[17,18]

Leukotriene levels are increased in the early as well as the late phase of the allergic reaction. Nasal insufflation studies show that both leukotriene C4 (LTC4) and leukotriene D4 (LTD4) induce an increase in nasal mucosal blood flow and nasal airway resistance.[19-21] Montelukast is an orally active, highly selective cysteinyl leukotriene type-1 receptor antagonist of leukotreine D4, with affinities approximately two-fold greater than the natural ligand. It is rapidly absorbed, achieving peak plasma concentration (Cmax) in three to four hours and with a mean bioavailability of 64% following a 10 mg oral administration. Montelukast is well tolerated and has a safety profile similar in pediatric and adult populations.

Optimal pharmacotherapy must not only control symptoms but also improve patients' quality of life.

The improvement in quality of life depends mainly on the reduction of nasal obstruction, as nasal blockage is a crucial symptom in persistent allergic rhinitis that leads to sleep impairment and subsequent daytime somnolence, fatigue, and reduced productivity.

The efficacy of montelukast in the treatment of AR has been studied quite extensively over the past few years as monotherapy, combined with a second generation antihistamine, and with or without intranasal corticosteroids.[22-26]

In our study, we compared the effects of desloratadine and desloratadine plus montelukast combination therapy on quality of life. Symptomatic patients were treated for six weeks with either desloratadine or desloratadine plus montelukast combination therapy.

In three reported studies, statistically significant endpoints in symptom scores were compared with placebo included daytime nasal symptoms scores, daytime eye symptom scores, nighttime symptom scores, and composite symptom scores. Nighttime symptoms (difficulty falling asleep, nighttime awakenings, and congestion upon awaking) appeared to have a better response with montelukast compared with antihistamines.[23,24,26]

In our study, there was no statistically significant difference observed in emotional symptoms, non-eye/nose symptoms, difficulty to fall asleep and nighttime awakening in the desloratadine group. Whereas in the desloratadine plus montelukast combined group, even though there was no difference in non-nose/eye and emotional symptoms, there was a statistically significant difference in sleep related symptoms. In both groups there was significant improvement in eye and nasal symptoms as well as practical problems and activities.

The results of our study demonstrate that desloratadine plus montelukast combined therapy results in significant improvement in the quality of life of patients suffering from persistent allergic rhinitis. The benefits of the desloratadine plus montelukast combined preparation were evident in most domains measured by RQLQ, specifically in nasal symptoms, eye symptoms, practical problems and activity limitations.

In our study the 0-3 point scale nighttime symptoms questionnaire was also evaluated. Group 2 had significantly improved nighttime symptoms scores. A significant improvement over baseline was observed in both groups 1 and 2 but patients treated with desloratadine plus montelukast combination therapy had a more significant benefit.

These results agree with those of previous studies, which show that monotherapy with montelukast[8] desloratadine[27] or levocetirizine[28-30] produces greater improvement in quality of life than placebo in patients affected by persistent and/or perennial allergic rhinitis.

Ciebiada et al.[31] demonstrated that montelukast was as efficacious in the improvement of nasal congestion as desloratadine or levocetirizine, and that it was more efficacious than placebo. Furthermore, combination therapy was more effective than monotherapy with montelukast alone and more effective than monotherapy with montelukast or desloratadine. Their study showed that combination therapy with montelukast and an antihistamine may have a positive impact on persistent allergic rhinitis and improve quality of life and nighttime symptoms.[31]

The improvement in nasal symptoms, eye symptoms, practical problems and activity limitations were nearly the same in patients treated with desloratadine and desloratadine plus montelukast combination therapy. Sleep symptom scores significantly decreased in patients treated with desloratadine plus montelukast combination therapy.

In conclusion, desloratadine plus montelukast combination therapy gave additional benefits in comparison to desloratadine alone and could be considered for patients whose quality of life is impaired by persistent allergic rhinitis. This study showed that desloratadine plus montelukast combination therapy has a considerable impact on quality of life, especially night symptoms.

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Declaration of conflicting interests

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REFERENCES

1. Dykewicz MS, Fineman S, Skoner DP, Nicklas R, Lee R, Blessing-Moore J, et al. Diagnosis and management of rhinitis: complete guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology. American Academy of Allergy, Asthma,

and Immunology. Ann Allergy Asthma Immunol 1998;81:478-518.
2. Tahamiler R, Edizer DT, Canakcioglu S, Guvenc MG, Inci E, Dirican A. Nasal sound analysis: a new method for evaluating nasal obstruction in allergic rhinitis. Laryngoscope 2006;116:2050-4.
3. Marshall PS, O'Hara C, Steinberg P. Effects of seasonal allergic rhinitis on selected cognitive abilities. Ann Allergy Asthma Immunol 2000;84:403-10.
4. Bousquet J, Van Cauwenberge P, Khaltaev N; Aria Workshop Group; World Health Organization. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001;108:S147-334.
5. Ledford DK, Lockey RF. Allergic rhinitis: Understanding the process (a major contributor to health problems-and on the rise). J Respir Dis 1998;19:576-84.
6. Meltzer EO, Prenner BM, Nayak A. Desloratadine Study Group. Efficacy and tolerability of once-daily 5 mg desloratadine, an H1 receptor antagonist, in patients with seasonal allergic rhinitis. Clin Drug Invest 2001;21:25-32.
7. Day JH, Briscoe MP, Rafeiro E, Ratz JD. Comparative clinical efficacy, onset and duration of action of levocetirizine and desloratadine for symptoms of seasonal allergic rhinitis in subjects evaluated in the Environmental Exposure Unit (EEU). Int J Clin Pract 2004;58:109-18.
8. Patel P, Philip G, Yang W, Call R, Horak F, LaForce C, et al. Randomized, double-blind, placebo-controlled study of montelukast for treating perennial allergic rhinitis. Ann Allergy Asthma Immunol 2005;95:551-7.
9. Juniper EF, Guyatt GH. Development and testing of a new measure of health status for clinical trials in rhinoconjunctivitis. Clin Exp Allergy 1991;21:77-83.
10. Dzaman K, Jadczak M, Rapiejko P, Usowski J, Jurkiewicz D. Life quality analysis based on a self-administered questionnaire in patient with nasal obstruction. Annales UMCS. 2005;90:416-20.
11. Lundbäck B. Epidemiology of rhinitis and asthma. Clin Exp Allergy 1998;28 Suppl 2:3-10.
12. Ciebiada M, Ciebiada MG, Kmiecik T, DuBuske LM, Gorski P. Quality of life in patients with persistent allergic rhinitis treated with montelukast alone or in combination with levocetirizine or desloratadine. J Investig Allergol Clin Immunol 2008;18:343-9.
13. van Adelsberg J, Philip G, Pedinoff AJ, Meltzer EO, Ratner PH, Menten J, et al. Montelukast improves symptoms of seasonal allergic rhinitis over a 4-week treatment period. Allergy 2003;58:1268-76.
14. Jordana G, Dolovich J, Briscoe MP, Day JH, Drouin MA, Gold M, et al. Intranasal fluticasone propionate versus loratadine in the treatment of adolescent patients with seasonal allergic rhinitis. J Allergy Clin Immunol 1996;97:588-95.
15. Graf P, Hallén H, Juto JE. Four-week use of oxymetazoline nasal spray (Nezeril) once daily at night induces rebound swelling and nasal hyperreactivity. Acta Otolaryngol 1995;115:71-5.
16. Graf P, Hallén H. Effect on the nasal mucosa of long-term treatment with oxymetazoline, benzalkonium chloride, and placebo nasal sprays. Laryngoscope 1996;106:605-9.
17. Bernstein DI, Levy AL, Hampel FC, Baidoo CA, Cook CK, Philpot EE, et al. Treatment with intranasal fluticasone propionate significantly improves ocular symptoms in patients with seasonal allergic rhinitis. Clin Exp Allergy 2004;34:952-7.
18. Singulair PI. Singulair prescribing information. Whitehouse Station, NJ: Merck & Co. Inc.; June 1998-2005.
19. Miadonna A, Tedeschi A, Leggieri E, Lorini M, Folco G, Sala A, et al. Behavior and clinical relevance of histamine and leukotrienes C4 and B4 in grass pollen-induced rhinitis. Am Rev Respir Dis 1987;136:357-62.
20. Okuda M, Watase T, Mezawa A, Liu CM. The role of leukotriene D4 in allergic rhinitis. Ann Allergy 1988;60:537-40.
21. Bisgaard H, Olsson P, Bende M. Effect of leukotriene D4 on nasal mucosal blood flow, nasal airway resistance and nasal secretion in humans. Clin Allergy 1986;16:289-97.
22. Meltzer EO, Malmstrom K, Lu S, Prenner BM, Wei LX, Weinstein SF, et al. Concomitant montelukast and loratadine as treatment for seasonal allergic rhinitis: a randomized, placebo-controlled clinical trial. J Allergy Clin Immunol 2000;105:917-22.
23. Nayak AS, Philip G, Lu S, Malice MP, Reiss TF; Montelukast Fall Rhinitis Investigator Group. Efficacy and tolerability of montelukast alone or in combination with loratadine in seasonal allergic rhinitis: a multicenter, randomized, double-blind, placebo-controlled trial performed in the fall. Ann Allergy Asthma Immunol 2002;88:592-600.
24. Philip G, Malmstrom K, Hampel FC, Weinstein SF, LaForce CF, Ratner PH, et al. Montelukast for treating seasonal allergic rhinitis: a randomized, double-blind, placebo-controlled trial performed in the spring. Clin Exp Allergy 2002;32:1020-8.
25. Philip G, Nayak AS, Berger WE, Leynadier F, Vrijens F, Dass SB, et al. The effect of montelukast on rhinitis symptoms in patients with asthma and seasonal allergic rhinitis. Curr Med Res Opin 2004;20:1549-58.
26. van Adelsberg J, Philip G, LaForce CF, Weinstein SF, Menten J, Malice MP, et al. Randomized controlled trial evaluating the clinical benefit of montelukast for treating spring seasonal allergic rhinitis. Ann Allergy Asthma Immunol 2003;90:214-22.
27. Van Cauwenberge P. Advances in allergy management. Allergy 2002;57 Suppl 75:29-36.
28. Potter PC; Paediatric Levocetirizine Study Group. Efficacy and safety of levocetirizine on symptoms and health-related quality of life of children with perennial allergic rhinitis: a double-blind, placebo-controlled randomized clinical trial. Ann Allergy Asthma Immunol 2005;95:175-80.
29. Bachert C, Bousquet J, Canonica GW, Durham SR, Klimek L, Mullol J, et al. Levocetirizine improves

quality of life and reduces costs in long-term management of persistent allergic rhinitis. J Allergy Clin Immunol 2004;114:838-44.
30. Walter Canonica G, Bousquet J, Van Hammée G, Bachert C, Durham SR, Klimek L, et al. Levocetirizine improves health-related quality of life and health status in persistent allergic rhinitis. Respir Med 2006;100:1706-15.
31. Ciebiada M, Górska-Ciebiada M, DuBuske LM, Górski P. Montelukast with desloratadine or levocetirizine for the treatment of persistent allergic rhinitis. Ann Allergy Asthma Immunol 2006;97:664-71.