# Desloratadine-montelukast combination improves quality of life and decreases nasal obstruction in patients with perennial allergic rhinitis

Cemal Cingi, MD[1], Fatih Oghan, MD[2], Gorkem Eskiizmir, MD[3], Aytekin Yaz, MD[4], Ahmet Ural, MD[5] and Nagehan Erdogmus, MD[1]

***Background:*** **The effects of desloratadine-montelukast combination on quality of life (QoL) and nasal airflow of patients with perennial allergic rhinitis (PAR) has not been reported. The objective of this work was investigate the efficacy of desloratadine-montelukast combination on nasal obstruction and health-related quality of life (HRQL) of patients with PAR.**

***Methods:*** **The patients with PAR (n = 40) were assessed using acoustic rhinometry (AcR) and Rhinoconjunctivitis QoL Questionnaire (RQLQ) before therapy. Desloratadine-montelukast fixed-dose combination treatment was applied to every patient once daily. The AcR and RQLQ score were reevaluated at the first and third months; and statistical comparison of pretreatment and posttreatment results was performed.**

***Results:*** **Nasal symptoms and signs such as itching, sneezing, discharge, congestion, and edema, and color change of turbinates have been decreased after treatment. In AcR, minimum cross-sectional area (MCA) measurements and volume results were increased after the treatment. Correlation was found between the volume results and nasal discharge and/or congestion in right nasal passages. In left nasal passages, statistical relation was observed between the MCA and itching and/or change of turbinate color ($p < 0.05$). A significant decrease in the overall RQLQ score was determined at the first and third months of therapy. The difference between scores at baseline and end of the first and third months for all domains was statically significant ($p < 0.001$). The treatment difference in change from the first month to the end of the third month was statistically significant ($p < 0.05$).**

***Conclusion:*** **Desloratadine-montelukast combination therapy causes subjective and objective decrease in nasal obstruction, reduces the other symptoms of PAR and improves the disease-specific QoL.** © 2013 ARS-AAOA, LLC.

*Key Words:*
**allergic rhinitis; quality of life; therapeutics; desloratadine; montelukast**

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Allergic rhinitis (AR) is a common chronic condition, estimated to affect up to 25% of adults and up to 40% of children in the developed countries.[1,2] AR presents with nasal symptoms (nasal obstruction, rhinorrhea, itching, and sneezing) and frequently causes eye signs and symptoms (redness, puffy lids, tearing, and itching) and mouth and throat symptoms (itching of the palate and pharynx and postnasal drainage). In many instances, patients also complain of headache and fatigue, and note significant decrease on their quality of life (QoL).[3] Traditionally, AR has been classified as either seasonal or perennial on the basis of the seasonality of allergen exposure. In seasonal AR, rhinitis symptoms show seasonal levels of such outdoor allergens as molds and pollens, usually during the spring and autumn. Perennial AR (PAR) involves an immunoglobulin E (IgE)-mediated reaction to allergens that display little or no seasonal variation and thus cause symptoms throughout the year; PAR is commonly caused by inhaled indoor

[1]*Department of Otorhinolaryngology, Faculty of Medicine, Osmangazi University, Eskisehir, Turkey;* [2]*Department of Otorhinolaryngology, Faculty of Medicine, Dumlupinar University, Kutahya, Turkey;* [3]*Department of Otorhinolaryngology, Faculty of Medicine, Celal Bayar University, Manisa, Turkey;* [4]*Department of Otorhinolaryngology, Tepecik Training and Research Hospital, Izmir, Turkey;* [5]*Department of Otorhinolaryngology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey*

Correspondence to: Cemal Cingi, MD, Osmangazi University, Faculty of Medicine, Department of Otorhinolaryngology, 26000, Meselik Kampus, Eskisehir, Turkey; e-mail: ccingi@ogu.edu.tr

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allergens such as dust mites, animal dander, cockroaches, and mold.[4]

Numerous mediators are implicated in the pathogenesis of AR, 2 of the most abundant being histamine and cysteinyl leukotrienes. The effect of intranasal administration of histamine and cysteinyl leukotrienes on AR symptoms is quite characteristic.[5] Histamine has been suggested to be primarily involved in the induction of sneezing, rhinorrhea, and nasal itching, but it has an obstructive effect only at relatively high concentrations. On the other hand, intranasal administration of leukotrienes causes mainly nasal blockage only, with very limited affects on the 3 other characteristic symptoms of AR.[6,7] Thus, the combination of these 2 anti-mediator therapies could theoretically provide additional benefits compared with the blockage of a single mediator only.

In the past 2 decades, acoustic rhinometry (AcR) has been used in studies involving nasal diseases and treatments, especially to analyze nasal congestion in various situations.[8–11] Acoustic rhinometry is a fast painless and noninvasive diagnostic method that requires little collaboration from the patient.[12] The test calculates cross-sectional areas at different points of the nasal cavity, providing area and distance mapping, with information on the location of sites with increased narrowing, called minimum cross-sectional areas (MCAs). It also provides information on nasal volume.[9,10,13,14] Some studies[8,15,16] have already used AcR to observe nasal geometry changes after treatment of nasal obstruction.

Because AR symptoms and individual Rhinoconjunctivitis QoL Questionnaire (RQLQ) domain scores have been shown to correlate only moderately in subjects with AR,[17] acquiring an accurate overall assessment of patient health needs depends on concomitant evaluation of symptom scores and health-related QoL (HRQL). HRQL has been recognized as an essential outcome measure in clinical studies.[18] The RQLQ, one of the most widely used rhinitis-specific questionnaires,[19] is composed of 28 questions focusing on 7 dimensions of health: activities, sleep, non-nose/eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotional functioning.[20] The purpose of this prospective study was to evaluate the effects of desloratadine-montelukast combination treatment on signs and symptoms of PAR and the impact on QoL in patients with PAR.

## Patients and methods

The research protocol was approved by the Eskisehir Clinical Research Ethical Committee.

### Study design

This was a prospective and multicentric clinical trial performed between March and June 2011 at 4 different medical centers including Eskisehir, Kutahya, Izmir, and Manisa. Fifty patients who were diagnosed with PAR were enrolled; however, only 40 patients completed the study. The patients were evaluated at 2 control visits after the diagnosis. All patients were treated with desloratadine-montelukast fixed-dose combination therapy (desloratadine 5 mg and montelukast 10 mg), which was taken daily for 3 months. All the participants were instructed to keep a diary of daily symptoms and medication use during the study; no rescue medications were allowed. The severity of sneezing, itching, nasal discharge, nasal congestion, and other findings, including turbinate edema and color change, were recorded before and after treatment on a 0 to 3 scale.

For evaluation of HRQL in study group, the RQLQ was used. Treatment difference was defined as the change from baseline to the end of the first and third months.

AcR was performed before and 90 days after treatment (SRE 2.100 rhinometer; RhinoMetrics A/S, Lynge, Denmark). The examinations were performed following Standardization Committee on Acoustic Rhinometry recommendations.[21] The patient's medical history was recorded, and the otolaryngology examination was performed in the same room as the AcR, which enabled a period of adaptation to the environment. This is an important aspect because nasal mucosal congestion is affected by changes in temperature and air humidity and by physical activity (walking to the test location). The tests were performed with the patient sitting down, with the head resting on the back of the chair to prevent it from moving. The mean value of the MCA ($cm^2$) and the distance (cm) from the tip of the nosepiece to the nasal cavity were used to calculate the volume of each nostril. Three alternate measurements were performed on each side of the nasal cavity. If any errors were detected, the area-distance curve for the specific measurement was discarded and the mean of the remainders was used. Fewer than 10% of measurements were discarded, and in no case were all 3 rejected.

### Patients

There were 40 patients (12 male, 28 female) in the study group, all of whom had a diagnosis of PAR at least for 2 years. Patients were healthy, nonsmoking adults aged 20 to 51 years. The diagnosis of AR was established in light of medical history, physical examination findings, and weal diameter of larger than 3 mm in the prick test. According to the Allergic Rhinitis and its Impact on Asthma (ARIA) classification, the diagnosis of PAR was determined for patients with allergic symptoms occurring more than 4 days per week or more than 4 weeks per year. The exclusion criteria were as follows: pregnancy; breast feeding; application to a physician in the previous 6 weeks for upper respiratory infections; sensitization to seasonal allergens (grass, trees and weed pollens); presence of asthma, vasomotor rhinitis, and/or nasal polyp, septal deviation; use of systemic or topical corticosteroids and antihistamines in the last month; and use of allergen-specific immunotherapy.

**TABLE 1.** Pretreatment and posttreatment mean MCA and volume values

| | Nasal passage | MCA ($cm^2$) | | Volume ($cm^3$) | |
|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD |
| Pretreatment | L | 0.31 | 0.08 | 2.7 | 0.55 |
| | R | 0.34 | 0.08 | 2.99 | 0.40 |
| Posttreatment | L | 0.38 | 0.07 | 3.1 | 0.40 |
| | R | 0.40 | 0.07 | 3.37 | 0.41 |

L = left; MCA = minimum cross-sectional area; R = right; SD = standard deviation.

### RQLQ

The RQLQ, which was originally developed by Juniper and Guyatt,[20] was administered to all patients. This questionnaire contains 28 questions related to symptoms grouped into 7 domains: sleep, non–hay fever symptoms, practical problems, nasal problems, eye symptoms, activities (ie, activities that have been limited by nose or eye symptoms), and emotional function. Patients were asked to provide their responses on a 7-point scale (0 = no impairment, 6 = severe impairment) at baseline, first month, and third month. Eligible participants completed the RQLQ and underwent measurement of nasal volume by AcR before starting the study and after the treatment at third month. The overall mean score for all 28 questions was determined. A high score corresponds to low QoL.

### Statistical analysis

SPSS for Windows version 15.0 (SPSS Inc., Chicago, IL) was used for statistical analysis. The statistical analysis was performed using the Wilcoxon matched signed ranks and Kolmogorov-Smirnov tests. The correlation analysis was used to determine the correlation between the AcR results and findings and/or symptoms of PAR. A $p$ value $> 0.05$ was considered statistically significant.

## Results

The study group (n = 40) comprised 28 females, with a mean ± SD age of 33.3 ± 10.5 years, and 12 males, with a mean ± SD age of 30.9 ± 8.8 years. There were no statistically significant differences between the female and male patients for age ($p = 0.491$).

Nasal symptoms and findings including itching, sneezing, discharge, congestion, and edema, and color change of turbinate have been decreased after treatment. In AcR, mean MCA measurements and volume results were statistically higher than before treatment (Table 1, $p < 0.001$). Pretreatment and posttreatment mean MCA values were given in a graphic modality (Fig. 1). Correlation was found between the volume results and nasal discharge and/or congestion in right nasal passages (r = 0.323, r = 0.391, $p < 0.05$). In left nasal passages, statistical relation was described between the MCA measurements and itching and/or change of turbinate color (r = 0.381, r = 0.373, $p < 0.05$). Correlations with AcR were generally low.

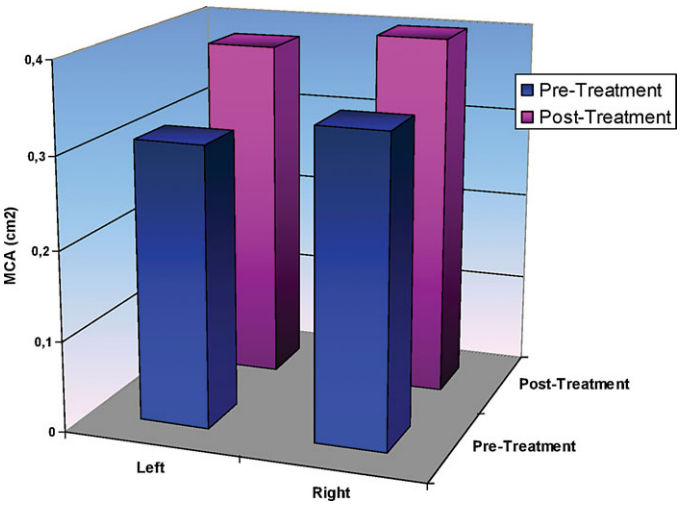


**FIGURE 1.** Pretreatment and posttreatment mean MCA values. MCA = minimum cross-sectional area.

There was a larger decrease in the overall RQLQ score for the group using desloratadine plus montelukast compared with the pretreatment scores. The difference between scores at baseline vs the end of the first and third months for all domains was statically significant (Table 2, $p < 0.05$). The treatment difference in change from the first month to the end of the third month was statically significant, in favor of the third month, for eye, nose, and non-nose/eye symptoms, sleep, practical problems, emotions, and activities that have been limited by nose or eye symptoms, and for overall score ($p < 0.05$, $p < 0.001$, $p < 0.001$, $p < 0.05$, $p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$, respectively).

## Discussion

Leukotrienes are proinflammatory lipid mediators.[22] Montelukast acts as a highly specific cysLT1 receptor antagonist and has a similar effect as loratadine; however, it is less effective than intranasally applied corticosteroids when used alone.[23] In literature, the indications and application of montelukast in AR are controversial. In a nasal challenge study, significant decreases in number of sneezes and nasal obstruction were reported either after montelukast alone or loratadine-montelukast combination.[24] When montelukast is used as a monotherapy in seasonal AR patients, it is more effective than placebo in curing daytime nasal symptoms, nighttime nasal symptoms, eye symptoms.[25–27] There is limited evidence on the efficacy of desloratadine plus montelukast in persistent and/or perennial AR, and also there is no study in the literature about the desloratadine-montelukast combination therapy. Patel et al.[28] reported that, after using montelukast for 6 weeks in the treatment of perennial AR patients, allergic symptoms and RQLQ improved significantly compared with placebo. A study using

**TABLE 2.** Descriptive statistics for domains and their comparison between the groups

| RQLQ (symptoms) | Baseline (mean ± SD) | $P_{BF}$ | First month (mean ± SD) | $P_{FT}$ | Third month (mean ± SD) | $P_{BT}$ |
|---|---|---|---|---|---|---|
| Eye problems | 3.68 ± 0.58 | <0.001 | 2.06 ± 0.32 | <0.05 | 3.25 ± 0.51 | <0.001 |
| Nasal problems | 3.21 ± 0.5 | <0.001 | 2.96 ± 0.46 | <0.001 | 2.78 ± 0.43 | <0.001 |
| None-nose/eye | 3.84 ± 0.6 | <0.001 | 3.46 ± 0.54 | <0.001 | 3.71 ± 0.58 | <0.001 |
| Sleep | 3.34 ± 0.52 | <0.001 | 3.0 ± 0.47 | <0.05 | 2.45 ± 0.38 | <0.001 |
| Activity | 4.12 ± 0.65 | <0.001 | 2.74 ± 0.43 | <0.001 | 3.87 ± 0.61 | <0.001 |
| Emotions | 4.87 ± 0.77 | <0.001 | 2.92 ± 0.46 | <0.001 | 4.41 ± 0.69 | <0.001 |
| Practical problems | 3.0 ± 0.47 | <0.001 | 2.68 ± 0.42 | <0.001 | 2.41 ± 0.38 | <0.001 |
| Overall | 15.32 ± 2.42 | <0.001 | 10.86 ± 1.71 | <0.001 | 13.22 ± 2.09 | <0.001 |

$P_{BF}$ = statistical significance between the baseline and first month; $P_{BT}$ = statistical significance between the baseline and third month; $P_{FT}$ = statistical significance between the first and third months; QoL = quality of life; RQLQ = Rhinoconjunctivitis QoL Questionnaire; SD = standard deviation.

zafirlukast found that it was more efficient on nasal obstruction in persistent AR patients.[29] In addition, Cingi et al.[30] found that montelukast was more effective for sleep, practical problems, nasal problems, and activities domains in patients with PAR. In persistent AR, nasal congestion is more pronounced than nasal itching and sneezing. This has been attributed to congestion and increased nasal resistance attributable to increased vasodilatation and permeability in which leukotrienes play a role. Understanding the role of leukotrienes in AR pathogenesis explains the higher rate of improvement provided by montelukast in some domains of the RQLQ that are related to the nasal condition.

In this study, we detected that combination desloratadine-montelukast treatment once daily for 3 months causes significant improvements in the daytime nasal symptoms score of patients with PAR. This medication was also significantly effective in improving nighttime symptoms, daytime eye symptoms, and all QoL parameters. On the other hand, particularly in patients with PAR, the coexistence of asthma should also be examined[4]; therefore, combination treatment modalities that may treat the upper and lower respiratory tracts efficiently and safely should be preferred. In this respect, desloratadine-montelukast combination is an ideal drug choice for the treatment of upper and lower respiratory tracts in patients with PAR. Our study is the first clinical trial in which the benefits of desloratadine-montelukast combination therapy in patients with PAR were demonstrated. Our study clinical results using with fixed-dose combination therapy for PAR are complement and validate previous researches demonstrated roles of cysteinyl leukotrienes plus histamines as inflammatory mediators in the pathophysiology of PAR.

Acoustic rhinometry is used to assess the geometry of the nasal cavities, including both the cross-sectional areas and the volume of the nasal cavities at various distances from the nostrils.[31] Roithmann et al.[32] suggested that AcR is especially useful in evaluating the response of nasal mucosa to allergen in allergic patients. However, it is actually used as an adjunctive diagnostic method, and the threshold for positive response is still needed. On the other hand, evaluating for rebound in a population with changing degrees of congestion as occurs in patients with PAR is difficult. Also, the arms of the study with effective treatments should favorably influence symptoms and airflow assessments. In this study, nasal obstruction was objectively evaluated by AcR and subjectively by symptom scores. AcR is often used for monitoring the therapeutic trials for seasonal rhinitis, impaired nasal patency, and nasal polyps.[33] Our study demonstrated that AcR is an ideal method for evaluating these changes in the prognosis of disease because it is accurate and objective and can be easily performed in patients with PAR.

The effects of desloratadine-montelukast combination therapy were seen most clearly in the nighttime symptoms including difficulty going to sleep and staying asleep, as well as nasal congestion on awakening, while daytime nasal, eye, and daily composite scores numerically favored desloratadine. The improvement in nasal congestion is not unexpected because nasal challenge with cysteinyl leukotrienes cause nasal blockage. We compared data at baseline, first month, and end of the treatment using with RQLQ. This multicenter study demonstrates that reductions in symptoms scores with desloratadine-montelukast combination therapy are accompanied by significant improvement in disease-related QoL in patients with PAR. The reduction of symptom scores with desloratadine-montelukast combination therapy is probably the major determinant of the QoL improvement. The improvement in QoL of patients with PAR has not been reported to date in the peer-reviewed literature after desloratadine-montelukast combination therapy. The improvements produced by fixed-dose combination therapy in QoL parameters—including sleep, activity, and emotions domains—are findings that have substantial clinical relevance, as PAR is now understood to significantly impair QoL for affected patients.[34] Desloratadine-montelukast combination therapy was shown to have a greater effect on RQLQ than nontreated patients with PAR. Ciebiada et al.[35] found that montelukast alone,

levocetirizine alone, desloratadine alone, and the montelukast/antihistamine combinations significantly improved nasal symptoms during the first 24 hours in patients with PAR. Improvement gradually increased during the 6 weeks of treatment, especially in patients receiving montelukast alone or in combination therapy with the antihistamine in both arms. Improvement at 42 days of treatment was significantly greater than that achieved on the first day of therapy in patients treated with the combination therapy, as well as in our study. McLeod et al.[36] reported that concomitant montelukast plus loratadine produces a greater degree of nasal decongestion compared with montelukast or loratadine alone in an experimental model of nasal congestion. They used AcR to determine nasal cavity dimensions and to compare volume ratios of nasal cavities for the control, montelukast alone, loratadine alone, and the montelukast plus loratadine-treated groups. In their review study, Cingi et al.[37] concluded that desloratadine plus montelukast therapy increase their potency when they are used in combination treatment when compared to their use separately. Adsule and Misra[38] emphasized that montelukast when used as monotherapy is efficacious and improves quality of life. Combination therapy (montelukast plus levocetirizine) is a more effective strategy than monotherapy in the treatment of PAR. Singh-Franco et al.[39] described that levocetirizine 5 mg/day is effective in reducing symptoms of PAR, seasonal AR, and improving QoL, with an acceptable tolerability profile when it is used alone. Ciebiada et al.[40] found that, montelukast, desloratadine, and levocetirizine significantly improved QoL. Combining montelukast with either levocetirizine or desloratadine gave additional benefits in comparison to each agent alone and could be considered for patients whose QoL is impaired by PAR. Wandalsen et al.[41] emphasized that patients with PAR had significantly higher score of symptoms when compared to controls, as well as lower nasal volumes. In addition, they used AcR to assess drug effects as an objective method. In our study, we used AcR to objectively evaluate drug effects on nasal obstruction.

## Conclusion

Desloratadine-montelukast combination therapy is beneficial for the reduction of nasal signs and symptoms and nasal obstruction of patients with PAR. Moreover, this treatment can provide a significant improvement in HRQL of patients whose QoL was impaired due to PAR. Desloratadine-montelukast combination therapy is well tolerated and provides significant benefits in patients with PAR, both in reduction of daytime and nighttime rhinitis symptoms. Desloratadine-montelukast combination therapy is better than desloratadine or montelukast monotherapy at improving the disease-specific QoL in the treatment of PAR. AcR is a practical measure used in diagnostic and prognostic procedures for patients with PAR. In addition, the benefits of desloratadine-montelukast combination therapy for patients with PAR can be evaluated by the parameters of AcR including MCA and volume. On the other hand, the main limitation of the study method was lack of a control group.

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