

ORIGINAL RESEARCH

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Comparison of therapeutic efficacy of antihistaminics and combinations of montelukast with allergic rhinitis**Erkan Yildiz¹, Selcen Koca Yıldız², Sahin Ulu³, Tulay Koca³**¹*Afyonkarahisar Suvat State Hospital, Department of Otorhinolaryngology, Afyonkarahisar, Turkey*²*Afyonkarahisar Healty Science University Hospital, Department of Pharmacist, Afyonkarahisar, Turkey*²*Afyonkarahisar Healty Science University Hospital, Department of Otorhinolaryngology, Afyonkarahisar, Turkey*³*Afyonkarahisar Healty Science University Hospital, Department of Physiology, Afyonkarahisar, Turkey*

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Abstract

Allergic Rhinitis is basically a chronic disease that decreases quality of life. Antihistaminics have been used for the first time in allergic rhinitis. In the search for an alternative treatment in resistant allergic rhinitis, Montelukasts and their combinations have been used. Randomized double-blind controlled study. In our study, the effect on the quality of life of the compounds used recently be compared after 3 months of treatment. In this study, 7 groups of 40 patients, 18-65 years old were planned for each group. The number of females and males was equal in each group (20). The patients in group A and group B will be called for checks after 3 months of medical treatment in the C-D-E-F-G-H group without treatment for 3 months. The patients in Group C received 10 mg Rupatadin Fumarate tablets orally (1 * 1 single dose) before bedtime, 5 mg Levosetirizine Dihydrochloride tablets in the patients in Group D orally (1 * 1 single dose) before bedtime, 10 mg Montelukast Sodium tablets in patients in Group E Before oral (1 * 1 single dose), patients in Group F 5 mg Desloratadin + 10 mg Montelukast Sodium tablets orally (1 * 1 single dose) before bedtime, and patients in Group G Levocetirizine Dihydrochloride + 10 mg Montelukast Sodium tablet orally before bedtime (1 * 1 single dose) will be given. These treatments will continue for 3 months without interruption. The Rinokonjucivations Quality of Life Questionnaire (RQLQ) will be completed with a total of 28 questions. No significant superiority of the Rupatadine molecule to levocetirizine was detected. The score of the Montelukast areas was significantly low when compared to the Rupatadine and Levosetirizine groups. Combined Montelukastes were found to be much more effective than single antihistaminics and single montelukast. There was no difference in quality of life between the combined Montelukast. Antihistaminics are the first treatment option in patients with allergic rhinitis, In resistant cases, combinations with montelukast should be used.

Keywords: Allergic rhinitis, quality of life, rupatadine, levosetirizine, montelukast, combined montelukast**Introduction**

Allergic rhinitis is a common chronic disease that affects 20-40% of children and adults in all centers [1,2]. Both nasal symptoms (nasal congestion, nosebleeds, itching, and sneezing) in allergic rhinitis, both eye symptoms (redness, swelling caps, tearing, and itching) and mouth symptoms (itching of the pharynx and palate) are seen [3]. In most cases, it is called headache and fatigue [4]; The aim of this study is to compare the effects of the drugs used in the intermittent and persistent form of the most common allergic rhinitis.

The first study of rupatadine in allergic rhinitis was conducted by Izquierdo I. et al., and after many studies, the use of the same light allergic rhinitis became widespread [5]. In the 2000s, the search for alternative treatment began instead of these chemicals which are not sufficient at times [7-10]. With the support of recent studies, both montelukast and combinations have been found to improve the quality of life in practice [11-15].

The effect of montelukast, desloratadine + montelukast and levosetirizine + montelukast combinations on the quality of life and the quality of life will be compared with non-sedative antihistaminics such as rupatadine, levocetirizine, which are given as the first treatment in mild allergic rhinitis. Thus, the most accurate and the most economical molecule in the treatment will be determined.

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Material and Methods

The study was carried out at the Otorhinolaryngology clinic. The study is planned to be conducted between April 2018 and April 2020. In this study, 7 groups of 40 patients, 18-65 years old (mean age 38), were planned for each group. The number of females and males was equal in each group (20 males and 20 females).

- 1) Smoking
- 2) Pregnancy and Lactation
- 3) Migrating Upper Respiratory Tract Infection in Last 6 Weeks
- 4) Oral and Topical Steroid Use
- 5) Patients with structural pathologies such as nasal septum deviation and polyp were the groups excluded

Study Design

The study was planned as a randomized controlled group. Group A Healthy People, Group B Allergic Rhinitis (Placebo), Group C Allergic rhinitis, Rupatadine areas, Group D Allergic rhinitis, Levosetirizine areas, Group E Allergic rhinitis, Montelukast areas, Group F Allergic rhinitis Desloratadin + Montelukast areas and Group G Allergic rhinitis and Levosetirizine + will be created by patients using Montelukast. The patients in Group A would consist of patients without any healthy disease, patients in Group B who were diagnosed as Allergic Rhinitis, who did not want to receive treatment (placebo), and all the patients in the other (C-D-E-F-G) groups were diagnosed with Allergic Rhinitis and treated separately. Patients in group A and group B will be called for control after 3 months of medical treatment in the C-D-E-F-G-H group without treatment for 3 months. Patients in Group C received 10 mg Rupatadin Fumarate tablets orally (1 * 1 single dose) before bedtime, 5 mg Levosetirizine Dihydrochloride tablets in patients in Group D orally (1 * 1 single dose) before bedtime, 10 mg Montelukast Sodium tablets in patients in Group E Before oral (1 * 1 single dose), patients in Group F 5 mg Desloratadin + 10 mg Montelukast Sodium tablets orally (1 * 1 single dose) before bedtime and patients in Group G Levocetirizine Dihydrochloride + 10 mg Montelukast Sodium tablet orally before bedtime (1 * 1 single dose) will be given. These treatments will continue for 3 months without interruption. The Rinokonjucivations Quality of Life Questionnaire (RQLQ) will be performed with a total of 28 questions.

The research protocol was approved by the Afyonkarahisar Health Sciences University Medical Faculty Clinical Research Ethics Committee (2018 1-2).

Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ)

The questionnaire consisted of 7 main subjects and 28 questions. There are 7 main headings in the questionnaire: eyes, nasal, emotional symptoms, symptoms other than the eyes and nasal, activities and problems in practice. There are 0 to 4 (0=none, 6=severe) scores in 4 questions in each title. The average scores were calculated for all 28 problems. The higher the score, the lower the quality of life.

Statistical Analysis

SPSS 21.0 (for Windows) was used for analysis. The ANOVA test and Bonferroni validation test were used in 7 group's RQLQ

questionnaire. The results were expressed as mean $\pm$ SD and $p < 0.05$ was considered statistically significant.

Results

Half of the patients in the study group ($n=40$) were male (20) and half (20) were female. The mean age was 36.1 ± 8.2 for the first group, 33.7 ± 9.1 for the 2nd group, 37.2 ± 8.9 for the third group, 37.7 ± 4.2 for the 4th group, 36.5 ± 5.8 for the 5th group, and $38.2 \pm$ for the 6th group. The mean score was 35.8 ± 5.8 for the 7th group. There was no difference between the groups in terms of age ($p=0.78$, p group 0.05).

When the control group was compared to all the groups, the difference was significant ($p < 0.05$). The scores decreased significantly in all the given drug groups. The placebo group was significantly different when compared to the other groups ($p < 0.05$). No significant difference was observed between the Rupatadine group and Levosetirizine group ($p > 0.05$). In the same way, a significant difference was observed in the groups of Desloratadin + Montelukast and Levosetirizine + Montelukast group against the Rupatadine and Levocetirizine monotherapy groups. ($p < 0.05$). The combined montelukast groups also showed a significant difference when compared to single montelukast group ($p < 0.05$). There was no significant difference observed in the Desloratadin + Montelukast and Levosetirizine + Montelukast group.

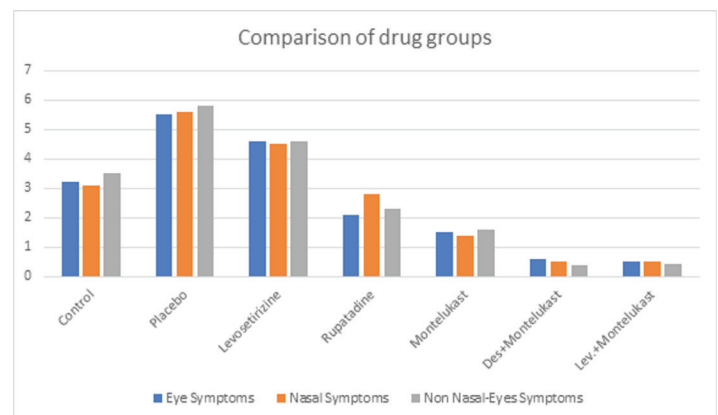


Figure 1. Comparison of drug groups (Eyes, nasal, non-nasal, and eye symptoms)

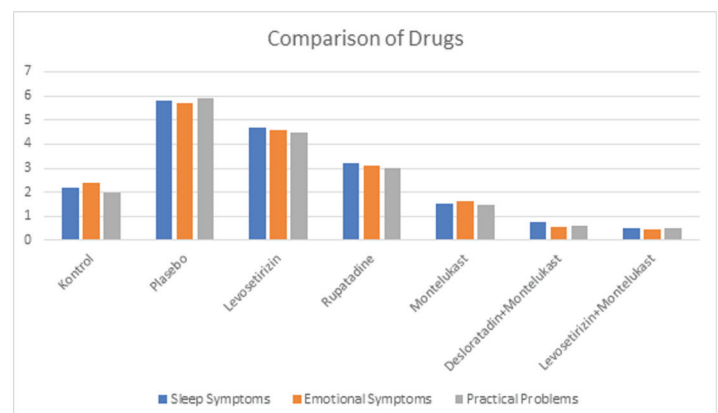


Figure 2. Comparison of drug groups (Sleep, emotional, and practical problem symptoms)

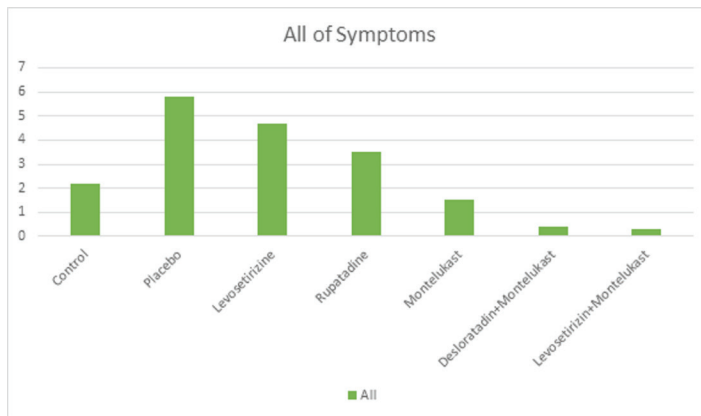


Figure 3. Comparison of drug groups (Comparison of the average of all symptoms)

When the results are compared,

- 1) No significant superiority of the Rupatadine molecule to levocetirizine was detected.
- 2) The score of the Montelukast areas was significantly low compared to the Rupatadine and Levocetirizine groups.
- 3) The combined montelukastes were found to be much more effective than the single antihistaminics and the single montelukast.
- 4) There was no difference in quality of life between the combined montelukast.

Discussion

Allergic rhinitis is a chronic disease affecting the quality of life in a significant part of the population (10-40%). Therefore, it results in high treatment costs. Two important areas in the treatment of allergic rhinitis are pharmacotherapy and immunotherapy. Today, the most commonly used treatments are oral or nasal antihistaminics, nasal steroids, leukotriene receptor antagonists and their combinations with antihistaminics [16].

According to the updated ARIA (Allergic Rhinitis Impact on Asthma) guideline, ranking according to the severity of the complaints is in the form of a antihistaminics, antihistaminics + nasal steroids, leukotriene antagonists + nasal steroids. The first option is antihistaminics. These are used to reduce symptoms by decreasing the histamine of the allergen released from the mast cell. These can be combined with nasal steroids. Later, leukotriene receptor antagonists were used. These are effective in persistent allergy rhinitis when compared to antihistaminics. Combinations with antihistaminics have been introduced for more resistant cases. These are the last choices in treatment [17].

Montelukasts are leukotriene D4 antagonists. In studies on nasal mucosa, they cause vasodilatation with α agonist action. They reduce the need for nasal spray treatment [18]. However, local steroids always increase the effect of combined montelukasts [19]. Combinations are also used successfully in Allergic Rhinitis associated with asthma [20]. In another study, these drugs have been shown to reduce pharyngolaryngeal symptoms in patients with allergic rhinitis [21]. In another study in which different combinations were tested, the effect of the combinations was determined to be stronger than monotherapy. Montelukast Cetirizine, Desloratadine and Fexofenadine were added, their potency was more than monotherapy [22]. It was seen that Montelukast decreased the allergy formation in patients with

allergic rhinitis [23]. In a study comparing Montelukast with antihistaminics, Montelukast and Levocetirizine were found to be superior to other antihistaminics [24].

Cingi C. et al. found a significant increase in quality of life when compared to patients treated with montelukast and placebo patients. In another study, Desloratadine + Montelukasts significantly increased the quality of life 3 months after treatment [25]. The Montelukast fexofenadine combination has also been shown to be more beneficial than monotherapy [26]. Montelukastes are also reported to be more effective with topical treatment. In the final phase studies, in vitro, a montelukast nasal spray was used and the desired effect was shown in the nasal mucosa alone [27].

The combination of montelukast with antihistaminics was thought to increase the treatment effect. In the literature, there has been no study showing the efficacy of antihistaminics, montelukast, and combinations at the same time. We found that Levocetirizine and Rupatadine significantly increased the quality of life when compared to the control group. We found that this effect increased in uncoordinated montelukast, and the greatest effect was in the combined montelukast. There was no significant difference between Levocetirizine and Rupatadine in terms of quality of life. We found that Montelukastes were more effective than antihistaminics. We found that the combinations were much more effective than the non-combination montelukast. There was no significant difference in age quality between the combinations.

Conclusion

In conclusion, antihistaminics should be the first choice of treatment in patients with allergic rhinitis. Montelukast can be used in the case of unsolvability. In more resistant cases, combinations with antihistaminics should be given.

Conflict of interest

The authors declare that there are no conflicts of interest.

Financial Disclosure

All authors declare no financial support.

Ethical approval

The research protocol was approved by the Afyonkarahisar Health Sciences University Medical Faculty Clinical Research Ethics Committee (2018 1-2).

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