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Original Article / Çalışma - Araştırma

Effect of montelukast on quality of life in subjects with nasal polyposis accompanying bronchial asthma

Montelukastın eşlik eden bronşiyal astımı bulunan nazal polipli hastaların yaşam kalitesi üzerindeki etkisi

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Objectives: In this study we investigated the effect of adding montelukast to the treatment of nasal polyposis patients with bronchial asthma on quality of life.

Patients and Methods: Thirty consecutive subjects with nasal polyposis accompanying bronchial asthma treated in our clinic were prospectively evaluated. Subjects with aspirin hypersensitivity and seasonal allergic rhinitis were excluded. Patients were evaluated using the Turkish version of rhinosinusitis disability index (RSDI) and visual analog scores before the montelukast therapy, one and three months after the therapy started. It must be noted that in addition to being treated with anti-leukotriene therapy, all of these subjects continued to receive routine nasal steroid treatment. In all subjects paranasal sinus tomography scans were obtained during the study. Lund-Mackay staging system, which is a radiological scoring system, was used in the staging of the disease severity.

Results: Rhinosinusitis disability index scores improved during the study period. Functional, emotional and physical sub-scales of RSDI were compared separately. But 1st and 3rd month scores are not statistically significant when compared with scores previous to montelukast therapy ($p>0.05$). Visual analog scale also showed a statistically significant decrease during the study period ($p<0.01$). Lund-Mackay staging did not show a statistically significant difference during the study period ($p>0.05$).

Conclusion: This study showed that montelukast therapy might have a clinical benefit as an adjunct to nasal steroids in subjects with nasal polyposis accompanying bronchial asthma.

Key Words: Montelukast; nasal polyposis; quality of life.

Amaç: Bu çalışmada bronşiyal astımlı nazal polipli hastaların tedavisine montelukast eklenmesinin yaşam kalitesine etkisi araştırıldı.

Hastalar ve Yöntemler: Kliniğimizde tedavi gören bronşial astımlı nazal polipli 30 ardışık hastanın semptomları ileriye dönük olarak değerlendirildi. Aspirin hipersensitivitesi ve mevsimsel alerjik riniti olan hastalar çalışma dışı bırakıldı. Hastalar montelukast tedavisi öncesinde ve tedaviye başlanmasından bir ve üç ay sonra rinosinüzit kısıtlılık ölçeğinin (RSKÖ) Türkçe versiyonu ve görsel analog ölçeği kullanılarak değerlendirildi. Belirtilmesi gereken önemli bir nokta da çalışma sırasında anti-lökotrien terapisiyle tedavi edilmelerine ilave olarak tüm hastalar rutin mazal steroid tedavilerini almaya devam etti. Çalışma sırasında tüm hastaların paranazal sinüs tomografileri çekildi. Hastalığın şiddetinin evrelenmesinde radyolojik skorlama sistemi olan Lund-Mackay evreleme sistemi kullanıldı.

Bulgular: Rinosinüzit kısıtlılık ölçeği puanlarında çalışma boyunca iyileşme oldu. Rinosinüzit kısıtlılık ölçeğinin fonksiyonel, emosyonel ve fiziksel alt skalaları ayrı ayrı karşılaştırıldı. Fakat 1. ve 3. aylardaki skorlar montelukast tedavisi öncesi skorlarla karşılaştırıldığında istatistiksel olarak anlamlı bulunmadı ($p>0.05$). Çalışma süresince görsel analog ölçekte de istatistiksel olarak anlamlı düşüş görüldü ($p<0.01$). Çalışma süresince Lund-Mackay radyolojik evreleme sisteminde istatistiksel olarak anlamlı fark gözlenmedi ($p>0.05$).

Sonuç: Bu çalışma, montelukast tedavisinin eşlik eden bronşiyal astımı olan nazal polipli hastalarda nazal steroidlere ek olarak klinik yararı olabileceğini gösterdi.

Anahtar Sözcükler: Montelukast; nazal polipozis; yaşam kalitesi.

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Nasal polyps are a frequently encountered problem in otolaryngology practice; however, the mechanisms underlying that condition are poorly understood. The main goals of management of nasal polyposis are to eradicate polyps, eliminate symptoms and prevent recurrence as well as improve life quality. After therapy, successful results cannot be obtained in all subjects. There is also a dilemma concerning the pathophysiology of nasal polyps. In recent years, there has been increasing interest in the potential role of leukotrienes (LT).[1]

Leukotrienes are inflammatory mediators which are the derivates of arachidonic acid via the 5-lipoxygenase pathway. Leukotrienes are produced by a number of cells including eosinophils, mast cells, macrophages, monocytes and basophils. LTC4 LTD4 and LTE4 are also called cysteinyl leukotrienes (C-LTs) as the target receptor of these molecules is the cysteinyl leukotriene receptor type 1 (CysLt1).[2] These molecules lead to contraction of human airway smooth muscle, chemotaxis, increased vascular permeability and modulation of airway mucus secretion.[3]

The LT pathway can be modified by two routes.[1] One is the inhibition of production of LTs by 5-lipoxygenase with zileuton and the other is the antagonism of the action of the LT at the CystLt1 receptor with zafirlukast, pranlukast or montelukast. Montelukast is the only available anti-LT in Turkey.

The roles of LTs has been emphasized in the pathogenesis of asthma, allergic rhinitis and nasal polyposis. For asthma pathogenesis LTs play a role in bronchoconstruction, airway hyperreactivity and airway inflammation. In addition it has been shown that the use of anti-LTs in mild and moderate asthma leads to clinical improvement in these groups of subjects. But results are insufficient to enable the optimum usage of anti-LTs in subjects with bronchial asthma. For allergic rhinitis it has also been shown that LTB4 and LTC4 levels are increased during allergen exposure.[1] Two recent studies showed clinical improvement of symptoms and quality of life in subjects with seasonal allergic rhinitis.

Leukotriene B4 and LTC4 are also increased in subjects with nasal polyposis.[3] Leukotriene C4 has also been found as prognostic for recurrence of nasal polyposis. Few studies reporting the utility of anti-LTs in subjects with nasal polyposis exist in the literature. The aim of this study is to evaluate the potential effect on life quality by the anti-LT montelukast, as an adjunct to nasal steroid medication in subjects with nasal polyposis accompanying bronchial asthma.

PATIENTS AND METHODS

This study was performed at the Ear Nose and Throat (ENT) Clinic Bakırköy Dr. Sadi Konuk Training and Research Hospital and the Experimental Ethics Committee of Bakırköy Training and Research Hospital approved the study protocol. Thirty subjects with nasal polyposis were included in this study. One subject was lost to follow-up and one subject did not complete the questionnaire. Two subjects were operated on during the study period at another ENT clinic and one subject had gastrointestinal side effects. Twenty-five subjects (16 males, 9 females; mean age 40.2±13.8 years; range 15 to 72 years) remained for inclusion. Nasal polyposis was diagnosed by nasendoscopy and radiology. Subjects with bronchial asthma, nasal polyposis and perennial allergic rhinitis were included. Pediatric subjects with a history of aspirin hypersensitivity or a history of seasonal allergic rhinitis were excluded. Systemic problems such as cystic fibrosis, Sjogren's syndrome, Wegener's granulomatosis and allergic fungal sinusitis which affect the sinuses were also excluded. Subjects with sinonasal malignancy and any previously prescribed systemic steroid medication were excluded from this study as well. All subjects were treated with daily nasal steroid (mometasone furoate monohydrate nasal spray, 50 mcg) for at least three months. The dosage of the spray was two sprays (50 mcg of mometasone furoate in each spray) in each nostril once daily (total daily dose of 200 mcg). The medication was continued and an additional 10 mg montelukast sodium (once daily, at night before the sleep) therapy was added. Subjects were evaluated using the Turkish version of the rhinosinusitis disability index (RSDI) previous to the montelukast therapy, and one and three months after the therapy started.[4] Computed tomography (CT) scans of all subjects were obtained during the study period. Disease severity was staged with the Lund-Mackay staging system radiologic score.[5]

The rhinosinusitis disability index is a 30-item questionnaire which includes 11 questions for physical status, nine questions for functional status and 10 questions for emotional status. Items of RSDI are listed in table 1. Responses are rated from 0 (never) to 4 (always) and the maximum score is 120. All subscale scores were also converted into a 100-point grading scale (0=good state, 100=bad state). After completing the RSDI, the subjects were asked to fully evaluate their nasal problems on a visual analog score (VAS) of 0 to 10 (0=mild; 10=severe).

Statistical analysis

Statistical analysis was performed using NCSS (Number Crunching Statistical System) 2007 & PASS 2008 Statistical Software (Utah, USA). All data were expressed as mean ± standard deviation. During the evaluation of the study data, along with the descriptive statistical methods, parameters with normal distribution for the comparison of qualitative data were evaluated using Kolmogorov-Smirnov test. When evaluating repeated parameters repeated measures ANOVA test was used. For evaluation of paired data Paired samples t-test was used. The relation between the parameters was assessed using the Pearson correlation analysis. Confidence interval was 95% and p value less than 0.05 was considered to be significant.

RESULTS

The RSDI emotional scores were decreased during the study period. Decrease of RSDI emotional scores on the 1st and 3rd months was not statistically significant when compared with pre-therapy scores ($p>0.05$). The RSDI functional scores did not show a statistically significant difference during the study period as well ($p>0.05$).

The RSDI physical scores improved in the study period. However, improvement at the 1st and 3rd months was not statistically significant compared to scores prior to therapy ($p>0.05$). The RSDI physical scores at the 1st month and 3rd month showed statistically significant decreases when compared with pre-therapy scores ($p=0.001$; $p<0.01$) It would be better to highlight that there was statistically significant improvement from baseline to follow-up (1 and 3 months; Table 2, Figure 1).

Visual analog scores also showed a statistically significant decrease during the study period ($p<0.01$). The values of VAS at the 1st month and 3rd month showed statistically significant decreases

Table 1. The rhinosinusitis disability index, domains and items

Physical status (11 items)
1. The pain or pressure in my face makes it difficult for me to concentrate.
2. The pain in my eyes makes it difficult for me to read.
3. I have difficulty stooping over to lift objects because of face pressure.
4. Because of my problem I have difficulty with strenuous yard work and housework.
5. Straining increases or worsens my problem.
6. I am inconvenienced by my chronic runny nose.
7. Food does not taste good because of my change in smell.
8. My frequent sniffing is irritating to my friends and family.
9. Because of my problem I don't sleep well.
10. I have difficulty with exertion due to my nasal obstruction.
11. My sexual activity is affected by my problem.
Functional status (9 items)
1. Because of my problem I feel handicapped.
2. Because of my problem I feel restricted in performance of my routine daily activities.
3. Because of my problem I restrict my recreational activities.
4. Because of my problem I feel frustrated.
5. Because of my problem I feel fatigued.
6. Because of my problem I avoid traveling.
7. Because of my problem I miss work or social activities.
8. My outlook on the world is affected by my problem.
9. Because of my problem I find it difficult to focus my attention away from my problem and on other things
Emotional status (10 items)
1. Because of my problem I feel stressed in relationships with friends and family.
2. Because of my problem I feel confused.
3. Because of my problem I have difficulty paying attention.
4. Because of my problem I avoid being around people.
5. Because of my problem I am frequently angry.
6. Because of my problem I do not like to socialize.
7. Because of my problem I frequently feel tense.
8. Because of my problem I frequently feel irritable.
9. Because of my problem I am depressed.
10. My problem places stress on my relationships with members of my family or friends.

Table 2. Summarized the mean scores of each rhinosinusitis disability index subscale, visual analog scores and Lund-Mackay staging scores mean values during the study period

	Previous therapy	1st month	3rd month	*p**
	Mean±SD	Mean±SD	Mean±SD	
RSDI emotional scores	43.50±22.67	39.00±25.41	35.30±24.27	0.088
RSDI functional scores	33.18±20.13	33.18±22.94	33.90±25.48	0.876
RSDI physical scores	49.60±24.07	38.88±25.08	35.44±24.58	0.003**
Visual analog scores	7.00±2.19	5.24±2.69	5.76±2.71	0.043*
Lund-Mackay staging	12.68±4.73	12.45±5.13	11.80±6.05	0.717

*: Repeated measures ANOVA test; **: p<0.05; RSDI: Rhinosinusitis disability index; SD: Standard deviation.

when compared with pre-therapy scores. (p=0.001; p<0.01) When compared the scores at 1st month and 3rd month there was no statistically significant decrease (p>0.05). Lund-Mackay staging did not show a statistically significant difference during the study period (p>0.05; Table 2).

DISCUSSION

This study showed that montelukast therapy might have a clinical benefit as an adjunct to nasal steroids in subjects with nasal polyposis accompanying bronchial asthma. This finding is consistent with the literature.[6] However, our preliminary results indicate that improvement was only seen in physical status, not in emotional and functional status.

Few studies exist in the literature that report the clinical benefit of montelukast therapy in subjects with nasal polyposis. Rosemary et al.[1] studied montelukast therapy in nasal polyposis. In the study group montelukast was added to oral and inhaled steroid therapy whereas the control group only received oral and nasal steroid therapy. When compared, subjects treated with montelukast showed a significant decrease in symptom scores including headache, facial pain and sneezing. However they were not able to show a significant effect on other symptoms including nasal blockage, anosmia or nasal discharge, overall symptom scores and quality of life parameters. They noted that there was a marked improvement in some subjects while other subjects had only marginal benefit. They also noted the difficulty of designing a therapeutic trial in nasal polyposis subjects and proposed larger, randomized and controlled studies which evaluated the effects of more prolonged therapy.

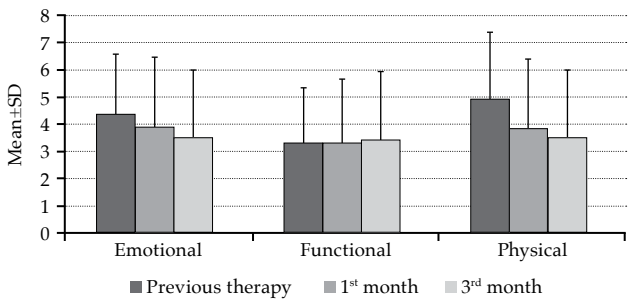

Figure 1. *Illustrated the mean scores of each subscale of rhinosinusitis disability index during the study period.*

Parnes and Chuma[2] reported 36 subjects treated with either zafirlukast, or zileuton. Overall they noted a 72% subjective improvement in patients' symptamotology. Fifty percent of the cases showed alleviation or stabilization in degree of nasal polyposis. Kieff and Busaba[7] reported 24 subjects who received montelukast therapy in addition to previous nasal steroid therapy. In 71% of the subjects symptoms were improved whereas the remaining 29% of the subjects' symptoms worsened. In addition to symptom scores polyp eosinophilia scores are also improved in 16 of the subjects.

These results showed that montelukast therapy resulted in convalescence in many subject's symptoms. It must be noted that in addition to being treated with anti-LT therapy, all of these subjects continued to receive routine nasal steroid treatment. The RSDI physical scores included such symptoms as facial pain, facial pressure, chronic draining nose, taste alteration, change in smell, sniffing and nasal obstruction. The decrease in subjects physical scores and overall VAS scores were also consistent with the literature. The therapeutic effect was seen on the first month visit. No additional clinical improvement was seen when the therapy was prolonged to three months.

In contrast to convalescence in physical scores and overall VAS scores, montelukast therapy did not change the disease severity when verified by Lund-Mackay radiologic staging. The observed benefit was found in the subjective measures (quality of life and visual analog scale) but not in the objective measures (such as Lund-Mackay score). These results may be influenced by a placebo effect.

This is one of the few studies evaluating the usefulness of montelukast in subjects with nasal polyposis accompanying bronchial asthma. We wanted to report our preliminary study results, recognizing that our bias is limited by small sample size and lack of randomization with a placebo control group. This is a single-group cohort trial and that it should be followed up with randomized clinical studies. For this study we excluded subjects with seasonal allergic rhinitis and aspirin hypersensitivity. Subjects with seasonal allergic rhinitis may exacerbate and need antihistamines. Therefore this exacerbation may have needed short time antihistamine use which could have affected the study results. To design a study in such distinct groups was proposed in previous studies.

We also need to note that when evaluated subject by subject, there are some cases which did not improve clinically during the study period in physical or overall VAS scores. We could not explain the exact reason for this finding. We think that this is why the pathogenesis of nasal polyposis is still unclear and variable.

In conclusion, this study showed that montelukast therapy might have a clinical benefit as an adjunct to nasal steroids in subjects with nasal polyposis accompanying bronchial asthma. Further randomized clinical trials are needed to demonstrate and establish the usefulness of anti-LT therapy in subjects with nasal polyposis.

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