Original Article / Çalışma - Araştırma

Effects of topical sprays on allergy-induced nasal obstruction in children

Çocuklarda topical spreylerin allerjiye bağlı burun tıkanıklığı üzerindeki etkileri

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Objectives: This study aims to evaluate the efficacy of mometasone furoate nasal spray, intranasal azelastine, and isotonic sea water nasal spray in the management of allergy-induced nasal obstruction.

Patients and Methods: Between October 2007 and August 2008 60 patients (37 males, 23 females; mean age 9.8±2.6 years; range 7 to 16 years) with a history of allergic rhinitis were included in the study. Laboratory assays including the skin prick test, nasal smear, phadiatop, total immunoglobulin E (IgE), and complete blood count test were performed. The patients were classified into three groups including 20 in each, according to the topical treatment administered. Patients in group 1 received azelastine, group 2 received mometasone furoate nasal spray, and group 3 received isotonic sea water nasal spray. Nasal passage volume was calculated using an acoustic rhinometry device.

Results: Azelastine and mometasone furoate decreased nasal congestion and increased nasal cavity volume more effectively, compared to isotonic sea water nasal spray.

Conclusion: Mometasone furoate and azelastine which decrease nasal congestion and increase nasal volume are effective in the management of allergic rhinitis in children.

Key Words: Acoustic rhinometry; allergic rhinitis; intranasal spray.

Amaç: Bu çalışmada allerjiye bağlı burun tıkanıklığının tedavisinde mometazon furoat burun spreyi, burun içi azelastin ve izotonik deniz suyu burun spreyinin etkinliği değerlendirildi.

Hastalar ve Yöntemler: Ekim 2007 - Ağustos 2008 tarihleri arasında alerjik rinit öyküsü olan 60 hasta (37 erkek, 23 kadın; ort. yaş 9.8±2.6 yıl; dağılım 7-16 yıl) çalışmaya dahil edildi. Laboratuvar yöntemleri olarak deri prik testi, burun sürüntü testi, fadiotop, total immünoglobulin E (IgE) ve tam kan sayımı yapıldı. Hastalar uygulanan topikal tedaviye göre 20'şerli üç gruba ayrıldı. Grup 1'deki hastalara azelastin, grup 2'dekilere mometazon furoat burun spreyi, grup 3'dekilere izotonik deniz suyu burun spreyi uygulandı. Burun pasaj hacmi, akustik rinometri aleti kullanılarak hesaplandı.

Bulgular: Mometazon furoat ve azelastin, izotonik deniz suyu burun spreyine kıyasla, daha etkin şekilde nazal konjesyonu azalttı ve burun hacmini artırdı.

Sonuç: Burun konjesyonunu azaltan ve burun hacmini artıran mometazon furoat ve azelastin, çocuklarda alerjik rinitin tedavisinde etkilidir.

Anahtar Sözcükler: Akustik rinometri; alerjik rinit; burun içi spreyi.

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Allergic rhinitis, a symptomatic disorder of the nose induced after exposure to allergens via immunoglobulin E (IgE)-mediated hypersensitivity reactions is characterized by four cardinal symptoms: rhinorrhea, nasal obstruction, nasal itching, and sneezing.[1] Recent studies show that the prevalence of allergic rhinitis is increasing all over the world. In the Turkish population, the prevalence of physician-diagnosed allergic rhinitis is 20.1%.[2] Allergic rhinitis is associated with an enormous economic burden, causing decreased quality of life, lowered work/school performance, and disturbed sleep.[3]

The diagnosis of allergic rhinitis is based on a typical history of allergic symptoms and positive diagnostic test results.[4] Allergic rhinitis is strongly suspected when two or more of the following symptoms persist for ≥1 hour on most days: rhinorrhea, sneezing, nasal obstruction, and nasal pruritus. The diagnosis should be confirmed by the skin prick test or the serum-specific IgE level.[5]

Various agents are used in the treatment of allergic rhinitis, however the use of these drugs are restricted in the pediatric population.[6,7] The intranasal corticosteroid mometasone furoate was effective and well tolerated in the relief of nasal symptoms, particularly obstruction, in subjects with seasonal and perennial allergic rhinitis in controlled clinical trials.[8] Azelastine exhibits a fast and long-acting effect based on a triple mode of action including anti-inflammatory, mast-cell stabilizing, and antiallergic effects. However, topical use of azelastine is more effective than the systemic antihistamine.[9] Nasal saline sprays have been recommended as an adjunct therapy to flush out mucus and irritants and improve the flow of air through the nose.[10]

The aim of our study was compare the efficacy of mometasone furoate, intranasal azelastine, and sea water in allergy-induced nasal obstruction by using acoustic rhinometry.

PATIENTS AND METHODS

This study was conducted on 60 children, (37 males, 23 females; mean age 9.8±2.6 years; range 7 to 16 years), admitted to the Cumhuriyet University Pediatric Allergy and Ear-Nose-Throat Departments between October 2007 and August 2008 with a diagnosis of persistent and intermittent allergic rhinitis.

After achieving written informed consent from all patients' parents. Informed consent was obtained from all participants after their parents were briefed regarding the treatment to be given and procedures to be followed. The study was permitted by the local ethics committee.

A thorough anamnesis was obtained from the parents of children who were admitted to the pediatric allergy and ear-nose-throat department with complaints of nasal obstruction, open mouth during sleep, sneezing, nasal flow, and itchy nose. Cases included in this study were chosen among patients with histories of allergic rhinitis. Laboratory methods including the skin prick test (SPT), nasal smear, phadiatop (this is a kind of method which measures specific IgE levels in blood serum), total IgE, and complete blood count tests were used to confirm the diagnosis of allergic rhinitis in all subjects and to formulate a differential diagnosis. When collecting the anamneses of the patients, all symptoms were categorized as mild, moderate, or severe.[5] Cases were included in the study if they exhibited at least two of the following symptoms: mild and/or moderate nasal flows, itchy nose, sneezing, headache, nasal cavity flow, and nasal obstruction.

Routine ear-nose-throat and endoscopic examinations were carried out in all cases. Acoustic rhinometry and nasal endoscopy were performed in order to group the cases as none, mild, moderate, and severe for turbinate edema.[5] Treatment was started for all individuals showing any sign of edematous turbinates and these individuals were included in the study. Children with septal deviation, nasal polyp, and adenoid pads and patients with rhinosinusitis who had received treatment in the past were not included in the study. All of the cases were scrutinized for treatment histories and family history of asthma and received physical treatment and respiratory function tests in order to probe into the coexistence of allergic rhinitis and asthma. The patients were classified into three groups of 20 on the basis of the topical treatment they received, and patients in all three groups received eight weeks of treatment. Patients in group 1 were administered two puffs of azelastine (Allergodil; Meda AB, Stockholm, Sweden), a topical antihistamine, in each nostril per day (1 puff= 0.14 mg). Patients in group 2 were administered two single dose puffs of mometasone furoate nasal spray (Nasonex; Schering Plough, USA), a topical steroid, in each nostril per day

(200 micrograms). Patients in group 3 were administered two puffs of isotonic sea water nasal spray (STÉRIMAR; Sofibel-Laboratoire Fumouze, France) in each nostril per day.

The skin prick tests was performed with a panel of 23 of the most common aeroallergens (Stallergenes, France) by using the standard prick method. The diameters of induration and erythema 20 minutes after test completion were separately measured and recorded on patient forms. Patients who were sensitive (+++) and very sensitive (++++) were accepted as one of the criteria for inclusion in the study.

Peripheral blood samples were collected from all patients and a cell count was made at the hematology laboratory using a cell counter device. Absolute eosinophil counts were determined, with >200/mm^3 defined as eosinophilia. The total IgE level in the blood was measured in all study participants and values above 100 U/mL were considered high. Nasal smears of all patients were examined in order to confirm the presence of nasal eosinophilia.

Acoustic rhinometry

Volumes were separately calculated for each nasal passage with our acoustic rhinometry device (Ecco Vision; Hood Instruments, Pembroke, Massachusetts) both before and after treatment. Children's noses were cleaned before taking any measurements. For measurement, the children were taken into a quiet room where the rhinometry device was located and were briefed about the procedure to be performed. They were told not to swallow, not to inhale or exhale from the nose, and not to move their noses. Three measurements were made for each passage, and the measurements were repeated three times at 10 minute intervals after the administration of decongestant spray. Two puffs of oxymetazoline hydrochloride (%0.025 concentration) were sprayed in each nasal passage for decongestion in an attempt to prevent mismeasurements associated with the nasal cycle. The values were recorded into an acoustic rhinometry device and archived for future calculations. The arithmetic mean of every three measurements was taken and the means were transferred into a computer program (Microsoft Excel). The means were decimalized and volumes of the nasal passage for a distance from 0 cm to 5 cm were calculated. Data were transferred to Origin graphic software (version 8.0; Microcal Software Inc., USA) and first used to reproduce a renogram curve. Data were subsequently used to calculate the respective area under the curve by taking the integral of the curve.

Statistical analysis

All statistical analyses were carried out using SPSS, version 14.0 for windows (SPSS Inc., Chicago, IL, USA). All data were presented as mean±SD. Comprasions among the groups volumes of the nasal passage were evaluated using Kruskal-Wallis test and Mann-Whitney U test. Wilcoxon matched-pairs rank test were used to compare the volumes of the nasal passage before and after treatment in each group. Chi-square testing was used to compare the categorical parameters of the groups. Differences were considered statistically significant at p value of <0.05.

RESULTS

There was no significant difference between age and gender distribution among the groups. The patient demographic characteristics for study populations are presented in Table 1.

Right nasal cavity volume (RNV), left nasal cavity volume (LNV), RNV with decongestant, and LNV with decongestant values of all groups included in our study were measured before and after treatment (Table 2). A comparison of values obtained from acoustic rhinometry evaluations before and after treatment in group 1 showed that

Table 1. Distribution of groups by age and gender

	Group 1		Group 2		Group 3		
	n	Mean±SD	n	Mean±SD	n	Mean±SD	p
Age (years)		10.25±2.73		9.90±2.64		9.30±2.61	>0.05
Gender							
Male	13		12		12		>0.05
Female	7		8		8		

SD: Standard deviation.

Table 2. Comparison of nasal cavity volume values in each group

	Pretreatment	Posttreatment	% change	*p*
	Mean±SD	Mean±SD		
Group 1				
Right nasal volume	3.69±1.3	3.95±1.4	7.0	<0.05*
Right nasal cavity volume with decongestant	4.00±1.3	4.31±1.3	9.2	<0.05*
Left nasal cavity volume	3.47±1.3	3.98±1.3	16.5	<0.05*
Left nasal cavity volume with decongestant	3.95±1.5	4.38±1.5	13.3	<0.05*
Group 2				
Right nasal volume	3.68±0.9	3.93±0.9	6.9	<0.05*
Right nasal cavity volume with decongestant	3.96±1.1	4.28±1.3	7.7	<0.05*
Left nasal cavity volume	3.41±0.9	3.79± 1.0	11.6	<0.05*
Left nasal cavity volume with decongestant	3.75±1.0	4.22±1.2	12.6	<0.05*
Group 3				
Right nasal volume	3.80± 1.1	3.76±1.2	1.0	NS
Right nasal cavity volume with decongestant	4.12±1.2	4.13±1.2	0.1	NS
Left nasal cavity volume	3.75±1.4	3.87±1.4	4.4	NS
Left nasal cavity volume with decongestant	4.09±1.3	4.15±1.4	1.7	NS

SD: Standard deviation; * Statistical analysis performed by Wilcoxon matched-pairs rank test; NS: Not significant.

the LNV, LNV with decongestant, RNV and RNV with decongestant values increased after treatment ($p<0.05$). Similarly, group 2 showed that the LNV, LNV with decongestant, RNV and RNV with decongestant values increased after treatment. However, in group 3 there were no statistically significant LNV, LNV with decongestant, RNV and RNV with decongestant values between before and after treatment ($p>0.05$).

The comparison of pretreatment left nasal cavity volume, left nasal cavity volume with decongestant, right nasal cavity volume, and right nasal cavity volume with decongestant means of groups yielded no statistically significant differences ($p>0.05$). However, changes in these measurements after treatment differed among the groups. The increases in nasal volumes measured by acoustic rhinometry were similar with azelastine and mometasone furoate and both were superior to isotonic sea water nasal spray ($p<0.05$) (Figure 1).

DISCUSSION

Allergic patients typically have an increase in nasal mucosal swelling, which leads to decreased nasal volume and area and, subsequently, to increased congestion.[12] Subjective assessment of nasal obstruction is commonly performed using a symptom severity score rating or a visual analog scale (VAS).[13] Common methods used to objectively measure nasal patency and resistances include rhinomanometry and acoustic rhinometry.

Objective measurements of nasal patency do not always correlate with the patient's subjective sensation of nasal obstruction.[14] Chan et al.[15] suggested that there is a poor correlation between the subjective symptoms of nasal obstruction and VAS and acoustic rhinometry measurements. Two different studies comparing the efficacy of acoustic rhinometry, rhinomanometry, and VAS to detect nasal airway patency were unable to demonstrate any difference among the three evaluation techniques.[16,17] Roithmann et al.[18] claimed that each of these objective and complementary measurement techniques provides a more reliable assessment of nasal patency than subjective evaluation by either patient or clinician and thus can provide valuable guidance in the management of nasal obstruction symptoms.

Acoustic rhinometry is a safe, non-invasive, objective, and validated measure of nasal obstruction that appears to be of practical use in the diagnosis and management of inflammatory diseases of the upper airways[19] It is a novel technique that acoustically measures the nasal cross-sectional area and the internal nasal cavity volume[20] and is a useful instrument for monitoring

the effectiveness of medical therapy for allergic rhinitis.[15] It is well tolerated, particularly by children. Straszek et al.[21] conducted a study in 2007 on the use of acoustic rhinometry to evaluate decongestion with 53 cases between 9 and 11 years old. They reported that classical minimum cross-sectional area values were not reliable for measuring decongestion and that the nasal cavity volume value was a more useful parameter.[22] We evaluated only the nasal cavity volumes in our study and observed a mean volume of 4.20 cm^3 after decongestion. The higher nasal cavity volume values in our study compared to those in the literature might be due to the high mean age of cases and increased passage volumes because of regular therapy administered over two months.

Nasal obstruction due to perennial allergic rhinitis is common in young children, and nasal saline or cromoglycate is often helpful in milder cases. For more severe obstruction, topical decongestants are very useful for short periods. However, to keep the nose open long-term, adequate intranasal glucocorticosteroids may be indicated.[13] Like intranasal corticosteroids, azelastine is effective in treating the symptoms of nasal congestion.[23] The efficacy of azelastine in decreasing nasal symptoms was evaluated by both subjective and objective methods in several studies, which showed that azelastine nasal spray improved nasal symptoms by decreasing nasal congestion. In another study, perennial rhinitis was treated with azelastine in children aged 5-12 years and its superiority to placebo in the relief of all symptoms was shown by VAS evaluation.[24] Azelastine nasal spray was significantly more effective than mometasone in the total nasal symptom score, which consists of sneezing, itchy nose, runny nose, and nasal congestion.[25] Azelastine nasal spray was reported to control all rhinitis symptoms, including nasal congestion, regardless of rhinitis diagnosis during a two-week study period.[26] The total nasal symptom score improved 27.1% with fluticasone nasal spray, 24.8% with azelastine nasal spray,

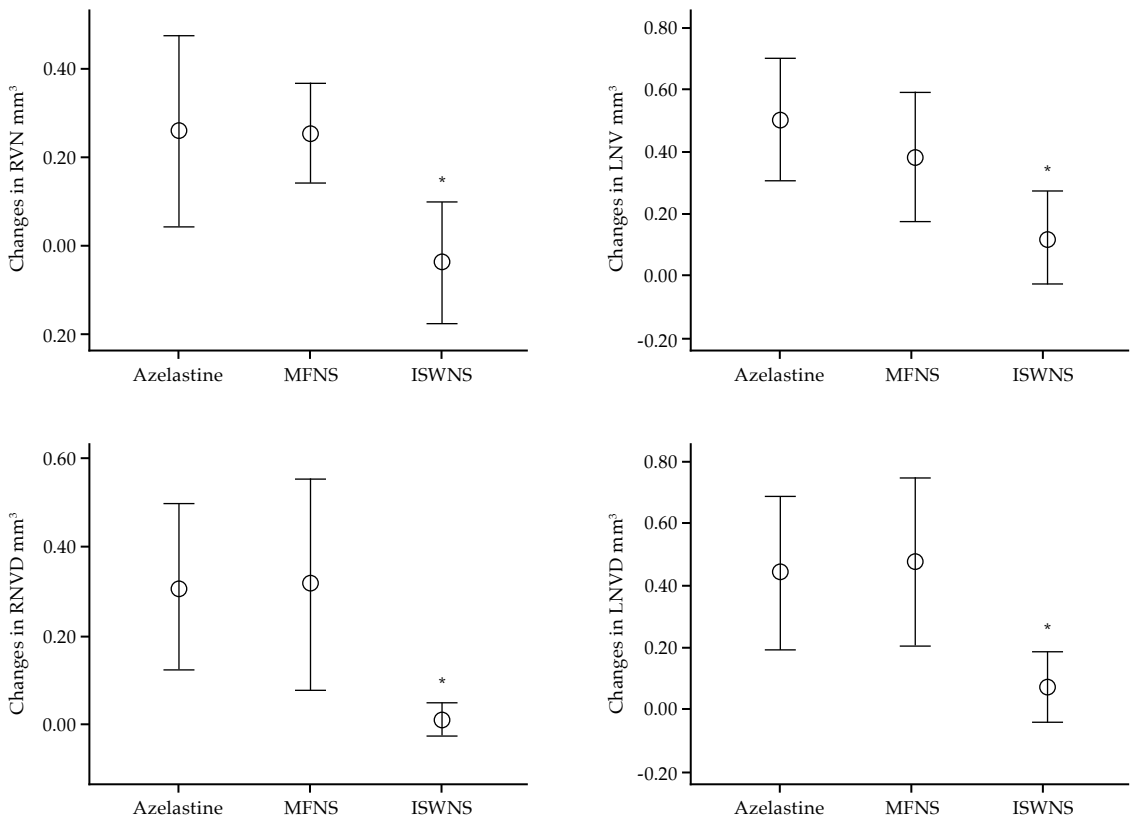

Figure 1. *The comparison of changes in RNV, LNV, RNVD, LNVD among groups.* statistically different from other groups (p<0.05). RNV: Right nasal volume; MFNS: Mometasone nasal spray; ISWNS: Isotonic sea water nasal spray; LNV: Left nasal cavity volume; RNVD: Right nasal cavity volume with decongestant; LNVD: Left nasal cavity volume with decongestant.*

and 37.9% with the two agents in combination ($p<0.05$ vs. either agent alone) after two weeks of treatment in another study.[27] Yamagiwa[28] evaluated the nasal cavity volumes and minimum cross-sectional area of 11 adult patients suffering from perennial allergic rhinitis with acoustic rhinometry at the end of the first and second weeks with azelastine (1 mg oral bid) therapy. He reported that minimum cross-sectional area increased between 21-39% at the end of the first week and 16-39% at the end of the second week. The nasal cavity volumes value increased from 16-24% to 19-24%. Spaeth et al.[29] demonstrated that azelastine is particularly effective in nasal obstruction by causing a statistically significant increase in nasal cavity volume. In our study, we applied azelastine (8 weeks) to the patients and detected a statistically significant increase in nasal volumes and this increase was significantly superior to that with isotonic sea water nasal spray.

The topical nasal corticosteroid (flunisolide) was more effective than an antihistamine nasal spray (azelastine hydrochloride) in reducing symptoms of allergic rhinitis evaluated by subjective methods.[30] We found similar effects with azelastine and mometasone furoate. Another study demonstrated that using topical nasal corticosteroid decreased nasal obstruction in perennial allergic rhinitis.[31] Chan et al.[15] used acoustic rhinometry and VAS to evaluate, compare, and correlate the efficacy of fluticasone propionate nasal spray therapy for four weeks. In VAS evaluation, a significant improvement in the symptoms of nasal blockage after fluticasone propionate treatment was observed. Acoustic rhinometry evaluation showed a significant increase in total volume ($p<0.01$) and total minimum cross-sectional area ($p<0.04$) after fluticasone propionate treatment, revealing a significant decongestive effect on the nasal mucosa after fluticasone propionate treatment.[15] Penagos et al.[32] found that mometasone furoate was associated with a significant reduction for nasal stuffiness/congestion compared to placebo. Topical mometasone furoate therapy for three weeks objectively reduced nasal congestion in moderate to severe persistent allergic rhinitis. After treatment with topical nasal steroid, patients with allergic rhinitis had significant reductions in the mean score for all nasal symptoms and in the total nasal score. Mean total nasal score was reduced by 53% and mean obstruction score was reduced by 50%. Furthermore, acoustic rhinometry was used to detect changes in nasal mucosa induced by three weeks therapy with topical nasal steroid; 14% mean increase in V5 (nasal volume between 0 and 5 cm) represents an impressive improvement in nasal congestion.[33] Hilberg[11] demonstrated that intranasal budesonide increased nasal cavity dimensions significantly more than oral terfenadine in a well-controlled comparison study with allergic rhinitis. Wilson et al.[34] evaluated two-week intranasal budesonide therapy in patients with seasonal allergic rhinitis and did not find any significant difference in the V5 values. We selected more severe patients and treated them for a longer period (8 weeks vs. 2 weeks) and we observed a significant increase in nasal volume after eight weeks of mometasone furoate therapy due to prevention of congestion. The increase with mometasone furoate was also superior to that with isotonic sea water nasal spray. However, no significant difference was found between the efficacies of azelastine and mometasone furoate in this study. Nasal volume did not change after isotonic sea water nasal spray therapy but increased with mometasone furoate and azelastine therapy. Isotonic sea water nasal spray may result in improved function of the nasal mucosa through several reported physiological effects including direct cleansing of irrigation, removal of inflammatory mediators, and improved mucociliary function demonstrated by increased ciliary beat frequency.[35] However, the exact mechanism of isotonic sea water nasal spray action is not known. Nasal saline irrigation can be viewed as an adjunctive treatment option for allergic rhinitis. This option permitted the reduced use of topical steroids for controlling allergic rhinitis in children, which may result in fewer side effects and less economic burden.[36]

The findings of this study showed that azelastine and mometasone furoate are effective treatment choices for allergic rhinitis because they decrease nasal congestion and remarkably increase nasal volume. The results could not demonstrate a superiority of the intranasal steroids compared to the antihistamine in the management of nasal obstruction.

Declaration of conflicting interests

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