Assessment of the Antiobstructive Effect of Fexofenadine on Nasal Allergy Challenge in Patients with Seasonal Allergic Rhinitis

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SUMMARY The oral administration of fexofenadine 120 mg daily is a common treatment of seasonal allergic rhinitis (SAR). It reduces the H_1 receptor-mediated symptoms, such as sneezing, pruritus, and nasal secretion as well as non-nasal symptoms such as conjunctivitis. The objective was to assess the effect of fexofenadine on nasal symptoms (such as nasal obstruction) in seasonal allergic rhinitis. A placebo-controlled, double-blind, randomized, cross-over study was performed which yielded evidence that two-week therapy with fexofenadine 120 mg daily in patients with SAR also relieves nasal obstruction and congestion. The parameters of nasal obstruction were evaluated by means of rhinoscopy, a subjective symptom score, and active anterior rhinomanometry. The subjective evaluation of nasal obstruction/congestion as recorded by the patient every 15 minutes for 4.5 hours after nasal allergen provocation showed a significant difference of the AUC (p = 0.025) between fexofenadine and placebo with a 12.8 % lower obstruction after fexofenadine. The swelling of the nasal mucosa, which was assessed by rhinoscopy for 4.5 hours after nasal allergen provocation, was 21% lower after treatment with fexofenadine (p = 0.041). In this double-blind, placebo-controlled trial, subjective patient ratings as well as objective investigator assessments demonstrate the anti-obstructive effect of fexofenadine in nasal allergen challenge.

Seasonal allergic rhinitis (SAR) causes H_1 receptor-mediated symptoms such as sneezing, pruritus, nasal secretion, and conjunctivitis. These symptoms represent the early phase of the allergic reaction; its primary mediator is histamine.[1] These symptoms are treated by oral administration of antihistamines such as fexofenadine.[2,3]

Nasal obstruction and congestion are other severe symptoms of SAR, leading to a markedly reduced quality of life. These symptoms occur predominantly during the late phase of the allergic reaction and are primarily caused by a vascular mechanism which is mediated by leukotrienes, prostaglandins and kinins, in particular LTC4, LTD4, PGD2, and IL-4.[4,5]

In the past, nasal obstruction was primarily treated by topically administered vasoconstrictors or glucocorticosteroids.[6-11] Recent studies show, however, that histamine is involved in the pathogenesis of the late-phase reaction as well and that some anti-

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histamines are also effective in reducing the release of several of the other mediators responsible for nasal blockage during the late-phase reaction.[1] These findings raise the question whether antihistamines can also serve as a sufficient treatment of nasal obstruction and congestion. The efficacy in relieving these nasal symptoms has already been proven for some second- and third-generation antihistamines such as cetirizine,[12] azelastine,[13,14] astemizole,[15,16] mizolastine[1] and desloratadine.[17,18] Moreover, a recent study in subjects with allergic rhinitis by Badorrek *et al.*[19] showed that a combination treatment with cetirizine and pseudoepinephrine was more effective than treatment with single substances. The aim of this placebo-controlled, double-blind, randomized, cross-over study was to clarify whether treatment with fexofenadine 120 mg daily reduces nasal obstruction and congestion as well as the H_1 receptor-mediated symptoms in patients with SAR.

MATERIAL AND METHODS

The investigational plan was approved by the ethical review board of the North-Rhine Medical Council and monitored according to the guidelines for good clinical practice. Patients were included in the study only after having given their informed written consent.

A randomized, two-phase, cross-over study was performed testing fexofenadine 120 mg daily versus placebo in patients with SAR (see Fig. 1 for the cross-over design). There were twelve patients included in this study. The selection of the patients for this study was carried out using the pre-ARIA nomenclature from 2001.[20,21] Randomization was performed in blocks of four in order to achieve balanced randomization. According to the randomization list, labeled medication was produced and emergency un-blinding envelopes were prepared with patient numbers written on the exterior of the envelope. On inclusion in the study, patients were assigned a sequential number within the open block. Following common double-blind design, neither patients nor investigators knew which treatment was administered. Each sealed envelope contained information about the treatment group to which the patient was assigned. The investigator obtained the envelopes for the patients he treated, and identical envelopes were kept by the director of the clinical study. The investigator was allowed to open the respective envelope only in case of an emergency in order to take appropriate action. Upon completion of the study, all envelopes were returned to the coordinating centre.

The study took place in late November approximately three months after the end of the pollen season to ensure that no natural airborne allergen interference could occur. Twelve patients between 18 and 50 years of age were enrolled. A skin prick test was performed to confirm the diagnosis of SAR and to ascertain the particular allergen of each patient. Inclusion criteria were seasonal or intermittent allergic rhinitis due to grass pollen sensitization. Exclusion criteria from this study were treatment with another antihistamine and/ or corticosteroids, and non-responsiveness to antihistamines in the past. None of the subjects suffered from perennial rhinitis. The study consisted of two treatment phases of 13 days each and four visits, one visit two days before the start and one on the last day of each treatment phase. Between the two treatment phases, there was a wash-out phase of eight days. Prior to the start of both treatment phases on Visits 1 and 3, all parameters were evaluated. Two days after these visits, patients started taking their study medication (fexofenadine 120 mg daily or placebo, respectively) for 13 days. On the last day of each treatment phase (Visits 2 and 4) all tests were performed again and all measures were reassessed. The primary parameter was the change of nasal air airflow (in ml/second, measured at 150 Pa) 4.5 hours (270 minutes) after nasal provocation according to the guidelines for nasal provocation by the German academies for otolaryngology and allergy,[22] evaluated by active anterior rhinomanometry at each visit. After the first measurement, the nasal mucosa was provoked mechanically with a saline nasal spray. The next measurement was performed 15 minutes later; a unilateral allergen provocation to the side with the higher airflow value was carried out thereafter. The allergen was applied to the nasal mucosa by means of a standardized commercially available solution (ALK-ABello®, Wedel, Germany). Four further rhinomanometry measurements of the nasal airflow were taken at 15, 45, 135, and 270 minutes after allergen provocation. The nasal airflow prior to both mucosal challenges was set to 0. The five following measurements were adjusted to this evaluation, thus indicating the change of the nasal airflow from the pre-challenge state.

At Visit 1, rhinomanometry was part of the screening. Subjects were included only if the decrease of the nasal airflow after mechanical provocation by a saline nasal spray did not exceed 20% of the pre-challenge airflow and if the decrease after allergen provocation was at least 40% of the airflow level after mechanical provocation. The rhinomanometry and the nasal allergen provocation were performed according to the recent guidelines of the German Association of Allergology and Clinical Immunology for nasal provocation tests in patients with upper respiratory tract diseases[25] and according to the guidelines of the International Committee on Objective Assessment of the Nasal Airways of the International Rhinologic Society.[23]

All secondary parameters (listed below) were assessed according to a four-level ordinal scale (0 = not present, 1 = mild, 2 = moderate, 3 = severe). Every 15 minutes after nasal allergen provocation for a total of 4.5 hours (270 minutes), the patients had to evaluate their nasal obstruction/congestion on their own as well as the symptoms of SAR including nasal itching, rhinorrhea, sneezing, and non-nasal symptoms (involvement of the eyes, ears or throat). The patients recorded these symptoms by means of a Palm® handheld computer, which they were provided with for the purpose of this study. Further secondary parameters were obtained by rhinoscopy using a nasal endoscope (Storz®, Tuttlingen, Germany, nasal endoscope 0°, 3 mm diameter), which was performed before and 15, 45, 135, and 270 minutes after nasal allergen provocation. The swelling of the nasal mucosa was evaluated as correlating symptom to nasal obstruction. Other symptoms assessed by rhinoscopy were erythema and secretion of the nasal mucosa. All rhinoscopy parameters were evaluated as a whole for both sides and for the challenged side separately.

Finally, an H_1 rhinitis score (European Agency for the Evaluation of Medicinal Products, EMEA) comprising the secondary parameters sneezing, rhinorrhea, nasal itching, and the sum score of these three symptoms were jointly evaluated by the patient and the investigator 15, 45, 135, and 270 minutes after nasal allergen provocation .

The statistical analysis was performed according to Hills and Armitage[24] by means of a Wilcoxon-Mann-Whitney test, using the evaluations from Visits 2 and 4. The Wilcoxon-Mann-Whitney test was applied to every single measurement as well as to the area under the curve (AUC) of each parameter. The AUCs of all parameters evaluated at Visits 1 and 3 were analyzed to ensure that the baseline conditions in the two treatment groups were comparable at the beginning of each treatment phase. Statistical analysis was performed using the SPSS (version 12, SPSS ® Inc., Chicago, Ill, USA).

RESULTS

All patients completed the study. None of the demographic parameters showed a significant difference between treatment groups. Eight of the 12 patients were allergic to grass, two to birch (betula verrucosa, betula pendula Roth), one to mugwort (arte-

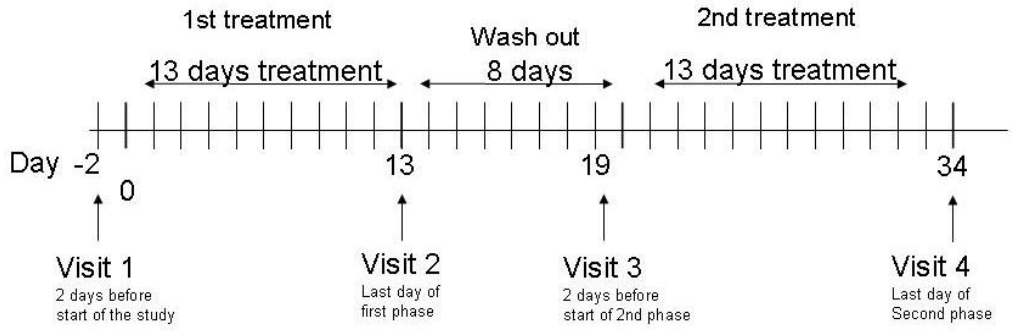

Fig. 1 Design of this two-phase, cross-over study, the vertical bars represent the four visits to the study centre and chronological overview of study visits.

misia vulgaris), and one to rye (secale cereale) pollen. No envelope containing the information about the medication or placebo group needed to be unsealed in order to administer rescue medication. With one exception, none of the parameters showed a significant difference between treatment groups in the beginning of each treatment phase at Visit 1 and Visit 3, respectively. Only the area under the curve (AUC) of the symptom "rhinorrhea" of the H1 rhinitis score was significantly higher at Visit 1 in Group 0 than in Group 1 ($p = 0.015$, exact Wilcoxon-Mann-Whitney Test). Group 0 received fexofenadine 120 mg daily in the subsequent treatment phase (see Figs. 1 and 2a). Fig. 2a shows the means of the summarized measurements of both treatment groups for fexofenadine versus placebo. Rhinomanometry was performed prior to nasal provocation (0 minutes), after mechanical provocation (15 minutes), and four times after allergen provocation (30, 60, 150, and 285 minutes). Fig. 2b shows the grade of nasal obstruction after treatment with fexofenadine or placebo, respectively, evaluated by the patient every 15 minutes for 4.5 hours after nasal allergen provocation. The means of the summarized measurements of both treatment groups for fexofenadine versus placebo are depicted in the diagram.

The extent of improvement of change of the nasal airflow following allergen challenge after a 13-day therapy with fexofenadine 120 mg daily against placebo can be characterized by the difference of the average AUCs. This difference was 15,329.13 minute*ml/second, equivalent to 919.7478 l, which is equivalent to an average improvement of 53.79 ml/second over the 4.5 hours after allergen challenge. To assess this measure, it was compared with the average pre-challenge nasal airflow at Visits 2 and 4, which was 269 ml/second, or with the mean of all nasal airflows measured at these visits. The latter relates to 230 ml/second.

Figs. 3a and b show the AUC of the swelling of the nasal mucosa, which was assessed by rhinoscopy for 4.5 hours after nasal allergen provocation. It was markedly lower after treatment with fexofenadine. Separate analysis of the challenged side ($p = 0.041$, Fig. 3a) and summarized measurements of both sides ($p = 0.041$, Fig. 3b) are depicted.

Since nasal obstruction is considered to be a particular symptom of the late-phase reaction, the improvement at the end of the 4.5-hour time period after allergen challenge was also analyzed. At this time, the average change of the nasal airflow was 55.77 ml/second higher after fexofenadine therapy as compared to placebo.

The recommendation for nasal provocation of the German guidelines[22] state that a bilateral challenge is possible, a unilateral application of allergens into the wider nostril, however, is recommended, to exclude variation of airflow by the nasal cycle. Ta-

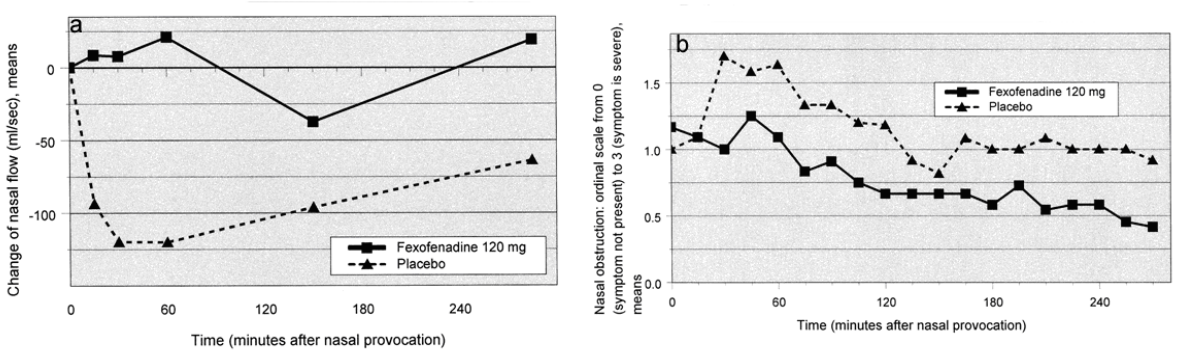

Fig. 2 A, change of nasal airflow after nasal provocation in patients with SAR after 13 days of treatment with fexofenadine 120 mg daily or placebo, respectively. The X-axis shows the time in minutes after nasal provocation, the y-axis the means of change of nasal flow in milliliter per second (ml/s). Dotted line with triangles, placebo, solid line with squares, fexofenadine 120 mg/day. B, Patient assessment of nasal obstruction. The X-axis shows the time in minutes after nasal provocation, the y-axis shows the mean of nasal obstruction on a symptom score from 0 (symptom is not present) to 3 (symptom is severe). Dotted line with triangles, placebo, solid line with squares, fexofenadine 120 mg/day.

ble 1 shows nasal obstruction measured by an all-day symptom score before and after 14 days treatment with triamcinolone acetonide nasal aerosol 27.5 µg daily or placebo during pollen season, as well as nasal obstruction in an all-day symptom score before and after 14 days of treatment with fluticasone propionate aqueous nasal spray 200 µg daily or placebo during pollen season on a 100-level score.

The subjective evaluation of nasal obstruction/congestion as recorded by the patient every 15 minutes for 4.5 hours after nasal allergen provocation showed a significant difference of the AUC (p = 0.025) between fexofenadine and placebo with a lower obstruction after fexofenadine (see Fig. 2b). A significant difference could also be observed for several single measurements at certain times (120, 210, 225, 255, and 270 minutes after nasal allergen provocation).

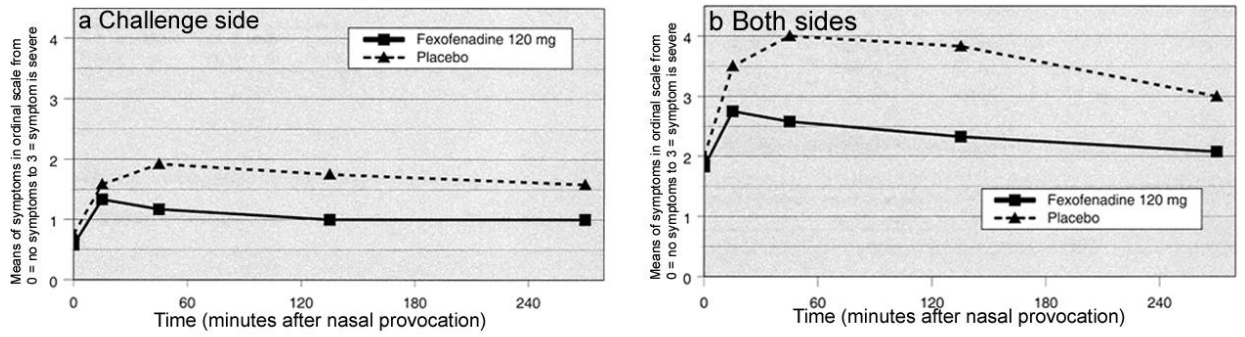

Fig. 3 The AUC of the swelling of the nasal mucosa. A, challenged side; B, both sides. The X-axes show the time in minutes after nasal provocation, the Y-axes show the means of symptoms in ordinal scale from 0 = no symptoms to 3 = symptom is severe. Dotted line with triangles, placebo, solid line with squares, fexofenadine 120 mg/day.

Table 1 Nasal obstruction: All-day symptom score before and after 14 days treatment with triamcinolone acetonide nasal aerosol 27.5 µg daily [29] or fluticasone propionate aqueous nasal spray 200 µg daily [9] or placebo during pollen season. Four-level ordinal scale (triamcinolone acetonide) and 100-level score (fluticasone proprionate).. Improvement in the change from baseline attributed to active medicine therapy.

	Triamcinolone acetonide nasal aerosol 27.5 µg daily or placebo		**Fluticasone propionate aqueous nasal spray 200 µg daily or placebo**	
	Active medicine	**Placebo**	**Active medicine**	**Placebo**
At baseline	2.25	2.4	76	78
Post therapy	not available	not available	43	62
Change from baseline	1.03	0.57	33	16
Improvement active medicine – placebo	0.46		17	
Percentage of the full range of the scale used	15.33 %		17 %	

The size of the therapeutic effect based on the analysis of the AUCs of this parameter was equivalent to an average improvement of 0.38 points during the 4.5 hour period after allergen challenge. Within the ordinal scale of this symptom ranging from 0 to 3 this represents 12.8%. The separate analysis of the measurements 4.5 hours after allergen challenge reveals an improvement of 0.5 points (16.7% of the full range of the scale).

Regarding the other four parameters evaluated by the patient every 15 minutes for 4.5 hours after nasal allergen provocation (nasal itching, rhinorrhea, sneezing, and non-nasal symptoms involving the eyes, ears or throat), there was no significant difference between the AUCs after treatment with fexofenadine or placebo, respectively. The only single measurement that showed a significant difference was rhinorrhea 150 minutes after provocation. Comparing the means of these parameters for both treatments, however, the tendency toward a therapeutic effect of fexofenadine was present as well: regarding rhinorrhea over the entire period of 4.5 hours; regarding nasal itching, sneezing, and non-nasal symptoms for the first hour after provocation. Thereafter, these three parameters diminished to an irrelevant level close to zero for placebo as well as for fexofenadine.

The swelling of the nasal mucosa, which was assessed by rhinoscopy for 4.5 hours after nasal allergen provocation, was markedly lower after treatment with fexofenadine. The AUC of this parameter showed a significant difference between the two treatment groups for both the separate analysis of the challenged side ($p = 0.041$, Fig. 3a) and the analysis of the summarized measurements of both sides ($p = 0.041$, Fig. 3b). The diagrams depicting the means confirm this tendency (Fig. 3).

The extent of improvement based on the analysis of the AUCs of this parameter was equivalent to an average improvement of 0.65 points for the challenged side separately and 1.24 points for the summarized figures of both sides. The full range of the scale for the challenged side is 0 to 3, for the latter it is 0 to 6. Thus, the percentages amount to 21.7% and 20.7%, respectively. The separate analysis of the measurements 4.5 hours after allergen challenge reveals an improvement of 0.58 points for the challenged side and 0.92 points for both sides (19.3% and 15.3% of the full range of the corresponding scale).

Table 2 Nasal airflow and subjective evaluation before and after treatment

	A: Change of nasal airflow (means) of Group 0 (fexofenadine before Visit 2, placebo before Visit 4). All values in ml/second		**B: Total symptom score (means) before and after 14 days of treatment with MFNS 200 µg daily or placebo, 6 hours after allergen challenge. Four-level ordinal scale. Improvement in the change from baseline attributed to active medicine therapy[8]**	
Visit 4 (placebo)			**Visit 2 (placebo)**	**Visit 4 (MFNS 200 µg)**
1	0.00	0.00	0.00	0.00
2	32.70	-81.00	-97.27	12.10
3	26.00	-106.00	-124.67	13.67
4	14.60	-98.40	-126.67	40.10
5	-55.55	-82.20	-107.92	0.30
6	-12.40	-94.65	-6.67	67.00

Measurement 1: prior to any provocation
Measurement 2: after mechanical provocation, 15 minutes after measurement 1
Measurement 3: 15 minutes after allergen provocation, 30 minutes after measurement 1
Measurement 4: 45 minutes after allergen provocation, 60 minutes after measurement 1
Measurement 5: 135 minutes after allergen provocation, 150 minutes after measurement 1
Measurement 6: 270 minutes after allergen provocation, 285 minutes after measurement 1

The other symptoms evaluated by rhinoscopy - erythema and secretion - showed the therapeutic effect of fexofenadine as well, but this was less distinct than for swelling. The AUCs of both symptoms were significantly lower after fexofenadine treatment for the provoked side separately (erythema, $p = 0.041$, secretion, $p = 0.041$) as well as for both sides (erythema, $p = 0.041$, secretion, $p = 0.026$).

Regarding the parameters of the H_1 rhinitis score, a significant difference was found between the AUCs of the two treatment groups for rhinorrhea ($p = 0.041$), sneezing ($p = 0.041$), and the sum score (0.015). The difference for nasal itching did not reach a level of significance. However, the results of the H_1 rhinitis score should be considered to have only limited validity, because the baseline evaluations of these parameters showed some significant differences between treatment groups at Visit 1, although in the opposite direction to the registered therapeutic effect after the treatment phase.

DISCUSSION

The treatment of seasonal allergic rhinitis with fexofenadine 120 mg daily relieves not only H_1-receptor-mediated symptoms such as sneezing, pruritus, secretion, and conjunctivitis, but also nasal obstruction and congestion. This was shown in this present placebo-controlled, double-blind, randomized, cross-over study performed on 12 patients with SAR after the end of the pollen season. The assessment of nasal obstruction and congestion was carried out for 4.5 hours after nasal allergen provocation after 13 days of treatment with fexofenadine 120 mg daily or placebo.

Table 2 shows the effects fexofenadine on nasal airflow and of MFNS on total symptom score. The primary parameter - the change of the nasal airflow - showed a clear tendency toward a positive influence of two weeks of premedication with fexofenadine on nasal obstruction after allergen provocation (Table 2, Fig. 2a). However, the difference be-

Table 3 Total symptom score and assessment of nasal obstruction before and after treatment with fexofenadine or desloratadine, respectively. Four-level ordinal scale. Improvement in the change from baseline by active medicine therapy

	Total symptom score (means) before and after 13 days of treatment with fexofenadine 120 mg daily or placebo, 4.5 hours after allergen challenge		**Nasal obstruction according to patients' evaluation: Means of the mean nasal congestion score based on the 4.5-hour periods after allergen challenge before and after 13 days of treatment with fexofenadine 120 mg daily or placebo**		Nasal obstruction: All-day symptom score before and after 14 days of treatment with desloratadine 5 mg daily or placebo during pollen season[18]	
	Active medicine	**Placebo**	**Active medicine**	**Placebo**	**Active medicine**	**Placebo**
At baseline	0.50	0.38	1.36	1.04	not available	not available
Post therapy	0.19	0.42	0.76	1.15	not available	not available
Change from baseline	0.31	-0.04	0.60	-0.11	0.5	0.4
Improvement Active medicine – Placebo	0.35		0.71		0.1	
Percentage of the full range of the scale used	11.67%		23.67%		3.33%	

tween treatment groups was not significant at any time of the measurements, neither was the AUC. Of this parameter, 21.5% of the scheduled evaluations (31 of 144) were missing, due to complete obstruction of the nasal cavity in which the nasopharyngeal pressure was to be determined.

Table 3 shows the total symptom score (means) before and after 13 days of treatment with fexofenadine 120 mg daily or placebo, 4.5 hours after allergen challenge. Improvement in the change from baseline by active medicine therapy, as well as the grade of nasal obstruction according to patients' evaluation is indicated by the means of the nasal congestion score based on the 4.5-hour periods after allergen challenge before and after 13 days of treatment with fexofenadine 120 mg daily or placebo. Further, nasal obstruction is measured on an all-day symptom score before and after 14 days of treatment with desloratadine 5 mg daily or placebo during pollen season.[18]

Significant results favoring fexofenadine were found in the analysis of an objective parameter, the rhinoscopically evaluated swelling of the nasal mucosa, as well as in the analysis of a subjective parameter, the patient's evaluation of nasal obstruction. The results of the nasal airflow as assessed by active anterior rhinomanometry confirmed this finding numerically; however, these results did not reach a statistically significant level.

It is difficult to compare the size of the therapeutic effect with other studies because of various study designs. Most other studies do not use an allergen challenge; some use non-comparable parameters. But nearly all studies examine the effect of different treatments on nasal obstruction in SAR by means of a symptom score as used in this present investigation, although the type of score varied. In accordance with the here presented findings, other studies showed a reduction of nasal obstruction by fexofenadine.[7,25-27]

Most previously published studies assessed the therapeutic effect by calculating the difference of a symptom score before (baseline) and after the treatment phase. This is why these figures (airflow/ nasal obstruction) were established for this present study to enable a comparison. However, for the tests on efficacy according to Hills and Armitage[24] in this cross-over study, these data were not needed in comparison to budesonide and fluticasone nasal steroids on reduction of the nasal airflow measured by rhinomanometry.

There was an improved airflow compared to topical intranasal steroid application, and the improvements (in percentage) achieved here reach up to the numbers achieved by intranasal steroid application.

In a comparable study, Ciprandi *et al.*[12] assessed a symptom score after a two-week treatment with mometasone furoate nasal spray (MFNS) 200 µg daily or placebo in patients with SAR. This symptom score comprised nasal itching, sneezing, rhinorrhea and congestion. Six hours after an allergen challenge the patient had to evaluate the symptom score according to the same four-level scale that was used in the here presented study. In Cipriandi's study,[8] the symptom score was evaluated before and after the 14-day treatment phase for active medicine and placebo. The mean improvement in the change from baseline that was achieved by the treatment with MFNS was 0.77 points on the 4-level scale, which is 25.7% of the full range of this scale (Table 2).

To compare this result with the here presented study, the same symptom score was created from the here presented database and the equivalent differences calculated based on the measurements 4.5 hours after allergen challenge, which were the latest ones we performed. The present therapeutic effect was about half the size of MFNS treatment according to this symptom score (Table 3).[18]

Separate figures for the symptom "nasal congestion" were not available for MFNS, which is why the total symptom score was compared alone. However, in this present study, nasal congestion was the symptom with the strongest therapeutic effect over the 4.5-hour period after allergen challenge.

Several other studies list precise figures for the symptom "nasal congestion" evaluated by means of a symptom score, which enables to calculate the improvement in the change from baseline for nasal congestion in the same manner as was conducted above for the total symptom score. However, none of these authors used the method of allergen-specific nasal challenge outside the pollen season. They assessed the all-day score of this symptom during the

pollen season. So here, the figures of these studies were not compared to the here presented ones from the single measurement 4.5 hours after allergen challenge, but with the mean of all measurements over the 4.5 hours (Table 3). The authors regard this procedure to achieve better comparability with an all-day symptom score, which takes into consideration the moments directly after a natural airborne allergen exposure as well as those several hours after or even free of allergen exposure.

In a study assessing the all-day nasal obstruction in patients with SAR before and after a 14-day treatment with desloratadine 5 mg daily or placebo the improvement in the change from baseline attributed to the active medicine therapy was 0.1 points on the same 4-level scale that was here used (Table 3).[18] This is equivalent to 3.3% of the full range of the scale, which is a much smaller effect size than was here observed for fexofenadine.

Another study testing triamcinolone acetonide nasal aerosol 27.5 µg daily versus placebo and applying the same four-level ordinal scale was carried out over four weeks. However, the interim results after two weeks were listed, showing a therapeutical effect about one third smaller than for fexofenadine (Table 1).[28]

The therapeutic effect of 14-day treatment with fluticasone propionate aqueous nasal spray at a dose of 200 µg daily or placebo on nasal obstruction in patients with SAR was evaluated in a study over two weeks.[9] Although in this study a 100-level score was used to assess this symptom instead of the more common four-level scale, this study was taken into consideration for comparison because precise figures for this study were available. In the study presented here, only the percentage of the full range of the used scale was taken into account for comparison of the size of the therapeutic effect, which is 17% (Table 1).

Hore *et al.*[29] described in a thorough review the effects of oral antihistamines for nasal obstruction. However, their patient group consisted of patients suffering from persistent allergic rhinitis. The here presented data focus on seasonal allergic rhinitis.

In a more recent study, Badorrek *et al.*[19] underline the beneficial effect of a combination of cetirizine and pseudoepinephrine on 49 patients suffering from intermittent allergic rhinitis, and confirmed the finding presented here.

Also, Raphael *et al.*[30] showed in their multicenter study of 610 patients with seasonal allergic rhinitis, that desloratadine and diphenhydramine reduce nasal symptoms, in accordance with our findings. In this double-blind, placebo-controlled trial, subjective patient ratings as well as objective investigator assessments demonstrate the anti- obstructive effect of fexofenadine in nasal allergen challenge.

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