Advanced Medical Journal, Vol.6, No.2, P.183-195, 2022 /https://doi.org/10.56056/amj.149

The effect of intranasal steroid in the treatment of allergic rhinitis with and without oral antihistamine (comparative study)

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Abstract

Backgrounds & objectives: Numerous studies have investigated the efficacies of steroid nasal sprays for adults with allergic rhinitis. However, research on their effectiveness in combination with oral antihistamines is limited. This study compared the efficacies of a steroid nasal spray (mometasone furoate) with an oral antihistamine (desloratadine tablet) in the treatment of allergic rhinitis.

Methods: A randomized clinical trial was conducted on 120 patients diagnosed with allergic rhinitis. The patients who attended the outpatient department at Rizgary Teaching Hospital in Erbil city were examined for clinical features of allergic rhinitis. Patients with moderate-severe and/or persistent symptoms were included in this study. In this study, 120 patients with allergic rhinitis were randomly assigned to receive mometasone furoate nasal spray alone (control group) and a combination of mometasone nasal spray and oral desloratadine (experimental group).

Results: This study showed a statistically significant effect of combination therapy in comparison with intranasal steroids alone. The effect of the combination therapy was more apparent among patients with moderate-severe persistent symptoms. The score was 11.05 in patients who received the combination therapy compared with 7.85 among patients who received single therapy.

Conclusions: This study showed that the efficacy of mometasone nasal spray in combination with antihistamine was higher than single steroid nasal sprays therapy.

Keywords: Allergic rhinitis; Mometasone furoate; Desloratadine tablet; Total symptom score.

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Introduction

Allergic rhinitis (AR) is a non-infectious nasal mucosa inflammation that is mediated by immunoglobulin E (IgE). Allergic rhinitis is the specific inflammation against allergen by immune defense cells on the nasal mucosa. This inflammation leads to chronic nasal symptoms such as sneezing, itching, runny nose, and nasal congestion[1-3]. The use of antihistamines and topical nasal steroids represents the cornerstones of pharmacologi c treatment for allergic rhinitis[4]. Allergic Rhinitis symptoms result in sleep disturbance, fatigue, depressed mood, and cognitive function compromise that impairs quality of life and productivity[5]. Non-allergic rhinitis is a dysfunction and non-infectious inflammation of the nasal mucosa. This condition is caused by provoking agents other than allergens or microbes. The prevalence of AR is between 10% and 20%. The patients experience the symptoms of nasal obstruction, anterior rhinorrhea, post-nasal discharge and sneezing. The subgroups of non-allergic are distinguished based on the triggers responsible for symptoms. The triggers are occupation, cigarette smoke, hormones, medication, food, and age[6].The Allergic Rhinitis and its Impact on Asthma (ARIA) classify the AR into four major groups. The groups are mild: normal sleep, no trouble with daily life, sport, and leisure, no trouble with working and study, and no troublesome symptoms. Intermittent symptoms: <4 days a week; or < 4 weeks. Persistent: symptoms are ≥4 days a week and ≥4 weeks and Moderate/severe: one or more items of following: sleep disorder, dustup daily life, sport, and leisure, symptoms occur at workplace or school, and troublesome symptoms[7]. The allergic rhinitis and its impact on asthma guidelines recommend intranasal corticosteroids as the first-line treatment for patients with moderate to severe and/or persistent rhinitis[8]. Immunotherapy, environmental control, oral 2nd generation antihistamine with or without Leukotriene Receptor Antagonists (LTRA) in patients with asthma were recommended for all classes of AR whereas intranasal steroids and LTRA for the moderate-severe intermittent, mild persistent, and moderate-severe persistent classes[9].Intranasal corticosteroids are used as the most common types of medication prescribed to patients with rhinitis or rhinosinusitis symptoms, including non-allergic rhinitis. However, it is not clear that intranasal corticosteroids, along with oral

antihistamines, are truly effective in these patients. Therefore, we aimed to compare the efficacies of a steroid nasal spray (mometasone furoate) with an oral antihistamine (desloratadine tablet) in the treatment of allergic rhinitis.

Patients and methods

One hundred twenty patients were selected who attended the ENT department, academic medical center in Rizgary Teaching Hospital/Erbil, Iraqi Kurdistan, from July 2019 to November 2019 for management of their allergic nasal symptoms. The patients were physically and clinically screened for eligibility criteria. The patients were randomly allocated to the control or experimental group. The patients in the control group received steroid nasal spray (mometasone furoate) and the experimental group received steroid nasal spray (mometasone furoate) with an oral antihistamine (desloratadine tablet).All patients informed about the study and signed the written informed consent. Detailed and relevant history was taken, and physical examination was carried out in all patients, including anterior rhinoscopy and endoscopic examination of the nasal cavity.

We selected 120 patients according to the eligibility criteria, they were randomly and equally divided into two groups. Each group was divided into three categories according to their severity from moderate to severe intermittent (n=20 patients), mild persistent (n=20 patients), and moderate to severe persistent (n=20 patients). The first 60 patients were prescribed intranasal steroid only (INS) Mometasone Furoate 200 micrograms once daily (two puffs each side) in the early morning. The other sixty patients were prescribed (INS) plus oral Desloratadine 5 mg once daily in the evening. Reevaluation was done at the first week, second, and fourth week. The patients were seen in the visits to ensure compliance with the medications and to complete their scale. The main inclusion criteria were; aged 13 years and older, patients with moderate-severe intermittent, mild persistent and moderate-severe persistent with one of the following symptoms; sleep disorder, disturb daily life, disturb sport and leisure, symptoms occur at workplace or school and troublesome symptoms. The main exclusion criteria were; children less than 13 years old, mild intermittent symptoms, nasal polyps, asthma on therapy, chronic rhinosinusitis, and other active respiratory diseases on steroid use. During the initial visit, patients

were asked to score their level of nasal complaints using 6 points Likert scale (0 to 5)[10]. The symptoms were sneezing, runny nose, nasal obstruction, post-nasal drip, hyposmia, conjunctivitis, sore throat, and cough. The severity of symptoms was rated on a scale that ranged from 0 (meant none) to 5 (meant severe). The patients with score 0-1 were considered to have mild severity; score 2-3 considered moderate and scored 4-5 with severe nasal complaints. The maximum score was 40. Data were summarized and analyzed using the Statistical Package for Social Sciences (SPSS, version 22). Chi-square test of association was used to compare proportions of two groups. McNemar test was used to compare the proportions of the same sample but at two different times. Student's t test of two independent samples was used to compare two means. A p-value of ≤ 0.05 was considered statistically significant.The ethical approval of the present study was taken from the local health ethics committee in Erbil city (KBMS health ethics committee). A written consent form was taken from all patients before recruitment into the study. The confidentiality of the personal information of the patients was protected throughout the study period.

Results

The mean age of the patients was 30.20±7.87 years, ranging from 17 to 54 years. The median was 30 years. Half of the patients (n = 60) were given INS (local steroid; Group I) only, and another half (n = 60) were given INS+ (local steroid with oral desloratadine: Group II).

The mean age of Group I was 29.6 years, and that of Group II was 30.7 years (p-value= 0.440). The largest proportion of the sample (39.2%) aged 25-34 years, but there was no significant difference in the age distribution of the two study groups (p = 0.709) as presented in table (1).

Table (1): Age distribution of the two study groups.

Age groups (years)	INS		INS+		Total		
	No.	(%)	No.	(%)	No.	(%)	p-value
< 25	19	(31.7)	15	(25.0)	34	(28.3)	
25-34	22	(36.7)	25	(41.7)	47	(39.2)	
≥ 35	19	(31.7)	20	(33.3)	39	(32.5)	0.709*
Mean (±SD)	29.6	(±7.5)	30.7	(±8.2)			0.440†

* By Chi-square test. †By t-test for two independent samples.

Around two-thirds of the sample (65.8%) were females, but there was no significant difference between the two groups regarding the gender distribution (p= 0.847), as presented in table (2).

Table (2): Gender distribution of the two study groups.

Gender	INS		INS+		Total		p-value
	No.	(%)	No.	(%)	No.	(%)	
Male	20	(33.3)	21	(35.0)	41	(34.2)	
Female	40	(66.7)	39	(65.0)	79	(65.8)	0.847*
Total	60	(100.0)	60	(100.0)	120	(100.0)	

*By Chi-square test. †By t-test for two independent samples.

Table (3) considers severity in patients who had moderate to severe intermittent symptoms. In each of the study groups (INS or INS+), there was an improvement of all the studied symptoms in week 4 compared with week 1. All the differences were either significant or can't be calculated (NA) (because of the difference in the number of categories in week 1 and week 4 as it is evident that none of the patients had severe symptoms in week 4).

Table (3): The severity of symptoms in week one and week four among patients with moderate to severe intermittent symptoms in each of the two study groups

	Week one			Week four			
	Score 0-1	**Score 2-3**	**Score 4-5**	**Score 0-1**	**Score 2-3**	**Score 4-5**	**p-value***
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
INS							
Sneezing	1 (5.0)	17 (85.0)	2 (10.0)	11 (55.0)	9 (45.0)	0 (0.0)	NA
Runny nose	2 (10.0)	17 (85.0)	2 (10.0)	11 (55.0)	9 (45.0)	0 (0.0)	NA
Nasal obstruction	4 (20.0)	16 (80.0)	0 (0.0)	15 (75.0)	5 (25.0)	0 (0.0)	0.001
Postnasal drip	1 (5.0)	15 (75.0)	4 (20.0)	10 (50.0)	10 (50.0)	0 (0.0)	NA
Hyposmia	5 (25.0)	14 (70.0)	1 (5.0)	12 (60.0)	8 (40.0)	0 (0.0)	NA
Conjunctivitis	11 (55.0)	9 (45.0)	0 (0.0)	18 (90.0)	2 (10.0)	0 (0.0)	0.016
Sore throat	7 (35.0)	13 (65.0)	0 (0.0)	14 (70.0)	6 (30.0)	0 (0.0)	0.016
Cough	5 (25.0)	14 (70.0)	1 (5.0)	15 (75.0)	5 (25.0)	0 (0.0)	NA
INS+							
Sneezing	4 (20.0)	16 (80.0)	0 (0.0)	15 (75.0)	5 (25.0)	0 (0.0)	0.001
Runny nose	5 (25.0)	15 (75.0)	0 (0.0)	17 (85.0)	3 (15.0)	0 (0.0)	<0.001
Nasal obstruction	7 (35.0)	13 (65.0)	0 (0.0)	20 (100.0)	0 (0.0)	0 (0.0)	NA
Postnasal drip	3 (15.0)	16 (80.0)	1 (5.0	19 (95.0)	1 (5.0)	0 (0.0)	NA

Hyposmia	6 (30.0)	14 (70.0)	0 (0.0)	18 (90.0)	2 (10.0)	0 (0.0)	<0.001
Conjunctivitis	13 (65.0)	7 (35.0)	0 (0.0)	20 (100)	0 (0.0)	0 (0.0)	NA
Sore throat	9 (45.0)	11 (55.0)	0 (0.0)	20 (100)	0 (0.0)	0 (0.0)	NA
Cough	9 (45.0)	11 (55.0)	0 (0.0)	19 (95.0)	1 (5.0)	0 (0.0)	0.002
* By McNemar test.							

Table (4) includes patients with mild persistent symptoms. The same pattern of Table (2) was observed in patients with mild persistent symptoms. There was an improvement in symptoms at week 4. In general, the improvement was better in combination therapy (INS+); the majority of the patients had mild symptoms after four weeks of therapy, while in monotherapy (INS), a considerable proportion of patients had moderate symptoms.

Table (4): The severity of symptoms in week one and week four among patients with mild persistent symptoms in each of the two study groups

	Week one			Week four			
	Score 0-1	**Score 2-3**	**Score 4-5**	**Score 0-1**	**Score 2-3**	**Score 4-5**	**p-value**
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
INS							
Sneezing	3 (15.0)	14 (70.0)	3 (15.0)	9 (45.0)	11(55.0)	0 (0.0)	NA
Runny nose	1 (5.0)	16 (80.0)	3 (15.0)	9 (45.0)	11(55.0)	0 (0.0)	NA
Nasal obstruction	1 (5.0)	15 (75.0)	4 (20.0)	10 (50.0)	10 (50.0)	0 (0.0)	NA
Postnasal drip	15 (75.0)	5 (25.0)	0 (0.0)	8 (40.0)	12 (60.0)	0 (0.0)	NA
Hyposmia	15 (75.0)	5 (25.0)	0 (0.0)	7 (35.0)	13 (65.0)	0 (0.0)	NA
Conjunctivitis	10 (50.0)	9 (45.0)	1 (5.0)	15 (75.0)	5 (25.0)	0 (0.0)	NA
Sore throat	7 (35.0)	13 (65.0)	0 (0.0)	15 (75.0)	5 (25.0)	0 (0.0)	0.008*
Cough	2 (10.0)	17 (85.0)	1 (5.0)	12 (60.0)	8 (40.0)	0 (0.0)	NA
INS+							
Sneezing	4 (20.0)	16 (80.0)	0 (0.0)	20 (100)	0 (0.0)	0 (0.0)	NA
Runny nose	3 (15.0)	15 (75.0)	2 (10.0)	18 (90.0)	2 (10.0)	0 (0.0)	NA
Nasal obstruction	6 (30.0)	13 (65.0)	1 (5.0)	17 (85.0)	3 (15.0)	0 (0.0)	NA
Postnasal drip	5 (25.0)	14 (70.0)	1 (5.0)	20 (100)	0 (0.0)	0 (0.0)	NA
Hyposmia	6 (30.0)	13 (65.0)	1 (5.0)	19 (95.0)	1 (5.0)	0 (0.0)	NA
Conjunctivitis	13 (65.0)	7 (35.0)	0 (0.0)	19 (95.0)	1 (5.0)	0 (0.0)	0.031*
Sore throat	4 (20.0)	14 (70.0)	2 (10.0)	16 (80.0)	4 (20.0)	0 (0.0)	NA
Cough	8 (40.0)	12 (60.0)	0 (0.0)	20 (100)	0 (0.0)	0 (0.0)	NA
* By McNemar test.							

Patients with moderate to severe persistent symptoms were included in table (5). Again, none of the patients had severe symptoms at week 4 in each of the study groups, but the study found that more than 90% of patients who took the combination therapy (INS+)

had mild symptoms at week four while a considerable proportion of patients of the monotherapy group (INS) had moderate symptoms at week 4.

Table (5): The severity of symptoms in week one and week four among patients with moderate to severe persistent symptoms in each of the two study groups.

	Week one			Week four			
	Score 0-1	**Score 2-3**	**score4-5**	**Score 0-1**	**Score 2-3**	**Score4-5**	**p-value**
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	
INS							
Sneezing	1 (5.0)	15 (75.0)	4 (20.0)	8 (40.0)	12 (60.0)	0 (0.0)	NA
Runny nose	2 (10.0)	17 (85.0)	1 (5.0)	10 (50.0)	10 (50.0)	0 (0.0)	NA
Nasal obstruction	3 (15.0)	13 (65.0)	4 (20.0)	10 (50.0)	10 (50.0)	0 (0.0)	NA
Postnasal drip	1 (5.0)	16 (80.0)	3 (15.0)	7 (35.0)	13 (65.0)	0 (0.0)	NA
Hyposmia	3 (15.0)	12 (60.0)	5 (25.0)	9 (45.0)	11 (55.0)	0 (0.0)	NA
Conjunctivitis	11 (55.0)	8 (40.0)	1 (5.0)	14 (70.0)	6 (30.0)	0 (0.0)	NA
Sore throat	6 (30.0)	13 (65.0)	1 (5.0)	13 (65.0)	7 (35.0)	0 (0.0)	NA
Cough	6 (30.0)	12 (60.0)	2 (10.0)	13 (65.0)	7 (35.0)	0 (0.0)	NA
INS+							
Sneezing	5 (25.0)	15 (75.0)	0 (0.0)	20 (100.0)	0 (0.0)	0 (0.0)	NA
Runny nose	5 (25.0)	15 (75.0)	0 (0.0)	19 (95.0)	1 (5.0)	0 (0.0)	NA
Nasal obstruction	4 (20.0)	15 (75.0)	1 (5.0)	18 (90.0)	2 (10.0)	0 (0.0)	NA
Postnasal drip	4 (20.0)	14 (70.0)	2 (10.0)	18 (90.0)	2 (10.0)	0 (0.0)	NA
Hyposmia	6 (30.0)	13 (65.0)	1 (5.0)	19 (95.0)	1 (5.0)	0 (0.0)	NA
Conjunctivitis	8 (40.0)	11 (55.0)	1 (5.0)	19 (95.0)	1 (5.0)	0 (0.0)	NA
Sore throat	9 (45.0)	11 (55.0)	0 (0.0)	20 (100.0)	0 (0.0)	0 (0.0)	NA
Cough	7 (35.0)	12 (60.0)	1 (5.0)	20 (100.0)	0 (0.0)	0 (0.0)	NA

It is evident in table (5) that in general, the mean total score on Day 0 was around 24 in each of the study groups and each of the The difference between the total score (week 1 score minus week four score) was more among patients taking the combination therapy (9.90) than the difference in scores (8.10) among patients taking the INS only (p-value = 0.007). Regarding patients with treatment groups. But after four weeks, the mean total score of Group I (INS) was around 10 compared to 5 in the Group II. mild persistent symptoms, the difference was also higher among patients taking the combination therapy (11.05) than those taking the single therapy (8.65), and the difference was significant (p-value = 0.005). The difference in mean score in combination

therapy among patients with moderate-severe persistent symptoms was 11.05 compared with 7.85 among patients who received the single therapy (P-value < 0.001) (Figure 1).

Table (6): Descriptive statistics of the total score according to time, and severity in each of the study groups

			Total score				
Group	**Severity**		**Day 0**		**Week 1**	**Week 2**	**Week 4**
INS	Moderate-severe intermittent	Mean	24.1		17.2	13.8	9.1
		SD	2.8		1.9	2.0	1.9
		Median	24.0		17.0	14.0	9.0
		Minimum	20.0		14.0	10.0	5.0
		Maximum	31.0		22.0	18.0	13.0
	Mild persistent	Mean	24.3		19.5	15.8	10.9
		SD	2.7		3.1	3.2	2.5
		Median	24.5		20.5	16.0	11.0
		Minimum	19.0		13.0	8.0	6.0
		Maximum	28.0		25.0	21.0	15.0
	Moderate-severe persistent	Mean	24.7		18.5	15.3	10.7
		SD	3.1		3.1	3.1	2.8
		Median	24.5		19.0	15.0	11.0
		Minimum	19.0		10.0	8.0	5.0
		Maximum	34.0		24.0	21.0	14.0
INS+	Moderate-severe intermittent	Mean	24.5		14.8	10.5	4.9
		SD	3.0		2.4	2.4	1.7
		Median	24.0		14.0	10.0	5.0
		Minimum	20.0		12.0	6.0	2.0
		Maximum	31.0		19.0	15.0	9.0
	Mild persistent	Mean	24.6		16.5	11.4	5.4
		SD	2.3		3.7	3.4	2.3
		Median	24.0		16.0	11.0	5.0
		Minimum	21.0		10.0	5.0	2.0
		Maximum	31.0		26.0	19.0	10.0
	Moderate-severe persistent	Mean	24.8		15.8	10.3	4.7
		SD	1.7		2.3	2.6	1.8
		Median	24.5		16.0	11.0	4.0
		Minimum	21.0		11.0	5.0	2.0
		Maximum	28.0		19.0	14.0	8.0

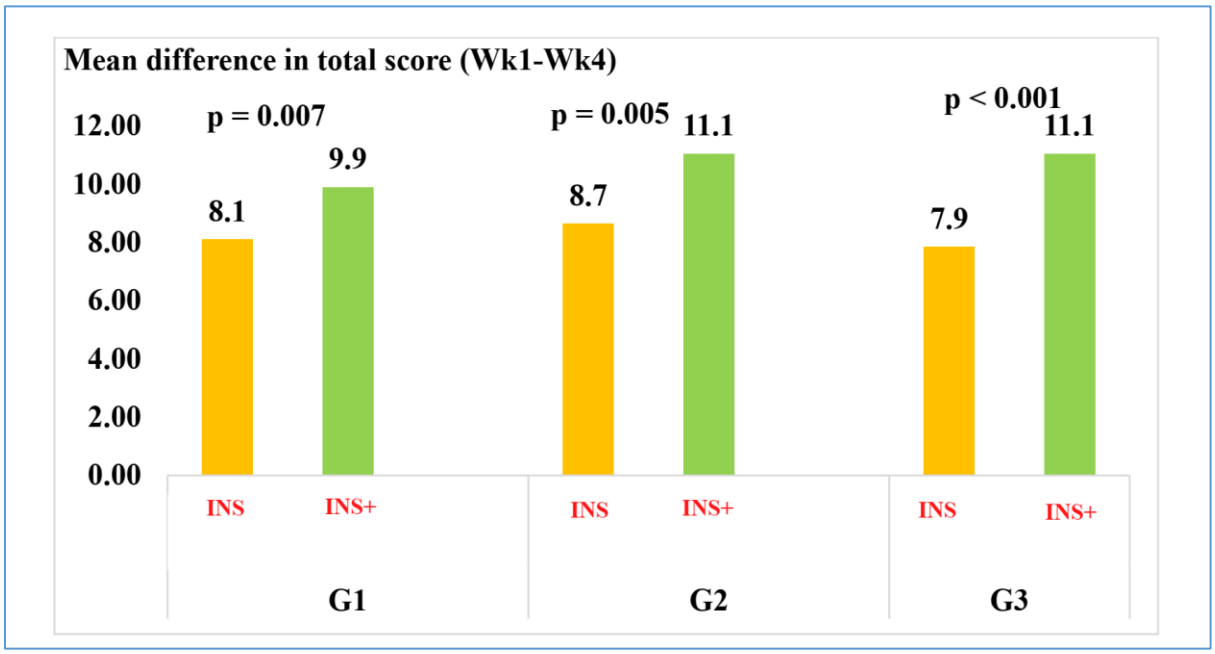

Figure (1): Mean difference in total scores (week 1 – week 4 scores) between INS and INS+ in each of the three groups of patients

Discussion

The effectives of mometasone furoate nasal spray in combination with an oral antihistamine compared to mometasone furoate nasal spray on symptoms in patients with allergic rhinitis have been approved in few studies. For example, Patel and Salapatek et al[11] allocated 180 patients into the following treatments. G1: received twice-daily GSP301 (665 mg of sponsor olopatadine and 25 mg of sponsor mometasone) GSP301 is an investigational fixed-dose combination nasal spray; G2: received once-daily GSP301 (665 mg of sponsor olopatadine and 50 mg of sponsor mometasone); G3 received 137 mg of azelastine and 50 mg of fluticasone (FDA-approved formulation of AzeFlu); G4: received twice daily olopatadine (665 mg; FDA-approved formulation), and G5 received twice daily placebo (based on the GSP301 formulation)[12]. The symptoms of the patients were rated on a scale of 0 (absent) to 3 (severe). They reported that the patients who received twice-daily or once-daily GSP301 had significantly higher improvement in the instantaneous total nasal symptom score compared to controls. The adverse events related to the treatment were observed in 22.2%, 30.6%, 25.0%, 22.2%, and 16.7% of the patients in the he twice-

daily GSP301, once-daily GSP301, AzeFlu, olopatadine, and placebo groups, respectively[12]. The comparable percentage of adverse events were reported among study groups. The adverse events were headache, dysgeusia, epistaxis, rash, treatment emergent, and withdrawal. We did not document the adverse events in the present study. We unable to make a between-study comparison about adverse events. But, the evidence reported that the benefits outweigh the potential risks[12]. Some other studies have approved on the effectiveness of combined treatment a nasal spray antihistamine and corticosteroid on reducing the AR symptoms compared to monotherapy[13-17].Patel and Salapatek et al [11] showed that twice-daily GSP301 is more rapid compared to the single-daily dose. The improvement in symptoms was occurred within 10 minutes of receiving the drug. We measured the score following one week and four weeks of the treatment, therefore, it may not be possible to make the exact comparison between the studies. In addition, the dose and antihistamines used in the literature are different from each other. A small sample study (n=24) compared mometasone furoate NS monotherapy with mometasone furoate NS plus loratadine reported similar results[18]. The patients were divided into two treatment groups to receive mometasone furoate NS plus loratadine (n=12) or mometasone furoate NS monotherapy (n=12). The improvements were observed in both groups compared to the baseline for total symptoms score (TSS), increases in peak nasal inspiratory flow (PNIF), and decreases in eosinophil levels. The greater improvement in symptoms with combination therapy than with monotherapy between two groups was observed at night time. But, no difference in treatment effect was noted between the two study groups. No significant differences were reported in other studies as well[19,20] and in a review study as well[19].The desire results among patients with AR for rapid and long-standing symptom relief could be obtained through combination of an antihistamine and a corticosteroid into a single intranasal formulation[20]. The different findings have been reported in this regard as well. For example, a study compared the efficacy of mometasone furoate nasal spray in combination with loratadine with that of monotherapy with the individual agents among patients aged 12 years and older. The study did not find significant difference between mometasone furoate NS plus loratadine and mometasone furoate NS monotherapy for the primary efficacy

variables[2]. The effect of these antihistamines starts within 1-2 hours, lasting for 12-24 hours, except for acrivastine, which has to be given at 8-hour intervals[21]. These results are agreement with the findings of our study, because we showed that antihistamines have the effect within the first week. However, the effect of steroid may be delayed for few days or for one week. The current evidence does not demonstrate life-threatening effects, and in addition, the second-generations are more advantageous compared to that of the older generation[22]. The delay effect of steroid could be a reason for the effect of single therapy at week 4.

The study was not exempt from the limitations. It was not possible for the investigators to follow the patients for more than this time period due to technical issues. In addition, all patients were selected from one geographic area that may preclude us from generalization the results to patients in other settings across the country. We did not record the risks of the treatment in the study groups, but the evidence reported in the literature recommends that benefits outweigh the potential risks[12].

Conclusions

The present study showed that using intranasal corticosteroids in combination with antihistamine is more effective than intranasal corticosteroids alone in patients with allergic rhinitis.

Conflict of interests

The authors recorded no conflict of interests.

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