International Journal of Otolaryngology Research

ISSN Print: 2664-6455
ISSN Online: 2664-6463
Impact Factor: RJIF 5.44
IJOR 2023; 5(2): 53-58
www.otolaryngologyjournal.in
Received: 27-06-2023
Accepted: 04-08-2023

Aml Ali Radwan
Department of Otorhinolaryngology, Faculty of Medicine, Tanta University, Tanta, Egypt

Mohamed Nasser El Sheikh,
Department of Otorhinolaryngology, Faculty of Medicine, Tanta University, Tanta, Egypt

Mohamed Hisham Aly Hamad
Department of Otorhinolaryngology, Faculty of Medicine, Tanta University, Tanta, Egypt

Mohamed Osama Tomoum
Department of Otorhinolaryngology, Faculty of Medicine, Tanta University, Tanta, Egypt

Corresponding Author:
Aml Ali Radwan
Department of Otorhinolaryngology, Faculty of Medicine, Tanta University, Tanta, Egypt

A prospective cohort study of intranasal combined corticosteroids and antihistamines versus intra nasal corticosteroids in management of allergic rhinitis

Aml Ali Radwan, Mohamed Nasser El Sheikh, Mohamed Hisham Aly Hamad and Mohamed Osama Tomoum

DOI: https://doi.org/10.33545/26646455.2023.v5.i2a.32

Abstract
Background: Allergic rhinitis (AR) is the predominant form of chronic rhinitis, impacting around 10-20% of the population. The objective of this research was to evaluate the efficacy of intranasal corticosteroids (INCS) with antihistamines in treating AR, with a focus on symptoms including itching, sneezing, runny nose, and nasal congestion, as compared to INCS alone.
Methods: This research was conducted on a sample of 100 patients, aged between 18 and 50 years old, who had a history of AR and were clinically diagnosed based on AR criteria. It was ensured that these patients had not used nasal steroids in the month before to the commencement of baseline measurements. The study design was randomized and prospective, using a controlled approach. The patients were randomly divided into 2 equal groups: Group 1: treated with local corticosteroids alone (Fluticasone). Group 2: treated with local corticosteroids and antihistaminic spray (Fluticasone + Azelastine).
Results: Nasal symptoms were insignificantly different between both groups before treatment. Two nasal symptoms were insignificantly different between the two groups while rhinorrhoea and sneezing were significantly improved in Group 2 than Group 1 after 1 and 2 months (P value<0.05). Nose symptoms were insignificantly different between both groups before treatment. Nasal congestion or stuffiness, nasal blockage or obstruction and trouble sleeping were insignificantly different between both groups while trouble breathing through the nose and unable to get enough through my nose during exercise or exertion were significantly improved in Group 2 than Group1 after 1and 2 months (P value<0.05).
Conclusions: Patients treated with Fluticasone nasal spray alone or in combination with Azelastine nasal spray experience significant improvement in various complaints as evidenced by improved VAS scale regarding (rhinorrhoea and sneezing) and A-NOSE score regarding (both trouble breathing through the nose and the inability to get enough breath during exercise).

Keywords: INCS, Antihistamines, AR

Introduction
Allergic rhinitis (AR) is the predominant form of chronic rhinitis, with a prevalence of 10-20% among the population [1]. The condition may manifest as either seasonal, occurring during certain periods like the pollen season, or perennial, persisting throughout the whole year [2]. The symptoms of AR, including rhinorrhoea, nasal blockage, itching, sneezing, watery eyes, and sometimes cough, are induced spontaneously with exposure to allergens and triggering factors, and may potentially be reversed [3]. Severe AR has been linked to substantial detriments in quality of life, sleep, and job productivity [1].
Co-occurrence of many illnesses in a patient, known as associated disease, is very prevalent in allergic disorders. Specifically, more than 85% of individuals with asthma also have AR. Conversely, the coexistence of asthma and AR is seen in only 20 - 30% of individuals. The presence of many chronic conditions in a patient amplifies the intensity of asthma [4].
The diagnosis mostly relies on clinical evaluation, taking into account the correlation between many symptoms. The key supplementary tests for diagnosing AR, with high specificity and sensitivity, are the acute hypersensitivity skin prick test (SPT) utilizing the puncture method and assessment of allergen-specific IgE levels in the blood [5, 6].

Avoiding allergens, allergen immunotherapy, and pharmacological intervention are relevant treatment efforts in AR.

INCS have been recognized as a safe and efficient first therapy for AR. Several INCS are available, such as beclomethasone dipropionate, budesonide, flunisolide, fluticasone propionate, mometasone furoate, and triamcinolone acetonide. Each of these treatments is efficacious for managing seasonal AR and may also be used as a prophylactic step for chronic AR. Generally, they relieve nasal congestion and itching, runny nose, and sneezing that occur during the first and last phases of an allergic response, with studies suggesting almost complete elimination of symptoms during the later phase [7].

Histamine is the primary pathophysiological mediator of AR, primarily acting via stimulating the H1 receptor [8]. Antihistamines used to treat AR are H1 receptor antagonists. Antihistamines may be categorized into two groups: oral and intranasal. Oral antihistamines may be categorized into two groups: older, first-generation antihistamines (such as chlorpheniramine) and newer, second-generation antihistamines (such as cetirizine). Intranasal antihistamines have a rapid onset of action, often within 15-30 minutes, surpassing the speed of oral antihistamines. Furthermore, no sedative effects have been seen with their use [9].

The objective of this research was to examine the effects of INCS and antihistamines together vs INCS alone in the treatment of AR, specifically in relation to symptoms such as itching, sneezing, rhinorrhoea, and nasal obstruction.

Methods and Patients

This study was conducted on a sample of 100 patients, aged between 18 and 50 years old, who had a history of AR and were clinically diagnosed based on specific criteria for AR symptoms (including sneezing, runny nose, nasal congestion, itching of the eyes, nose, and palate, postnasal drip, cough, irritability, and fatigue). It is important to note that none of the patients had used nasal steroids in the month prior to the start of the study.

The research was conducted with clearance from the Ethical Committee of Tanta University Hospitals. Informed written agreement was acquired from either the patient or their family. The research was conducted from December 2021 to December 2022.

Exclusion criteria were severe asthma, planned surgery of nasal cavity, patient with adrenal disease, patient with cataract or glaucoma, nasal fungal infection, other causes of elevated IgE level like (parasite infection, allergic bronchopulmonary aspergillosis and churg-stauss / polyarteritis nervosa).

Randomization

Using a computer-generated software, patients were divided into two equal groups at random: Group 1: AR were treated with local corticosteroids alone (Fluticasone) two puffs in each nostril once daily for two weeks then lowered to one puff in each nostril once daily based on patient improvement. Group 2: AR was treated with local corticosteroids and antihistaminic spray (Fluticasone + Azelastine) two puffs in each nostril once daily for two weeks then lowered to one puff in each nostril once daily based on patient improvement.

All patients were subjected to complete history taking, assessed before treatment and after first and second month of treatment using: visual analogue scale (VAS) [10] and questionnaire to evaluate nasal obstruction symptoms done by Arabic version of nose scale (A-NOSE) [11], general examination, otorhinolaryngological clinical examination including anterior rhinoscopy and diagnostic nasal endoscopy and serum IgE level test.

The VAS is a technique used to evaluate the subjective perception of nasal symptoms, such as sneezing, nasal congestion, nasal itching and rhinorrhoea. The scale ranges from 0, denoting the complete lack of symptoms, to 10, representing the existence of intense symptoms. Patients were directed to mark a cross on a line that symbolizes their unique experiences with nasal symptoms.

A-NOSE: The Nasal Obstruction Symptom Evaluation (NOSE) survey is a scientifically verified tool specifically developed to assess and quantify nasal obstruction. The questionnaire is concise and includes 5 questions that individuals judge themselves on, with scores ranging from 0 to 4. The NOSE score is calculated by adding up the replies to the 5 separate questions, resulting in a range of values from 0 to 20. The Arabic version of the NOSE scale, known as A-NOSE, was created via cross-cultural adaptation and accurate translation of the original form.

Statistical analysis

Statisticians at IBM Inc. in Armonk, NY, USA, used SPSS v26 to compile and analyse the data. The range, standard deviation (SD), and mean were the quantitative variables. To compare the two groups, an unpaired Student's t-test was used. The Chi-square test was used to evaluate the qualitative variables, which were presented as percentages and frequencies. Statistical significance was determined by a two-tailed P value that was less than 0.05.

Results

A total of 126 patients were evaluated for their eligibility in this research. Out of these, 11 patients did not match the required requirements, while 5 patients declined to participate. Additionally, there were missing data from 10 patients, with 4 patients from Group 1 and 6 patients from Group 2 failing to complete the follow-up. The remaining 100 patients were randomly assigned to two groups, with 50 patients in each group. The patients who were assigned to certain groups were monitored and subjected to statistical analysis. Figure 1

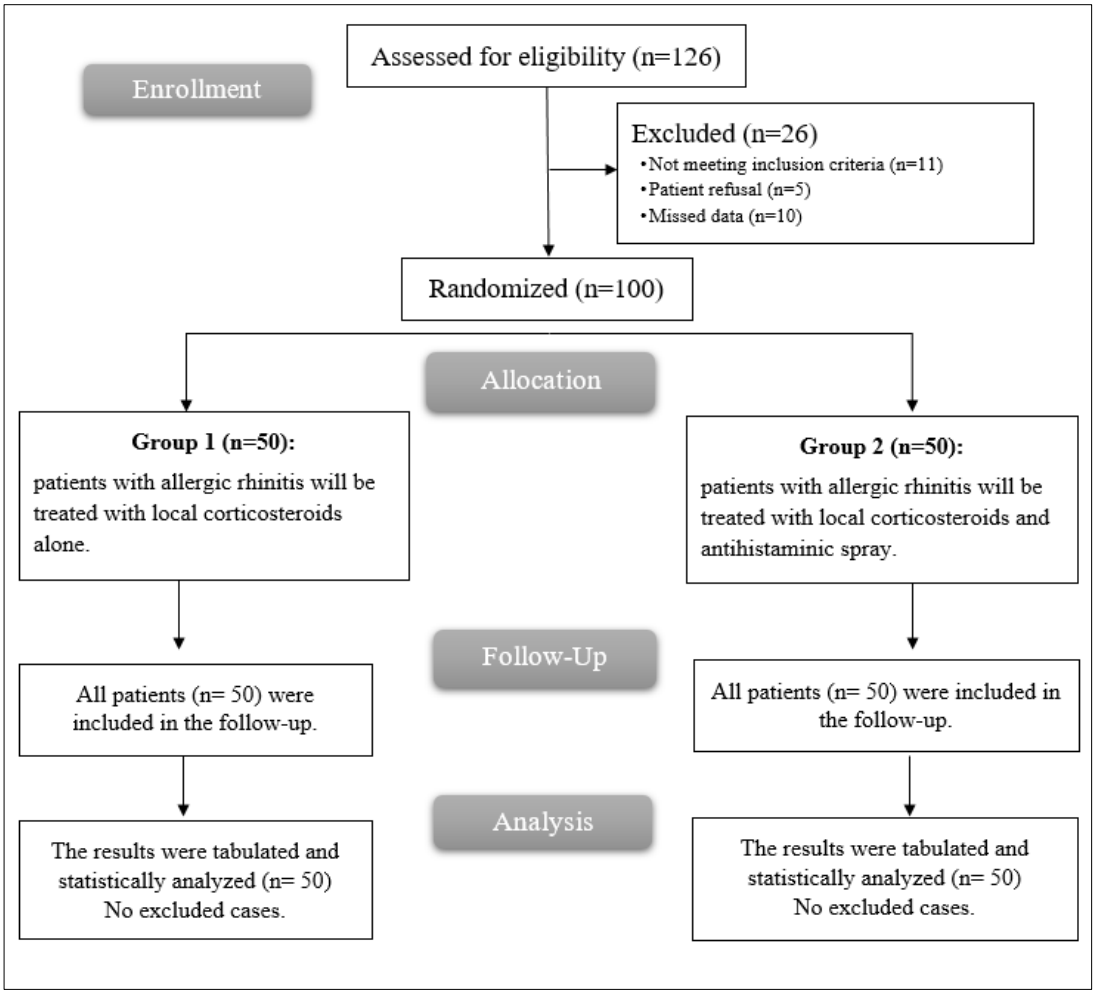

Fig 1: Consort flowchart of the enrolled patients

The age, sex, bronchial asthma, skin allergy, allergic conjunctivitis, type of AR, total serum IgE were Insignificantly different between both groups. Table1

Table 1: Demographic data, bronchial asthma, skin allergy, allergic conjunctivitis type of AR and total serum IgE

		Group 1 (n=50)	Group 2 (n=50)	P value
Age (years)		34.5 ± 10.22	32.8 ± 9.16	0.378
Sex	Male	19 (38%)	22 (44%)	0.542
	Female	31 (62%)	28 (56%)	
Bronchial asthma		15 (30%)	18 (36%)	0.523
Skin Allergy		9 (18%)	12 (24%)	0.461
Allergic conjunctivitis		13 (26%)	12 (24%)	0.817
Type of AR	Seasonal	23 (46%)	20 (40%)	0.545
	Perennial	27 (54%)	30 (60%)	
Total serum IgE (IU/ml)		220.9 ± 170.7	167.2 ± 128.32	0.079

The two groups did not vary significantly in terms of nasal symptoms prior to therapy, which include irritation, itching, rhinorrhea, and sneezing. Concerning stuffiness and itching in the nose, neither group differed significantly from the other. Compared to Group 1, Group 2 showed a significant improvement in rhinorrhea and sneezing at the 1- and 2-month marks. Table 2

Table 2: Comparison between both groups according to VAS of different complaints before and after treatment.

	Nasal congestion	Nasal itching	Rhinorrhoea	Sneezing
Before treatment				
Group 1	6.6 ±2.15	6.22 ±2.23	5.9 ±2.02	5.9 ±2.02
Group 2	5.8 ± 2.14	5.6 ± 2.86	5.7 ± 2.33	5.1 ± 2.54
P value	0.072	0.216	0.648	0.085
After 1 month				
Group 1	3.42 ±1.94	3.42 ±2.28	3.22 ±2.1	3.56 ±2.05
Group 2	2.8 ± 1.93	2.6 ± 2.35	2.1 ± 2.42	2.5 ± 2.67
P value	0.137	0.066	0.015*	0.023*

After 2 months				
Group 1	2.04 ±1.74	2.08 ±1.77	2.18 ±1.96	2.46 ±1.72
Group 2	1.5 ± 1.36	1.4 ± 1.53	1.1 ± 1.67	1.4 ± 2.03
P value	0.076	0.056	0.003*	0.006*

The presence of nose symptoms (such as nasal congestion, nasal blockage, difficulty breathing, difficulties sleeping, and inadequate nasal airflow during exercise or exertion) showed no significant difference between the two groups prior to therapy. The occurrence of nasal congestion or stuffiness, nasal blockage or obstruction, and difficulty sleeping did not show significant differences between both groups. However, there was a significant improvement in the ability to breathe through the nose and the ability to get enough air through the nose during exercise or exertion in Group 2 compared to Group 1 after 1 and 2 months. (P value<0.05). Table 3

Table 3: Comparison between both groups according to nose score of different complaints before and after treatment

	Nasal congestion or stuffiness	**Nasal blockage or obstruction**	**Trouble breathing through the nose**	**Trouble sleeping**	**Unable to get enough through my nose during exercise or exertion**	**Total score**
Before treatment						
Group 1	2.5 ± 0.81	2.8 ± 0.93	2.8 ± 0.79	2.5 ± 1.18	3.5 ± 0.74	14.12±3.37
Group 2	2.5 ± 0.97	2.6 ± 1.15	2.5 ± 0.99	2.2 ± 1	3.2 ± 0.83	12.98±3.64
P value	0.912	0.295	0.098	0.124	0.058	---
After 1 month						
Group 1	1.3 ± 0.53	1.4 ± 0.64	1.5 ± 0.65	1 ± 0.86	1.8 ± 0.62	6.98±2.21
Group 2	1.2 ± 0.69	1.2 ± 0.7	1.1 ± 1.05	0.8 ± 0.84	1.4 ± 0.73	5.74±3.23
P value	0.871	0.105	0.042*	0.198	0.003*	---
After 2 months						
Group 1	1.1 ± 0.51	1.2 ± 0.58	1.3 ± 0.62	1 ± 0.84	1.6 ± 0.64	6.18±1.86
Group 2	1 ± 0.59	1 ± 0.71	1 ± 0.95	0.7 ± 0.8	1.2 ± 0.82	4.98±2.61
P value	0.468	0.128	0.027*	0.238	0.033*	---

Discussion

The major findings in our study showed that the nasal symptoms (nasal congestion, nasal itching, rhinorrhea and sneezing) were insignificantly different between both groups before treatment. Our results were supported by study of Ilyina *et al*. [12] they found that the individual nasal symptoms were insignificantly different before treatment between intranasal Azelastine hydrochloride and fluticasone propionate group or Azelastine hydrochloride group. Supporting our results, Kim *et al*. [13] found that baseline individual nasal symptoms were insignificantly different between the groups who received 200 µg ciclesonide, 5 mg levocetirizine, or a combination of both. In the study of Ratner *et al*. [14] demonstrated that the baseline individual nasal symptoms (congestion, itching, sneezing, rhinorrhea) were insignificantly different between combination therapy (with intranasal azelastine and fluticasone group) and fluticasone alone group.

In the present study, nasal symptoms were significantly improved after 1month and after 2month compared to before treatment in Fluticasone group and Fluticasone + Azelastine group (P value <0.001).

In agreement with our results, Kim *et al*. [15] they found that INCS/INAH combination and INCS monotherapy significantly improved the total mean rhino-conjunctivitis VAS score and nasal symptoms compared to baseline. Supporting our results, Price *et al*. [16] The research showed that MP-AzeFlu was linked to enhanced VAS ratings in all areas examined, such as the intensity of AR symptoms, asthma symptoms, sleep quality, daily job or school activities, daily social activities, and daily outdoor activities. In the present study, two nasal symptoms (nasal congestion and nasal itching) were insignificantly different between the two groups. But rhinorrhea and sneezing were significantly improved in Fluticasone + Azalastine group than Fluticasone group after one and two months.

Consistent with our findings, Kim *et al*. [15] observed that the combination of INCS and intranasal antihistamines (INAH) led to a substantial improvement in the overall mean score of the Rhino conjunctivitis Quality of Life Questionnaire (RQLQ) compared to using INCS alone. Similarly, Du *et al*. [17] showed that the combined treatment of INAH and INCS was more effective than INCS alone in reducing symptoms such as rhinorrhea and sneezing, as measured by the VAS scale. In this study, the severity of various nasal complaints (such as nasal congestion, nasal blockage, difficulty breathing through the nose, trouble sleeping, and inability to get enough air through the nose during exercise or exertion) was found to be statistically insignificant between the two groups before the treatment.

Our results were in contrary with study of Kim *et al*. [13] A study showed that the baseline individual nasal symptoms, as measured by the total nasal symptom score (TNSS), and the reflective total ocular symptom score (rTOSS) were comparable among the three treatment groups who were given 200 µg ciclesonide, 5 mg levocetirizine, or a combination of both. These scores represent the signs and symptoms that caused significant discomfort and interfered with daily activities.

In the present study, the nose ratings of several symptoms (nasal congestion or stuffiness, nasal blockage or obstruction, difficulties sleeping) were insignificantly different between both groups. However, the symptoms of difficulty breathing through the nose and insufficient airflow during exercise or exertion were considerably alleviated in the group receiving both local corticosteroids and antihistaminic spray, compared to the group receiving just local corticosteroids, after one and two months.

Our results were in contrary with study of Pinar *et al*. [18] The investigation revealed a substantial difference between the groups for daily nasal symptoms, including nasal blockage, nasal discharge, sneezing, and itching, throughout

the second week and first month evaluations ($p< 0.05$). Additionally, Kim *et al*. [15] The study discovered that the combination therapy of INCS and INAH was more effective than INCS alone in reducing the average morning and evening 12-hour reflective TNSS to a greater extent (mean difference -0.44, 95% confidence interval -0.61 to -0.27, $P<0.00001$, I2 = 8%). Additionally, the combination therapy also resulted in a significant decrease in the total ocular symptom score (mean difference -0.62, 95% confidence interval -1.05 to -0.19, P = 0.005, I2 = 36%).

According to our results, nasal congestion or stuffiness, nasal blockage or obstruction and trouble sleeping were insignificantly different between both groups. Trouble breathing through the nose and unable to get enough through my nose during exercise or exertion were significantly improved in local corticosteroids and antihistaminic spray group than local corticosteroids alone group after one month and two months (P value =0.042 and 0.003 respectively).

In agreement with our results, Kim *et al*. [15]. The study discovered that the combined treatment of INCS and INAH was notably more effective in relieving nasal and ocular symptoms and enhancing the quality of life compared to the use of INCS alone in individuals with AR. In a similar vein, Ilyina *et al*. [12] shown that patients treated with MP-AzeFlu reported considerably more substantial decreases in reflected rTNSS, reflecting total ocular symptom score (rTOSS), and reflective total of 7 symptom scores (rT7SS) compared to those treated with AZE. According to our results, Total serum IgE was insignificantly different between both groups.

Similar to our results, Segundo *et al*. [19] they found that there was no significant change in IgE level between the studied groups.

Our study had some limitations as it was a single center study, the study lacked comparison with controlled group and adverse effects weren't evaluated.

Conclusions

Patients treated with Fluticasone nasal spray alone or in combination with Azelastine nasal spray experience significant improvement in various complaints as evidenced by improved VAS scale regarding (rhinorrhoea and sneezing) and A-NOSE score regarding (both trouble breathing through the nose and the inability to get enough breath during exercise).

Financial support and sponsorship: Nil.

Conflict of Interest: Nil.

References

1. Dykewicz MS, Hamilos DL. Rhinitis and sinusitis. Journal of Allergy and Clinical Immunology. 2010 Feb 1;125(2):S103-15.
2. Klimek L, Bachert C, Pfaar O, Becker S, Bieber T, Brehler R, *et al*. ARIA guideline 2019: treatment of allergic rhinitis in the German health system. Allergol Select. 2019;3:22-50.
3. Muñoz-Cano R, Ribó P, Araujo G, Giralt E, Sanchez-Lopez J, Valero A. Severity of allergic rhinitis impacts sleep and anxiety: results from a large Spanish cohort. Clin Transl Allergy. 2018;8(1):23-8.
4. Amaral R, Fonseca JA, Jacinto T, Pereira AM, Malinovschi A, Janson C, *et al*. Having concomitant asthma phenotypes is common and independently relates to poor lung function in NHANES 2007-2012. Clin Transl Allergy. 2018;8(1):13-9.
5. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, *et al*. European position paper on rhinosinusitis and nasal polyps Rhinology. 2020;58:1-464.
6. Hamerschmidt R, Hamerschmidt R, Moreira AT, Tenório SB, Timi JR. Comparison of turbinoplasty surgery efficacy in patients with and without allergic rhinitis. Braz J Otorhinolaryngol. 2016;82:131-9.
7. Hembrom R, Ghosh S, Paul S, Maiti R, Mandal S, Das S, *et al*. Role of vitamin D3 supplementation in allergic rhinitis: an outpatient department based prospective analytical observational study. Int J Basic Clin Pharmacol. 2019;8:10-40.
8. Sly RM. Changing prevalence of allergic rhinitis and asthma. Ann Allergy Asthma Immunol. 1999;82(3):233-52.
9. Kaliner MA, Berger WE, Ratner PH, Siegel CJ. The efficacy of intranasal antihistamines in the treatment of allergic rhinitis. Ann Allergy Asthma Immunol. 2011;106(2):6-11.
10. Delgado DA, Lambert BS, Boutris N, McCulloch PC, Robbins AB, Moreno MR, *et al*. Validation of digital visual analog scale pain scoring with a traditional paper-based visual analog scale in adults. J Am Acad Orthop Surg Glob Res Rev. 2018;2(3):88-90.
11. Amer MA, Kabbash IA, Younes A, Elzayat S, Tomoum MO. Validation and cross-cultural adaptation of the arabic version of the nasal obstruction symptom evaluation scale. The Laryngoscope. 2017;127(11):2455-9.
12. Ilyina NI, Edin AS, Astafieva NG, Lopatin AS, Sidorenko IV, Ukhanova OP, *et al*. Efficacy of a novel intranasal formulation of azelastine hydrochloride and fluticasone propionate, delivered in a single spray, for the treatment of seasonal allergic rhinitis: results from russia. Int Arch Allergy Immunol. 2019;178(3):255-63.
13. Kim CH, Kim JK, Kim HJ, Cho JH, Kim JS, Kim YD, *et al*. Comparison of intranasal ciclesonide, oral levocetirizine, and combination treatment for allergic rhinitis. Allergy Asthma Immunol Res. 2015;7(2):158-66.
14. Ratner PH, Hampel F, Van Bavel J, Amar NJ, Daftary P, Wheeler W, *et al*. Combination therapy with azelastine hydrochloride nasal spray and fluticasone propionate nasal spray in the treatment of patients with seasonal allergic rhinitis. Ann Allergy Asthma Immunol. 2008;100(1):74-81.
15. Kim M, Ryu G, Kang SY, Kim MA, Yang SI, Lee IH, *et al*. Intranasal antihistamine and corticosteroid to treat allergic rhinitis: A systematic review and meta-analysis. Allergy. 2022;77(11):3436-40.
16. Price D, Klimek L, Gálffy G, Emmeluth M, Koltun A, Kopietz F, *et al*. Allergic rhinitis and asthma symptoms in a real-life study of MP-AzeFlu to treat multimorbid allergic rhinitis and asthma. Clin Mol Allergy. 2020;18:15-25.
17. Du K, Qing H, Zheng M, Wang X, Zhang L. Intranasal antihistamine is superior to oral H(1) antihistamine as an add-on therapy to intranasal corticosteroid for

treating allergic rhinitis. Ann Allergy Asthma Immunol. 2020;125(5):589-96.
18. Pinar E, Eryigit O, Oncel S, Calli C, Yilmaz O, Yuksel H. Efficacy of nasal corticosteroids alone or combined with antihistamines or montelukast in treatment of allergic rhinitis. Auris Nasus Larynx. 2008;35(1):61-6.
19. Segundo GR, Gomes FA, Fernandes KP, Alves R, Silva DA, Taketomi EA. Local cytokines and clinical symptoms in children with allergic rhinitis after different treatments. Biologics. 2009;3:469-74.

How to Cite This Article
Radwan AA, El Sheikh MN, Aly Hamad MH, Tomoum MO. A Prospective Cohort Study of Intranasal Combined Corticosteroids and Antihistamines versus Intra Nasal Corticosteroids in Management of Allergic Rhinitis. International Journal of Otolaryngology Research 2023; 5(2): 53-58.