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Original Research Article

Comparative clinical assessment of mometasone furoate-azelastine hydrochloride intranasal spray (Ryaltris AZ®) with fluticasone furoate-azelastine hydrochloride intranasal spray in patients with allergic rhinitis in India

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ABSTRACT

Background: Allergic rhinitis is a type of IgE-mediated hypersensitivity reaction. ARIA recommends a combination of intranasal corticosteroid and intranasal antihistamine as first-line treatment for allergic rhinitis in moderate to severe AR. The current study aimed to compare the effectiveness and safety of Mometasone furoate-Azelastine hydrochloride Nasal Spray and Fluticasone furoate-Azelastine hydrochloride Nasal Spray for the treatment of allergic rhinitis in India.
Methods: A multicentric, comparative study was carried out across 30 ENT clinics in India. From September to November 2022, medical records were scrutinised for information such as medical history, symptoms, treatment details, clinical results, and adverse events. The mean change in total nasal and non-nasal symptom scores from baseline to the end of treatment was used to assess effectiveness.
Results: 235 received mometasone furoate-azelastine hydrochloride intranasal spray and 221 received Fluticasone furoate-Azelastine hydrochloride (FF-Az) Intranasal Spray. The mean change from the baseline TNSS score at day 14 in the MF-AZ and FF-Az groups was -6.89 (±3.32) and -6.82 (±3.20) respectively, with no significant difference (p=0.81) between the two. Bitterness and nasal irritation was significantly higher in the FF-Az group. There was no hospitalization, SAE, or treatment discontinuation due to AEs among patients in either group.
Conclusions: The study found that intranasal mometasone-azelastine and fluticasone furoate-azelastine sprays were equally effective in relieving nasal and non-nasal symptoms by days 7 and 14, respectively. However, patients in the fluticasone furoate-azelastine group reported more bitter taste and nasal irritation.

Keywords: Mometasone, Azelastine, Fluticasone furoate, Nasal spray, Allergic rhinitis

INTRODUCTION

Allergic rhinitis (AR) is a heterogeneous IgE-mediated hypersensitivity reaction characterized by nasal itch, sneezing, watery or mucous rhinorrhoea, nasal obstruction, and nasal or pharyngeal irritation. AR, if left untreated, can significantly reduce patients' overall quality of life (QOL).[1] The Allergic Rhinitis and Its Impact on Asthma (ARIA) guideline recommend a combination of intranasal corticosteroid (INCS) along with intranasal

antihistamine (INAH) as first-line treatment for allergic rhinitis, especially for treatment of moderate to severe AR, particularly if nasal congestion is the major symptom.[2] Second-generation intranasal corticosteroids, such as triamcinolone acetonide, fluticasone propionate, mometasone furoate, and fluticasone furoate, have lower systemic bioavailability but bind more potently to receptors. Fluticasone furoate and mometasone furoate have been found to be effective treatments for both nasal and ocular symptoms of allergic rhinoconjunctivitis in studies.[3] But only Azelastine hydrochloride and olapatidine hydrochloride are FDA-approved INAH for allergic rhinitis. Fixed-dose combinations of INCS and intranasal H1-antihistamine are more effective than the individual compounds administered separately, are well tolerated, and have faster symptom improvement.[4] There has been no head-to-head study comparing combinations of INCS and INAH in the treatment of allergic rhinitis to our knowledge. Although each have their own unique properties like fluticasone furoate (FF) has a higher receptor affinity than mometasone furoate (MF) and MF has the lowest systemic bioavailability of all INCS, the clinical advantage of FF or MF over each other has yet to be demonstrated in clinical studies. Therefore, the current study was planned to compare the effectiveness and safety of Mometasone furoate-Azelastine hydrochloride NS (Ryaltris AZ ®; Glenmark Pharmaceuticals Ltd., India) and fluticasone furoate-Azelastine hydrochloride NS in clinical practice for the treatment of allergic rhinitis patients in India.

METHODS

This was a multicentric, comparative, retrospective study conducted across 30 ENT clinics across India. Patients aged ≥ 12 years with allergic rhinitis who were prescribed Mometasone furoate-Azelastine hydrochloride intranasal spray (Ryaltris AZ®) or Fluticasone furoate-Azelastine hydrochloride intranasal spray by their treating physician were enrolled. The study was conducted after obtaining permission from Independent ethics committee. The study was conducted in accordance with the Declaration of Helsinki and ICH-Good Clinical Practice guidelines. Data confidentiality was maintained throughout the study period. Because this was a retrospective study in which participants were de-identified or could not be contacted, informed consent was not required, and waiver of consent was considered for the study in accordance with the Indian council of medical research (ICMR) National Ethical guidelines for biomedical and health research involving human participants, 2017.

Medical records, from September to November 2022, of patients being treated with MF-Az or FF-Az were evaluated for information such as medical history, symptoms, treatment details, clinical results, and adverse events. The effectiveness was measured by the mean change in total nasal and non-nasal symptom scores from baseline to the end of treatment (14 days), and the safety was measured by the number of treatment-emergent adverse events (TEAEs), treatment-related AEs, and AEs/SAEs that led to study withdrawal. The study also compared patients' sensory attributes, such as bitterness of taste or nasal irritation caused by the study medications.

Data was recorded in a predesigned case record form and compiled in Microsoft excel version 2019 and analysed. Descriptive statistics for quantitative variables were represented as mean±SD. Qualitative variables were represented as frequency and percentages. Unpaired t test or Mann Whitney test was used to compare differences between two independent groups depending on the normality of distribution. Paired t-test/Wilcoxon matched paired t test were used for comparing dependent variable depending on the normality of distribution. Normality of data was tested using Kolmogorov-Smirnov test. Graphical representations were done wherever applicable. Level of significance will be considered as $P < 0.05$. Data will be analysed using Graph pad prism software version 3.06.

RESULTS

A total of 619 patient's medical records were reviewed, of which 456 had complete medical records and were available for analysis. Of these, 235 received Mometasone furoate-Azelastine hydrochloride (MF-Az) Intranasal Spray and 221 received Fluticasone furoate-Azelastine hydrochloride (FF-Az) Intranasal Spray. The baseline characteristics of patients in both groups were similar (Table 1).

Table 1: Age and gender wise comparison of patients in both the group.

Parameters	Mometasone furoate-azelastine hydrochloride intranasal spray (Ryaltris AZ®) (N=235)	Fluticasone furoate-azelastine hydrochloride intranasal spray (N=221)	Inter group p value (unpaired t test)
Age (years)			
Mean	34.03	33.59	0.7330
SD	13.77	13.62	
Gender			
Male	130	104	0.09
Female	105	117	

Table 2: Comparison of TNSS among patients in both the group (n=456).

Parameters	Mometasone furoate-azelastine hydrochloride intranasal spray (Ryaltris AZ®) (N=235)	Fluticasone furoate-azelastine hydrochloride intranasal spray (N=221)	Inter group p value (unpaired t test)
Day 0			
N	235	221	
Mean	7.74	7.70	
SD	3.45	3.23	0.8985
Median	9.00	8.00	
Day 7±1			
N	235	221	
Mean	3.06	3.00	
SD	2.26	2.19	0.7738
Median	3.00	3.00	
Mean change from baseline	-4.68	-4.70	
Intragroup p value (paired t Test)	<0.0001	<0.0001	
Day 14±2			
N	235	221	
Mean	0.85	0.88	
SD	1.11	1.15	0.7770
Median	0.00	0.00	
Mean Change from Day 7±1	-2.21	-2.12	
Intragroup p-value (Paired t Test)	<0.0001	<0.0001	
Mean Change from Baseline to Day 14±2			
Mean change from baseline	-6.89	-6.82	
Intragroup p value (Paired t Test)	<0.0001	<0.0001	

Majority of patients in both groups (76.06% in the MF-Az group (N=188) and 70.05% in the FF-Az group (N=180) were classified as moderate-severe AR. Similarly, 58.19% of the MF-Az group (N=126) and 56.19% of the FF-Az group (N=121) had persistent disease.

At baseline, the total nasal symptoms score (TNSS) in the MF-AZ group was 7.74±3.45 and in the FF-Az group was 7.70±3.23, (p=0.89). The mean change from the baseline TNSS score at day 14 in the MF-AZ and FF-Az groups was -6.89 (±3.32) and -6.82 (±3.20) respectively. Intergroup comparison showed no significant difference (p=0.81) between the two, whereas intragroup comparison showed a significant reduction in TNSS from baseline in both groups (p<0.0001) (Table 2). Similarly, there was no significant difference in baseline Total non-nasal symptoms score (TNNSS) between the two groups of patients (p=0.97). The mean change from the baseline TNNSS score at day 14 in the MF-Az and FF-Az groups was -3.83 (±3.18) and -4.07 (±3.13) respectively. The intergroup comparison showed no significant difference (p=0.42) between the two, whereas the intragroup comparison showed a significant reduction in TNNSS from baseline in both groups (p<0.0001) (Table 3).

Sensory attributes among enrolled patients revealed that the VAS score for bitterness was significantly higher in the FF-Az group than in the MF-Az group, 3.09 (±2.87) vs. 2.42 (±2.55), p=0.009. Similarly, nasal irritation was significantly higher in the FF-Az group, 1.64 (±2) vs. 1 (±1.77), p=0.0004. There was no hospitalization, SAE, or treatment discontinuation due to AEs among patients in either group. There were no TEAEs reported among patients in either group. Overall, both treatments were tolerated well by the patients.

DISCUSSION

The present study comparing the two INCS- Azelastine nasal spray is first of its kind in India. INCS are important and effective treatment option available for management of AR and has shown to affect both nasal and non-nasal (ocular) symptoms of AR. A systemic review of 2267 patients with allergic rhinitis in 16 randomised controlled trials, showed superioriority of INCS over oral antihistamines as first line treatment for allergic rhinitis. [5] Mometasone and fluticasone furoate are second generation INCS that have higher glucocorticoid receptor binding affinity, resulting in higher topical potency.

Table 3: Comparison of TNNSS among patients in both the group.

Parameters	Mometasone furoate-azelastine hydrochloride intranasal spray (Ryaltris AZ®) (N=235)	Fluticasone furoate-azelastine hydrochloride intranasal spray (N=221)	Inter group p value (unpaired t test)
Day 0			
N	219	200	
Mean	4.25	4.07	
SD	3.27	3.60	0.9754
Median	4.00	3.00	
Day 7±1			
N	219	200	
Mean	1.19	1.23	
SD	1.54	1.69	0.7332
Median	0.00	0.00	
Mean change from baseline	-2.88	-2.84	
Intragroup p value (paired t Test)	<0.0001	<0.0001	
Day 14±2			
N	219	200	
Mean	0.18	0.24	
SD	0.58	0.60	0.2782
Median	0.00	0.00	
Mean Change from Day 7±1	-1.00	-0.99	
Intragroup p-value (Paired t Test)	<0.0001	<0.0001	
Mean Change from Baseline to Day 14±2			
Mean change from baseline	-3.88	-3.83	
Intragroup p value (Paired t Test)	<0.0001	<0.0001	

They also have low bioavailability, resulting in lower systemic exposure and thus a lower risk of side effects. In India, Azelastine is the only approved intranasal antihistamine that is available as a monotherapy as well as in combination with INCS. It is a second-generation antihistamine that has been shown to be effective in allergic rhinitis patients.[6] A systematic review and meta-analysis found that combining intranasal corticosteroid (INCS) and intranasal antihistamine (INAH) therapy is a more effective treatment for allergic rhinitis (AR) than INCS monotherapy.[7] In our study both the combination i.e., MF-Az and FF-Az was found to be prescribed commonly in patients with moderate to severe and persistent AR. This is in line with the ARIA guideline, where, it recommends the use of INCS-Azelastine combinations in symptomatic treated or untreated patients who have persistent symptoms.[2] It also suggested that a combination of an INCS and INAH might act faster than an INCS alone, which might be preferable to some patients at the outset of treatment (the first two weeks).

In our study, the overall control of nasal and non-nasal symptoms was similar across both groups of patients, and both combinations showed a significant decrease in nasal and non-nasal symptoms at day 7 and 14, indicating that both INCS-Azelastine combinations are equally effective. These findings were consistent with previous studies, which found that MF nasal spray and FF nasal spray significantly reduced nasal and non-nasal symptoms.[8-10] An 8-week study on patients with persistent rhinoconjunctivitis found that mometasone and fluticasone furoate improved allergic rhinoconjunctivitis subjectively and objectively.[3] Karpishchenko et al evaluated the combination of intranasal azelastine hydrochloride and mometasone furoate and found that it significantly improved nasal symptoms and quality of life compared to intranasal mometasone furoate alone and intranasal mometasone furoate in combination with an oral third-generation antihistamine.[11] We also evaluated and compared patients' sensory attributes and found that nasal irritation and bitterness were significantly higher in patients on fluticasone furoate azelastine combination. Patients' adherence and preference to treatment are also affected by sensory attributes, and those with better sensory attributes are more likely to be used for an extended period of time, helping to maintain quality of life. Azelastine is thought to be associated with bitterness in the combination, so masking the bitterness of azelastine was

thought to be important in improving its usage among patients. The bitterness of the MF-Az formulation is masked with neotame and the use of a 70 mcl Vp3 pump rather than a 140 mcl Vp3 pump, resulting in less vehicle for the same dose.[12] Bitter taste can also be associated with poor dosing technique. [13] Improving dosing technique through patient education is essential in such cases to decrease bitterness of any product. The study's retrospective nature and relatively small sample size are its two main limitations; similarly designed and executed large-scale prospective studies would help in providing additional value to the comparison.

CONCLUSION

Current study showed that intranasal mometasone-azelastine has similar effectiveness to fluticasone furoate-azelastine intranasal spray, showing significant improvement in nasal and non-nasal symptoms at both days 7 and 14, along improving sensory attribute among patients with significantly less bitter taste and nasal irritation.

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