Azelastine/fluticasone intranasal spray for allergic rhinoconjunctivitis

JESSIE A. LEE MB BS
CONSTANCE H. KATELARIS MB BS, PhD, FRACP

The azelastine/fluticasone intranasal spray is a new option for treating allergic rhinoconjunctivitis. With clinical efficacy and prompt onset of action, it may be associated with increased patient satisfaction and improved medication compliance in the initial treatment period.

Allergic rhinoconjunctivitis (ARC) is a common health problem with an increasing prevalence worldwide. Self-reports from the 2007–2008 National Health Survey suggest that it affects approximately 15% of the Australian population.[1] In a population-based study conducted in Tasmania in 1991-93, the reported prevalence of hayfever in an adult cohort was 41%.[2]

The societal burden of ARC is significant and includes the direct costs of treatment and medical consultations as well as indirect impacts such as decreased productivity, time away from work or school and impairment of quality of life. In an Australian survey of adults and children with physician-diagnosed ARC, the majority of patients reported sleep disturbance and over 40% of patients described interference with school or work performance.[3] Management of comorbid conditions, including sinusitis and asthma, can also add to the financial cost of ARC.

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Dr Lee is Immunology Advanced Trainee, Department of Medicine, Division of Allergy and Clinical Immunology at Campbelltown Hospital, Sydney.
Professor Kataleris is Senior Staff Specialist, Department of Medicine, and Head of Unit, Division of Allergy and Clinical Immunology at Campbelltown Hospital; and Professor of Immunology and Allergy, University of Western Sydney, Sydney, NSW.

ARC is characterised by an acute histamine-mediated reaction triggered by the binding of antigen-specific IgE antibodies to mast cells and basophils. This results in the release of mediators, including histamine, leukotrienes and prostaglandins, and the development of symptoms such as sneezing, itching and rhinorrhoea. In the eye, this reaction results in watering, itching and mild injection. The acute reaction is followed by a late-phase reaction that involves the recruitment and infiltration of inflammatory cells in the nasal mucosa – this perpetuates the inflammatory response, producing persistent rhinorrhoea and prominent nasal congestion.[4]

Current gaps in treatment

Intranasal corticosteroids and intranasal antihistamines are recommended for the treatment of ARC and have been shown to be highly effective and well tolerated in this setting.[5] When used separately, however, these medications have limitations that may compromise patient satisfaction and necessitate the use of multiple simultaneous agents. Intranasal corticosteroids have been shown to provide greater relief of nasal symptoms than intranasal antihistamines,[6] but the onset of action is delayed and achieving maximal benefit can take several weeks.[7] Intranasal antihistamines have a rapid onset of action and result in increased patient satisfaction in the short term but are less efficacious than intranasal corticosteroids.[8]

What is azelastine/fluticasone intranasal spray?

Azelastine/fluticasone is now available in an intranasal spray that combines the most commonly prescribed intranasal antihistamine (azelastine) with the most commonly prescribed intranasal corticosteroid (fluticasone propionate).[9] It was approved by the TGA in December 2013 (and amended in February 2014) for symptomatic treatment of moderate to severe allergic rhinitis and rhinoconjunctivitis in adults and children of at least 12 years of age where use of a combination (intranasal antihistamine and glucocorticoid) is appropriate. It is presented in a metered-dose spray pump unit that administers azelastine 125 µg and fluticasone 50 µg per spray. The recommended dose for adults and adolescents

is one spray in each nostril twice daily (morning and evening).[9]

Efficacy

As single agents, fluticasone and azelastine have known efficacy in the treatment of ARC. Intranasal corticosteroids, which are potent suppressors of inflammatory activity, are the most efficacious single maintenance treatment for ARC.[5] In a double-blinded, randomised trial conducted in an environmental exposure chamber, patients reported significantly better symptom relief within 15 minutes of using azelastine compared with placebo.[10] As an intranasal spray, azelastine offers greater local tissue penetration and a significantly quicker onset of action than the oral antihistamines cetirizine and loratadine for seasonal allergic rhinitis.[11]

Intranasal azelastine/fluticasone has been studied in four randomised, double-blinded, placebo-controlled trials that have assessed the efficacy and tolerability of the combination therapy in over 4000 patients aged 12 years and over with seasonal ARC.[12] Each of these trials, which were conducted over a two-week period during allergy seasons in the USA, demonstrated that intranasal azelastine/fluticasone significantly improved nasal symptoms when compared with a placebo. In two of these studies, azelastine/fluticasone demonstrated an onset of action within 30 minutes. A meta-analysis of three of these studies found that use of azelastine/fluticasone demonstrated superiority for improvement of symptoms (including rhinorrhoea, nasal congestion, nasal itch and sneezing) compared with azelastine or fluticasone alone.[13]

In 2013, results were published of an open-label safety study of intranasal azelastine/fluticasone conducted in India, in which 612 patients with perennial ARC were followed over the course of a year in 37 centres.[14] Compared with patients using fluticasone only, patients using azelastine/fluticasone experienced significantly greater relief of nasal symptoms until 28 weeks, with rapid efficacy demonstrated for azelastine/fluticasone.[14] Between 28 weeks and 52 weeks, patients using azelastine/fluticasone had a trend towards greater relief of symptoms; however, the difference between the two groups was not statistically significant.[14]

Safety

Topical intranasal therapy is a safe option for the management of ARC because it allows for concentrated, targeted application with little systemic absorption of the medications used. The systemic bioavailability of fluticasone propionate when given as a nasal spray at twelve times the recommended daily dose has been shown to be only 0.5%.[15] Thus, the risk of adverse effects that are often associated with oral corticosteroid use is minimal. Local irritation of the nasal mucosa is the most common adverse effect of intranasal corticosteroid use.

Azelastine commonly results in taste disturbance; there have been reports of increased sedation with use of this agent but this has not been supported by placebo-controlled trials.[16]

Azelastine/fluticasone was well tolerated in short-term safety trials, in which over 95% of more than 3000 patients completed a full two-week study period.[12] No patients discontinued treatment due to serious or unexpected adverse events. The most commonly reported adverse event was an unpleasant taste due to azelastine (4% of patients), which was slightly less frequent than for the patients receiving azelastine alone (5%). Smaller numbers of patients experienced headache and epistaxis.

In the one-year safety study of intranasal azelastine/fluticasone that has been conducted in 612 patients in India, no serious safety concerns were identified.[14] Fewer than 3% of patients discontinued the study due to an adverse event; this discontinuation rate was not significantly different to the control group that received fluticasone alone.

Limitations

For optimal results, the azelastine/fluticasone nasal spray should ideally be used regularly. In clinical practice, use of azelastine/fluticasone could be limited by the cost of the medication and the odd taste could have an impact on patient adherence.

It is important to consider that the blinded azelastine/fluticasone randomised control trials were only two weeks in duration in patients with seasonal ARC. Although greater clinical efficacy compared to monotherapy was demonstrated over this period, there are limited data on whether this difference persists over a longer period of time. As single agents, intranasal antihistamines have particular utility in providing rapid symptomatic relief in the immediate setting. Regular prophylactic use of intranasal corticosteroids decreases the occurrence of nasal symptoms over time;[8] it would follow that prompt symptom relief would become a less prominent requirement.

Conclusion

The new azelastine/fluticasone combination intranasal spray could provide a solution to some of the inadequacies of single agents for the treatment of ARC. The combination medication addresses one of the major reasons for noncompliance (slow onset of action) with intranasal corticosteroids. Patients with seasonal ARC are usually advised to commence their intranasal corticosteroids prior to the start of the pollen season, but this often does not occur. With its prompt onset of action, azelastine/fluticasone may therefore have particular benefit in patients with seasonally occurring symptoms, and also in patients with poor medication compliance. Whether there is any advantage in persisting with dual agent therapy over single intranasal corticosteroid therapy after the initial treatment period is unknown. MT

References

A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

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