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Combined intranasal treatment for allergic rhinitis: an option for children under 12 years of age

Alberto Vidal[1*], Pedro Cortez[2]

[1]Unit of Pediatric Pulmonology, Clínica MEDS, Lo Barnechea, Santiago 7690000, Chile
[2]Unit of Otorhinolaryngology, Clínica MEDS, Lo Barnechea, Santiago 7690000, Chile

***Correspondence:** Alberto Vidal, Unit of Pediatric Pulmonology, Clínica MEDS, Av. José Alcalde Délano 10.581, Lo Barnechea, Santiago 7690000, Chile. alberto.vidal@meds.cl
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Abstract

Intranasal treatments combining corticosteroids with antihistamines are a safe and effective alternative for treating moderate to severe seasonal allergic rhinitis in children over 12 years of age and adults. Evidence for their use in children under 12 years of age is limited and based on four studies: three examining azelastine hydrochloride and fluticasone propionate combination (AzeFlu) (including one placebo-controlled efficacy study, one comparative efficacy study, and one safety study) and one examining olopatadine hydrochloride and mometasone furoate combination (OloMom) (a placebo-controlled study). The recommendations from these studies could be conditional for school children aged 6 to 11 years with seasonal (non-perennial) allergic rhinitis, but only when symptoms cannot be controlled with a single drug.

Keywords

allergic rhinitis, combined treatment, corticosteroids, antihistamines, children

Introduction

Treatment for allergic rhinitis includes avoidance of aeroallergens, saline irrigation, oral or nasal antihistamines, nasal corticosteroids, combinations of nasal corticosteroids and antihistamines, antileukotrienes, and immunotherapy [1–3]. Leading guidelines recommend the use of combinations of nasal corticosteroids and nasal antihistamines (INCS/INAH) in adolescents and adults when rhinitis cannot be controlled with a nasal corticosteroid inhaler with or without an oral antihistamine [4, 5]. Current scientific evidence has shown that nasal inhalation delivery devices that combine corticosteroids and antihistamines such as azelastine hydrochloride (Aze) and fluticasone propionate (Flu) combination (AzeFlu) and olopatadine hydrochloride (Olo) and mometasone furoate (Mom) combination (OloMom) can significantly reduce symptoms and improve the quality of life (QoL) of patients over 12 years of age and adults suffering from moderate to severe seasonal allergic rhinitis, with superior effectiveness to placebo and the use of each of them separately [6–11]. Some pediatric guidelines, such as the New EUFOREA

Algorithm, have also recommended the use of these combinations in children over 6 years of age, but only conditionally, since the possible side effects and possible interactions of co-administration of these drugs must be considered [12, 13]. These recommendations are based on the studies discussed below.

Method

A review of the scientific evidence on combined INCS/INAH treatment in children under 12 years of age with allergic rhinitis was conducted between October and November 2025. Articles in English were collected from various scientific databases (Medline, Web of Science, EBSCOhost, ScienceDirect, and Scopus). MeSH terms and free terms were used in their English versions. The terms were grouped into two dimensions: i) seasonal or perennial allergic rhinitis; ii) pharmacological treatment in children. The Boolean operator "AND" was used to integrate the three dimensions.

Intranasal corticosteroid/intranasal antihistamine studies in children

In 2016, Berger et al. [14] published a multicenter, double-blind, controlled study measuring the clinical effects of the AzeFlu combination in preschool and school-aged children with moderate to severe seasonal allergic rhinitis compared with placebo. This study demonstrated significant improvement of the QoL at day 15 of treatment compared with placebo and reported that the differences with treatment were more evident when nasal/ocular symptoms were reported in a higher percentage by the children than by their caregivers [14]. The second was a prospective, randomized, parallel study, involving patients treated with the AzeFlu combination and the other with Flu alone. This study demonstrated that patients treated with AzeFlu achieved significantly greater and earlier symptom control than those treated with Flu alone [15]. A third study sharing conditions with the previous evaluated the safety of the AzeFlu combination compared with Flu alone in children under 12 years of age. In this study, adverse effects (AEs) reported by children or their caregivers were low, most were mild, resolved spontaneously, and there was no difference between the two groups [16]. Finally, Prenner et al. [17] published a multicenter, double-blind, parallel-group randomized trial in 2022 that measured the efficacy and safety of the OloMom combination versus placebo. This study showed that the OloMom group significantly improved nasal symptoms, ocular watering, and overall QoL, achieving a good safety profile [17]. Table 1 shows the most important methodological characteristics and results of these 4 studies.

Table 1. Studies of combined nasal therapy in children under 12 years of age with allergic rhinitis.

Author	Age (years)	Number of patients	Study groups	Follow-up	Efficacy outcomes	Safety outcomes
Berger et al. [14]	4–11	348 (304 children aged 6–11 years, 44 children < 6 years excluded for statistical analysis)	AzeFlu (Aze 137 µg/Flu 50 µg) 1 puff in each nostril twice daily vs. placebo	15 days	Average QoL at day 15 decreased by –0.29 points in the AzeFlu group (p = 0.027). Children with > 90% self-reported symptoms: fewer nasal (p = 0.002) and ocular (p = 0.009) symptoms; children with < 10% self-reported symptoms: no significant differences in symptoms.	No significant differences were found in AEs, most of which were mild (dysgeusia, epistaxis).
Berger et al. [15]	6–11	353	AzeFlu vs. Flu (Aze 137 µg/Flu 50 µg) 1 puff in each nostril twice daily vs. Flu (50 µg) 1 puff in each nostril twice daily	3 months	AzeFlu group reduction of –0.68 points, Flu group reduction of –0.54 points (p = 0.04). The AzeFlu group controlled symptoms 16 days earlier than the Flu group.	Not applicable.
Berger et al. [16]	4–11	404	AzeFlu (Aze 137 µg/Flu 50 µg) 1 puff in each nostril twice daily vs. Flu (50 µg) 1 puff in each nostril twice daily	3 months	Not applicable.	Incidence of AEs: AzeFlu (16%), Flu (13%). Epistaxis and headache were the most frequent AEs.

Table 1. Studies of combined nasal therapy in children under 12 years of age with allergic rhinitis. (*continued*)

Author	Age (years)	Number of patients	Study groups	Follow-up	Efficacy outcomes	Safety outcomes
Prenner et al. [17]	6–11	446	OloMom (Olo 665 µg/Mom 25 µg) 1 puff in each nostril twice daily vs. placebo	14 days	The OloMom group significantly improved individual symptom scores (p = 0.001), physician symptom scores (p < 0.01), and QoL scores (p < 0.001) compared to placebo.	Treatment-related AEs: OloMom (12.0%) and placebo (10.4%): most common: dysgeusia, headache, epistaxis.

QoL: quality of life; AEs: adverse effects; Aze: azelastine hydrochloride; Flu: fluticasone propionate; Olo: olopatadine hydrochloride; Mom: mometasone furoate; AzeFlu: Aze and Flu combination; OloMom: Olo and Mom combination.

These studies have some limitations that warrant consideration. The first is the limited follow-up, which in some was very short [14, 17] and in others only medium-term [15, 16], making it difficult to assess whether this beneficial effect is lost over time or whether adverse reactions appear with prolonged use of the treatment. Another limitation is the lack of analysis of the efficacy and safety of the combination therapy compared to inhaled corticosteroid monotherapy, which was only measured with the AzeFlu combination [15, 16]. Another important limitation is that the three studies on AzeFlu belong to the same lead author and possibly the same research group [14–16], which suggests a possible overlap of patient samples and study centers, and raises some concerns such as limited external validation of the findings, possible systematic bias in the study design in patient selection or outcome assessment, and less generalizability to different clinical settings and populations. Although two of the four studies [15, 16] compared AzeFlu with FLu, the results prevent us from inferring that this combination is better than the one most commonly used in real life in children with moderate to severe allergic rhinitis, which is INCS plus an oral antihistamine. All these studies only examined children with seasonal allergic rhinitis, so their results cannot be applied to children with perennial allergic rhinitis. These results also cannot be applied to children with allergic rhinitis and asthma, who also use inhaled corticosteroids and require closer monitoring of the doses and duration of the corticosteroids received. Regarding the total daily doses of INCS/INAH, the studies that evaluated AzeFlu administered high doses for this age group, similar to those recommended for adults with allergic rhinitis, and only the Olo/Mom study used half the dose recommended for those over 12 years of age or adults [1, 2]. The total daily dose of Flu should be evaluated with caution at this age due to its potential effects on growth. Although fluticasone furoate is known to be a molecule with a different chemical structure and greater affinity for corticosteroid receptors than Flu, it has also been shown as a nasal corticosteroid to significantly reduce growth velocity in children treated with allergic rhinitis compared to placebo [18]. This raises some questions: Could the studies with Aze/Flu have had the same clinical results with half the adult dose? Would treatment with AzeFlu reduce the total amount of inhaled corticosteroids administered compared to the use of intranasal corticosteroids plus an oral antihistamine? Could the on-demand treatment strategy (only in case of symptoms) with INCS/INAH be considered at this age, as it has already begun to be proposed in adults [19]? The lack of clinical efficacy studies in the preschool population is also considered a limitation, so these studies do not allow us to recommend treatment with INCS/INAH in children under 6 years of age. The reasons for the limited available evidence in children under 12 years of age are multifactorial. On the one hand, there are difficulties obtaining informed consent from parents for research using drugs whose efficacy and safety have not been measured, given that other proven alternatives for treating allergic rhinitis are also available, such as inhaled corticosteroid monotherapy with or without concomitant oral antihistamines. Furthermore, in preschool and school children, the interpretation of allergic rhinitis symptoms is complex. There are symptom scales directed at caregivers that may be subjective, and others applicable to children that often require significant time and effort to administer. Finally, administering intranasal drugs in preschool and young school-age children is challenging and often not tolerated, which constitutes a significant barrier to the acceptance or continuation of these types of studies.

A recent network meta-analysis examined the clinical effects of different treatments in children with allergic rhinitis, assessing the mean improvement in clinically relevant variables. This meta-analysis, which

included three of the four studies mentioned above, demonstrated that INCS/INAH treatment significantly improves mean ocular symptom scores and QoL compared with nasal corticosteroid monotherapy in seasonal rhinitis; however, the authors suggest the need for further studies in this population [20].

Based on the analysis of these studies, these products can be used in children aged 6 to 11 years with seasonal allergic rhinitis that remains symptomatic after initiating environmental management measures, application of saline nasal sprays, oral antihistamines, and nasal corticosteroids. The most studied combination in terms of efficacy and safety is Aze/Flu, which could be used in the clinical setting for 3 months under strict clinical control that includes recording the improvement of symptoms, the appearance of the most frequent local effects such as headache, epistaxis or dysgeusia, and a careful monitoring of the growth curve even after the end of the treatment period.

Conclusion

Efficacy and safety studies for INCS/INAH (AzeFlu and OloMom) show encouraging results in school children aged 6 to 11 years with seasonal rhinitis. This may be a valid option for patients with seasonal allergic rhinitis who do not respond to treatment with inhaled corticosteroids or combinations of inhaled corticosteroids with oral antihistamines. The limited evidence available for the combination INCS/INAH at this age makes it necessary for the decision to start treatment to be agreed upon by the parents and the treating physician, with careful follow-up of the therapy to confirm its clinical effectiveness and the early detection of potential AEs. Before recommending the routine use of INCS/INAH, further studies are needed, including safety and efficacy studies in children under 6 years of age, adherence studies, tolerability studies, comparisons with nasal corticosteroids alone or with combinations of nasal corticosteroids and oral antihistamines, and evaluation of the response in children with rhinitis and concomitant asthma. More research is also needed to measure the potential long-term effect on growth, for example, if used in perennial allergic rhinitis. Finally, cost-effectiveness studies comparing INCS/INAH with inhaled corticosteroid monotherapy or combinations of oral antihistamines and inhaled corticosteroids should be considered.

Abbreviations

AEs: adverse effects

Aze: azelastine hydrochloride

AzeFlu: azelastine hydrochloride and fluticasone propionate combination

Flu: fluticasone propionate

INCS/INAH: combinations of nasal corticosteroids and nasal antihistamines

Mom: mometasone furoate

Olo: olopatadine hydrochloride

OloMom: olopatadine hydrochloride and mometasone furoate combination

QoL: quality of life

Declarations

Author contributions

AV: Conceptualization, Formal analysis, Supervision, Visualization, Validation, Writing—original draft, Writing—review & editing. PC: Formal analysis, Supervision, Visualization, Writing—review & editing. Both authors read and approved the submitted version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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