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Review article

Pharmacologic and anti-IgE treatment of allergic rhinitis ARIA update (in collaboration with GA^{2}LEN)

The pharmacologic treatment of allergic rhinitis proposed by ARIA is an evidence-based and step-wise approach based on the classification of the symptoms. The ARIA workshop, held in December 1999, published a report in 2001 and new information has subsequently been published. The initial ARIA document lacked some important information on several issues. This document updates the ARIA sections on the pharmacologic and anti-IgE treatments of allergic rhinitis. Literature published between January 2000 and December 2004 has been included. Only a few studies assessing nasal and non-nasal symptoms are presented as these will be discussed in a separate document.

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Background

The management of allergic rhinitis includes patient education, allergen and pollutant (e.g. tobacco) avoidance, pharmacotherapy and allergen-specific immunotherapy (1–3).

Pharmacologic treatment encompasses efficacy, safety and cost-effectiveness of medications, patient preference and the objective of treatment (4), likely adherence to recommendations (5), severity of the disease as well as the presence of co-morbidities. Medications used for rhinitis are usually administered intranasally or orally. The efficacy of medications may differ among patients.

The pharmacologic treatment of allergic rhinitis proposed by ARIA is an evidence-based and step-wise approach based on the classification of the symptoms. The ARIA workshop, held in December 1999, published a report in 2001 (2) and new information has subsequently been published. The initial ARIA document lacked some important information on issues such as complementary and alternative medicine (CAM) and occupational rhinitis.

Objectives

This document updates the ARIA sections on the pharmacologic and anti-IgE treatments of allergic rhinitis. Literature published between January 2000 and December 2004 has been included. Complementary and alternative medicine is not evaluated in this document as it is discussed in a separate section (G. Passalacqua, unpublished data). Moreover, only a few studies assessing nasal and non-nasal symptoms are presented as these will also be discussed in a separate document (A.A. Cruz et al., unpublished data).

Abbreviations: ARIA, Allergic Rhinitis and its Impact on Asthma; BID, twice a day; CAM, complementary and alternative medicine; HPA, hypothalamic-pituitary-adrenal; OD, once a day; PAF, platelet activating factor; PRN, as needed; QOL, quality-of-life; RQLQ, rhinoconjunctivitis quality of life questionnaire (Juniper).

Methods

Search strategy

- Studies were sought from MEDLINE (1 January 2000 to 31 December 2004) and EMBASE. Moreover, we used the expert group database to assess whether certain papers may not have been retrieved by the electronic search.
- The following key words were used for the search strategy:
- Antihistamine, H1-blocker, (intra)nasal corticosteroid, intranasal steroid, anti-cholinergic, decongestant, immunotherapy, leukotriene receptor antagonist, Azelastine, Beclomethasone, Budesonide, Cetirizine, Chlorpheniramine, Clemastine, Cromoglycate, Desloratadine, Diphenhydramine, Ebastine, Emedastine, Fexofenadine, Fluticasone, Ipratropium, Ketotifen, Levocetirizine, Loratadine, Mizolastine, Mometasone, Montelukast, Olopatadine, Omalizumab, Oxatomide, Pranlukast, Pseudoephedrine, Rupatadine, Triamcinolone and Zafirlukast.
- [AND] rhinitis.
- [AND] conjunctivitis.
- [AND] placebo.
- Moreover, we searched for rhinitis [OR] conjunctivitis [AND] systematic review.

Selection criteria

- Only randomized, double-blind, placebo-controlled clinical trials published as full papers were selected including some key studies on safety.
- Key case reports and observational studies were used for drug safety information.
- Full manuscripts published in peer-reviewed journals. Abstracts were not considered.

Exclusion criteria

- Studies using methods which make it very difficult to assess efficacy and/or safety.
- Challenge studies including chamber and park models (6–13).
- Skin test studies.
- Methodological papers using single-blind trials (14–19).
- Reviews in which the methodology was not clearly stated (20).
- Studies on non-allergic rhinitis, rhino-sinusitis or nasal polyposis (21–28) or sleep disordered breathing (29, 30).

All studies meeting the search strategy were examined by two of the experts, reviewed by the chair of the group and discussed during plenary sessions of the ARIA Scientific Committee.

Pharmacologic treatment of allergic rhinitis

Oral H_1 antihistamines. H_1-blockers or H_1-antihistamines block histamine at the H_1 receptor level (neutral antagonists or inverse agonists) (31). Some also possess additional anti-allergic properties. During the last 20 years, pharmacologic research has produced compounds with minimal sedative effect and impairment: the so-called second-generation H_1-antihistamines, as opposed to the first-generation H_1-antihistamines (32). The term 'third' generation should be reserved for an H_1-antihistamine with novel properties.

Oral H_1-antihistamines improve the quality-of-life of patients by their effectiveness against symptoms mediated by histamine, including rhinorrhea, sneezing, nasal itching and eye symptoms. They are, however, less effective on nasal congestion.

Long-term treatment (years) with an oral H_1-antihistamine is safe, including little or no sedation or impairment. Some, but not all, oral H_1-antihistamines undergo hepatic metabolism via the cytochrome P450 system and are prone to drug interactions. Although cardiotoxicity is not a class effect (33), major concerns existed about the arrhythmogenic action of terfenadine, astemizole and high doses of diphenhydramine, which have rarely been associated with fatalities.

H_1-antihistamines have been approved for young children (34).

Table 1 summarizes the desirable characteristics of an anti-histamine medication for use in allergic rhinitis (35).

Recently, Loratadine, a major second-generation anti-histamine medication in the USA, has taken on a non-prescription or over the counter (OTC) status (36). This has resulted in increased out of pocket expenses for patients as OTC medications are not part of an insurance or drug benefit program. Insurers are continuing to adjust drug benefits for other anti-histamines in view of the 44% drop in anti-histamine use by patients who have lost drug benefits for anti-histamine medications (37).

Cetirizine. Cetirizine provides a positive impact on work/school-related productivity and activity impairment in patients with pollen-induced rhinitis (38).

Table 1. Optimal properties of oral H_1-antihistamines

Pharmacologic properties
Potent and selective H_1 receptor blockage
Additive anti-allergic activities
No clinically relevant pharmacokinetic interference by foods, medications or intestinal transport proteins
No known interaction with cytochrome P4503A (CYP3A)
No known interaction with other diseases to avoid toxic reactions
Efficacy
Effective in the treatment of intermittent and persistent rhinitis as defined in the ARIA document (2)
Effective for all nasal symptoms including nasal obstruction
Improvement of allergic eye symptoms
If a claim for asthma is made
Improvement of asthma symptoms (short-term studies)
Reduction of asthma exacerbations (long-term studies)
An improvement of the pulmonary function tests, even though in pollen-induced bronchial symptoms, FEV1 and peak flow rates are usually not altered
If a claim for a preventive effect is proposed, appropriate trials should be conducted
Studies should be carried out in young children and old age patients to assess efficacy
Side effects
No sedation, cognitive or psychomotor impairment
No anti-cholinergic effects
No weight gain
No cardiac side effects (prolongation of the QT interval)
Possible use in pregnancy and breast feeding
Studies should be carried out in young children and old age patients to assess safety
Pharmacodynamics
Rapid onset of action, so that clinical benefits are noted quickly and so drugs can be used also prn
Long duration of action, at least persistence of clinical effects over 24 h, so the drug can be administered once a day
No likelihood of development of tolerance (tachyphylaxis).
Comparison with other drugs used to treat rhinitis (conjunctivitis)

Long-term (6 months) treatment with Cetirizine reduces allergic symptoms and the need for rescue medication in children with mite allergy as compared with placebo (39).

In infants 6–11 months of age, a double-blind, placebo-controlled study has demonstrated the safety of Cetirizine (40). Another study produced no adverse effects on behavior, and learning processes were associated with the prolonged use of Cetirizine in young children with atopic dermatitis (41).

Although, in children, Chlorpheniramine and Cetirizine increased P300 latency (an event-related potential used as an objective test of sedation) when compared with baseline (42), the significant increase in P300 latency was not accompanied by a change in subjective somnolence as measured on a visual analog scale.

Cetirizine, compared with placebo, delays or, in some cases, prevents the development of asthma in a subgroup of infants with atopic dermatitis sensitized to grass pollen and, to a lesser extent, house dust mite (43). Further studies are required focusing specifically on sensitized groups to substantiate this finding.

Desloratadine. Desloratadine in 5 mg dosage provided significant 24 h relief of seasonal allergic rhinitis signs and symptoms. There were no statistically significant differences among the four largest doses suggesting that Desloratadine 5 mg OD offers the best therapeutic profile (44). Recommended OD doses of Fexofenadine and Desloratadine were equally effective in improving nasal peak flow and nasal

symptoms in seasonal allergic rhinitis (45). Desloratadine reduces nasal congestion (46), rapidly and safely reduces the symptoms of perennial allergic rhinitis, and its efficacy did not diminish during 4 weeks of treatment (47). In two studies, Desloratadine also reduced bronchial symptoms during the pollen season in patients with seasonal asthma and seasonal rhinitis (48, 49).

At the recommended dose of 5 mg, Desloratadine appears to be free of adverse effects on psychomotor performance, daytime sleep latencies, and subjective sleepiness and could prove suitable for those involved in skilled activity and transportation (50). Desloratadine at a therapeutic dose does not impair driving performance (51). Desloratadine has no clinically relevant electrocardiographic or pharmacodynamic interactions with Ketoconazole (52), Erythromycin (53) or Azithromycin (54).

Ebastine. In pollen-induced rhinitis, Ebastine 20 mg OD was significantly superior to Loratadine 10 mg OD. It improved the total rhinitis symptom score throughout the day and in the morning when awakening at the end of the 24 h dosing interval over a 4-week period (55–57).

At its recommended therapeutic dose, it did not alter objective measures of psychomotor and cognitive function (58, 59). At five times the recommended therapeutic dose, it did not cause clinically relevant changes in the QTc interval (60). There is no effect of food intake in the efficacy of Ebastine (61).

Fexofenadine. In one study, Fexofenadine (120 mg OD) was significantly more effective than Loratadine in relieving eye symptoms and nasal congestion and was significantly better than Loratadine in improving the rhinitis-quality-of-life questionnaire (RQLQ) (62).

In 259 patients, no differences were found between the Fexofenadine and placebo groups on reaction times, decision-making or driver behaviour (63).

Fexofenadine was efficacious and safe in 6- to 11-year-old children with seasonal allergic rhinitis (64, 65).

Emedastine. Emedastine was studied in a double-blind, randomized, parallel-group trial without a placebo group (66).

Levocetirizine. In the treatment of seasonal allergic rhinitis, by comparison with other dosages, Levocetirizine 5 mg OD has an optimal benefit/risk ratio (67). Levocetirizine is effective for the relief of nasal congestion in adolescents and adults (perennial allergic rhinitis) sensitized to house dust mites (68). In this study, somnolence was reported in 2.8% of the placebo group and in 6.0% of the Levocetirizine group.

An important trial examined the effect of Levocetirizine given for over 6 months to 551 patients with moderate to severe persistent allergic rhinitis (XPERT® study). It was found that, compared with placebo, Levocetirizine improves nasal symptoms including nasal obstruction and quality of life (RQLQ and SF-36) and reduces medical costs involved in the long-term management of these patients (69). Levocetirizine is currently the only antihistamine with the indication of persistent allergic rhinitis in Europe.

Single and repeated doses of Levocetirizine have no effect on cognitive and psychomotor functions in healthy volunteers (70–72) and on driving performance (73).

Loratadine. Loratadine syrup 5 or 10 mg OD was effective in improving the symptom scores of children aged 3–12 years with allergic rhinitis without side effects (74). Loratadine was well tolerated by a selected group of children aged 2–5 years at a dose similar to the adult dose (i.e. 10 mg per day) (75). Learning and response time in children attending a laboratory school were not significantly affected by Loratadine or Diphenhydramine (76). This report differs from previous studies (38, 77).

Mizolastine. Over a 4-week period, Mizolastine 10 mg OD was as effective as Loratadine 10 mg OD in relieving symptoms of perennial allergic rhinitis in adult patients, and the tolerability was good (78).

Rupatadine. Rupatadine is a new second-generation H_1-antihistamine with OD dosing that may have the potential to provide better control of symptoms than the currently used oral H_1-antihistamines. This is due to its dual pharmacologic profile (anti-PAF and anti-H_1) which does, however, require testing in controlled comparative studies. Rupatadine 10 mg per day was superior to placebo and non-significantly superior to Ebastine 10 mg in alleviating the symptoms of seasonal allergic rhinitis over a 2-week period (79). Somnolence was reported in 2.4% of patients treated with placebo, 10.8% with Ebastine and 17.7% with Rupatadine.

Topical H_1-antihistamines. Intranasal H_1-antihistamines are effective in reducing itching, sneezing, runny nose and nasal congestion. Given ocularly, they are effective in reducing allergic eye symptoms. They can be effective within 20 min of administration. Topical H_1-antihistamines require twice a day dosing. In general, topical H_1-antihistamines are well tolerated. However, both oral and topical antihistamines are significantly less effective than intranasal glucocorticosteroids for the treatment of allergic rhinitis, particularly for the symptom of nasal congestion.

Nasal administration. Azelastine nasal spray was found to be an effective treatment for patients with seasonal allergic rhinitis who do not respond to loratadine and is an alternative to switching to another oral antihistamine or to using multiple antihistamines (80). Azelastine nasal spray is effective in treating severe seasonal allergic rhinitis patients who remain symptomatic after treatment with Fexofenadine (81).

Ocular administration. A 10-week, randomized, double-blind, parallel group compared olopatadine 0.1% ophthalmic solution BID *vs* placebo in 131 patients with pollen-induced rhinitis and conjunctivitis. Olopatadine controlled ocular and nasal symptoms and was well tolerated (82).

Epinastine has been tested in a randomized, double-blind, parallel-group study without a placebo arm in patients with allergic conjunctivitis (83).

Intranasal glucocorticosteroids. Glucocorticosteroids are the most efficacious medications available for the treatment of allergic and non-allergic rhinitis. The rationale for using intranasal glucocorticosteroids in the treatment of allergic rhinitis is that high drug concentrations can be achieved at receptor sites in the nasal mucosa, with minimal risk of systemic adverse effects. Because of their mechanism of action, efficacy appears after 7–8 h of dosing, but maximum efficacy may require up to 2 weeks. These medications are effective at improving all symptoms of allergic rhinitis. For nasal congestion or frequent symptoms, an intranasal glucocorticosteroid is the most appropriate first-line treatment. Intranasal glucocorticosteroids are well tolerated and adverse effects are uncommon, of mild severity and have approximately the same incidence as placebo. Evidence shows that the long-term use of intranasal glucocorticosteroids is free of the concerns associated with the long-term use of oral glucocorticosteroids.

Ideal properties which should be met by intranasal Glucocorticosteroids are listed in Table 2 (35).

Table 2. Optimal properties of intranasal glucocorticosteroids

Pharmacologic properties
Potent action on transcription factors
Inhibition of cytokine synthesis
First pass hepatic metabolism
Limited systemic bioavailability
Efficacy
Effective in the treatment of intermittent and persistent rhinitis as defined in the ARIA document (2)
Effective for all nasal symptoms
Improvement of eye symptoms
If a claim for asthma is proposed
Improvement of asthma symptoms (short-term studies)
Reduction of asthma exacerbations (long-term studies)
An improvement in pulmonary function tests, even though in pollen-induced bronchial symptoms, FEV_1 and peak flow rates are usually not altered
If a claim for nasal polyposis or sinusitis is proposed, adequate appropriate trials should be conducted
If a claim for a preventive effect is proposed, appropriate trials should be conducted
Side effects
Minimal local side effects
No HPA axis effects
Especially in children
And in association with the inhaled (intrabronchial) form
No long-term effect on growth in children
No eye or bone side effects
Possible use in pregnancy
Pharmacodynamics
Assessment of the onset of action
Long duration of action, at least 24 h, ability to be administered once a day
If a claim for a prn use is proposed, appropriate trials should be conducted
Comparison with other drugs used to treat rhinitis

Clinical and pharmacologic effects. The onset of action of intranasal corticosteroids may be shorter than previously thought (84, 85). Budesonide is effective after 12 h of administration (86).

Cost-effectiveness studies of intranasal corticosteroids are important but may depend on local costs. Few studies are available.

Side effects of intranasal glucocorticosteroids. In children, the rate of growth was slightly reduced in those regularly treated twice a day with intranasal Beclomethasone over 1 year (87). However, no growth slowing has been observed in 1 year follow-up studies of children treated with Fluticasone propionate (88) or Mometasone furoate (89–91). Moreover, a pharmacokinetic/pharmacodynamic model of the relationship between systemic corticosteroid exposure and growth velocity has been proposed and may be useful for the development of future locally acting corticosteroids (90, 91).

Budesonide aqueous nasal spray does not affect the HPA-axis in children with allergic rhinitis (92). Concurrent use of intranasal and orally inhaled Fluticasone propionate does not affect hypothalamic-pituitary-adrenal-axis function (93).

In a study of 360 patients with allergic rhinitis, Fluticasone propionate, Mometasone furoate and Beclomethasone dipropionate caused variations in the intraocular pressure measured by Goldman's tonometry at 3 weeks, 6 weeks, 3 months, 6 months and 1 year, but the variations were within normal limits (94).

In the elderly, intranasal corticosteroids, at the recommended dose, have not been associated with an increased risk of fractures (95).

Budesonide. Allergic contact dermatitis has occasionally been reported after the intranasal or inhaled administration of Budesonide (96, 97).

Fluticasone propionate. Fluticasone propionate aqueous nasal spray [when used as needed (PRN) (84, 85)] improves nasal symptoms of seasonal allergic rhinitis. PRN has a lower incidence of adverse events than typically associated with regular one per day use (85). The PRN use of Fluticasone propionate has been approved in some countries. Future studies are still needed to show the optimal use of intranasal glucocorticosteroids in the controlling of nasal symptoms, especially in persistent allergic rhinitis. It has been confirmed by one of the studies that a significant difference of total symptom scores between the treatment of fluticasone propionate aqueous and placebo was found only after 5 days of treatment (84). Whether there is a need for a minimum duration of treatment by intranasal glucocorticosteroids in PRN remains to be investigated.

A randomized placebo-controlled trial compared Fluticasone propionate aqueous nasal spray in mono-therapy, Fluticasone propionate plus Cetirizine, Fluticasone propionate plus Montelukast and Cetirizine plus Montelukast for seasonal allergic rhinitis (98). The results of this comparative study showed that Fluticasone propionate is highly effective for treating patients with allergic rhinitis, with an efficacy exceeding that of Cetirizine plus Montelukast in combined therapy. This study also suggested that there was little advantage in adding Cetirizine or Montelukast to Fluticasone propionate.

Intranasal Fluticasone propionate is also effective for treating perennial non-allergic rhinitis with or without eosinophilia (99) and significantly improves ocular symptoms in patients with seasonal allergic rhinitis (100).

The effect of drugs on sleep in allergic rhinitis has already been reported. A recent study reported an improvement in subjective sleep disturbances in perennial allergic rhinitis treated with intranasal Fluticasone propionate for 8 weeks. However, polysomnography, the current gold standard for sleep studies, was unchanged (101).

Rhinitis during pregnancy, a common condition with long-standing nasal congestion, is troublesome for the mother. A study of 53 pregnant women showed no effect of Fluticasone propionate on fetal growth or pregnancy outcome (102). Although safe in pregnant women, it was not very effective for this condition.

Intranasal Fluticasone propionate was tested for its effect on the bioavailability and pharmacokinetics of single-dose intranasal Hydromorphone hydrochloride in patients with allergic rhinitis (103). Hydromorphone was rapidly absorbed after nasal administration, with maximum concentrations occurring for most subjects within 30 min suggesting that Fluticasone propionate does not modify its absorption.

Mometasone furoate. Mometasone furoate nasal spray relieves cough and nasal symptoms associated with seasonal allergic rhinitis (104).

Triamcinolone acetonide. Intranasal Triamcinolone acetonide given for 4 weeks improves symptom scores and RQLQ in patients with perennial allergic rhinitis. The ability of Triamcinolone to relieve nasal congestion symptoms was correlated with improvements in RQLQ (105). The Food and Drug Administration (FDA) recently approved the HFA formulation of Triamcinolone acetonide.

Decongestants. The decongestant effect of an H_1-antihistamine Pseudoephedrine fixed-dose combination was demonstrated by using the novel method of endoscopic inferior turbinate photography, in addition to acoustic rhinometry and visual analogue scale scores (106). Pseudoephedrine has been banned for Olympic athletes. This has important implications for the correct and prominent labeling of pharmacologic treatments for rhinitis, particularly for over-the-counter remedies.

Antileukotrienes. Several pivotal studies of seasonal allergic rhinitis compared Montelukast and placebo, and in some studies the combination Montelukast-Loratadine (107–111). Montelukast, in trials involving a large number of patients, was consistently more effective than placebo for all nasal and ocular symptoms and there was no significant difference between Montelukast and Loratadine, even for nasal obstruction. Moreover, contrary to the first study (112), the combination Montelukast-Loratadine did not provide any statistically significant additive beneficial effect to the two drugs given alone. In all these studies, Montelukast improved all nasal symptoms of rhinitis, symptoms of conjunctivitis and RQLQ, and was well tolerated. Montelukast is equally effective in patients exposed to low and high pollen counts (111). In a study carried out in patients with seasonal allergic rhinitis and asthma, Montelukast was found to improve nasal and bronchial symptoms (113). As-needed beta-agonist use (puffs/day) was also reduced with Montelukast. Combined Montelukast and Cetirizine treatment, when started 6 weeks before the pollen season, is effective in preventing AR symptoms and reduces allergic inflammation in the nasal mucosa during natural allergen exposure (114).

Leukotriene receptor antagonists are less effective in allergic rhinitis than intranasal corticosteroids and have an efficacy similar to oral H_1-antihistamines (98, 115, 116).

Montelukast does not modify skin prick test results (117, 118) and therefore does not need to be discontinued before skin testing.

Humanized monoclonal antibodies against IgE

The recombinant humanized monoclonal anti-IgE antibody (Omalizumab) forms complexes with free IgE, blocking its interaction with mast cells and basophils and lowering free IgE levels in the circulation. In a large pivotal trial, Omalizumab decreased serum free IgE levels and provided clinical benefit in a dose-dependent fashion in patients with seasonal allergic rhinitis (119). Omalizumlab was found to decrease all nasal symptoms and improve RQLQ in patients with rhinitis induced by birch and ragweed pollens as well as in patients with sensitization to outdoor allergens (adults and adolescents) (120, 121). Moreover, the treatment was safe and well tolerated (122, 123). In patients with asthma and rhinitis, Omalizumab improved nasal and bronchial symptoms and reduced unscheduled visits to physicians for asthma (124). The clinical benefit of treatment with Omalizumab is associated with an anti-inflammatory effect on cellular markers in blood and nasal tissue (125, 126) as well as a reduction in mast cell FcεRI expression and function (127). Omalizumab inhibits allergen challenge-induced nasal response (128). Omalizumab rapidly decreases nasal allergic response and FcεRI on basophils (129) and dendritic cells (130). The relative efficiency of this treatment compared to H_1-antihistamines and intranasal glucocorticosteroids needs to be established.

Specific immunotherapy (SIT) and treatment with monoclonal anti-IgE antibodies have complementary modes of action. Omalizumab conferred a protective effect independent of the type of allergen. Additional clinical benefit was demonstrated in both pollen seasons, whether there was coverage by SIT or not (131). The co-seasonal application of Omalizumab after pre-seasonal SIT decreases ocular and nasal symptom scores and rescue medication use in grass pollen allergic children (132). This combination might prove useful for the treatment of allergic rhinitis, particularly for polysensitized patients.

Table 3. Level of evidence

	Seasonal rhinitis		Perennial rhinitis		
	Adult	Children	Adult	Children	Persistent rhinitis†
Oral H1-antihistamines	A	A	A	A	A
Intranasal H1-anthistamines	A	A	A	A	B*
Intranasal corticosteroids	A	A	A	A	B*
Intranasal chromones	A***	A***	A***	A***	
Anti-leukotrienes	A	A			B**
Anti-IgE mab	A	A	A	A	B*

B*: by extension of studies in persistent allergic rhinitis of 4 weeks and longer, but studies using the new classification have to be performed to confirm efficacy in this indication.
B**: by extension of studies in seasonal allergic rhinitis of 4 weeks.
A***: most studies included small numbers of patients.
†Adolescents and adults.

Treatment of infants and young children

Perennial rhinitis in children under 4 years of age is a difficult problem to treat safely and effectively. A randomized, multicentre, double-blind, double dummy, placebo-controlled study compared intranasal Fluticasone propionate and ketotifen (133). Generally, except for nasal itching/rubbing over weeks 1–3, the patients taking Fluticasone propionate had lower recorded symptom scores for all individual symptoms measured. Nasal blockage, in particular, was significantly reduced over the 4–6-week periods. There were no reports of serious adverse events, the incidence of drug-related adverse events was low and there was no statistical difference in regard to safety between the groups.

Conclusions

New studies have been performed since the ARIA workshop report and they are listed in this report. A revised level of evidence can be proposed (Table 3). It is clear that studies using the new ARIA classification (intermittent and persistent rhinitis) should be carried out for all treatments in order to fully appreciate the efficacy of treatments used in allergic rhinitis.

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