The selection of pharmacotherapy for patients with allergic rhinitis (AR) depends on several factors, including age, prominent symptoms, symptom severity, control of AR, patient preferences, and cost. Allergen exposure and the resulting symptoms vary, and treatment adjustment is required. Clinical decision support systems (CDSSs) might be beneficial for the assessment of disease control. CDSSs should be based on the best evidence and algorithms to aid patients and health care professionals to jointly determine treatment and its step-up or step-down strategy depending on AR control. Contre les symptômes variés, et traitement ajustement est nécessaire. Les plans de traitement dépendent de plusieurs facteurs, y compris l'âge, les symptômes prédominants, la sévérité des symptômes, le contrôle de l'AR, les préférences du patient, l'exposition aux allergènes et les symptômes résultants varient, et l'ajustement du traitement est requis. Les systèmes de décision clinique (CDSS) pourraient être bénéfiques pour l'évaluation de la contrôle de maladie. Les CDSS devraient être basés sur la meilleure preuve et les algorithmes pour aider les patients et les professionnels de la santé à déterminer conjointement le traitement et sa mise à niveau ou stratégie de traitement à rebours en fonction du contrôle de l'AR.
The selection of pharmaceutical therapy for patients with allergic rhinitis (AR) depends on several factors, such as age, prominent symptoms, symptom severity, control of AR, patient preferences, availability of treatment, and cost.1 With allergen exposure and the resulting symptoms varying daily, patients with AR would benefit from regular monitoring of their symptoms to facilitate treatment adjustment. Clinical decision support systems (CDSSs) might be beneficial for the accomplishment of this task by assessing disease control, such as in response to treatment. A CDSS is a health information technology system designed to assist health care professionals and patients with clinical decision-making.
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Box 1. Summary of recommendations for the treatment of AR and conjunctivitis used in the algorithm

- Oral or intranasal H1-antihistamines are less effective than intranasal corticosteroids for the control of all rhinitis symptoms.28-33
- Leukotriene receptor antagonists are usually considered less effective than oral H1-antihistamines.30,34,35
- Comparisons between oral and intranasal H1-antihistamines differ between recommendations, and thus no definite conclusions have yet been reached.
- Combined intranasal fluticasone propionate and azelastine hydrochloride in a single device is more effective than monotherapy and is indicated for patients when monotherapy with either an intranasal H1-antihistamine or glucocorticoid is considered inadequate.1,34-37
- Intranasal antihistamines and intranasal corticosteroids are effective for ocular symptoms, with no significant difference between them.38,39 However, the combination of azelastine and fluticasone propionate was more effective than fluticasone propionate alone.36,37
- In most studies, combinations of oral antihistamines or leukotriene receptor antagonists and intranasal corticosteroids are in general not more effective than monotherapy with intranasal corticosteroids.40,41
- Intracocular H1-antihistamines or cromones are effective for ocular symptoms.42 The importance of decongestants is debatable.43 However, the efficacy of treatment varies with individual patient response.
- In clinical practice, intranasal corticosteroids need a few days to be fully effective, whereas intranasal H1-antihistamines or combined intranasal fluticasone and azelastine are rapidly effective.43
- All recommended medications are considered safe at the usual dosage. First-generation oral H1-antihistamines are sedating and should be avoided.34
- Oral or nebulized corticosteroids can be helpful in patients with severe disease whose symptoms are uncontrolled by other treatment, although studies are lacking in patients with AR.45
- Further studies are needed in preschool children to make more firm recommendations possible, although recent studies show the efficacy of oral H1-antihistamines.46

The symptoms of AR can cause considerable morbidity in physical and emotional comfort, as well as in functional capacity and quality of life (QOL). The control and severity of AR have been defined in a similar manner to asthma.2,14,15 Measures of AR control include symptom scores, patients’ self-administered visual analog scales (VASs), objective measures of nasal obstruction, a recent modification of the Allergic Rhinitis and its Impact on Asthma severity classification, and patients’ reported outcomes, such as QOL or scores with several items.16,17 However, the challenges of managing AR are increased by the fact that patients do not often recognize their AR symptoms or confuse them with those of asthma.47 Therefore it is important for patients to be able to use an AR symptom scoring system that is simple to use and rapidly responsive to change.

As is the case for asthma, the best control of AR should be achieved as early as possible to (1) improve patient satisfaction and concordance to treatment and (2) reduce the consequences of AR, including symptoms, reduced QOL, and school and work absenteeism. Untreated AR can impair driving ability and put patients at risk.48 The ultimate goal of AR control is to reduce the costs incurred by AR.20,23

A step-up/step-down approach to AR pharmacotherapy based on patient response might hold potential for optimal AR control and cost of treatment.2 Mask has proposed that electronic daily monitoring with VASs might help patients achieve optimal control of AR symptoms.4 Well-controlled AR is defined as a VAS score of 2 or less of 10. VAS cutoff values to step up or down treatment were proposed by comparison with pain VAS scores and step-up schemes or from the literature in the field of allergy (see the additional material in this article’s Online Repository at www.jacionline.org).24,26

RECOMMENDATIONS FOR THE TREATMENT OF AR AND RHINOCONJUNCTIVITIS

The treatment of AR also requires the consideration of (1) the type (rhinitis, conjunctivitis, and/or asthma) and severity of symptoms, (2) the relative efficacy of the treatment, (3) the speed of onset of action of treatment, (4) current treatment, (5) historic response to treatment, (6) patient’s preference, (7) interest to self-manage, and (8) resource use. Guidelines27 and various statements by experts for AR pharmacotherapy usually propose the approach summarized in Box 1.28-46

Allergen immunotherapy appears to be as effective as pharmacotherapy47,48 but is also regarded as a disease modifier intervention with the potential of altering the natural history of allergic diseases.49,50 Nonpharmacologic interventions, such as nasal filters31 or saline, have been found to be effective.

PATIENTS’ VIEWS

Many patients with AR are not satisfied with their current treatment,52-54 and this results in frequent nonadherence to therapy.55,56 In some studies, most patients were satisfied with their treatment, but full control was rarely achieved.54-57,59 Despite the vast availability of treatment options, most patients are “very interested” in finding a new medication,56,60 and around 25% are “constantly” trying different medications to find one that “works.”56 Patients want more effective treatments that can control all their symptoms, including ocular ones,61,62 and a more rapid onset of action.63

Some patients believe that their health care provider does not understand their allergy treatment needs or does not take their allergy symptoms seriously.52 Many patients self-medicate with over-the-counter drugs for a long period of time and usually only consult a physician when their treatment is ineffective.64 Over-the-counter drugs for a long period of time and usually only consult a physician when their treatment is ineffective.64

In one study, patients chose a step-down therapy to speed up the control of symptoms.64

A patient’s individual preference for an oral or intranasal route treatment needs to be considered.52,64,65 In addition, health care professionals need to inform the patient of the relative benefits and harms of each prescribed treatment to support their decision making.
**ALGORITHM DECISION AID**

A step-up/step-down individualized approach to AR pharmacotherapy might hold the potential for optimal control of AR symptoms while minimizing side effects and costs. However, the following should be considered:

- as in asthmatic patients, treated and untreated patients should be considered differently (Figs 1 and 2);
- most patients have received a previous treatment that should guide health care professionals with regard to the current prescription; and
- patterns of medication use in previously treated patients should be evaluated when future treatment is initiated.

The step-up or step-down strategy should be discussed with the patient and should consider the following:

- efficacy of previous treatments;
- adherence to treatment;
- the patient’s preference (route of administration, fear of side effects, and experience of the patient regarding the treatment);
- possible side effects or harms; and
- costs.

The step-up approach consists of the following:

- **Step 1:** For mild symptoms, use intranasal or oral nonsedating \( H_1 \)-antihistamines.
- **Step 2:** For moderate-to-severe symptoms and/or persistent AR, use intranasal corticosteroids. The dose of some intranasal corticosteroids can be increased according to the package insert.
- **Step 3:** For patients with uncontrolled symptoms at step 2 (current or historical), use a combination of intranasal corticosteroids and intranasal \( H_1 \)-antihistamines. However, depending on the physician’s experience, other therapeutic strategies can be used.

- **Step 4:** It is possible that an additional short course of oral steroids might help to establish control and continue control by step 3. Intraocular cromones or \( H_1 \)-antihistamines can be added to improve the control of ocular symptoms.

- Treatment should be reassessed quickly (eg, 1-7 days) to confirm control by using a step-up approach.

- Patients whose symptoms are uncontrolled at step 3 should be considered as having severe chronic upper airway disease and might benefit from specialist referral and assessment for allergy workup and nasal examination.

Alternatively, a step-down approach can be used, and step 3 treatment should be considered as the first option in patients with a previous treatment failure or resistance to monotherapy. After a few days of achieving complete control, consideration could be given to treatment reduction. However, the step-down approach is based on consensus, and more data are needed.

The duration of treatment is determined by the type of rhinitis (intermittent or persistent). In the patient with intermittent rhinitis, treatment should be continued daily for 2 weeks or for the duration of the pollen season or other specific allergen exposure. In the patient with persistent rhinitis, a longer course...
Assessment of control in treated symptomatic patient

CONCLUSION

We propose a simple algorithm to step up or step down AR treatment globally. However, its use varies depending on the availability of medications in different countries and depending on resources. These issues have not been approached in the present article because of their variability between countries. Inherently, algorithms are a combination of individual decision nodes that represent separate recommendations. They require testing as a complete algorithm and comparison with alternative strategies to explore whether the combination of these separate recommendations leads to more benefit than harm when applied in practice. Thus this algorithm, as with other algorithms, requires testing in large-scale trials to provide the necessary certainty in available evidence. The current algorithm is being developed by MASK² for a CDSS that will be available on Apple and Android and that will provide opportunities for evaluation.

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RATIONAL FOR USING A VAS IN THE ALGORITHM

Certain differences between groups in their VAS scores or changes in scores might have no clinical relevance, even if they achieve statistical significance. A wide range of minimal clinically important differences (MCIDs) in change scores on the pain VAS have been reported by using different methods. MCIDs ranged from 9 to 30 mm (of 100 mm) in emergency departments. E2-E6 In other settings, changes of 33 mm E7 and 31 mm E8 have been shown to be clinically meaningful. In patients with endometriosis, the pain MCID was set at 10 mm. E9 The MCID for the fatigue VAS was around 10 mm in a large rheumatoid arthritis clinical practice and similar to that seen in clinical trials. E10 The MCID in the VAS pain score does not differ with sex, age, and cause-of-pain groups E11 or with the severity of pain being experienced. E11 However, the linearity of the pain VAS is found in some E12 but not all E13, E14 studies. Pain VAS measurement error has been reported to be up to 20 mm. Consequently, change scores and the calculations of aspects, such as MCIDs, can be carefully considered by the potential lack of interval scaling of the VAS and further compromised by the magnitude of measurement error. Repeated pain VAS data meet the strict requirements of the Rasch model, including unidimensionality, and they were internally valid. E11 However, the pain VAS does not behave linearly, and the MCID can underestimate or overestimate true change during repeated pain VAS. E17

In patients with AR, to our knowledge, there is a single study that has estimated MCIDs in the VAS during treatment. E18 By using receiver operating characteristic curve analysis, a appropriate method for estimation of MCIDs, the established cutoff variation of 23 mm for the VAS was associated with a cutoff variation of 0.5 for the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). Sensitivity analysis with RQLQ and Total Symptom Score 6 scales confirmed the aptitude of the cutoff value (23 mm) to discriminate changes in symptoms and QOL. The MCID was the same whatever the baseline VAS level. E18 A level of more than 23 mm appears to be a relevant cutoff. VAS changes appear to encompass both symptoms and disease-specific QOL. E18,E19 Another study, the Control of Allergic Rhinitis and Asthma Test, E20,E21 approximated the VAS MCDI. In CARAT, the MCID is 4 (range, 0-30). E22 The real-life study of Demeny et al. E23 in primary care used the same methods as a cluster randomized trial carried out in specialist practices. E23 Both studies, which were carried out in France in large populations, showed a very similar change in VAS levels during treatment depending on total symptom scores and RQLQ scores. These studies suggest that the cutoff of 23 mm E18 is appropriate to find a clinically significant difference.

VAS levels appear to be similar in different countries in patients with severe intermittent or persistent rhinitis. A VAS can be used in all age groups, including preschool children (guardian evaluation) E24 and the elderly. E25 Furthermore, it can be used in a wide variety of languages. E25-E32 VAS levels vary with the Allergic Rhinitis and its Impact on Asthma classification in many languages. E28,E33-E35 A VAS level of 50 (>100 mm) is suggestive of moderate-to-severe AR E19,E36,E37 although in some studies the cutoff was greater than 60 mm. E30 AVAS was used to define severe chronic upper airway disease. E24 Thus the MCDI found in 2 large French populations can be generalized to other countries with different languages and cultures across the lifecycle. However, future studies should refine this cutoff level.

REFERENCES


