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Allergic Rhinitis Special Issue

This special issue of the Acta Medica Philippina on allergic rhinitis comes at a time when the pollution in Philippine cities is at an all time high. The traffic problem, as well as the fumes emanating from large industrial complexes have no doubt significantly contributed to the problem. The sulfur, dust, carbon, among others, have increased the incidence of respiratory ailments, among other diseases, in the Metro, and allergic rhinitis is one of the more significant maladies that plague our population.

Almost everyone I know has some degree of rhinitis. Some days are worse than others. And each one has some sort of remedy: antihistamines, anti-allergies, decongestants – you name it. There are so many of them out there in the market, that it seems a confused mess. This issue tries to help resolve these issues, and has a comprehensive review of all these medications and treatments available. It is a multidisciplinary issue, with pediatricians, otolaryngologists and allergy specialists joining forces to come up with these parameters and guidelines to best help alleviate or treat this very significant problem.

I congratulate Dr. Ruzanne M. Caro and Dr. Marysia T. Recto, and all those who are responsible for this special issue of Acta, which is sure to be a part of the library of any specialist or general practitioner seeing patients with allergic rhinitis, which I am sure shall be in the clinics at some very significant months of each year.

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Joint Practice Parameters on the Management of Allergic Rhinitis

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Disclosure

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Drs. Ruzanne Caro, Marysia Recto and Madeleine Sumpaico are speakers of Glaxo Smith-Kline and MSD. They are also speakers and members of the advisory board of other pharmaceutical companies. The following are speakers of pharmaceutical companies other than MSD and GSK: Drs. Mary Anne Castor, Julie De Leon, Gwyneth Velez and Josefino Hernandez. The rest of the working group have nothing to disclose.

Introduction

Allergic rhinitis is a common disease entity that may be easily misdiagnosed and mistreated. It is a global concern, affecting 10% to 25% of the population worldwide, that has to be controlled since it can be disabling affecting the quality of life of patients. The Philippine Society of Otolaryngology-Head and Neck Surgery is currently updating its 2006 guideline on Allergic Rhinitis. The Section of Rhinology, Department of Otorhinolaryngology together with the Section of Allergy and Immunology, Departments of Pediatrics and Internal Medicine, came up with practice parameters in the diagnosis and management of adult and pediatric patients suspected to have allergic rhinitis to guide clinicians in managing these patients. Locally, it is the first collaboration of otorhinolaryngologists and allergists.

Scope of the Guideline

This practice parameter was developed to guide general physicians, otorhinolaryngologists and allergists in the diagnosis and management of adult and pediatric patients with allergic rhinitis in an ambulatory care setting.

Objectives

This guideline aims to (1) assist general physicians, otorhinolaryngologists and allergists diagnose true allergic rhinitis; (2) evaluate current techniques and practices in diagnosing allergic rhinitis; and (3) describe treatment and management options for allergic rhinitis.

Development process

The Section of Rhinology of the Department of Otorhinolaryngology and Section of Allergy and Immunology of the Departments of Pediatrics and Internal Medicine of the UP-Philippine General Hospital convened a working group to create a consensus document to be used primarily for the Allergic Rhinitis Clinic, a joint clinic of the aforementioned sections in the Out-Patient Department of the UP-PGH, and to serve as a guide to general physicians, otorhinolaryngologists and allergists.

The working group agreed to come up with an algorithm for the diagnosis and management of a patient with allergic rhinitis. Clinical questions were subsequently formulated based on the algorithm. The members then searched for relevant literature (including clinical practice guidelines, systematic reviews) in the National Library of Medicine's PubMed database, Herdin database and unpublished local articles on allergic rhinitis. Appraisal of literature was done by an epidemiologist and evidence was presented and discussed within the working group. Applicability and availability of the diagnostic tests and therapeutic interventions were considered. All materials were assessed for relevance and further classified according to levels of evidence and grades of evidence based on guidelines. Recommendations were based on nominal approval of the working group.

The document was then presented to stakeholders---consultants and residents of four clinical departments (Family Medicine, Internal Medicine, Otorhinolaryngology, Pediatrics), medical interns, medical students, nurses and patients. The opinions of the stakeholders were considered in the final draft.

Levels of recommendation and evidence adapted from American Academy of Otolaryngology-Head & Neck Surgery guideline development.

Guideline Definitions for Evidence-Based Statements

Statement	Definition	Implication
Strong Recommendation	A strong recommendation means the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation) and that the quality of the supporting evidence is excellent (Grade A or B).[a] In some clearly identified circumstances, strong recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	A recommendation means the benefits exceed the harms (or that the harms exceed the benefits in the case of a negative recommendation), but the quality of evidence is not as strong (Grade B or C).[a] In some clearly identified circumstances, recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms.	Clinicians should also generally follow a recommendation but should remain alert to new information and sensitive to patient preferences.
Option	An option means that either the quality of evidence that exists is suspect (Grade D)[a] or that well-done studies (Grade A, B, or C)[a] show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role.
No Recommendation	No recommendation means there is both a lack of pertinent evidence (Grade D)[a] and an unclear balance between benefits and harms.	Clinicians should feel little constraint in their decision making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient preference should have a substantial influencing role.

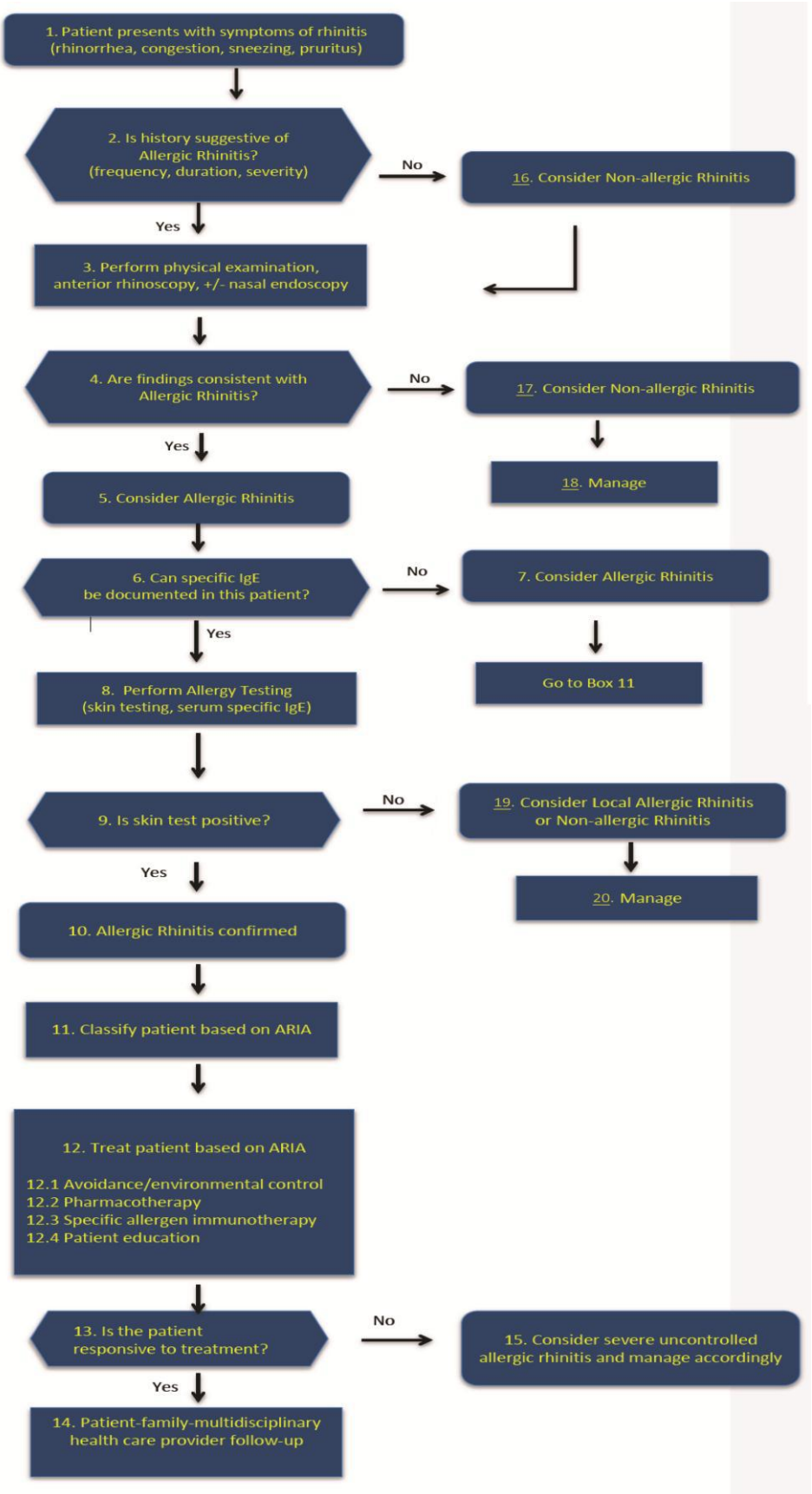
[a]American Academy of Pediatrics classification scheme.[25]

Evidence Levels for Grades of Evidence.[a]

Grade	Evidence Quality for Diagnosis	Evidence Quality for Treatment and Harm
A	Systematic review of cross-sectional studies with consistently applied reference standard and blinding	Well-designed randomized controlled trials performed on a population similar to the guideline's target population
B	Individual cross-sectional studies with consistently applied reference standard and blinding	Randomized controlled trials; overwhelmingly consistent evidence from observational studies
C	Nonconsecutive studies, case-control studies, or studies with poor, nonindependent, or inconsistently applied reference standards	Observational studies (case control and cohort design)
D	Mechanism-based reasoning or case reports	
X	Exceptional situations where validating studies cannot be performed and there is a clear preponderance of benefit over harm	

[a]American Academy of Pediatrics classification scheme[25] updated for consistency with current level of evidence definitions.[26]

Algorithm


1. Patient presents with symptoms of rhinitis (rhinorrhea, congestion, sneezing, pruritus)
2. Is history suggestive of Allergic Rhinitis? (frequency, duration, severity)
No
16. Consider Non-allergic Rhinitis
Yes
3. Perform physical examination, anterior rhinoscopy, +/- nasal endoscopy
4. Are findings consistent with Allergic Rhinitis?
No
17. Consider Non-allergic Rhinitis
18. Manage
Yes
5. Consider Allergic Rhinitis
6. Can specific IgE be documented in this patient?
No
7. Consider Allergic Rhinitis
Go to Box 11
Yes
8. Perform Allergy Testing (skin testing, serum specific IgE)
9. Is skin test positive?
No
19. Consider Local Allergic Rhinitis or Non-allergic Rhinitis
20. Manage
Yes
10. Allergic Rhinitis confirmed
11. Classify patient based on ARIA
12. Treat patient based on ARIA
12.1 Avoidance/environmental control
12.2 Pharmacotherapy
12.3 Specific allergen immunotherapy
12.4 Patient education
13. Is the patient responsive to treatment?
No
15. Consider severe uncontrolled allergic rhinitis and manage accordingly
Yes
14. Patient-family-multidisciplinary health care provider follow-up

Joint Practice Parameters on Allergic Rhinitis

Box 1. Patient presents with symptoms of rhinitis (rhinorrhea, nasal congestion, sneezing, nasal pruritus)

Rhinitis is defined as an inflammation of the lining of the nose that may present with one or more of the following symptoms: rhinorrhea (anterior and posterior), nasal congestion, sneezing, and nasal pruritus, that may occur for 2 or more consecutive days lasting for at least an hour on most days. These may or may not be associated with symptoms involving the eyes, ears and throat.[1,2]

Rhinitis may be classified as allergic and non-allergic. Approximately 50% of cases are allergic.[3] Occupational rhinitis, however, has both allergic and non-allergic components.

Rhinitis "mimickers" include nasal polyps, structural or mechanical factors (septal wall abnormalities, trauma, foreign bodies, nasal tumors, choanal atresia, cleft palate, adenoidal hypertrophy, pharyngonasal reflux and acromegaly), cerebrospinal fluid rhinorrhea and ciliary dyskinesia syndrome.[1]

References

1. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63(Suppl. 86):8–160.
2. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2 Suppl):S1-84.
3. Skoner DP. Allergic rhinitis: Definition, epidemiology, pathophysiology, detection, and diagnosis. J Allergy Clin Immunol. 2001; 108(1 Suppl);S2-8.

Box 2: Is history suggestive of allergic rhinitis?

Allergic rhinitis is considered in the presence of the following symptoms: rhinorrhea, nasal congestion, sneezing, and/or nasal pruritus triggered by allergen exposure. Symptoms may be associated with conjunctival redness, itchy and/or teary eyes.

The diagnosis of allergic rhinitis should begin with a thorough history and complete physical examination.

Allergic rhinitis symptoms (rhinorrhea, nasal congestion, sneezing, nasal pruritus) are reversible spontaneously or with treatment. The British Society for Allergy and Clinical Immunology emphasized the same set of symptoms to strengthen the diagnosis of allergic rhinitis with the inclusion of nasal crusting.[1] Nasal congestion alone is rarely associated with allergy. However, in preschool children, allergic rhinitis may present with just nasal obstruction.[2]

Although the clinical manifestations of both allergic and non-allergic rhinitis may be similar, nasal pruritus, sneezing and seasonal exacerbations are more common in allergic rhinitis. Eyes, ears and throat symptoms frequently accompany allergic rhinitis.[3] In a local retrospective study of 424 pediatric patients' charts, the most commonly observed nasal symptoms were sneezing, rhinorrhea, nasal congestion and nasal pruritus in descending order.[4] The presence of allergic conjunctivitis best differentiates allergic rhinitis from other forms of rhinitis, with an odds ratio of 2.85.[5] Bouts of sneezing, itchy eyes and a family history make a diagnosis of allergic rhinitis more probable.[3] In a prospective cross-sectional study of 85 pediatric patients done in a local hospital, the presence of sneezing, rhinorrhea, and nasal congestion showed good sensitivity (80%) compared to a skin test in diagnosing allergic rhinitis; however, these symptoms showed poor specificity (<30%) since they are also seen in patients with non-allergic rhinitis.[6]

Based on a study on the accuracy of history in diagnosing allergic rhinitis, the following points in the history would lead to an accurate diagnosis of allergic rhinitis: (1) allergy triggers, (2) presence of nasal symptoms and watery-itchy eyes, (3) positive personal history and (4) positive family history of atopy with positive likelihood ratios ranging from 2.49 to 6.69.[7]

The following supportive clinical information should always be part of history taking: (1) pattern or frequency, duration or chronicity (intermittent or persistent) and severity of symptoms with effect on patient's quality of life; (2) age of onset; (3) precipitating factors or triggers; (4) result of previous allergy testing; (5) response to previous treatment; and (6) presence of other atopic and co-morbid conditions.

A detailed environmental history, including occupational exposure, is also important. The updated practice parameter on the diagnosis and management of allergic rhinitis states that questions relating symptoms to pollen and animal exposure have positive predictive value for diagnosing allergic rhinitis.[8]

References

1. Angier E, Willington J, Scadding G, Holmes S, Walker S. Management of allergic and non-allergic rhinitis: a primary care summary of the BSACI guideline. Prim Care Respir J. 2010; 19(3):217-22.
2. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63(Suppl. 86): 8-160.
3. Keil T, Bockelbrink A, Reich A, et al. The natural history of allergic rhinitis in childhood. Pediatr Allergy Immunol. 2010; 21(6):962–9.
4. Aquino CC, Sumpaico MW, Recto MT, Castor MR, de Leon JC. Clinical profile of pediatric patients with allergic rhinitis seen at the allergy clinic out-patient department of the Philippine General Hospital, A five year review (2008-2012). 2013. Unpublished.
5. Greiner AN, Hellings PW, Rotiroti G, Scadding GK. Allergic rhinitis. Lancet. 2011; 378(9809): 2112-22.
6. Mallillin JI, Castor MR, de Leon JC, Recto MT, Sumpaico MW, et al. Correlation of skin prick test with symptoms and physical examination findings in Allergic Rhinitis among Filipino children. 2014. Unpublished.
7. Gendo K, Larson EB. Evidence-based diagnostic strategies for evaluating suspected allergic rhinitis. Ann Intern Med. 2004; 140(4):278-89.
8. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2 Suppl):S1-84.

Box 3. Perform physical examination, anterior rhinoscopy, +/- nasal endoscopy.

A complete physical examination should be done in a patient with allergic rhinitis, paying close attention to the organ systems where co-morbidities as well as other atopic diseases may manifest. Anterior rhinoscopy supports but does not definitely establish the diagnosis of rhinitis. Nasal endoscopy may be warranted in certain situations.

Recommendation, Grade B evidence

History and physical examination is usually sufficient for a presumptive diagnosis of rhinitis. (Table 1) The presence of facial grimaces, nasal creases, allergic shiners and Dennie-Morgan lines are suggestive of allergic rhinitis. A local retrospective chart review noted that the most common physical examination findings in pediatric patients with allergic rhinitis are allergic shiners, posterior pharyngeal wall cobblestoning, congested turbinates, pink turbinates, pale turbinates and clear, watery nasal discharge.[1] Although allergic shiners may be found in non-atopic persons, one study in Taiwan using digital photographs, showed that dark shiners had an excellent specificity (100%) for allergic rhinitis and that the darkness of allergic shiners positively correlated with the chronicity of allergic rhinitis.[2] This was a prospective cohort study involving patients with allergic rhinitis with a healthy control group. However, a recent local prospective cross-sectional study among pediatric patients seen at the allergy clinic at UP-PGH revealed that the presence of allergic shiners is highly sensitive (90%) but poorly specific (<10%) in diagnosing allergic rhinitis.[3] Another local study reported that allergic shiners, allergic salute, and bunny red nose were seen in only less than 10% of patients.[4] (Table 2)

Patients with history of rhinitis should undergo examination of the nose which includes evaluation of the nasal passageways, turbinates, and septum, presence or absence of nasal discharge and/or nasal polyps.[5,6] Traditional rhinoscopy consists of inspection with a nasal speculum following mucosal decongestion and the use of mirrors to examine the nasopharynx and larynx.[5,6] The nasal mucosa appears pale (may also be hyperemic) and swollen with a bluish-gray appearance when mucosal edema is severe. Mucus threads may be seen. Nasal secretions are usually watery in character.[5,6]

Mucosal appearance may not distinguish between allergic and non-allergic rhinitis because non-allergic rhinitis may also present with mucosal pallor, edema, or hyperemia.[6] A local prospective cross-sectional study showed that both pale and hyperemic turbinates may be present in patients with allergic rhinitis, with pale turbinates (74%) more common than hyperemic ones,[3] similar to another local cross-sectional survey which showed a higher percentage (73%) of patients having pale, boggy mucosa.[7]

In a study of children with allergic rhinitis, anterior rhinoscopy findings typically reveal congestion of the nasal mucosa and presence of pale, thin secretions. Areas of congestion, defined as (1) inferior turbinate contact with the inferior meatus and (2) middle turbinate contact with adjacent structures such as the uncinate process and septum, were reported as predictive factors for the diagnosis of allergic rhinitis with positive predictive values of 83.8% and 86.2%, respectively. Anterior rhinoscopy findings of pale turbinates were only present in 39.8% of the study population of children with allergic rhinitis (N=176), with a reported sensitivity of 60.6%.[8]

Nasal endoscopy is indicated in the following: (1) presence of atypical symptoms or physical findings; (2) occurrence of complications or other conditions; and (3) inappropriate response to therapy.[5] It is usually performed in the office following decongestion and topical anesthesia; however, some children my require sedation prior to the procedure.[5,6]

References

1. Aquino CC, Sumpaico MW, Recto MT, Castor MR, de Leon JC. Clinical profile of pediatric patients with allergic rhinitis seen at the allergy clinic out-patient department of the Philippine General Hospital, A five year review (2008-2012). 2013. Unpublished.
2. Chen CH, Lin YT, Wen CY, et al. Quantitative assessment of allergic shiners in children with allergic rhinitis. J Allergy Clin Immunol. 2009; 123(3):665-71.
3. Mallillin JI, Castor MR, de Leon JC, Recto MT, Sumpaico MW. Correlation of skin prick test with symptoms and physical examination findings in allergic rhinitis among Filipino children. 2014. Unpublished.
4. Lim LA. Profile of patients with allergic rhinitis at the UP-PGH. Acta Med Philipp. 1990; 26(1):17-24.
5. Dykewicz MS, Fineman S, Skoner DP, et al. Diagnosis and management of rhinitis: complete guidelines of the joint task force on practice parameters in allergy, asthma and immunology. Ann Allergy Asthma Immunol. 1998; 81(5 Pt 2):478–518.
6. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2 Suppl):S1-84.
7. Valencia MS, Andaya AG, Uy BL. Allergic rhinitis: a study on the prevalence, clinical and personality profiles among adolescents. Sto Tomas Journal of Medicine. 1997; 46(4):156-65.
8. Ameli, F, Brocchetti F, Tosca MA, Signori A, Ciprandi G. Nasal endoscopy in children with suspected allergic rhinitis. Laryngoscope. 2011; 121(10):2055-9.
9. Small P, Kim H. Allergic rhinitis. Allergy Asthma Clin Immunol. 2011; 7 Suppl 1:S3.
10. Agbayani BF, Rojas J. Clinical features of allergic rhinitis cases. Acta Med Philipp. 1981; 17(4):127-36.

Table 1. Components of a complete history and physical examination for patients with suspected allergic rhinitis[9]

History	Physical Examination
Personal	Outward signs
• Rhinorrhea	• Mouth breathing
• Sneezing	• Rubbing of the nose / transverse nasal crease
• Nasal pruritus	• Frequent sniffling and / or throat clearing
• Nasal congestion	• Allergic shiners (dark circles under eyes)
• Eye involvement (pruritus, lacrimation, redness)	Nose
• Seasonality	• Color of the mucosa
• Triggers	• Mucosal swelling / bleeding
Quality of Life	• Pale, thin secretions
Response to Previous Medications	• Polyps and other structural abnormalities
• Antihistamines	Sinuses
• Corticosteroids	• Palpation of sinuses for signs of tenderness
Medication Use	• Maxillary tooth sensitivity
• Beta-blockers	Ears
• Aspirin	• Normal
• NSAIDs	• Pneumatic otoscopy to assess for Eustachian tube dysfunction
• ACE inhibitors	• Valsalva's maneuver to assess for fluid behind the tympanic membrane
• Hormone therapy	Eyes
• Recreational drugs	• Hyperemia
Co-Morbidities	• Lacrimation
• Asthma	Posterior oropharynx
• Sinusitis	• Postnasal drip
• Nasal polyps	• Lymphoid hyperplasia ("cobble stoning")
• Otitis Media	• Tonsillar hypertrophy
• Conjunctivitis	Chest
• Sleep disorders (snoring, obstructive sleep apnea)	• Wheezing
Past Medical History	• Rales / rhonchi
• Allergy	Skin
• Asthma	• Rashes
Family History	
• Allergy	
• Asthma	
Environmental	
• Flooring / upholstery / curtains	
• Animals / insects (cockroaches)	
• Pollen	
• Tobacco exposure	
• Molds	
• Humidity	

Table 2. Local studies showing the clinical profile of patients with allergic rhinitis

Study	Population	Most Common Clinical Manifestations		Physical Examination Finding		Age Group Commonly Affected	
Agbayani BF, Rojas J.[10]	N = 144	Sneezing	68.06%			15-19 yrs	25.00%
(1981)	UP-PGH Allergy	Nasal congestion	43.75%			25-29 yrs	17.36%
Retrospective chart review	Clinic Patients	Pruritus	53.47%			20-24 yrs	16.67%
		Lacrimation	44.44%			10-14 yrs	10.42%
		Rhinorrhea	40.97%				
Lim LA[2]	N = 152	Rhinorrhea	95.0%	Pale turbinates	48.8%	26-30 yrs	22.3%
(1990)	UP-PGH Allergy	Sneezing	92.7%	Nasal discharge	48.1%	21-25 yrs	16.2%
Retrospective chart review	Clinic Patients	Nasal congestion	91.5%	Hyperemic turbinates	38.2%	31-35 yrs	10.8%
		Nasal pruritus	71.8%	Tonsillar congestion / hypertrophy	36.7%	16-20 yrs	10.1%
						36-40 yrs	10.1%
Valencia MS, Andaya AG, Uy BL[5]	N = 1,459	Rhinorrhea	73%	Pale / boggy		15 yrs	26.9%
(1997)	Students from the Sto.	Sneezing	71%	nasal mucosa	73%	14 yrs	21.9%
Cross-sectional survey using	Tomas University	Nasal congestion	71%			16 yrs	21.3%
allergic rhinitis questionnaire	High School	Headache	53%			13 yrs	20.2%
(ARQ)	Department	Itchy eyes	45%				
		Nasal pruritus	43%				

Box 4. Are findings consistent with allergic rhinitis?

Box 5 and Box 7. Consider allergic rhinitis

Allergic rhinitis is a symptomatic disorder of the nose induced after allergen exposure by an immunoglobulin E (IgE)-mediated inflammation of the membranes lining the nose.[1] It is characterized by rhinorrhea, nasal congestion, sneezing and nasal pruritus. It is also associated with several comorbid respiratory conditions.

Allergic rhinitis affects 10% to 30% of adults and 40% of children. It is more common than pure non-allergic rhinitis with a ratio of 3:1.[2] Its prevalence still continues to increase worldwide.[3] In the 1996 International Study of Asthma and Allergies of Childhood (ISAAC), allergic rhinitis prevalence among Filipino children was 26.2% (aged 6 to 7 years) and 32.5% (aged 13 to 14 years).[4] The 2008 National Nutrition and Health Survey reported a prevalence of 20.0% among adult Filipinos.

Allergic rhinitis symptoms commonly develop before the age of 20 years in 80% of cases.[6] Symptoms of allergic rhinitis develop in 20% children by 2 to 3 years of age and in approximately 40% by age 6 years. Approximately 30% develop symptoms during adolescence.[7]

A prospective study looking at the correlation of allergy skin prick test results and symptoms and physical examination findings of allergic rhinitis among Filipino children showed that sneezing, rhinorrhea, and nasal congestion showed satisfactory sensitivity (>80%) in determining allergic rhinitis when compared to skin prick test. However, these symptoms have a high probability of being present even in patients without allergic rhinitis (specificity <30%). The same relationship is exhibited for allergic shiners (sensitivity >90%, specificity <10%). No significant relationship was found between ocular and nasal pruritus, sneezing, rhinorrhea, and nasal congestion, and skin prick test positivity (p-value > 0.05). Likewise, the presence of allergic shiners; congested & pale turbinates; clear, watery nasal discharge; and throat cobblestoning showed no significant relationship with the skin prick test result (p-value > 0.05).[19]

Children in families with a bilateral family history of allergy generally have symptoms before puberty; those with a unilateral family history tend to have symptoms later in life or not at all.[8] The presence of a bilateral family history (odds ratio 3.1 [1.1–9.3]) was significantly associated with allergic rhinitis.[9]

Risk factors for allergic rhinitis include genetic and environmental factors. In the International Conference on Allergic Rhinitis in Childhood, they listed the following genetic factors: atopic family history, male sex, sustained elevated total and specific IgE levels, chromosomal mutations and immune response genes. Environmental factors include: early cow's milk formula feeding, solid food exposure, critical aeroallergen exposure during infancy, spring or autumn births, specific and early infections with viruses and exposure to products of pollution.[8] One study found a protective effect of childhood farm living on the prevalence of allergic rhinitis as well as an increasing prevalence with increasing degree of urbanization, both in subjects raised on a farm and in those who were not.[10]

Allergic rhinitis is not a life-threatening disease but it may significantly affect a patient's quality of life. Allergic rhinitis patients experience a significant reduction in quality of life in terms of reduced work and school productivity such as increased absenteeism and lack of sleep.[9] Children can have difficulties at school because of learning impairment secondary to distraction, fatigue, poor sleep, or irritability. S ome patients might be unable to take part in family or social events, resulting in emotional disturbances that manifest as anger, sadness, frustration, and withdrawal.[9]

Allergic rhinitis is associated with other mucosal inflammatory disorders, including asthma, rhinosinusitis, otitis media, and allergic conjunctivitis. The naso-ocular reflex is implicated in the presence of both nasal and ocular symptoms in allergic rhinitis. Pathophysiology of ocular symptoms in allergic rhinitis may be direct (to the eye) or indirect (by nasal mucosa) deposition of allergen. Baroody et al. proposed several mechanisms for the occurrence of the reflex: (1) allergen deposited on the nasal mucosa can stimulate afferent reflexes propagating centrally, and the efferent arm of these reflexes may not only affect the contralateral nasal cavity but also to proximal areas such as conjunctivae, and maxillary sinus; (2) nasal allergic reaction leads to the release of mediators from the nose and up-regulation of circulating cells, which, when attracted to the eye, are primed to release more mediators and cause more severe symptoms; and (3) the nasolacrimal duct may act as conduit in the transfer of allergen and mediators of allergic reactions.[10]

Asthma and allergic rhinitis are closely linked together such that Simons has even proposed a new term "allergic rhinobronchitis". Both diseases often have similar natural histories, seasonal exacerbations and provoking factors. Parallel immunopathologies and immunopathophysiologies have been documented for these two conditions leading to the concept called the "one airway-one disease" phenomena.[1,11] Pollen allergy is more clearly associated with rhinitis than with asthma while some non-specific provoking factors such as cold, dry air are more clearly associated with asthma than with rhinitis. Epidemiologic evidence shows that allergic rhinitis often precedes asthma and that asthmatic patients with severe allergic rhinitis tend to have worse asthma than those with mild allergic rhinitis.[12] In a review of studies linking allergic rhinitis and asthma, it was concluded that allergic rhinitis is a risk factor for the development of asthma.[13]

Allergic rhinitis probably predisposes to sinusitis because of nasal infl ammation, resulting in nasal congestion and obstruction of sinus ostia. Decreased sinus ventilation leads to ciliary dysfunction, transudation of fluids, and stagnation of mucus, thereby promoting growth of bacterial pathogens.[9] A local study showed that sinusitis was significantly associated with allergic rhinitis (OR = 3.06 [1.48-6.31]).[14]

Studies have shown that there is a strong association between acute otitis media with effusion (OME) and allergic rhinitis. The prevalence of nasal allergy in children with OME ranges from 35% to 50%, and, conversely, about 21% of allergic children have OME.[15] Conjunctivitis is related to both direct allergen contact with the conjunctival mucosa and activation of the nasal-ocular reflex.[9]

Orthodontic malocclusions have been reported in some children with allergic rhinitis. A stuffy, blocked nose leads to mouth breathing, and the incidence of malocclusions is almost three times greater in mouth breathers than in nose breathers.[16]

A systematic review on the association between allergic rhinitis and sleep-disordered breathing in children showed that majority of the studies had significant association between the two.[17] Allergic rhinitis is one of the risk factors for obstructive sleep apnea syndrome. Sleep-disordered breathing has been attributed to multilevel anatomic obstruction.[18]

References

1. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63 Suppl 86:8-160.
2. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2 Suppl):S1-84.
3. Small P, Kim H. Allergic rhinitis. Allergy, Asthma Clin Immunol. 2011; 7 Suppl 1:S3.
4. Cua-Lim F, Roa C Jr, Ferreria M, et al. Prevalence of asthma in Metro Manila, Philippines. Philipp J Allergy Immunol. 1997; 4:9-20.
5. Abong JM, Kwong SL, Alava HA, Castor MA, de Leon JC. Prevalence of allergic rhinitis in Filipino adults based on the National Nutrition and Health Survey (NNHeS) 2008. Asia Pac Allergy. 2012; 2(2):129-35.
6. Greiner AN, Hellings PW, Rotiroti G, Scadding GK. Allergic rhinitis. Lancet. 2011; 378(9809):2112-22.
7. Skoner DP. Allergic rhinitis: Definition, epidemiology, pathophysiology, detection, and diagnosis. J Allergy Clin Immunol. 2001; 108(1 Suppl):S2-8.
8. International conference on allergic rhinitis in childhood. Allergy. 1999; 54: 7-34.
9. Keil T, Bockelbrink A, Reich A, et al. The natural history of allergic rhinitis in childhood. Pediatr Allergy Immunol. 2010; 21(6):962–9.
10. Eriksson J, Ekerljung L, Lotvall J, et al. Growing up on a farm leads to lifelong protection against allergic rhinitis. Allergy. 2010; 65(11):1397-403.
11. Baroody FM, Naclerio RM. Nasal-ocular reflexes and their role in the management of allergic rhinoconjunctivitis with intranasal steroids. World Allergy Organ J. 2011; 4(1 Suppl):S1-5.
12. Simons FE. Allergic rhinobronchitis: the asthma-allergic rhinitis link. J Allergy Clin Immunol. 1999; 104(3 Pt 1):534-40.
13. Leynaert B, Neukirch F, Demoly P, Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. J Allergy Clin Immunol. 2000; 106(5 Suppl): S201-5.
14. Tam LJ, Andaya AG. Association of sinusitis with allergic rhinitis and bronchial asthma in children. St Tomas J Med. 2005; 52(3):101-7.
15. Spector SL. Overview of comorbid associations of allergic rhinitis. J Allergy Clin lmmunol .1997; 99(2):S773-80.
16. Bresolin D, Shapiro PA, Shapiro GG, Chapko MK, Dassel S. Mouth breathing in allergic children: its relationship to dentofacial development. Am J Orthod.1983; 83(4):334-40.
17. Lyn SY, Melvin TA, Boss EF, Ishman SL. The association between allergic rhinitis and sleep-disordered breathing in children: a systematic review. Int Forum Allergy Rhinol. 2013; 3(6):504-9.
18. Georgalas C. The role of the nose in snoring and obstructive sleep apnoea: an update. Eur Arch Otorhinolaryngol. 2011; 268(9):1365-73.
19. Mallillin JI, Castor MR, de Leon JC, Recto MT, Sumpaico MW. Correlation of skin prick test with symptoms and physical examination findings in allergic rhinitis among Filipino children. 2014. Unpublished.

Box 6. Can specific IgE be documented in this patient?

Specific IgE can be documented by either a skin prick test or in vitro assay. It confirms that a specific allergen suggested by medical history has induced an Immunoglobulin E (IgE) antibody response.

Strong Recommendation, Grade A evidence

The diagnosis of specific IgE mediated allergies, suggested by a clinical history and the physical examination, should be based on validated allergy tests such as the skin prick test (SPT) and/or specific IgE in the serum, when indicated.[1]

When properly performed, skin testing is generally considered to be the most convenient, most effective and least expensive screening tool for determining the presence of IgE-mediated sensitivity. It gives the clinician and the patient immediate information on reactivity to individual allergens.[2] It provides evidence of an allergic basis for and to confirm suspected causes of the patient's symptoms.

Seasonal rhinitis/conjunctivitis should be skin tested in treatment-resistant cases and in cases of associated pollen-induced asthma or severe pollen-food syndrome. Perennial rhinitis/conjunctivitis cases should be skin tested in all cases as the causal allergen is not always immediately apparent.[1,3]

Vital to the accuracy and reproducibility of the results of skin testing are quality control measures and proper performance of skin testing.[4,5] Various factors dictate the number of skin tests that are necessarily performed, namely age, potential allergen exposures and area of the country. Moreover, it is essential to know which aeroallergens are present locally and are clinically important to properly interpret skin tests.[4]

Specific IgE immunoassays may be preferable to skin testing under special clinical conditions such as widespread skin disease, uncooperative patients, history suggestive of an unusually greater risk of anaphylaxis from skin testing and patient inability to cease antihistamines or other skin test suppressive therapy.[6,7]

The precise sensitivity of these immunoassays compared with prick/puncture skin tests has been reported to range, depending on the immunoassay assessed, from less than 50% to greater than 90%, with the average being approximately 70% to 75% for most studies.[8]

If symptoms are narrowly confined to certain seasons, a limited number of relevant allergens to be tested would suffice for confirmation of the clinical diagnosis. By contrast, perennial symptoms would require a more extended allergen panel of both indigenous outdoor and indoor inhalants.[8]

There is general agreement that significant indoor all ergens such as house dust mite, prevailing indoor fungal allergens (*Penicillium* species, *Aspergillus* species, *Alternaria alternata*), cockroach, and epidermals (cat, dog, feathers), should be tested in patients with perennial respiratory symptoms.[8] In the Philippines, the most common allergens that cause sensitization are: housedust mite, cockroach, pollens and cat dander .[9]

Because the constitutive allergenicity, potency, and stability are variable among commercial allergen extract reagents, sensitivity and the positive predictive value of both prick/puncture and specific IgE tests generally tend to be higher among pollens, house dust mite, certain epidermals, and fungi.[8]

In general, SPT and most commercial specific IgE assays display a good sensitivity, but a lower specificity. However, these depend largely on the antigen tested. Skin testing and specific IgE tests are complementary and in certain circumstances only (e.g. when a test is negative despite a suggestive history), a combined use of both tests enhances their diagnostic accuracy.[1]

Because these tests are expensive, they are not affordable to many patients. Cost, geographic constraints, availability and quality control of skin tests should be considered by the clinician as important clinical modulating factors in our setting.

References

1. Eigenmann PA, Atanaskovic-Markovic M, O'B Hourihane J, et al. Testing children for allergies: why, how, who and when: an updated statement of the European Academy of Allergy and Clinical Immunology (EAACI) Section on Pediatrics and the EAACI-Clemens von Pirquet Foundation. Pediatr Allergy Immunol. 2013; 24(2):195–209.
2. Chiriac AM, Bousquet J, Demoly P. In vivo methods for study and diagnosis of allergy. In: Adkinson NF, Bochner BS, Burks AW, et al, eds. Middleton's Allergy, Principles and Practice, 8th ed. Pennsylvania: Saunders; 2014. Pp. 1119-1129.
3. American Academy of Allergy, Asthma and Immunology. Consultation and referral guidelines citing the evidence: How the allergist-immunologist can help. J Allergy Clin Immunol. 2006; 117(2 Suppl Consultation): S495-523.
4. Conner SJ. Evaluation and treatment of the patient with allergic rhinitis. J Fam Pract. 2002; 51(10):883-4, 887-90.
5. Angier E, Willington J, Scadding G, et al. Management of allergic and non-allergic rhinitis: a primary care summary of the BSACI guideline. Prim Care Respir J. 2010; 19(3): 217-22.
6. Smith W. Skin prick testing for the diagnosis of allergic disease. Australasian Society of Clinical immunology and Allergy Inc [Online]. 2012 [cited 2013 April]. Available from www.allergy.org.au.
7. Leith E, Bowen T, Butchey J, et al. Consensus guidelines on practical issues of immunotherapy – Canadian Society of Allergy and Clinical Immunology (CSACI). Allergy Asthma Clin Immunol. 2006; 2(2): 47-61.
8. Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: an updated practice parameter (AAAAI, ACAAI). Ann Allergy Asthma Immunol. 2008; 100 (3 Suppl 3):S1-148.
9. Estrella PS, Recto MT, Castor MA, et al. Sensitization patterns to aeroallergens and food allergens among pediatric patients with common allergic diseases. 2013. Unpublished.

Box 8. Perform Allergy Testing (skin testing, serum specific IgE)

The skin test is done by performing a prick or puncture test. Strong Recommendation, Grade A evidence

When the prick/puncture test results are negative despite a convincing history of symptoms upon exposure, an intracutaneous test (ICT) is done as it will identify a larger number of patients with lower skin test sensitivity.

Contraindications to the performance of skin prick testing include the following: (1) diffuse dermatological conditions (2) severe dermatographism (3) poor subject cooperation and (4) when the patient is unable to cease antihistamines or other interfering drugs.[1,2]

Relative contraindications, on the other hand, include the following: (1) persistent severe or unstable asthma (2) pregnancy (3) babies and infants and (4) patients on beta blockers.[1] In situations in which there is a high risk of systemic anaphylaxis, the use of beta-blockers is contraindicated while the use of ACE inhibitors may be a relative contraindication as these drugs may interfere with normal compensatory mechanisms in anaphylaxis.[1,2] Other medications that may interfere with skin prick testing include anti-depressants such as doxepin, tricyclics and tetracyclics, phenothiazines, over-the-counter remedies such as analgesics, antitussives, antiemetics, sedatives, relaxants, cyproheptadine and pizotifen which are migraine prophylactics, and topical corticosteroids. [1,2]

Commercially available assays for allergen specific IgE in the serum are based on the principle of immunoadsorption. The amount of the IgE bound to the allergen is quantitated using a labeled anti-human IgE.

High accuracy and low adverse effects are benefits of allergy testing. Skin prick test has better positive predictive value than total serum Ig-E.[3]

Procedure for Skin Testing[4]

Prick Test

A sharp instrument (hypodermic needle, solid bore needle, blood lancet) is passed through a drop of extract or control solutions (histamine, saline) at a 45° to 60° angle to the skin. The skin is then gently lifted, creating a small break

in the epidermis through which the suspected allergen solution penetrates.

Puncture Test

The skin test device is instead passed through the drop at a 90°angle to the skin. Devices used in this manner generally are designed with a sharp point and a shoulder (0.9 or 1 mm) to prevent excess penetration into the dermis. With some devices, the technique can be modified with a slight rotating twist after the puncture is made.

Other devices are used with no need to place a drop of the allergen extract on the skin beforehand. Some devices are submerged in a well containing the allergen extract before performing the prick test. There are also devices with multiple heads developed to apply several skin tests at the same time using the puncture technique.

The site of skin testing may affect the results. The back as a whole is more reactive than the forearm. When the forearm is used, the tests should not be placed in areas 5 cm from the wrist or 3 cm from the antecubital fossae. It is recommended that there should be sufficient space (approximately 2 to 2.5 cm) between each applied allergen.

Intracutaneous test should be performed with small volumes (0.02-0.05 ml) of allergens injected intracutaneously using a disposable 1 ml (tuberculin) syringe with an attached gauge 26-30 needle. The intracutaneous tests are placed on the upper arm or volar surface of the forearm.

The size of the reaction read after 15-20 minutes will be recorded as Mean Wheal Diameter=D + d/2 (with D indicating the largest diameter of the wheal and d indicating the largest diameter perpendicular to D).

Procedure for Serum Specific IgE [4]

As previously stated, commercially available assays for allergen specific IgE in the serum are based on the principle of immunoadsorption. The allergen specific IgE of interest binds to the allergen, which has either been previously bound to a solid phase or becomes bound to a solid phase after the IgE has been bound. IgE that does not bind to the allergen, together with other irrelevant proteins, are then washed away from the solid phase. The amount of the IgE bound to the allergen is quantitated using a labeled anti-human IgE (monoclonal or mixture of monoclonal) antibodies. The label can be a radioactive isotope, an enzyme, or a ligand to which an enzyme or antiligand conjugate is bound. The ImmunoCAP system, a fluorescent immunoassay, is available locally as an in-vitro test for specific IgE.

References

1. Smith W. Skin prick testing for the diagnosis of allergic disease. Australasian Society of Clinical Immunology and Allergy Inc [Online]. 2012 [cited 2013 April]. Available from www.allergy.org.au.
2. Leith E, Bowen T, Butchey J, et al. Consensus guidelines on practical issues of immunotherapy – Canadian Society of Allergy and Clinical Immunology (CSACI). Allergy Asthma Clin Immunol. 2006; 2(2): 47-61.
3. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63 Suppl. 86:8-160.
4. Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: an updated practice parameter (AAAAI, ACAAI). Ann Allergy Asthma Immunol. 2008; 100(3 Suppl 3):S1-148.
5. Soderstrom L, Kober A, Ahlstedt S, et al. A further evaluation of the clinical use of specific IgE antibody testing in allergic diseases. Allergy. 2003; 58(9):921-8.

Box 9. Is skin test positive?

A prick/puncture/intracutaneous test with a response of at least 3-mm diameter (with equivalent erythema) more than diluent control done at the same time or a 0.35 kUA/ml report from an Immunocap in vitro assay system is required as proof of the presence of cutaneous allergen specific IgE.[1]

The proper interpretation of the skin test requires a thorough knowledge of the medical history and physical examination findings. A positive skin test alone in an asymptomatic patient does not automatically mean that the individual is allergic. It may, however, predict subsequent clinical allergy especially if the wheal size is ≥ 4mm.[1] However, a positive skin test that correlates with a history suggestive of clinical sensitivity strongly indicates the allergen as the cause of the disease. Conversely, a negative skin test with a negative clinical history makes an allergic condition unlikely.[2]

ImmunoCAP specific IgE detects IgE antibodies in the range 0 to 100 kUA/ml. The result is reported quantitatively. In clinical practice, 0.35 kUA/ml has commonly been used as a cut off.[3]

References

1. Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: an updated practice parameter (AAAAI, ACAAI). Ann Allergy Asthma Immunol. 2008; 100(3 Suppl 3):S1-148.
2. Wallace DV, Dykewics MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2): S1-84.
3. Soderstrom L, Kober A, Ahlstedt S, et al. A further evaluation of the clinical use of specific IgE antibody testing in allergic diseases. Allergy. 2003; 58(9):921-8.

Box 10. Allergic Rhinitis is confirmed.

Specific IgE documentation should be done either by skin test or by in vitro assays as it represents the primary diagnostic tool to confirm that a specific allergen suggested by medical history has induced an Immunoglobulin E (IgE) antibody response.[1]

Crobach and colleagues demonstrated, with reference to experts' diagnosis, that the predictive value of the clinical history alone for the diagnosis of allergic rhinitis was 82% to 85% for intermittent seasonal allergens and at least 77% for persistent allergens and the rate increased to 97% to 99% when skin prick tests or specific IgE tests were performed.[2]

The recommendation to document the presence of specific IgE places a high value on adequate allergy testing as a prerequisite for optimal care including allergen avoidance, pharmacotherapy and immunotherapy even if there is a high positive likelihood ratio 2.08 (95% CI; 1.68-2.59). and low negative likelihood ratio 0.58 (95% CI;0.48-0.71) of history and PE in making a correct diagnosis of allergic rhinitis and a low value on cost and complications of allergy testing.[3]

References

1. AAAI Work Group Report. Allergy Diagnosis in Clinical Practice. November 2006.
2. Crobach MJ, Hermans J, Kaptein AA, Ridderikhoff J, Petri H, Mulder JD. The diagnosis of allergic rhinitis: how to combine the medical history with the results of the radioallergosorbent tests and skin prick tests. Scand J Prim Health Care. 1998; 16(1):30-6.
3. Williams P, Ahlstedt S, Barnes JH, Söderström L, Portnoy J. Are our impressions of allergy test performances correct? Ann Allergy Asthma Immunol. 2003; 91(1):26–33.

Box 11. Classify patient based on ARIA

Using the internationally accepted ARIA standard for the management of allergic rhinitis, patients are classified based on the duration and severity of symptoms. [1]
Strong Recommendation, Grade A

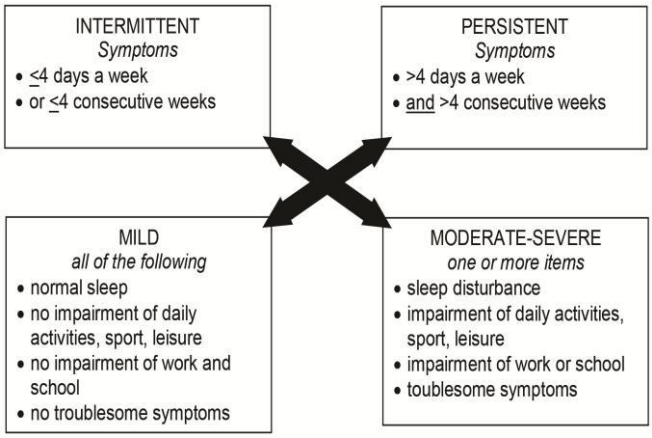


Figure 1. ARIA classification

Reference

1. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63 Suppl. 86:8-160.

Box 12. Treat patient based on ARIA.

Treatment is based on the classification of the patient.[1]
Recommendation, Grade B

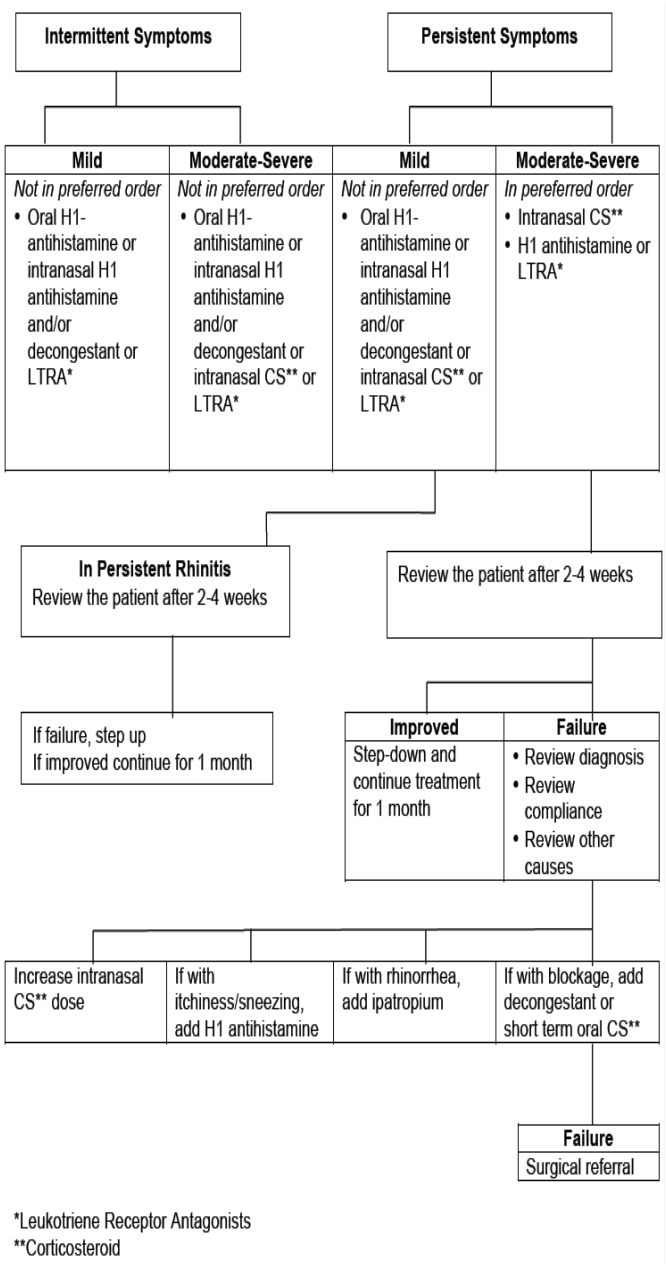


Figure 2. Algorithm for the management of allergic rhinitis

Reference

1. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63 Suppl 86:8-160.

Box 12.1 Allergen Avoidance or Environmental Control

The clinical benefits of inhalant allergen and air pollution control measures, with the exception of multi-faceted house dust mite control measures, in treating allergic rhinitis symptoms are controversial due to lack of adequate clinical trials.
Recommendation, Grade B evidence

In the pathophysiology of allergic disease, the presence of specific IgE, or allergen sensitization to different environmental allergens is mandatory.[1,2] A range of environmental inhalant allergens have been associated with allergic rhinitis such as pollen, fungi, animal dander, insect debris and, most commonly, house dust mites.[3] There is a dose-dependent relationship between exposure to inhalant allergens and sensitization, as well as an association between sensitization and disease exacerbation.[1,4] Evidence by which the use of allergen avoidance or environmental control measures may be useful for the management and prevention of allergic disease are the following:[1]

- Development of specific IgE or sensitization to specific inhalant allergens is a major risk factor for asthma, rhinitis and eczema;
- Exposure of individuals with established allergic disease to high levels of allergens cause symptom exacerbation and worsening of inflammation;
- Complete removal from exposure leads to improvement in disease control.

Hence, environmental control interventions should aim to achieve targeted, significant and effective removal from specific allergen exposure (as identified by clinical history and identification of specific IgE through allergy testing) early in the natural history of the disease or during disease exacerbation. Environmental control or allergen avoidance interventions may be used for allergic disease in two scenarios: for prevention of the development of allergic disease (primary prevention) and for the treatment of existing allergic disease (tertiary prevention).[3,4]

Use of environmental control measures as adjuncts for treatment of allergic rhinitis

The house dust mite (HDM) has been documented globally as the most common airborne allergen triggering respiratory allergies.[5] Several methods of reducing dust mite levels have been proposed with varying degrees of clinical effectiveness (Table 3). These clinical trials were of poor methodological quality and small in number.[6,7] However, the recent clinical reviews noted that only multifaceted house dust mite control measures (HDM impermeable beddings, acaricides plus high-efficiency particulate air filters) to reduce exposure to house dust mites and improve symptoms of allergic rhinitis can be strongly recommended despite the moderate quality of evidence for their effectivity.[6,8] The use of multifaceted HDM control measures is recommended in the local setting based on the following facts: (1) HDM is the most ubiquitous airborne allergen in the Philippines; (2) there is a strong connection of house dust mite exposure and triggering of allergic rhinitis symptoms; and (3) that HDM avoidance measures a relatively available in the Philippine setting.

Regarding the effectivity of allergen avoidance measures against other inhalant allergens, the evidence is weak to make any definite recommendations. Despite the apparent inconclusive effect of allergen avoidance measures in the treatment of allergic rhinitis, allergen exposure remains strongly associated with allergic disease in cross-sectional studies and are key prognostic factors is several allergic conditions such as asthma and atopic dermatitis [4,9]

Air pollutants may exacerbate allergic rhinitis. These come in the form of tobacco smoke, aerosols, formaldehyde, perfumes, traffic emissions and fungal and bacterial irritants.[10,11,12] Despite the lack of disease control effectiveness in environmental pollution interventional studies, the absence of adverse effects of avoiding environmental pollutants would justify these measures based on a biologic rationale. Available studies evaluating pollution control interventions are still wanting in methodological quality.

The clinical benefits of inhalant allergen avoidance measures in treating allergic rhinitis symptoms, in general, are still controversial mainly due to the number and quality of clinical trials done to assess treatment efficacy. Most allergen-avoidance intervention trials have dealt with asthma symptoms and very few have studied rhinitis symptoms. Furthermore, the use of meta-analyses in assessing clinical trials on environmental interventions may not be valid evaluation tools for determining clinical efficacy of these measures. Several meta-analyses have produced variable and controversial results mainly due to poor screening of literature, inappropriate statistical analysis and poor quality of the studies being analyzed.[13]

The difficulty in designing an ideal randomized controlled clinical trial evaluating environmental intervention measures has been noted. These studies are difficult to blind because patients enrolled in these types of studies tend to change their behavior towards compliance (Hawthorne effect).[14] Furthermore, the exact processes by which allergen exposure can exacerbate allergic disease must be understood fully and definitively before developing and testing the effectiveness of interventions.[10]

Despite the lack of good quality studies, avoidance of documented airborne allergen triggers and indoor and outdoor air pollutants is still recommended in patients with allergic rhinitis. These strategies have a great potential in the reduction in allergic symptoms and medication needs with minimal effects on cost and psychosocial downsides.

References

1. Custovic A. Allergen control in the prevention and management of allergic disease. In: Adkinson NF, et al, eds. Middleton's Allergy: Principles and Practice, 7th ed. Elsevier Inc.; 2009. pp. 1447-1458.

2. Gentile DA, Skoner DP. Allergic Rhinitis. In: Leung DYM, et al, eds. Pediatric Allergy: Principles and Practice, 2nd ed. Elsevier Inc.; 2010. pp. 291-300.
3. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63 Suppl 86:8-160.
4. Halken S. Prevention of allergic disease in childhood: clinical and epidemiological aspects of primary and secondary allergy prevention. Pediatr Allergy Immunol. 2004; 15 Suppl16:9-32.
5. Estrella PS, Recto MT, Castor MA, et al. Sensitization patterns to aeroallergens and food allergens among pediatric patients with common allergic diseases. 2013. Unpublished.
6. Brozek JL, Bousquet J, Baena-Cagnani CE, et al. Allergic rhinitis and its impact on asthma (ARIA) guidelines: 2010 revision. J Allergy Clin Immunol. 2010; 126(3):466-76.
7. Nurmatov U, van Schayck CP, Hurwitz B, Sheikh A. House dust mite avoidance measures for perennial allergic rhinitis: an updated Cochrane systematic review. Allergy. 2012; 67(2):158-65.
8. Van Schayck OC, Maas T, Kaper J, Knottnerus AJ, Sheikh A. Is there any role for allergen avoidance in the primary prevention of childhood asthma? J Allergy Clin Immunol. 2007; 119(6):1323-8.
9. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2 Suppl):S1-84.
10. Tovey ER, Marks GB. It's time to rethink mite allergen avoidance. J Allergy Clin Immunol. 2011; 128(4):723-7.
11. Leung TF, Ko FW, Wong GW. Roles of pollution in the prevalence and exacerbations of allergic diseases in Asia. J Allergy Clin Immunol. 2012; 129(1):42-7.
12. Peden D, Reed CE. Environmental and occupational allergies. J Allergy Clin Immunol. 2010; 125(2 Suppl 2):S150-160.
13. Platts-Mills TA. Allergen avoidance in the treatment of asthma: problems with the meta-analyses. J Allergy Clin Immunol. 2008; 122(4):694-6.
14. Platts-Mills TA. Allergen avoidance. J Allergy Clin Immunol. 2004; 113(3):388-91.

Table 3. Effectiveness of avoidance measures in rhinitis and asthma for certain indoor allergens.[3]

Measure	Evidence of Effect on Allergen Levels	Evidence of Clinical Benefit
House dust mites		
Encase bedding in impermeable covers	Some	None (adults): Evidence A Some (children): Evidence B
Wash bedding in a hot cycle (55-60C)	Some	None: Evidence B
Replace carpets with hard flooring	Some	None: Evidence A
Acaricides and/or tannic acid	Weak	None: Evidence A
Minimize objects that accumulate dust	None	None: Evidence B
Use vacuum cleaners with integral HEPA filter and double-thickness bags	Weak	None: Evidence B
Remove, hot wash or freeze soft toys	None	None: evidence B
Pets		
Remove cat/dog from the home	Weak	None: evidence B
Keep pet from main living areas/bedrooms	Weak	None: evidence B
Use HEPA-filter air cleaners	Some	None: evidence B
Wash pet	Weak	None: evidence B
Replace carpets with hard flooring	None	None: Evidence B
Use vacuum cleaners with integral HEPA filter	None	None: evidence B
Set of allergen control measures	Some	Some: Evidence B

*derived from ARIA 2008 guidelines using SIGN levels of evidence (appendix A)

Box 12.2 Pharmacologic Treatment of Allergic Rhinitis

Pharmacotherapy plays a crucial role in symptom control of patients with allergic rhinitis.[1]
Strong Recommendation, Grade A evidence

In deciding on the proper medication(s) for patients with allergic rhinitis, it is important to first consider various patient factors such as (1) most prominent symptoms (2) presence of co-morbidities (3) severity and control of symptoms (4) age and preference and (5) safety, efficacy, and cost-effectiveness of the different drugs to be prescribed.[2]

Treatment options, either used singly or in combination, include oral and intranasal antihistamines, leukotriene receptor antagonists, oral and intranasal corticosteroids, oral and topical decongestants, anticholinergics, anti-IgE therapy (omalizumab) and saline solution.

Oral Antihistamines

Oral H1-antihistamines, are recommended for use as first line of treatment among patients with mild or moderately severe allergic rhinitis, even among children.[1, 2, 3,4] ***Among them, the newer generation of antihistamines are strongly preferred because of less side effects on cognition and sedation.***[2]

Antihistamines are the mainstay of treatment in allergic disease and can be used for both intermittent and persistent symptoms. They are important in reducing the rhinorrhea, sneezing and itching in allergic rhinitis but have little relief in those with nasal congestion. They exert systemic effects and are helpful as well in reducing ocular symptoms in those who have allergic conjunctivitis. Although oral antihistamines are effective on a need basis, they work best when given continuously.[5]

Oral H1-antihistamines are divided into 2 groups: the older or first generation antihistamines (chlorpheniramine, diphenhydramine, hydroxyzine) and the newer or second generation antihistamines (cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine, ebastine, bilastine).

First generation antihistamines have a much greater chance of causing sedation, impairment of performance and anticholinergic effects (e.g. dry mouth, urinary retention). These anticholinergic effects may actually be responsible for the better control of rhinorrhea compared to using second generation antihistamines.[6,7] The first generation antihistamines currently have limited use despite being effective in relieving allergic rhinitis symptoms because of their sedating effects and negative impact on cognition. Their propensity for causing sedation and impairment of cognition is due to their ability to cross the blood brain barrier and block histamine in the central nervous system.[4,8] They are, therefore, not routinely recommended for use in the treatment of allergic rhinitis.[9,10]

On the other hand, second generation antihistamines do not cross the blood brain barrier and are associated with lesser or even no risks for the aforementioned adverse effects.[9] The second generation antihistamines are non-sedating and are recommended for use over the older antihistamines. They are more specific for H1-receptors with less penetration of the blood brain barrier, accounting for their increased safety and less impairment of the central nervous system.[4,8] They have been found to have an anti-inflammatory effect aside from their ability to strongly antagonize histamine receptors, allowing them to be equally effective in reducing symptoms of itching, sneezing, watery rhinorrhea, conjunctivitis, and nasal congestion.[2,6,9,10]

In determining the safety of the currently used classes of H1-antihistamines, examination of their therapeutic index is essential. The therapeutic index of an antihistamine is defined by its benefit-to-risk ratio, which is also called the efficacy-to-safety ratio. This pertains to the range of doses and plasma concentrations that the drug can be given safely and effectively. Having a broad therapeutic index is essential to the safety of an antihistamine because some of these drugs when taken beyond the recommended dose may have the potential for dose-related CNS effects. The lower limit of the benefit-to-risk ratio is based on the drug's minimally effective dose, defined as the lowest dose or plasma concentration for which a beneficial clinical effect may be elicited. The upper limit is the highest dose that can be safely given without eliciting any of the adverse pharmacologic effects.

The first generation antihistamines have a narrower therapeutic index than the second generation antihistamines. Their ability to cross the blood brain barrier causes them to have the higher potential of having CNS adverse effects, limiting the range of doses that can be safely given. A broad therapeutic index should always be considered when giving antihistamines because of the potential of overcompliance by the patient, wherein they increase their dosage to achieve symptomatic relief. For antihistamines with a broad therapeutic index, specifically the second generation antihistamines, even when their recommended dose is exceeded, the patient is unlikely to develop any adverse effects.[11]

In patients with allergic rhinitis, second generation antihistamines are recommended over the first generation antihistamines because it places a higher value on its less adverse reactions regardless of the uncertain comparative efficacy between the two.[12-14] (Tables 4 and 5)

For those whose symptoms are not fully controlled by oral H1-antihistamines, and do not experience adverse reactions to oral decongestants, an alternative choice might be a combination of both. However, this should not be given for more than 10 days. It has also been suggested that research should be done to determine the efficacy and adverse effects in the local setting.

Bilastine

Bilastine is a new second generation antihistamine effective for the symptomatic treatment of allergic rhinoconjunctivitis. It has a very high and selective affinity for the H1 receptor. It is not metabolized in the hepatic or intestinal system, since it does not inhibit the CYP450 or CYP1A4 or CYP3A4 enzymes. Randomized controlled trials have noted comparable efficacy of bilastine with cetirizine and desloratidine.[15,16] The 20 mg tablet is given once a day 1 hour before or 2 hours after food intake. At 20 mg, it does not cause significant sedation and it has no demonstrable cardiotoxicity.[17]

Chlorpheniramine

Chlorpheniramine is a first generation antihistamine drug that is effective in relieving the symptoms of sneezing, nasal discharge, nasal congestion, and pruritus, but it also has the adverse effect of sedation. Comparative studies of chlorpheniramine and fexofenadine showed that both drugs were similar in efficacy in relieving symptoms of sneezing, nasal discharge, and nasal congestion. However, nasal pruritus, anosmia, and other physical signs of allergy were better relieved by chlopheniramine. Its use is limited, however, by its adverse effects, most notably drowsiness, as compared to fexofenadine.[18]

Cetirizine

Cetirizine, an active metabolite of hydroxyzine, is a second generation antihistamine commonly used for the treatment of allergic rhinitis. Studies have shown that it has a rapid onset of action as compared to loratadine, with effects being noted 1.5 hours after its administration. Cetirizine is active immediately after it is absorbed, as compared to loratadine which needs to be metabolized in the liver before transforming into its active metabolite.[19] In comparison to the other second generation antihistamines, such as loratadine, cetirizine has the potential of causing sedation with its daily dosage of 10 mg. It can be safely given to pregnant women but dosage adjustment is needed when being given to patients with hepatic or renal impairment.[20]

Desloratadine

Desloratadine is a second generation antihistamine with a very high affinity for H1 receptors. It is different from the other antihistamines because of its ability to avoid interactions with drugs that inhibit the cytochrome P-450 or P-glycoprotein transport system, avoiding potential adverse effects. It has been shown to have no dose-related adverse effects, with headache as the most common side effect. It is effective at relieving symptoms of allergic rhinitis with its once daily 5 mg dosage with effects lasting for 24 hours.[21] Desloratadine has also been shown to have a higher patient satisfaction rate because it is able to significantly reduce the

frequency of nighttime awakenings due to allergic symptoms, as compared to loratadine and fexofenadine.[22]

Diphenhydramine

Diphenhydramine is a first generation antihistamine with sedative effects that is still commonly used for the treatment of emergent cases of acute allergic reactions.[11]

Ebastine

Ebastine is a second generation antihistamine with a daily dose of 10 mg once daily, but has also been shown to have increased efficacy at a higher dose of 20 mg once daily for patients with severe allergic rhinitis as compared to other antihistamines such as cetirizine. It is effective in relieving symptoms of nasal discharge, sneezing, and pruritus, but with less ability to relieve nasal congestion. Studies using 10 mg and 20 mg dosage of ebastine for a 12-week period showed no dose-related adverse effects.[23]

Fexofenadine

Fexofenadine is a second generation antihistamine with a wide therapeutic index. Studies have shown that a daily dose of 20 mg twice daily is considered as its minimally effective dose, and even when exceeding the recommended daily dose of 120 mg to 180 mg, no adverse CNS effects were noted.[11,18] Studies have shown that despite dosages being increased to as high as 360 mg/day, no dose related increase in sedation or decrease in cognition was noted.[20] Fexofenadine is rapidly absorbed with effects noted 1-2 hours after intake and remains apparent even up to 24 hours. It is effective in reducing symptoms of sneezing, nasal discharge, and nasal congestion comparable to chlorpheniramine, but has less ability to effectively relieve anosmia and nasal pruritis.[9]

Levocetirizine

Levocetirizine is the active enantiomer of cetirizine and is an effective second generation antihistamine. It has both the ability to block antihistamine as well as have anti-inflammatory effects. This means that aside from relieving symptoms of nasal discharge, sneezing, and pruritus, levocetirizine has the ability to reduce symptoms of nasal congestion. The recommended dose of 5 mg once daily has been found to be effective and well-tolerated. Studies comparing levocetirizine 10 mg monotherapy with montelukast 10 mg monotherapy showed that relief of nasal symptoms was more effective with levocetirizine alone than montelukast, but combining the two provided a more superior control of symptoms.[24]

Loratadine

Loratadine is a second generation antihistamine and is a selective antagonist of peripheral H1-receptors commonly used for the treatment of allergic rhinitis because of its minimal side effects on the CNS. It is effective in improving symptoms of nasal discharge, blockage, pruritus, and sneezing. It is also capable of relieving ocular symptoms of allergic rhinitis such as tearing, pruritis and redness.[25,26] However, in comparison to cetirizine, it has a slower onset of action. It is transformed to its active metabolite in the liver, as compared to cetirizine which is active immediately after its absorption.[19] Despite this, loratadine is an effective and safe treatment for allergic rhinitis, with a dose of 10 mg once daily producing relief among patients[26] and it can be given even to pregnant women.[20]

References

1. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63 Suppl 86:8-160.
2. Brozek JB, Bousquet J, Baena-Cagnani CE, Bonini S, et al. Allergic rhinitis and its impact on asthma (ARIA) guidelines: 2010 revision. J Allergy Clin Immunol. 2010; 126(3):467-76.
3. Potter PC. Effectiveness and safety of new generation antihistamines in allergenic rhinitis and urticaria. SA Fam Pract. 2004; 47(1):24-8.
4. Ng KH, Chong D, Wong CK, et al. Central nervous system side effects of first- and second-generation antihistamines in school children with perennial allergic rhinitis: A randomized, double-blind, placebo-controlled comparative study. Pediatrics. 2004; 113(2):e116-21.
5. Okano M. Mechanisms and clinical implications of glucocorticosteroids in the treatment of allergic rhinitis. Clin Exp Immunol. 2009; 158(2):164-73.
6. Sur DK, Scandale S. Treatment of allergic rhinitis. Am Fam Physician. 2010; 81(12):1440-6.
7. Mosges R, Klimek L. Today's allergic rhinitis patients are different: New factors that may play a role. Allergy. 2007; 62(9):969-75.
8. Simons FE. Advances in H1-antihistamines. N Engl J Med. 2004; 351(21):2203-17.
9. Small P, Kim H. Allergic rhinitis. Allergy Asthma Clin Immunol. 2011; 7 Suppl 1:S3.
10. Van-Cauwenberge P, Bachert C, Passalacqua G, et al. Consensus statement on the treatment of allergic rhinitis. Allergy. 2000; 55(2):116-34.
11. Simons FE. The value of a broad therapeutic index for antihistamines. Adv Studies Med. 2002; 2(24):872-6.
12. Ciprandi G, Passalacqua G, Mincarini M, Ricca V, Canonica GW. Continuous versus on demand treatment with cetirizine for allergic rhinitis. Ann Allergy Asthma Immunol. 1997; 79(6):507-11.
13. Hindmarch I. Psychometric aspects of antihistamines. Allergy. 1995; 50(24 Suppl):48-54.
14. Shamsi Z, Hindmarch I. Sedation and antihistamines: A review of inter-drug differences using proportional impairment ratios. Hum Psychopharmacol. 2000; 15(S1):S3-S30.
15. Bachert C, Kuna P, Sanquer F, et al. Comparison of the efficacy and safety of bilastine 20 mg vs. desloratadine 5 mg in seasonal allergic rhinitis patients. Allergy. 2009:64(1):58-65.
16. Kuna P, Bachert C, Nowacki Z, et al. Efficacy and safety of bilastine 20 mg compared with cetirizine 10 mg and placebo for the symptomatic treatment of seasonal allergic rhinitis: a randomized, double-blind, parallel-group study. Clin Exp Allergy. 2009:39(9):1338-47.
17. Church MK. Safety and efficacy of bilastine: A new H1-antihistamine for the treatment of allergic rhinoconjunctivitis and urticaria. Expert Opin Drug Saf. 2011; 10(5):779-93.
18. Ramesh L. A comparative study of fexofenadine with chlorpheniramine maleate and betamethasone in allergic rhinitis. Int J Pharm Bio Sci. 2013; 4(1):128-34.
19. Frossard N, Walsh GM. Comparing the H1 profile of second-generation antihistamines. Allergy. 2000; 55 Suppl 60:40-5.
20. Banerji A, Long AA, Camargo CA Jr. Diphenhydramine versus nonsedating antihistamines for acute allergic reactions: A literature review. Allergy Asthma Proc. 2007; 28(4):418-26.
21. Salmun LM, Lorber R. 24-hour efficacy of once-daily desloratadine therapy in patients with seasonal allergic rhinitis. BMC Fam Pract. 2002; 3:14.
22. Glass D, Harper AS. Assessing satisfaction with desloratadine and fexofenadine in allergy patients who report dissatisfaction with loratadine. BMC Fam Pract. 2003; 4:10.

23. Bousquet J, Gaudano EM, Palma Carlos AG, Staudinger H. A 12-week placebo-controlled study of the efficacy and safety of ebastine, 10 and 20 mg once daily, in the treatment of perennial allergic rhinitis. Allergy. 1999; 54(6):562-8.
24. Mullol J, Bachert C, Bousquet J. Management of persistent allergic rhinitis: Evidence-based treatment with levocetirizine. Ther Clin Risk Manag. 2005; 1(4):265-71.
25. Hindmarch I, Shamsi Z, Stanley N, Fairweather DB. A double-blind, placebo-controlled investigation of the effects of fexofenadine, loratadine and promethazine on cognitive and psychomotor function. Br J Clin Pharmacol. 1999; 48(2):200–6.
26. Katelaris C. Comparative effects of loratadine and azatadine in the treatment of seasonal allergic rhinitis. Asian Pac J Allergy Immunol. 1990; 8(2):103-7.

Table 4. Usual Dosage of Oral H1-Antihistamines[8]

H1-antihistamine	Onset and Duration of Action (hours)	Usual Adult Dosage
First Generation Drugs		
Chlopheniramine	3, 24	4mg/tab TID or QID 12mg/tab (sustained release formula) BID
Diphenhydramine	2, 12	25-50mg/tab TID or QID or ODHS
Hydroxyzine	2, 24	25-50mg/tab TID or ODHS
Second Generation Drugs		
Bilastine	1,24	20 mg/tab OD
Cetirizine	1, 24	5-10mg/tab OD
Desloratadine	2, 24	5mg/tab OD
Ebastine	2, 24	10-20mg/tab OD
Fexofenadine	2, 24	60mg/tab BID or 120 or 180mg/tab OD
Levocetirizine	1, 24	5mg/tab OD
Loratadine	2, 24	10mg/tab OD

Intranasal Antihistamines

***The oral second generation H1-antihistamines are preferred over intranasal antihistamines for patients with intermittent or persistent allergic rhinitis.*[1]**

Intranasal H1-antihistamines, which include azelastine and olopatadine, can be used as a first line of treatment for patients with seasonal allergic rhinitis.[1,2] These topical antihistamines are able to more effectively reduce nasal symptoms associated with allergic rhinitis, such as nasal congestion and obstruction. They have a faster onset of action than oral antihistamines (15 minutes for azelastine versus 150 minutes for desloratadine) and less risk of systemic side effects because of the more direct delivery of the medication to the tissues.[2,3,4]

Despite having a more rapid onset of action, they are not recommended for use over oral antihistamines for patients with more severe or persistent allergic rhinitis because of their uncertain efficacy, bitter taste, and the need to administer them several times a day which can affect the patient's compliance to the treatment.[1,2,4] They have been found to cause sedation. For patients with symptoms of sneezing, rhinorrhea, itchiness, and eye redness, oral antihistamines are preferred because of their ability to relieve these symptoms as compared to the intranasal preparations.[4]

For those patients with different values and preferences, or those who may have adverse reactions to newer generation oral H1-antihistamines, intranasal antihistamines may be an alternative choice. (Table 5)

Azelastine

Azelastine nasal spray is a second-generation antihistamine, approved for the treatment of allergic rhinitis, both in adults and children. Azelastine 0.15% nasal spray at 2 sprays per nostril once or twice daily significantly improved the nasal symptoms associated with seasonal allergic rhinitis with an onset of action within 15 to 30 minutes.[5,6,7] Bitter taste was the most common adverse event with use of azelastine.[6,7]

Olopatadine

Olopatadine is an antihistamine with selective H(1)-receptor antagonist and mast cell stabilizer activity.[8,9] It is available in oral, intranasal and ocular preparations.[8] Olopatadine, 0.6% nasal spray is approved for the relief of seasonal allergic rhinitis symptoms in children 6 years of age and older.[1,2]

In a study done by Kaliner et al. comparing olopatadine 0.6% nasal spray versus fluticasone propionate 50 mcg in the treatment of seasonal allergic rhinitis, both treatments were safe and well tolerated. Olopatadine and fluticasone nasal sprays both reduced nasal and ocular seasonal allergic rhinitis symptoms with no significant between-treatment differences except for a faster and greater onset of action with olopatadine.[10,11]

References

1. Meltzer EO, Blaiss M, Fairchild CJ. Comprehensive report of olopatadine 0.6% nasal spray as treatment for children with seasonal allergic rhinitis. Allergy Asthma Proc. 2011; 32(3):213-20.
2. Shah SR, Nayak A, Ratner P, Roland P, Michael Wall G. Effects of olopatadine hydrochloride nasal spray 0.6% in the treatment of seasonal allergic rhinitis: A phase III, multicenter, randomized, double-blind, active-and placebo-controlled study in adolescents and adults. Clin Ther. 2009; 31(1):99-107.
3. Simons FE, Simons KJ. Histamine and H_1-antihistamines: Celebrating a century of progress. J Allergy Clin Immunol. 2011; 128(6):1139-50.
4. Chipps BE, Harder JM. Antihistamine treatment for allergic rhinitis: Different routes, different outcomes. Allergy Asthma Proc. 2009; 30(6):589-94.
5. Horak F, Zieglmayer UP. Azelastine nasal spray for the treatment of allergic and nonallergic rhinitis. Expert Rev Clin Immunol. 2009; 5(6):659-69.
6. Shah S, Berger W, Lumry W, La Force C, Wheeler W, Sacks H. Efficacy and safety of azelastine 0.15% nasal spray and azelastine 0.10% nasal spray in patients with seasonal allergic rhinitis. Allergy Asthma Proc. 2009; 30(6):628-33.
7. van Bavel J, Howland WC, Amar NJ, Wheeler W, Sacks H. Efficacy and safety of azelastine 0.15% nasal spray administered once daily in subjects with seasonal allergic rhinitis. Allergy Asthma Proc. 2009; 30(5):512-8.
8. Nickels AS, Dimov V, Wolf R. Pharmacokinetic evaluation of olopatadine for the treatment of allergic rhinitis and conjunctivitis. Expert Opin Drug Metab Toxicol. 2011; 7(12):1593-9.
9. Roland PS, Ryan MW, Wall GM. Olopatadine nasal spray for the treatment of seasonal allergic rhinitis in patients aged 6 years and older. Expert Opin Pharmacother. 2010; 11(9):1559-67.
10. Katial RK, Salapatek AM, Patel P. Establishing the onset of action of intranasal corticosteroids: is there an ideal study design? Allergy Asthma Proc. 2009; 30(6): 595-604.
11. Kaliner MA, Storms W, Tilles S, et al. Comparison of olopatadine 0.6% nasal spray versus fluticasone propionate 50 microg in the treatment of seasonal allergic rhinitis. Allergy Asthma Proc. 2009; 30(3):255-62.

Table 5. Oral and Intranasal Antihistamines[12]

Generic drug	Dosage form	Age limit	Adult dose	Pediatric dose
Second generation oral antihistamine				
Azelastine	0.1% nasal spray	5 years	1-2 sprays per nostril bid	5-11 years: 1 spray per nostril bid
Bilastine	20 mg tablet	12 years	1 tablet od	
Cetirizine	10 mg tablet 10mg/ml drops 5 mg/5ml syrup 2.5 mg/10 ml drops 1 mg/ml solution	6 months	5-10 mg qd	6-11mos: 2.5 mg qd 12-23 mos: 2.5 mg qd or bid 2-5 years: 2.5 or 5 mg qd or 2.5 mg bid 6-11 years: 5-10 mg qd
Desloratadine	5 mg tablet 2.5 mg/5 ml syrup	6 months	5 mg qd	6-23 mos: 1 mg qd 2-5 years: 1.25 mg qd 6-11 years: 2.5 mg qd
Fexofenadine	120 mg tablet 180 mg tablet	2 years	120 mg qd	6-23 mos: 15 mg bid 2-11 years: 30 mg bid
Levocetirizine	5 mg tablet 2.5 mg/5ml syrup	6 months	5 mg qd	6 mos–5 years: 1.25 mg qd 6-11 years: 2.5 mg qd
Loratadine	10 mg tablet 5 mg/5 ml syrup	2 years	10 mg qd	2-5 years: 5 mg qd ≥ 6 years: 10 mg qd
First generation oral antihistamine				
Chlorpheniramine	4 mg tablet 0.5 mg/ml drops 1 mg/5ml syrup		4 mg every 4-6 hours, maximum of 24 mg/day	*Drops:* 1-3 mos: 0.25 ml qid 4-6 mos: 0.5 ml qid 7-12 mos: 0.75 ml qid 1-2 years: 1 ml qid *Syrup:* 2-6 years: 2.5 ml qid 7-12 years: 5 ml qid ≥ 12 years 10ml qid
Diphenhydramine	25 mg tablet 50 mg tablet 12.5mg/5ml syrup	2 years	25 mg bid-qid	1 mg/kg/dose tid-qid
Hydroxyzine	10 mg tablet 25 mg tablet 2mg/ml syrup	all ages	25 mg bid-qid	1-2 mg/kg/day to be given in 2-3 divided doses

Intranasal Corticosteroids

Intranasal corticosteroids are considered the most effective pharmaceutical treatment for allergic rhinitis and are recommended as first-line therapy for moderate-to-severe symptoms.

Intranasal corticosteroids are the single, most effective treatment for allergic rhinitis. Topical steroids are able to control and reduce the four main symptoms of allergic rhinitis: nasal congestion, sneezing, nasal itchiness and rhinorrhea.

For patients with severe symptoms of allergic rhinitis, intranasal corticosteroids can be given alone or in combination with oral antihistamines.[1] Intranasal corticosteroids (fluticasone propionate, mometasone furoate and triamcinolone) have an anti-inflammatory effect on the nasal mucosa[2] without the adverse systemic effects. In comparison to the oral corticosteroids, they are not readily absorbed into the systemic circulation and are metabolized rapidly after its absorption into the nasal mucosa. This gives them the advantage of avoiding systemic effects despite being used for prolonged periods of time, even for a year.[3] They have an added beneficial effect of reducing lower airway symptoms for asthmatic patients with allergic rhinitis.[1]

Intranasal corticosteroids may be given as initial treatment even without previously giving a trial of antihistamines with or without decongestants. They should also be given before starting oral corticosteroids.[4]

If administered in children, they should be given at the lowest effective dose. Giving on a need basis (55-62% of days) has been effective in patients with seasonal allergic rhinitis but may not be as effective as continuous use.[5,6]

For elderly patients with allergic rhinitis, intranasal corticosteroids have the most favorable safety and efficacy profiles.[7]

Local side effects may include epistaxis, crusting and drying without nasal mucosal atrophy. Patients should be advised to spray away from the nasal septum. Other local side effects can be avoided with proper technique.[8,9]

Intranasal corticosteroids are the drug of choice in those with seasonal as well as persistent allergic rhinitis in both adults and children. (Table 6) These are based on studies supporting their higher efficacy. They are more efficacious than oral H1-antihistamines, intranasal antihistamines, oral leukotriene receptor antagonists as well as oral leukotriene receptor antagonists plus oral H1 antihistamines. However, if cost, route of administration and adverse effects are an issue, alternative choices may be looked into.[10-16]

Budesonide

Budesonide is an intranasal corticosteroid with documented use in allergic rhinitis. As a corticosteroid it has low systemic bioavailability, quickly metabolized to less active metabolites with minimal systemic effects. In a study comparing budesonide and formoterol, it was found that budesonide given in 250 mcg once daily demonstrates greater efficacy compared to formeterol 200 mcg once daily in relieving nasal congestion as well as having a faster onset of action.[1] This greater efficacy may be attributed to the long duration of anti-inflammatory effects secondary to its bioavailability intracellularly in fatty acids.

Ciclesonide

Ciclesonide is the newest approved intranasal corticosteroid available in the market. It does not contain benzylalkonium chloride or phenylethyl alcohol, excipients that have been associated with reduced mucociliary transport, and unpleasant sensory perceptions. It is formulated in a hypotonic suspension that has been shown to optimize intranasal absorption and it has a lower volume of spray and indicated for seasonal and perennial allergic rhinitis. Efficacy can be achieved with a dosing of 200 μg per day. Additionally, its onset of action is as early as one hour after administration. Ciclesonide nasal spray has also been shown to have an acceptable safety profile in patients with allergic rhinitis as young as 2 years of age.[2]

Fluticasone propionate

Fluticasone propionate is an established intranasal steroid for the treatment of allergic rhinitis. Its favorable pharmacological profile, combining high local efficacy with low systemic bioavailability (<1%), has established fluticasone propionate as an effective intervention.[18]

Treatment with intranasal fluticasone propionate 200 μg once daily significantly improved not only nasal symptoms, daytime sleepiness but also cognitive performance, as measured by the test of variables of attention (TOVA) in patients with seasonal allergic rhinitis.[19]

It can also be used in combination with an oral antihistamine particularly fexofenadine (100 μg twice daily as an initial drug or 60 mg twice daily as an additional drug) which can improve outcomes for nasal symptoms. [20]

Fluticasone furoate

Fluticasone furoate is fluticasone with furoate as the side-chain. Based on a systematic review by Rodrigo et al. in 2010, the administration of fluticasone furoate 110 μg once daily significantly improved nasal symptoms (congestion, rhinorrhea, sneezing, and itching) in adolescents and adults with seasonal allergic rhinitis and perennial allergic rhinitis, compared with placebo.[21] A striking finding was the consistent efficacy of intranasal fluticasone furoate in reducing ocular symptoms (itching or burning, tearing or watering, and redness) in both seasonal and perennial allergic rhinitis patients.[21] Meltzer et al. found that in patients aged 6 to 11 years, intranasal fluticasone furoate 110 μg once daily significantly improved reflective and instantaneous total nasal symptom scores (rTNSS and iTNSS) compared with placebo.[22]

Maspero et al. also reported that intranasal fluticasone furoate at doses of 110 or 55 μg once daily in children 2 to 11 years was beneficial for both rTNSS and iTNSS scores compared with placebo.[23]

Mometasone furoate

Mometasone furoate is an intranasal corticosteroid that has a systemic bioavailability of <0.1%.[8] With a dosing of 200 μg per day, it effectively treats itchy ear and palate in individuals with seasonal allergic rhinitis.[24,25]

In a study by Yamada et al, a significant reduction of the sleepiness scale was also observed in the MFNS group with high sleep disturbance. A significant decrease of nasal nitric oxide was found in the MFNS group, especially among patients with severe nasal symptoms. This prospective study indicated that mometasone furoate significantly improves nasal symptoms, quality of life, sleep quality, and upper airway condition in Japanese subjects with perennial allergic rhinitis.[26]

Triamcinolone

Triamcinolone is a synthetic glucocoticoid in aqueous nasal spray form. It is poorly water-soluble and non polar. This formulation makes the spray a highly viscous compound as it enters the nasal mucosa. In a study done in Turkey, it was proven that Triamcinolone effectively reduces

nasal congestion in patients with seasonal allergic rhinitis and bronchial hyperresponsiveness. The outcome measures were subjective reports of the participants and acoustic rhinometry as the objective measure.[28]

References

1. Day J, Carrillo T. Comparison of the efficacy of budesonide and fluticasone proprionate aqueous nasal spray for once daily treatment of perennial allergic rhinitis. J Allergy Clin Immunol 1998; 102(6 Pt 1):902-8.
2. Small P, Kim H. Allergic rhinitis. Allergy, Asthma Clin Immunol. 2011; 7 Suppl 1:S3.
3. van Cauwenberge P[1], Bachert C, Passalacqua G, et al. Consensus statement on the treatment of allergic rhinitis. European Academy of Allergology and Clinical Immunology. Allergy. 2000; 55(2):116-34.
4. Okano M. Mechanisms and clinical implications of glucocorticosteroids in the treatment of allergic rhinitis. Clin Exp Immunol. 2009; 158(2):164-73.
5. Meltzer EO. The role of nasal corticosteroids in the treatment of rhinitis. Immunol Allergy Clin North Am. 2011; 31(3):545-60.
6. Benitez HH, Arvizu VM, Gutiérrez DJ, et al. Nasal budesonide plus zafirlukast vs nasal budesonide plus loratadine-pseudoephedrine for controlling the symptoms of rhinitis and asthma. Rev Alerg Mex. 2005; 52(2):90-5.
7. Neffen H, Wingertzahn MA. Ciclesonide, a hypotonic intranasal corticosteroid. Allergy Asthma Proc. 2010; 31 Suppl 1: S29-37.
8. Slavin RG. Special considerations in treatment of allergic rhinitis in the elderly: role of intranasal corticosteroids. Allergy Asthma Proc. 2010; 31(3):179-84.
9. Allergic Rhinitis. In: Leung DYM, Sampson HA, Geha R, eds. Pediatric Allergy: Principles and Practice, 2nd ed. Saunders; 2010. pp. 291-300.
10. Adkinson NF, et al. Middleton's Allergy: Principles and Practice, 7th ed. Allergic and Non-Allergic Rhinitis, 2009.
11. Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: A systematic review of randomized controlled trials. BMJ. 1998; 317(7173):1624-9.
12. Nathan RA, Yancey SW, Waitkus-Edwards K, et al. Fluticasone propionate nasal spray is superior to montelukast for allergic rhinitis while neither affects overall asthma control. Chest. 2005; 128(4):1910-20.
13. Jen A, Baroody F, de Tineo M, Haney L, Blair C, Naclerio R. As-needed use of fluticasone propionate nasal spray reduces symptoms of seasonal allergic rhinitis. J Allergy Clin Immunol. 2000; 105(4):732-8.
14. Dykewicz MS, Kaiser HB, Nathan RA, et al. Fluticasone propionate aqueous nasal spray improves nasal symptoms of seasonal allergic rhinitis when used as needed (prn). Ann Allergy Asthma Immunol. 2003; 91(1):44-8.
15. Di Lorenzo G, Pacor ML, Pellitteri ME, et al. Randomized placebo-controlled trial comparing fluticasone aqueous nasal spray in mono-therapy, fluticasone plus cetirizine, fluticasone plus montelukast and cetirizine plus montelukast for seasonal allergic rhinitis. Clin Exp Allergy. 2004; 34(2):259–67.
16. Pullerits T, Praks L, Ristioja V, Lötvall J. Comparison of a nasal glucocorticoid, antileukotriene, and a combination of antileukotriene and antihistamine in the treatment of seasonal allergic rhinitis. J Allergy Clin Immunol. 2002; 109(6):949-55.
17. Yanez A, Rodrigo GJ. Intranasal corticosteroids versus topical H1 receptor antagonists for the treatment of allergic rhinitis: A systematic review with meta-analysis. Ann Allergy Asthma Immunol. 2002; 89(5):479-84.
18. Kariyawasam HH, Scadding GK. Seasonal allergic rhinitis: fluticasone propionate and fluticasone furoate therapy evaluated. J Asthma Allergy. 2010; 21(3):19-28.
19. Mansfield LE, Posey CR. Daytime sleepiness and cognitive performance improve in seasonal allergic rhinitis treated with intranasal fluticosone propionate. Allergy Asthma Proc. 2007; 28: 226–229.
20. Takahashi G, Matsuzaki Z, Okamoto A, et al. A randomized control trail of stepwise treatment with fluticasone propionate nasal spray and fexofenadine hydrochloride tablet for seasonal allergic rhinitis. Allergol Int. 2012; 61(1):155-62.
21. Rodrigo GJ, Neffen H. Efficacy of fluticasone furoate nasal spray vs. placebo for the treatment of ocular and nasal symptoms of allergic rhinitis: A systematic review. Clin Exp Allergy. 2011; 41(2):160-70.
22. Meltzer EO, Lee J, Tripathy I, Lim J, Ellsworth A, Philpot E. Efficacy and safety of once-daily fluticasone furoate nasal spray in children with seasonal allergic rhinitis treated for 2 weeks. Pediatr Allergy Immunol. 2009; 20(3):279-86.
23. Maspero JF, Rosenblut A, Finn A Jr, Lim J, Wu W, Philpot E. Safety and efficacy of fluticasone furoate in pediatric patients with perennial allergic rhinitis. Otolaryngol Head Neck Surg. 2008; 138(1):30-7.
24. Bernstein DI, Teper A, Gopalan G, Gates D. Effects of intranasal mometasone furoate on itchy ear and palate in patients with seasonal allergic rhinitis. Ann Allergy Asthma Immunol. 2012; 108(5):359-62.
25. Clement P, Gates D. Symptom suppression in subjects with perennial allergic rhinitis treated with mometasone furoate nasal spray. Int Arch Allergy Immunol. 2012; 157(4):387-90.
26. Yamada T, Yamamoto H, Kubo S, et al. Efficacy of mometasone furoate nasal spray for nasal symptoms, quality of life, rhinitis disturbed sleep, and nasal nitric oxide in patients with perennial allergic rhinitis. Allergy Asthma Proc. 2012; 33(2):e9-16.
27. www.MIMS.com/Philippines [accessed 9 March 2014]
28. Oztürk F, Türktaş I , Asal K , Ileri F , Münevver Pinar N. Effect of intranasal triamcinolone acetonide on bronchial hyperresponsiveness in children with seasonal allergic rhinitis and comparison of perceptional nasal obstruction with acoustic rhinometric assessment. Int J Pediatr Otorhinolaryngol. 2004; 68(8):1007-15.

Table 6. Steroids Available in Local Market[26]

Intranasal Steroid	Usual Dosage
Fluticasone furoate	Adult & adolescent ≥12 yr : 1-2 sprays/nostril od Children 2-11 yr : 1-2 sprays/nostril od
Fluticasone proprionate	Adult including elderly & children >12 years: 2 sprays/nostril od Children 4-11 years:1 spray/nostril od or bid
Mometasone furoate monohydrate	Adult & adolescent: 2-4 sprays/nostril od Children 2-11 years: 1 spray/nostril od
Ciclesonide, 50mcg	Adult & children ≥6 years: 2 sprays/nostril od
Olopatadine HCl + fluticasone propionate	Adult, elderly & adolescent ≥12 years: 2 sprays/nostril bid Children 6-11 years: 1 spray/nostril bid

Oral Corticosteroids

Oral corticosteroids may be recommended for patients with severe or intractable symptoms of allergic rhinitis for a short duration.

Oral corticosteroids significantly reduce symptoms of sneezing, nasal congestion, rhinorrhea, and itchiness comparable to intranasal steroids.[1] However, given the known risks of systemic corticosteroids, use should be limited to severe and intractable cases and for a short duration.

They should not be considered as first line of treatment for allergic rhinitis. Oral corticosteroids should be avoided in children, pregnant women, and patients with known contraindications. [2,3]

Oral corticosteroids, given as a short course of 5-7 days, may be considered in those who have severe persistent

disease not responding to usual treatment or those presenting with nasal polyposis, not responding to intranasal corticosteroids. Parenteral corticosteroids, either given as a single dose or multiple/recurrent doses, are contraindicated because of the great potential for adverse reactions.

Methylprednisolone

A study done by Loeb in 1961 compared the therapeutic effects of methylprednisolone given by two different routes – oral and intramuscular in 36 patients with seasonal allergy. Participants receiving oral medications were given an initial dose of 20 to 24 mg on the first day, tapered by 4mg daily until a maintenance dose of 4 to 8 mg daily was reached. The other group received an initial dose of 80 mg of injectable methylprednisolone intramuscularly, and, subsequent doses at 40 and 80 mg were given as required when patients complained of recurrence of symptoms of a moderate or severe degree respectively. Improvement was measured based on the following criteria: (1) subjective improvement, (2) detailed history of symptoms, and (3) periodic examination of the eyes, nose, throat, and chest. Their results showed that both routes of administration of methylprednisolone generally have the same effect during the first week of treatment. However, in the subsequent weeks, a lower total dose of oral methylprednisolone was slightly more effective in reducing symptoms. In addition, the patients belonging to the intramuscular methylprednisolone group were observed to need other medications such as antihistamines in controlling allergic rhinitis symptoms probably because they would have to wait for the next office visit in order for them to receive additional injections. The advantages noted in using injectable steroid over oral form include: (1) no gastric side effects; (2) more uniform absorption of steroid with more efficient utilization of the active ingredient; and (3) complete control by the physician of the use of potent medications reducing the possibility of irregular intake or abuse of drugs.[5]

Prednisone

Acute episodes of allergic rhinitis are controlled by loading an initial dose of prednisone 10 mg given four times daily for the first 48 hours with subsequent daily maintenance dose of 10-20mg.[4]

Other oral steroids

Locally, betamethasone and dexamethasone oral tablets are available in most pharmacies. These are very potent anti-inflammatory agents with potencies up 25 times that of hydrocortisone. Although clinical studies have indicated efficacy in treating severe uncontrolled allergic rhinitis, these are not routinely recommended as first-line drugs for this condition due to their very long half-lives and greater tendency for adverse effects. [6]

Betamethasone is also available in combination with some oral antihistamines (e.g. loratadine, chlorpheniramine) but clinical trials evaluating their safety and efficacy in treating allergic rhinitis are lacking. One randomized, double-blind controlled study of 299 adult patients with severe allergic rhinitis given betamethasone-loratadine combination tablet for seven days noted the superiority of oral steroids in controlling nasal symptoms in allergic rhinitis ($p<0.013$); however, there was no significant difference of additional loratadine in a combination tablet with betamethasone.[7] In a prospective multicenter study, children aged 6 to12 years old with severe perennial allergic rhinitis were given betamethasone-loratadine oral suspension for 5 days. Significant reduction in nasal and ocular symptoms were noted with no adverse effects described. It was recommended in this study that combination treatment of loratadine with betamethasone in an oral solution was effective and safe as initial, short-term treatment for children with severe perennial allergic rhinitis.[8]

References

1. Karaki M, Akiyama K, Mori N. Efficacy of intranasal steroid spray (mometasone furoate) on treatment of patients with seasonal allergic rhinitis: Comparison with oral corticosteroids. Auris Nasus Larynx. 2013 Jun; 40(3): 277-81.
2. van Cauwenberge P, Van Hoecke H, Vandenbulcke L, Van Zele T, Bachert C. Glucocorticosteroids in allergic inflammation: clinical benefits in allergic rhinitis,rhinosinusitis, and otitis media. Immunol Allergy Clin North Am. 2005; 25(3):489-509.
3. Joos GF, Brusselle GG, Van Hoecke H, van Cauwenberge P, Bousquet J, Pauwels RA. Positioning of glucocorticosteroids in asthma and allergic rhinitis guidelines (versus other therapies).Immunol Allergy Clin North Am. 2005; 25(3):597-612.
4. Freedman SO. The treatment of allergic rhinitis. Can Med Assoc J. 1964; 91:602-5.
5. Loeb LJ. The use of methylprednisolone in seasonal allergy. Can Med Assoc J. 1961; 85:480-2.
6. Schimmer BP and Parker KL. Adrenocorticotropic Hormone: Adrenocortical steroids and their synthetic analogues; Inhibitors of the synthesis and actions of adrenocortical hormones in Goodman & Gilman's The Pharmacologic Basis of Therapeutics.10th edition. Hardman JG, Limbird LE (eds.)@2001 McGraw-Hill Medical Publishing Division.1655-1666.
7. Snyman JR, Potter PC, Groenewald M, Levin J; Claricort Study Group. Effect of betamethasone-loratadine combination therapy on severe exacerbations of allergic rhinitis: a randomized, controlled trial. Clin Drug Investig. 2004; 24(5):265-74.
8. De Morales TM, Sanchez F. Clinical efficacy and safety of a combined loratadine-betamethasone oral solution in the treatment of severe pediatric perennial allergic rhinitis. World Allergy Organ J. 2009; 2(4):49-53.

Leukotriene Receptor Antagonists

Oral leukotriene receptor antagonists (LTRA) alone or in combination with antihistamines, may be recommended for patients with allergic rhinitis.

Leukotriene receptor antagonists (LTRAs) are a group of drugs that block the effects of leukotrienes on cysteinyl

receptors known to correlate with the pathophysiology of allergic rhinitis, thereby reducing its symptoms. They are potent inflammatory mediators resulting from the enzymatic action of membrane phospholipids. Researches on LTRAs, particularly montelukast, whether as monotherapy or in combination with other drugs, have already been performed. Several studies have shown its efficacy for allergic rhinitis in terms of daytime nasal symptoms (including rhinorrhea, sneezing, itchiness, and congestion), nighttime nasal symptoms, and overall improvement in the quality of life.[1,2,3] However their effects are less predictable than intranasal corticosteroids or antihistamines. Combination with antihistamines however showed superior efficacy over monotherapy.[4,5,6,7,8] Safety profile of LTRA particularly montelukast has been shown to be comparable to placebo.[3,8] Utilization of LTRA in allergic rhinitis has been recommended in recent guidelines including ARIA. Since patients more often present with concomitant asthma, anti-leukotrienes are recommended for both of these conditions.[1] (Table 7)

References

1. Cingi C, Ozlugedik S. Effects of montelukast on quality of life in patients with persistent allergic rhinitis. Otolaryngol Head Neck Surg. 2010; 142(5):654-8.
2. Okubo K, Baba K. A double-blind non-inferiority clinical study of montelukast, a cysteinyl leukotriene receptor 1 antagonist, compared with pranlukast in patients with seasonal allergic rhinitis. Allergol Int. 2008; 57(4):383-90.
3. Okubo K, Baba K. Therapeutic effect of montelukast, a cysteinyl leukotriene receptor 1 antagonist, on Japanese patients with seasonal allergic rhinitis. Allergol Int. 2008; 57(3):247-55.
4. Lu S, Malice MP, Dass SB, Reiss TF. Clinical studies of combination montelukast and loratadine in patients with seasonal allergic rhinitis. J Asthma. 2009; 46(9):878-83.
5. Ho CY, Tan CT. Comparison of antileukotrienes and antihistamines in the treatment of allergic rhinitis. Am J Rhinol. 2007; 21(4):439-43.
6. Cingi C, Gunhan K, Gage-White L, Unlu H. Efficacy of leukotriene antagonists as concomitant therapy in allergic rhinitis. Laryngoscope. 2010; 120(9):1718-23.
7. Ciebiada M, Gorska-Ciebiada M, DuBuske LM, Gorski P. Montelukast with desloratadine or levocetirizine for the treatment of persistent allergic rhinitis. Ann Allergy Asthma Immunol. 2006; 97(5):664-71.
8. Gupta V, Matreja PS. Efficacy of montelukast and levocetirizine as treatment for allergic rhinitis. J Aller Ther. 2010; 1:103.

Oral Decongestants

Oral and intranasal decongestants may be recommended for allergic rhinitis with prominent nasal congestion. Intranasal decongestants should be used for a short duration due to the risk of developing rebound rhinitis.

Decongestants reduce nasal congestion by stimulating the alpha-adrenergic receptors in the nasal mucosa causing vasoconstriction of underlying blood vessels and decreased swelling and edema. Several studies on the use of oral decongestants have showed its efficacy in the improvement of nasal congestion in patients with allergic rhinitis but no effect on sneezing, itchiness, rhinorrhea, and non-nasal symptoms.[1,2,3] Oral decongestants, specifically phenylephrine, are recommended for patients presenting with nasal congestion. Moreover, combining with oral antihistamines showed superior results.[4,5,6] Side effects include loss of appetite, insomnia and irritability. An increase in blood pressure may occasionally be noted in those with controlled hypertension, so monitoring of blood pressureis advised.[2]

It has been recommended to give oral decongestants, if needed, for not more than 10 days, to avoid adverse reactions.

Intranasal decongestants are catecholamines utilized mainly for short-term (not longer than 5 days and preferably shorter) relief of nasal congestion, as long-term use may result in rebound rhinitis (rhinitis medicamentosa). Rebound rhinitis may occur as early as within the first three days of use or as late as more than a week after treatment; proper advice is definitely important.[1] Local adverse reactions may include burning, stinging and occasional bleeding. The addition of intranasal decongestant, such as oxymetazoline, to intranasal steroids produced greater nasal decongestion with faster onset of action and longer duration of effect.[7, 8]

References

1. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63 Suppl 86:8-160.
2. Horak F, Zieglmayer P, Zieglmayer R, et al. A placebo-controlled study of the nasal decongestant effect of phenylephrine and pseudoephedrine in the Vienna Challenge Chamber. Ann Allergy Asthma Immunol. 2009; 102(2):116-20.
3. Sherkat AA, Sardana N, Safaee S, Lehman EB, Craig TJ. The role of pseudoephedrine on daytime somnolence in patients suffering from perennial allergic rhinitis (PAR). Ann Allergy Asthma Immunol. 2011; 106(2):97-102.
4. Badorrek P, Dick M, Schauerte A, et al. A combination of cetirizine and pseudoephedrine has therapeutic benefits when compared to single drug treatment in allergic rhinitis. Int J Clin Pharmacol Ther. 2009; 47(2):71-7.
5. Anolik R. Desloratadine and pseudoephedrine combination therapy as a comprehensive treatment for allergic rhinitis and nasal congestion. Expert Opin Drug Metab Toxicol. 2009; 5(6):683-94.
6. Grubbe RE, Lumry WR, Anolik R. Efficacy and safety of desloratadine/ pseudoephedrine combination vs. its components in seasonal allergic rhinitis. J Investig Allergol Clin Immunol. 2009; 19(2):117-24.
7. Baroody FM, Brown D, Gavanescu L, DeTineo M, Naclerio RM. Oxymetazoline adds to the effectiveness of fluticasone furoate in the treatment of perennial allergic rhinitis. J Allergy Clin Immunol. 2011; 127(4):927-34.
8. Meltzer EO, Bernstein DI, Prenner BM, Berger WE, Shekar T, Teper AA. Mometasone furoate nasal spray plus oxymetazoline nasal spray: Short-term efficacy and safety in seasonal allergic rhinitis. Am J Rhinol Allergy. 2013; 27(2):102-8.

Table 7. Montelukast

Generic drug	Dosage form	Age limit	Adult dose	Pediatric dose
Montelukast	4 mg chewable tablet	6 months	10 mg od	6 months 5 years: 4 mg od
	5 mg chewable tablet			6 – 14 years : 5 mg od
	10 mg tablet			≥15 years: 10 mg od

Omalizumab

Omalizumab is a monoclonal antibody against IgE which binds to the constant region of the IgE molecule, blocking the interaction of the antibody with the mast cells and basophils. It reduces free IgE concentrations and is currently approved for treatment of severe persistent allergic asthma that is refractory to all other available treatment. [1]

It has not been approved for **routine** use in the treatment of allergic rhinitis over presently and currently approved therapy. This is because of the limited information on its improvement in selected patients and its high cost.

Reference

1. Chervinsky P, Casale T, Townley R, et al. Omalizumab, an anti-IgE antibody, in the treatment of adults and adolescents with perennial allergic rhinitis. Ann Allergy Asthma Immunol. 2003; 91(2):160-7.

Combination Drugs

Combination drugs are also available in the local market for the treatment of allergic rhinitis and they have different preparations (syrup, tablet, nasal spray). Examples are loratadine and betamethasone, cetirizine and phenylephrine, levocetirizine and montelukast, olopatadine and fluticasone propionate. Several studies demonstrating efficacy of these combination drugs have been done. However, there is a need for more supporting evidence regarding the role of combination drugs in the management of allergic rhinitis.

It is emphasized that oral steroids, whether as a single drug or as part of a combination drug, should be limited to short duration of use (5 to 7 days of therapy).

Snyman, et al demonstrated the benefit of a short course (5 to 7 days of treatment) of systemic low dosage corticosteroids with and without antihistamine therapy during acute severe exacerbations of allergic rhinitis. In their study, 299 patients diagnosed with severe allergic rhinitis were randomly allocated to receive (1) betamethasone 1.0mg, or (2) betamethasone 1.0 plus loratadine 10mg, or (3) betamethasone 0.5mg plus loratadine 10mg, or (4) loratadine 10mg alone; and then evaluated for improvement in disease severity based on: symptom score, nasal obstruction, patient and doctor perceptions of improvement. Significant reduction of relapse rate was noted in the treatment group which received the combination of betamethasone 1.0 plus loratadine 10mg. it was also noted that there was a significant difference in doctor and patient perceptions of improvement for all groups who received corticosteroids, compared to antihistamines alone.[1]

Lanier, et al. compared the efficacy of combined use of fluticasone plus olopatadine with fluticasone plus fexofenadine in alleviating signs and symptoms of allergic rhinoconjunctivitis. Eighty subjects were randomly assigned into 3 treatment groups—(1) fluticasone with olopatadine, (2) fluticasone with fexofenadine, and (3) placebo—who underwent conjunctival allergen challenge pre- and post-medication for two weeks. Allergic signs and symptoms (i.e. ocular itching, ocular redness, and overall nasal symptoms) were compared before and after the assigned intervention. Results revealed that the 2 treatment groups had similar effects on total nasal symptom efficacy scores; but in terms of ocular itching.[2]

References

1. Snyman JR, Potter PC, Groenewald M, Levin J, Claricort Study Group. Effect of betamethasone-loratadine combination therapy on severe exacerbations of allergic rhinitis: a randomized, controlled trial. Clin Drug Investig. 2004; 24(5):265-74.
2. Lanier BQ, Abelson MB, Berger WE, et al. Comparison of the efficacy of combined fluticasone propionate and olopatadine versus combined fluticasone propionate and fexofenadine for the treatment of allergic rhinoconjunctivitis induced by conjunctival allergen challenge. Clin Ther. 2002; 24(7):1161-74.

Saline Solution

Saline irrigation with either isotonic or hypertonic solutions are utilized for adjunctive therapy and they help reduce symptoms and improve quality of life in patients with allergic rhinitis. They may be less effective than intranasal steroids and no more effective than other active agents for allergic rhinitis, but their low cost and overall good patient acceptance are of modest benefit in easing patient symptoms. Minimal adverse effects include burning sensation, irritation and nausea. They are less effective than intranasal steroids and no more effective than other forms of treatment for allergic rhinitis.[1,2]

When it comes to nasal saline concentration, there have been many studies that have shown conflicting results between isotonic and hypertonic nasal saline irrigations. Some studies advocate hypertonic solution use over hypotonic solution and vice versa (Table 8). The evidences available at this moment seem to be inconclusive as to which particular concentration is better. One thing is common though, the exact mechanism on how nasal saline irrigation provides improvement is unclear.

There are many hypotheses on how nasal saline irrigation promotes improvement of nasal symptoms. They include: (1) improve mucociliary clearance; (2) decrease mucosal edema; (3) decrease inflammatory mediators; and (4) mechanically clear nasal crusts and thick mucous .[3]

Although several studies have shown that hypertonic saline solutions improve saccharine transit time, other studies have likewise shown that hypertonic saline solutions affect ciliary beat frequency negatively.[1-3] For this reason, isotonic saline solutions which do not affect ciliary beat frequency may be more appropriate than hypertonic saline solution for nasal irrigation. However, the mucolytic effect induced by the hyperosmolarity of hypertonic solutions cannot be ignored since there is an improvement in saccharine transit time. Further studies can be undertaken to finally determine which solution, isotonic or hypertonic, would be better to use as nasal saline irrigation for the different sinonasal disorders.

References

1. Harvey R, Hannan SA, Badia L, Scadding G. Nasal saline irrigations for the symptoms of chronic rhinosinusitis. Cochrane Database Syst Rev. 2007; (3):CD006394.
2. Heatley DG, McConnell KE, Kille TL, Leverson GE. Nasal irrigation for the alleviation of sinonasal symptoms. Otolaryngol Head Neck Surg. 2001; 125(1):44-8.
3. Papsin B, Mc Tavish A. Saline nasal irrigation: Its role as an adjunct treatment. Can Fam Physician. 2003; 49:168-73.

Table 8. Clinical Studies of Nasal Saline Irrigation[3]

STUDY	PATIENTS	DESIGN	COMPARATORS	FINDINGS
Georgitis 1994	30 allergic rhinitis	Crossover	Nasal hyperthermia (molecular or large- particle water vapour) versus simple irrigation	Histamine levels fell with all treatments; greatest decline seen with irrigation (P < .05 and < .01) Leukotriene C4 levels significantly reduced by irrigation (P < .05) Prostaglandin D_2 levels unaffected by treatment
Krayenbuhl and Seppey 1995	104 intranasal surgery	Retrospective	Saline stream versus passive saline instillation	Stream patients required significantly fewer ostoperative recovery days (*P* <.05) and visits to physicians (*P* <.05)
Seppey et al 1995	209: 151 rhinosinusitis; 58 endonasal surgery	Treatment at physicians' discretion	Medium saline stream versus strong stream	Significant decrease in signs and symptoms in all patients (*P* < .0005)
Seppey et al 1996	28 endonasal surgery	Randomized	Saline stream versus passive saline instillation	Stream significantly more effective than drops at 9 days after surgery (*P* <.01) Stream significantly more tolerable at 9, 15, and 30 days after surgery (*P* <.02)
Adam et al 1998	143 cold or sinus infection	Randomized placebo-controlled	Hypertonic saline versus normal saline versus obser vation	No differences in nasal symptom scores among the three groups
Pigret and Jankowski 1996[1]	20 ethmoidectomy	Randomized, single-blind	Pressurized seawater nasal lavage versus nasal irrigation with antiseptic or mucolytic	Irrigation methods equally effective
Shoseyov et al 1998[1]	30 chronic sinusitis	Randomized, double-blind	Hypertonic saline versus normal saline	Improved cough and radiologic scores for hypertonic saline group (P ≤.05) Improved nasal secretion scores for both groups (P ≤ .05)
Heatley et al 2001	150 chronic sinusitis	Crossover	Saline delivery via bulb syringe versus irrigation pot	Irrigation methods equally effective

Box 12.3. Allergen Specific Immunotherapy

Allergen specific immunotherapy is the treatment option that may potentially alter the course of IgE-mediated respiratory allergies and thus possibly provide long-term effects.
Strong Recommendation, *Grade A evidence*

Allergen specific immunotherapy may potentially alter the course of respiratory allergies with documented IgE-mediated triggers.[1] It is effective for the treatment of allergic rhinitis, allergic conjunctivitis, allergic asthma, and stinging insect hypersensitivity. It is also indicated in atopic dermatitis patients with aeroallergen sensitization.[2]

Immunotherapy should also be considered depending on the following factors: (1) severity and duration of symptoms, (2) responsiveness to other forms of therapy, (3) unacceptable adverse effects of medications, (4) the patient's desire to avoid long-term pharmacotherapy, (5) reduction of the risk of future asthma, and (6) the presence of comorbid conditions, such as sinusitis or asthma.[1]

Contraindications for allergen immunotherapy include patients with medical conditions that would reduce their ability to survive allergen immunotherapy systemic allergic reactions or the resultant treatment. Examples include severe asthma uncontrolled by pharmacotherapy and significant cardiovascular disease.[1]

The adverse reactions of allergen immunotherapy include common local reactions, swelling and induration at the injection site, and in rare instances, life-threatening and fatal anaphylaxis. The estimated allergen immunotherapy

fatality rate was one per 2.5 million injections (average of 3.4 deaths per year).[1]

Allergen immunotherapy should be administered under the direct supervision of an appropriately trained physician, qualified physician extender (nurse practitioner or physician assistant), or both in a facility with the appropriate equipment, medications, and personnel to treat anaphylaxis.[2]

Allergen immunotherapy is effective in both adults and children. There is no specific upper or lower age limitation for allergen immunotherapy. It is important to know appropriate indications, the absence of significant comorbid conditions, and the patients' ability to comply or cooperate with allergen immunotherapy.[2]

Immunotherapy is most commonly administered as a series of subcutaneous injections requiring a build-up period until an optimal therapeutic dose is reached, followed by a maintenance period of three to five years.

Efficacy of Specific Allergen Immunotherapy

Effects on quality of life

Specific allergen immunotherapy is effective in reducing allergic rhinitis symptoms scores, improving quality of life and reducing use of medications.[3]

In suitably selected patients with seasonal allergic rhinitis, specific allergen immunotherapy is recommended because it significantly (1) reduces overall symptom scores (SMD 0.57, 95% CI 0.82-0.33); (2) reduces symptom scores for nasal (SMD 1.59, 95% CI 2.29-0.89), bronchial (SMD 0.59, 95% CI 1.06-0.11) and ocular (SMD 1.80, 95% CI 3.28-0.31) symptoms;[3] (3) improves rhinoconjunctivitis quality of life scores (SMD 0.52, 95% CI 0.69-0.34);[3] and (4) reduces use of medications (SMD 0.48, 95% CI 0.67-0.29)[3]. The result of the meta-analysis places a relatively high value on relieving the symptoms of allergic rhinitis and a relatively low value on avoiding adverse effects and on cost of therapy. Only randomized studies on seasonal allergic rhinitis were included.

Effects on the development of asthma

Allergen immunotherapy reduces the risk for future development of asthma in patients with allergic rhinitis.[1,4]

Immunotherapy in children with allergic rhinitis may be given to reduce the risk of developing asthma. This benefit is seen at completion of treatment (OR 0.40, 95% CI 0.20-0.79)[4], at 2 years after discontinuation (OR 0.40, 95% CI 0.18-0.88)[5] and at 7 years after discontinuation of treatment (OR 2.48, 95% CI 1.1-5.4)[6]. This takes into consideration the evidence on the paradigm of one airway-one disease and that patients with allergic rhinitis alone are at high risk of developing asthma. Although the drop-out rates for the studies were significant, the potential to prevent another allergic airway disease was considered more important.

Duration of effect

The clinical benefits of allergen specific immunotherapy may be sustained years after discontinuation of treatment.[1]

Allergen immunotherapy is recommended for allergic rhinitis because of its persistent benefits.[4] Eng et al., through observational studies, examined children with allergic rhinitis (sensitive to seasonal allergens) who were given immunotherapy for 3 years and were followed up after 6 and 12 years of discontinuation of immunotherapy.[7,8] The reduction in symptom scores remained significant after 6 years (mean 4.5, 95% CI 2.7-7.1)[7] and after 12 years (mean 35.2, 95% CI 2.0-74.1)[8] of discontinuation of immunotherapy. Randomized studies on children with allergic rhinitis given immunotherapy for 3 years also show the persistent benefits of reducing asthma risk after 2 and 7 years of discontinuation of immunotherapy.[5,6] The lasting effects on decreasing symptoms and risk of future asthma outweighs the cost of three years of immunotherapy.

Effects on the development of sensitization to new allergens

Allergen immunotherapy for allergic rhinitis may prevent the development of new allergen sensitization.[1]

Immunotherapy may prevent new sensitizations in patients with allergic respiratory disease. This was seen with immunotherapy with housedust mite by Inal et al (RR 0.46, 95% CI 0.14-0.58),[9] Pajno et al (RR 0.43, 95% CI 0.3-.62)[10] and Des Roches et al (OR 0.3, 95% 0.001-0.49).[11] This was also seen with immunotherapy with grasses by Eng et al (RR 0.58, 95% CI 0.36-0.94)[8] and Purello et al (RR 0.35, 95% CI 0.33-0.37).[12] Thus, sensitization to new allergens not included in the immunotherapy may be prevented although the evidence were mostly observational studies.

Local studies also show a trend towards the prevention of new sensitizations in adult (23% vs 71%, p=0.0126)[13] and pediatric (14.3% vs 78.5%, p=0.001)[14] populations but the sample sizes were small (14 patients per arm).

References

1. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2):S1-84.
2. Cox L, Nelson H, Lockey R, et al. Task force report. Allergen immunotherapy: A practice parameter third update. J Allergy Clin Immunol. 2011; 127(1 Suppl):S1-55.
3. Calderon MA, Alves B, Jacobson M, Hurwitz B, Sheikh A, Durham S. Allergen injection immunotherapy for seasonal allergic rhinitis. Cochrane Database Syst Rev. 2007; (1):CD001936.
4. Moller C, Dreborg S, Ferdousi HA, et al. Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study). J Allergy Clin Immunol. 2002; 109: 251-256.
5. Niggeman B, Jacobsen L, Dreborq S, et al. Five-year follow-up on the PAT study: specific immunotherapy and long-term prevention of asthma in children. Allergy. 2006; 61(7):855-9.
6. Jacobsen L, Niggemann B, Dreborg S, et al. Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study. Allergy. 2007; 62(8):943-8.
7. Eng PA, Reinhold M, Gnehm HP. Long-term efficacy of preseasonal grass pollen immunotherapy in children. Allergy. 2002; 57(4):306-12.

8. Eng PA, Borer-Reinhold M, Heijnen IA, Gnehm HP. Twelve-year follow-up after discontinuation of preseasonal grass pollen immunotherapy in childhood. Allergy. 2006; 61(2):198-201.
9. Inal A, Altintas DU, Yilmaz M, Karakoc GB, Kendirli SG, Sertdemir Y. Prevention of new sensitizations by specific immunotherapy in children with rhinitis and/or asthma monosensitized to house dust mite. J Investig Allergol Clin Immunol. 2007; 17(2):85-91.
10. Pajno GB, Barberio G, De Luca F, Morabito L, Parmiani S. Prevention of new sensitizations in asthmatic children monosensitized to house dust mite by specific immunotherapy: A six-year follow-up study. Clin Exp Allergy. 2001; 31(9):1392-7.
11. Des Roches A, Paradis L, Menardo JL, Bouges S, Daures JP, Bousquet J. Immunotherapy with a standardized Dermatophagoides pteronyssinus extract. VI. Specific immunotherapy prevents the onset of new sensitizations in children. J Allergy Clin Immunol. 1997; 99(4):450-3.
12. Purello-D'Ambrosio F, Gangemi S, Merendino RA, et al. Prevention of new sensitizations in monosensitized subjects submitted to specific immunotherapy or not: A retrospective study. Clin Exp Allergy. 2001; 31(8):1295-302.
13. Chato VV, Abong JM, Aleta LA, Sumpaico MW. Prevention of new sensitization in adults and adolescents with respiratory allergies undergoing allergen immunotherapy as measured by repeat skin prick test: a cohort study. Phil J Allergy Asthma Immunol. 2010; 15(2):32-8.
14. Millanes IG, Sumpaico MW, Recto MT, Castor MR. The effect of allergen immunotherapy on the development of new sensitizations among children and adolescents with allergic respiratory diseases as measured by skin prick test: a cross-sectional study. Phil J Allergy Asthma Immunol. n.d.; 17(1):3-12.

Box 12.4. Patient education

Education of the patient, family members, and caregivers is crucial in promoting compliance to management and maximizing treatment outcomes in allergic rhinitis.
Strong Recommendation, Grade B evidence

According to Sheikh et al., standardized allergy education given to primary healthcare professionals results in modest improvements in disease-specific quality of life in patients with perennial rhinitis. Thirty-nine percent of patients who received care from an allergy-trained primary healthcare professional showed a clinically significant $p<0.5$ improvement in the rhinitis quality of life questionnaire compared with 28% of patients who received standard care (risk difference=11%, number needed to treat=9, P=0.1).[1]

Patient education includes sensitivity to the socioeconomic and demographic characteristics of the patient. A partnership is established from the time of the first visit, and is reinforced during subsequent visits. The physician should (1) stress the chronicity of the disease; (2) set realistic treatment goals and discuss environmental allergen avoidance and control; and (3) properly instruct the patient and his caregivers on the administration of medications and the use of the devices, the benefits of adherence to such, and possible side effects. The patient should also be informed of co-morbidities such as bronchial asthma, and complications such as otitis media, nasal polyposis and sinusitis. Lastly, he and his caregivers should be informed of the positive impact that disease control could have on quality of life.[2]

References

1. Sheikh A, Khan-Wasti S, Price D, Smeeth L, Fletcher M, Walker S. Standardized training for healthcare professionals and its impact on patients with perennial rhinitis: a multi-centre randomized controlled trial. Clin Exp Allergy. 2007; 37(1):90–9.
2. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2):S1-84.

Box 13. Is the patient responsive to treatment?

The management of allergic rhinitis follows a stepped-care approach, the outcome of which must be reassessed periodically for effectiveness and presence of adverse effects of treatment. Patients with partial or refractory disease must be thoroughly re-evaluated and specialized treatment given for individual conditions.
Strong Recommendation, Grade A evidence

The general approach to treatment of allergic rhinitis based on global guidelines emphasizes a stepped-care management plan. In patients with mild intermittent rhinitis, oral or intranasal antihistamines are usually effective for controlling sneezing, rhinorrhea, nasal pruritus and congestion on a short term or intermittent basis. A leukotriene antagonist may be used as an alternative if there are complications with use of antihistamines. If the rhinitis develops into the moderate-severe or persistent type, especially with significant nasal congestion, then an intranasal steroid (INS) is the preferred medication. With any grade of severity there should be appropriate follow-up after two weeks, and medications are stepped-up or stepped-down after at least one month of compliant treatment as indicated by clinical evaluation.[1,2]

Majority of patients will respond to this type of management. However, patients with only partial responses to treatment should be evaluated and treated for residual complaints and comorbid diseases. Concomitant ophthalmologic symptoms (tearing, eye redness, swelling and pruritus) may be treatment with an intraocular antihistamine. For residual nasal congestion, oral or intranasal decongestants and/or intranasal antihistamines may be given.[2]

If there is poor response to maximal medical therapy and quality of life and functioning is adversely affected, then referral to an allergy and/or an ENT specialist may be warranted. Referral to an allergist is warranted for allergy testing in order to identify the sensitizing allergen and thus give allergen-specific treatment options such as directed allergen avoidance measures and immunomodulation in the form of specific allergen immunotherapy.[2] Furthermore, if the patient experiences adverse reactions to maintenance allergy medications, immunotherapy is an alternative option for treatment . Allergy evaluation and management is also necessary if the patient presents with other comorbid disease such as asthma, allergic conjunctivitis and atopic dermatitis.[3] Referral to the ENT specialist may be warranted if other

symptoms develop (such as ear pain, throat discomfort) or when symptoms worsen despite adequate and appropriate therapy. If the diagnosis becomes uncertain, re-evaluation and re-examination may be useful. A complete head and neck examination or special diagnostic tests such as fiberoptic nasal endoscopy or imaging may be of benefit.

Nasal symptom score monitoring, quality of life assessments, monitoring of olfactory function and adverse-events monitoring such as signs of sedation and hypothalamic pituitary axis suppression may be in order especially for younger patients. It must be noted that it is not only the disease that may adversely affect health-related quality of life, but administered therapy, even if perceived to be beneficial, may also cause health impairment.[4]

References

1. Greinier AN, Meltzer EO. Pharmacologic rationale for treating allergic and non-allergic rhinitis. J Allergy Clin Immunol. 2006; 118(5):985-98.
2. Corren J, Baroody FM, Pawankar R. Allergic and non-allergic rhinitis. In: Adkinson NF, et al., eds. Middleton's Allergy Principles and Practice, 8th ed. Saunders; 2014. pp. 678-679.
3. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2):S1-84.
4. Juniper EF, Stahl E, Doty RL, Simons FE, Allen DB, Howarth PH. Clinical outcomes and adverse effect monitoring in Allergic Rhinitis. J Allergy Clin Immunol. 2005; 115(3 Suppl 1):S390-413.

Box 14. Patient-family-multidisciplinary health care provider follow-up

A multidisciplinary approach among the patient, his family & caregivers, the primary care physician, the allergist/immunologist, and the otorhinolaryngologist is the key to a successful management outcome in patients with allergic rhinitis.
Strong Recommendation, Grade A evidence

To achieve the goals of reduction of symptoms, improvement in quality of life and increased ability to function, united and cooperative efforts are necessary to manage exacerbations and minimize complications. Allergen avoidance, use of medications and immunotherapy are optimized when there is constant communication among the involved physicians.

During follow-up, the patient's response to his medications should be assessed. For those who have improved, tapering of medications should always be considered to avoid the risk of side effects or adverse reactions. Symptoms of these should be vigilantly sought at every visit. The patient's quality of life should be assessed as well. For those whose symptoms did not improve, a step up in treatment should be considered.

Every visit is an opportunity for patient education, review of environmental control, compliance to medications, and the technique in the use of devices. Co-morbidities such as bronchial asthma and complications of allergic rhinitis such as nasal polyps, sinusitis, obstructive sleep apnea and otitis media should be addressed.

Optimal management of patients with allergic rhinitis involves an effective collaboration among the patient, his family or caregivers, and his physicians.

Reference

1. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2):S1-84.

Box 15. Consider severe uncontrolled allergic rhinitis.

Patients are diagnosed to have severe uncontrolled allergic rhinitis when their symptoms are inadequately controlled despite effective, safe, and acceptable pharmacologic treatment based on guidelines.

Clinicians are guided by various protocols (ARIA, BSACI, etc.) in treating allergic rhinitis. There is a substantial percentage of patients whose symptoms are inadequately controlled despite adequate treatment. Classified under SCUAD (Severe Chronic Upper Airway Diseases), they have impaired quality of life, social functioning, sleep, and work or school performance.[1]

In the trea tment of these patients, several factors are considered: (1) disease-related factors (environmental factors, hormonal status of the patient, genetics); (2) diagnosis-related factors such as the presence of one or more of the following diseases (granulomatous diseases, aspirin intolerance, asthma, COPD, bronchiectasis, Churg-Strauss syndrome, cystic fibrosis, primary ciliary dyskinesia) which may affect the appropriate management for the patient; (3) patient-related factors (compliance to medication use, proper administration of treatment); 4) treatment-related factors (best choice of treatment by the physician, re-evaluation of pharmacotherapy, need for immunotherapy).[2]

References

1. Hellings PW, Fokkens WJ, Akdis C, et al. Uncontrolled allergic rhinitis and chronic rhinosinusitis: where do we stand today? Allergy. 2013; 68(1):1-7.
2. Bousquet J, Bachert C, Canonica GW, et al, on behalf of the extended Global Allergy and Asthma European Network, World Allergy Organization and Allergic Rhinitis and its Impact on Asthma Study Groups. Unmet needs in severe chronic upper airway disease (SCUAD). J Allergy Clin Immunol. 2009; 124(3):428-33.

Box 16 and Box 17. Non-allergic Rhinitis

If a patient presents with chronic nasal symptoms, such as obstruction and rhinorrhea, but has negative skin prick test and/or absence of serum IgE, consider non-allergic rhinitis.

Non-allergic rhinitis (NAR) is a heterogenous group of nasal conditions which occur in relation to non-allergic, non-infectious triggers without associated allergic disease, determined by negative skin prick test for relevant allergens

and/or negative allergen-specific antibody tests. In December 2008, NAR Consensus Panel was held, which came up with 8 subtypes that fulfill the criteria of NAR. These are the following: 1) non-allergic rhinopathy, previously known as vasomotor rhinitis, or idiopathic non-allergic rhinitis, 2) non-allergic rhinitis with eosinophilia, 3) atrophic rhinitis, 4) senile rhinitis, 5) gustatory rhinitis, 6) drug-induced rhinitis, including rhinitis medicamentosa, 7) hormonal-induced rhinitis, including the rhinitis of pregnancy, and 8) cerebrospinal fluid leak.[1]

Patients with NAR more often report nasal congestion and rhinorrhea, compared with patients with allergic rhinitis, who commonly complain of sneezing and itching. The former group also develop symptoms at a later age. Common triggers of NAR are changes in weather and temperature, food, perfumes, odors, smoke, and fumes. Exposure to animals does not lead to nasal symptoms. In addition, patients with NAR have few complaints of concomitant symptoms of allergic conjunctivitis (itching, watering, redness, and swelling). They do not have other atopic diseases and have no family history of atopy.[2]

Mixed rhinitis (allergic and non-allergic) occurs in 44-87% of patients with allergic rhinitis and is more prevalent than pure allergic or non-allergic rhinitis.[3]

References

1. Tran N, Vickery J, Blaiss M. Management of Rhinitis: Allergic and Non-Allergic. Allergy Asthma Immunol Res. 2011; 3(3):148-56.
2. Schroer B, Pien LC. Nonallergic rhinitis: common problem, chronic symptoms. Cleve Clin J Med. 2012; 79(4):285-93.
3. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2):S1-84.

Box 18. Manage Non-allergic Rhinitis

Management of non-allergic rhinitis involves avoidance of environmental triggers, use of antihistamines, steroids and decongestants.

Recommendation, Grade B

Avoidance

Environmental triggers such as strong odors (perfumes, soaps, paint, etc.) and air pollutants (smoke fumes, tobacco smoke) are respiratory irritants and should be avoided by patients whose symptoms worsen upon exposure.[1]

Antihistamines

The anticholinergic activity of first-generation oral antihistamines is beneficial to patients with non-allergic rhinitis (NAR). Oral second-generation antihistamines are not as effective. Topical antihistamines have been found to be very effective for the overall treatment of NAR. In a multicenter, randomized, placebo-controlled trial, Banov and Lieberman evaluated the efficacy of the azelastine nasal spray in patients with vasomotor rhinitis and found a significant improvement in total vasomotor rhinitis symptom scores (TVRSS) in those patients receiving azelastine (2 sprays per nostril twice a day, 1.1 mg) versus placebo.[2] In an open label, two-week study done by Lieberman et.al, with azelastine (2 sprays per nostril twice a day) given to patients with allergic rhinitis, mixed rhinitis, and vasomotor rhinitis, it was found that azelastine had improvement in control of all rhinitis symptoms including nasal congestion, postnasal drip, sneezing, and sleeping difficulty.[3]

Steroids

Intranasal corticosteroids have been found to be effective in NAR, especially in vasomotor rhinitis and non-allergic rhinitis with eosinophilia syndrome (NARES). Fluticasone propionate and beclomethasone are the only topical corticosteroids approved by the FDA in the US for the treatment of NAR. Clinically, there does not appear to be a difference among the intranasal steroids available at this time.[1]

Decongestants

No specific studies looking at the effectiveness of oral decongestants in the treatment of NAR are currently available, but they should be considered as adjunctive therapy (used on a need basis for nasal congestion that is not responsive to intranasal corticosteroids, topical antihistamines, or a combination of both).[1]

Nasal saline

Nasal saline has been found to be helpful alone or as an adjuvant therapy in patients with chronic rhinorrhea. It is best performed immediately prior to intranasal corticosteroids and may be especially helpful in reducing postnasal drip, sneezing, and congestion. A 2007 Cochrane database review found eight randomized controlled trials in which saline was evaluated in comparison with placebo, other treatments or as an adjunct to other treatments. There was favorable evidence for saline as adjuvant therapy. Saline irrigations are well tolerated with very minor side effects.[4]

References

1. Wallace DV, Dykewicz MS, Bernstein DI, et al. The Joint Task Force on Practice Parameters, representing the AAAAI, ACAAI, JCAAI. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2):S1-84.
2. Banov CH, Lieberman P, Vasomotor Rhinitis Study Groups. Efficacy of azelastine nasal spray in the treatment of vasomotor (perennial nonallergic) rhinitis. Ann Allergy Asthma Immunol. 2001; 86(1):28-35.
3. Lieberman P, Kaliner MA, Wheeler WJ. Open-label evaluation of azelastine nasal spray in patients with seasonal allergic rhinitis and nonallergic vasomotor rhinitis. Curr Med Res Opin. 2005; 21(4):611-8.
4. Harvey R, Hannan SA, Badia L, Scadding G. Nasal saline irrigations for the symptoms of chronic rhinosinusitis. Cochrane Database Syst Rev. 2007; (3):CD006394.

Box 19. Local Allergic Rhinitis

If a patient presents with symptoms similar to allergic rhinitis but has negative skin prick test and positive nasal production of specific IgE antibodies, consider local allergic rhinitis.
Recommendation, Grade B

Local allergic rhinitis (LAR) is a localized nasal allergic response in the absence of systemic atopy characterized by (1) local production of specific IgE (sIgE) antibodies; (2) Type 2 helper cell inflammatory pattern of mucosal cell infiltration during natural exposure to aeroallergens; and (3) positive nasal allergen provocation test (NAPT) response with release of inflammatory mediators (tryptase and eosinophil cationic protein).[1]

The nasal allergen provocation test, albeit not a standardized test, is an 'in vivo' diagnostic tool which resembles the natural exposure of patients to allergen, and consequently, the development of allergic reaction. It can be utilized in clinical practice, but its value is more appreciated in investigational research, particularly in understanding the pathophysiology, immunology and pharmacotherapy of allergic diseases. In clinical practice, indications for NAPT include multi-sensitized patients, patients with local allergic rhinitis or occupational allergic rhinitis, and correlation between allergy and other morbidities. In research, NAPT is done to elucidate mechanisms of allergic reaction and mechanisms of immunotherapy and to evaluate the efficacy of new treatments.[3] In the UP-PGH setting, it is recognized that NAPT has very limited use in the clinical diagnosis of allergic rhinitis.

Local allergic rhinitis presents with clinical nasal symptoms similar to allergic rhinitis, (itching, sneezing, rhinorrhea, and obstruction) and is often associated with ocular symptoms. Patients with LAR may have both persistent and intermittent symptoms with severity that can be classified as mild, moderate, or severe. For the diagnosis of LAR, neither skin prick testing nor determination of the presence of serum sIgE antibodies is useful, and a nasal allergen provocation test is needed to identify the culprit allergen or allergens.[2]

References

1. Rondon C, Campo P, Togias A, et al. Local allergic rhinitis: concept, pathophysiology, and management. J Allergy Clin Immunol. 2012; 129(6): 1460-7.
2. Rondon C, Fernandez J, Canto G, Blanca M. Local allergic rhinitis: concept, clinical manifestations, and diagnostic approach. J Investig Allergol Clin Immunol. 2010; 20(5):364-71.
3. Loureiro G, Tavares B, Machado D, Pereira C. Nasal provocation test in the diagnosis of allergic rhinitis, Allergic Rhinitis. Prof. Marek Kowalski (ed.) @2012. ISBN: 978-953-51-0288-5, InTech, Available from: http://www.intechopen.com/books/ allergic-rhinitis/nasal-provocation-test-in-the-diagnosis-of-allergic-rhinitis

Box 20. Manage local allergic rhinitis

If a patient presents with symptoms consistent with local allergic rhinitis, manage as allergic rhinitis.
Strong Recommendation, Grade B

A number of patients present with persistent local allergic rhinitis (LAR) with moderate to severe symptoms that require incessant use of nasal corticosteroids and oral antihistamines; hence, it is important to verify whether they will benefit from specific immunotherapy for the responsible allergen. Further research is necessary to determine whether patients with LAR respond favorably to specific immunotherapy with aeroallergens.[1]

A follow-up study by Rondon et al on local allergic rhinitis which aimed to evaluate the natural history of patients with LAR (194 LAR patients and 130 healthy controls) and the development of asthma and allergic rhinitis showed that, after five years, patients with LAR experienced worsening of rhinitis (26.1%), perceived impairment in their health (17.6%), quality of life (40.3%), and, in 5.6%, showed an evolution toward asthma. One of the main outcomes of this study was the detection of *de* novo systemic atopy among LAR patients and healthy controls, which were evaluated by objective measures (skin prick test and serum IgE determination) and showed that after the first five years, a similar rate of conversion to systemic atopy was detected in 6.25% and 5.25% respectively. With these results, the authors concluded that LAR and classic AR may be two independent entities, and that LAR may produce significant impairment in health and quality of life. [1]

Reference

1. Rondon C, Campo P, Zambonino M, et al. Follow-up study in local allergic rhinitis shows a consistent entity not evolving to systemic allergic rhinitis. J Allergy Clin Immunol. 2014; 133(4):1026-31.

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