BULETIN FARMATERA
E-ISSN: 2528-410X

LITERATURE REVIEW

Latest Pharmacological Therapies in Allergic Rhinitis

Rudfi Rizky S Nainggolan
Faculty of Medicine, Universitas Islam Sumatera Utara, Jl STM No. 77 Medan, Sumatera Utara
Corresponding Email: rudfirizky@gmail.com

Abstract: Allergic rhinitis is a chronic inflammatory disease of the nasal mucosa due to a type 1 hypersensitivity reaction that has a major impact on the quality of life and the global economy. This study aims to review the pathophysiological mechanisms and evaluate the effectiveness of current pharmacological therapies to support more personalised and evidence-based treatment. The method used was a systematic literature review of 2021–2025 publications from the PubMed, Scopus, and Web of Science databases, including clinical studies, meta-analyses, and systematic reviews. Results show that second-generation antihistamines, intranasal corticosteroids, and combination therapies such as GSP301 are effective in controlling symptoms. Additional approaches, such as cromolyn sodium, montelukast, ipratropium bromide, as well as biologic agents (omalizumab, dupilumab), show promising results, especially in severe or resistant cases. SCIT and SLIT immunotherapies have also been shown to be effective with good safety and compliance profiles. The MASK-air data and the ARIA–EAACI guidelines support a phased and individualised approach to therapy. In conclusion, pharmacological therapy of allergic rhinitis continues to evolve towards more effective, safe, and personalised treatment, with multidisciplinary collaboration as the key to improving patients' quality of life.

Keywords: Allergic rhinitis, pharmacological therapy

INTRODUCTION

Background of allergic rhinitis

Definition and classification (intermittent vs. persistent, mild vs. severe)

Allergic rhinitis is a medical condition that arises as a result of a type 1 hypersensitivity reaction in the lining of the nasal mucosa, in response to airborne allergens such as pollen from grass and trees, house dust mites, and animal dander. The main symptoms include nasal congestion, discharge from the nose (rhinorhea), itching (pruritus), and sneezing that occurs repeatedly or suddenly.UT and poho, house dust mites, animal hair, with the main symptoms of nasal congestion, watery rhinorhea, pruritus and paroxysmal sneezing.[1]

Global and regional epidemiology

It is estimated that around 20% of the UK population suffers from allergic rhinitis, which has also become a global health issue, with the number of sufferers reaching

E-ISSN: 2528-410X

around 400 million people worldwide [1,2] Globally, allergic rhinitis (AR) disease is reported to impact about 25% of children and 40% of adults. In most cases, about 80% of cases, show symptoms before the age of 20, with the highest intensity occurring in the age range of 20 to 40 years, then gradually decreasing with age.[2] During the first five years of life, the prevalence of allergic rhinitis (AR) in children is reported to be about 17.2%, with the most common age at diagnosis being in the range of 24 to 29 months, which is 25%.[2] The condition is more common in boys in childhood, while its prevalence increases in girls as they enter adolescence.[2] The incidence of allergic rhinitis (AR) continues to increase from year to year, which is suspected to be closely related to the urbanisation process and high exposure to environmental pollution as the main triggering factors. In addition, RA is often accompanied by other medical conditions such as asthma, eczema, chronic or recurrent sinusitis, prolonged cough, and complaints such as a tight head and migraines.[1]

Disease on the quality of life and the economy

The high incidence of allergic rhinitis (AR) poses great pressure on the welfare of the community as a whole and has a significant economic impact, both through direct and indirect costs in its treatment. A study in the Netherlands estimated that the total expenditure on AR reached 4,827 euros per patient each year.[3]

Allergic rhinitis (AR) poses a significant socioeconomic burden, as this condition can reduce the quality of life of sufferers, disrupt sleep patterns and cognitive abilities, and trigger irritability and fatigue.[4]

In addition, this condition also has an impact on declining performance in the school and workplace environment, especially during the peak season of pollen spread.[4]

Allergic rhinitis (AR) is also one of the common causes of patients seeking medical services, both to general practitioners, primary health care centres, and hospitals.[4]

Pathophysiology of allergic rhinitis

The role of IgE, mast cells, eosinophils, and inflammatory mediators

Allergic rhinitis is a form of type 1 hypersensitivity reaction that occurs in the nasal mucosa and is mediated by *immunoglobulin E (IgE).* This condition arises when individuals who have been sensitised are re-exposed to allergens, such as pollen or house dust. Such exposure triggers the production of *allergen-specific IgE (sIgE),* which then binds to high-affinity receptors on the *surface of mast cells*. This bond triggers the release of inflammatory mediators such as *histamine, tryptase, prostaglandins*, and *leukotrienes*, which are responsible for early symptoms such as *rhinorhea, nasal congestion, pruritus*, and *recurrent sneezing*.

This allergic response consists of two phases: an initial phase that occurs in a matter of minutes, and an advanced phase that can last up to 24 hours. One method to study this mechanism is *the Nasal Allergen Challenge (NAC),* which is the procedure of

E-ISSN: 2528-410X

administering aerosol allergens into the nasal cavity to monitor the immune response. After NAC, there is an increase in inflammatory mediators locally and systemically, as well as a surge *in type 2 cytokines* such as *IL-5* and *IL-13*, which play a role in the activation and recruitment of *eosinophils* to the nasal mucosa. These eosinophils contribute to inflammation and aggravate clinical symptoms.

In addition to eosinophils, *basophils*, *T lymphocytes*, and various *antigen-presenting cells* such as *monocytes*, *dendritic cells*, and *ILC2* also play a role in strengthening the immune response. Within a few hours of exposure to the allergen, there is an increase in the number of such immune cells in the blood circulation, accompanied by increased levels of sIgE and inflammatory cytokines. This systemic response can last up to a month, suggesting that allergic rhinitis is not just a local reaction, but also involves thorough immune activation.

Despite the availability of various therapies such as antihistamines and allergen immunotherapy, about *60% of patients* are still dissatisfied with the results of treatment. This confirms the importance of a deep understanding of the *pathophysiology of allergic rhinitis*, particularly the role of IgE, mast cells, eosinophils, and inflammatory mediators, in order to develop a more effective and personalised therapeutic approach. [5]

Neuro-immunological mechanisms and involvement of the autonomic nervous system

Allergic rhinitis not only involves the immune system, but it also shows a close affinity with the central and autonomic nervous systems—including sympathetic, parasympathetic, and enteric. This complex interaction between the nervous system and the immune system contributes greatly to the appearance and development of allergic symptoms. *Neurons* can communicate directly with various *immune cells*, especially *mast cells,* that play a central role in allergic reactions. When immune cells are activated, they release *proinflammatory mediators* such as *cytokines, neurotrophins, chemokines*, and *neuropeptides*, which then stimulate sensory neurons.

In contrast, neuron activation also triggers the release of *neurotransmitters* and *neuropeptides* that can affect immune cell function, creating a decisive reciprocal relationship in neuroimmunological processes. Evidence of the existence of this interaction is strengthened by the successful application *of Pavlovian conditioning* in the management of allergic disorders, which suggests the presence of a psychoneuroimmune component in type 1 hypersensitivity reactions.

Homeostasis reflexes mediated by the nervous system, such as *sneezing in allergic rhinitis*, *coughing in asthma*, and *vomiting in food allergies*, are manifestations of neuroimmune communication aimed at maintaining the body's balance. However, when these interactions are *dysregulated*, the immune system can become overactive, triggering severe symptoms and extreme hemodynamic responses that have the

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potential to lead to serious conditions such as *anaphylaxis*.

Recent research has systematically reviewed the role of neuroimmune interactions in a wide range of common allergic diseases, including *allergic rhinitis, chronic rhinosinusitis, allergic asthma, food allergies, atopic dermatitis*, and *urticaria*. A deeper understanding of neurological tissues that have been underpaid for by immunologists and allergists is essential. These tissues not only function in maintaining homeostasis, but they can also interact pathologically with familiar immune pathways, triggering what is referred to as *neuroimmunological inflammation*.

By understanding these mechanisms, we can identify *new allergy phenotypes and endotypes*, as well as pave the way for a more *personalised and patient-focused* approach to therapy, in line with the evolving era of medicine.. [6]

Purpose of pharmacological therapy

Control symptoms, prevent exacerbations, and improve quality of life.

The main goal of pharmacological therapy in allergic rhinitis is to control annoying symptoms such as sneezing, nasal congestion, and rhinorrhea, so that the patient can go about their daily activities more comfortably. In addition, treatment aims to prevent exacerbations or recurrences of symptoms that can worsen the condition and decrease productivity. With proper management, pharmacological therapy also plays an important role in improving the quality of life of sufferers, both from physical, emotional, and social aspects, so that they can function optimally in the family, school, and workplace environment.

Reasons for the importance of this literature review

The literature review on allergic rhinitis therapy plays an important role in supporting the development of new therapies that are more effective and safe, as well as encouraging the application of evidence-based approaches in clinical practice. With the continued development of the immunological and molecular mechanisms of the disease, the scientific literature is becoming a major source for evaluating the effectiveness of current interventions, including biological therapies and allergen-specific immunotherapy. In addition, updates to clinical *guidelines* are needed to keep treatment recommendations relevant, accurate, and in accordance with the latest scientific findings, so as to improve the quality of care and clinical outcomes for patients.

METHOD

This method of writing a *literature review* is carried out through a systematic literature search strategy using several scientific databases such as PubMed, Scopus, and Web of Science. The search focused on relevant keywords, namely "allergic rhinitis", "pharmacologic therapy", "antihistamines", "intranasal corticosteroids", "biologics", and "immunotherapy", in the publication range of 2021 to 2025, and included articles in

E-ISSN: 2528-410X

English and Indonesian. Inclusion criteria include clinical studies, meta-analysis, and *systematic reviews*, while articles involving animal studies, case reports, and non-peer-reviewed publications are excluded. The analysis was carried out narratively by emphasising the aspects of effectiveness, safety, and conformity to *the recommendations of the applicable clinical* guidelines.

RESULT

Classification of the latest pharmacological therapies

Second-generation antihistamines (cetirizine, fexofenadine, bilastine)

Second-generation antihistamines such as cetirizine, fexofenadine, and bilastine are widely used to treat allergic rhinitis due to their minimal sedative effects. Bilastine, as a non-sedative antihistamine, is effective and safe based on a meta-analysis of five randomised controlled trials involving 3,329 patients. Compared to placebo, bilastine significantly improved total, nasal, and non-nasal quality of life, and reduced discomfort due to rhinitis. Its efficacy is comparable to that of other antihistamines, but it has advantages in terms of side effects, especially with a lower incidence of drowsiness compared to cetirizine. The available evidence shows moderate to high quality, supporting the use of bilastine as an effective and tolerable therapy for allergic rhinitis.[7]

Kortikosteroid intranasal (fluticasone furoate, mometasone)

Management of persistent allergic rhinitis of moderate to severe severity is still a global challenge, and combination therapy is often used to optimise clinical outcomes. One common approach is the use of intranasal corticosteroids (INCS) such as fluticasone furoate or mometasone, in combination with oral antihistamines or leukotriene receptor antagonists (LTRAs), depending on the presence of comorbidities such as asthma. An experimental study with a double-blinded randomised clinical trial design compared the effectiveness of the combination of fluticasone furoate with cetirizine versus fluticasone furoate with montelukast in patients with persistent allergic rhinitis. Assessments were conducted based on nasal eosinophil count and five-symptom total score (T5SS) using a visual analogue scale (VAS) before and after four weeks of treatment. Results showed that both combination therapies provided significant improvement, but the combination of fluticasone furoate and montelukast resulted in a statistically greater reduction in nasal obstruction and rhinorhea compared to the combination with cetirizine. Although the decrease in eosinophils and T5SS was higher in the montelukast group, the difference was not statistically significant. These findings support the use of fluticasone furoate, particularly when combined with montelukast, as a more effective option in managing symptoms of certain allergic rhinitis, such as nasal congestion and rhinorrhea.[8]

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Decongestants (oxymetazoline, pseudoephedrine) – limited use

The use of decongestants such as oxymetazoline and pseudoephedrine in the pharmacological therapy of allergic rhinitis should be limited and carried out with great caution. Based on various international guidelines, including ARIA as well as guidelines from the United States, Japan, and China, decongestants are only recommended for severe nasal congestion conditions and, in certain indications, are even considered second-line options, especially in children. Long-term and excessive use of decongestants can trigger drug-induced rhinitis, which is non-allergic inflammation of the nasal mucosa characterised by cilia damage, vasomotor disorders, and rebound congestion. The main symptom of this condition is a persistent nasal congestion, with histopathological changes such as mucosal swelling, loss of cilia, and infiltration of inflammatory cells. Studies show that most patients with drug-induced rhinitis have a history of decongestant use over a long period of time, even up to decades. To prevent and manage this condition, intranasal glucocorticoids (INCS) are recommended, and when ineffective, they can be combined with antihistamines or oral corticosteroids. However, the effectiveness and safety of combining INCS with decongestants still require further research, especially in patients with chronic rhinitis who do not respond to standard therapy.[9]

Anticholinergic intranasal (ipratropium bromide)

Intranasal anticholinergics, specifically ipratropium bromide, have become a concern in pharmacological therapy of allergic rhinitis (AR), especially to address persistent rhinorrhea even after the patient has undergone treatment and immunotherapy. RA itself is a hyperreactive condition of the nose characterised by symptoms such as rhinorhea, nasal congestion, itching, and sneezing. Ipratropium bromide works by inhibiting the activity of acetylcholine on muscarinic receptors in the nasal cavity, thereby reducing mucus secretion. This drug shows good clinical effectiveness and has a high safety profile, with minimal systemic side effects. Although there is no agreement on the timing and optimal indication of its use, ipratropium bromide is considered an adjunct therapy that is beneficial for patients with symptoms of difficult-to-control rhea. In the future, more in-depth clinical trials are needed to establish the role and application of intranasal anticholinergics more broadly in the management of RA.[10]

Stabiliser mast cell (cromolyn sodium)

Cromolyn sodium, as a mast cell stabiliser, has been used in pharmacological therapy of allergic rhinitis, both seasonal and chronic. The drug works by inhibiting the degranulation process in the mast cells that have been sensitised, thereby preventing the release of inflammatory and allergic mediators that trigger the symptoms. The intranasal use of cromolyn has been shown to be able to relieve the symptoms of allergic rhinitis, especially rhinorhea and sneezing, and is effective as a

E-ISSN: 2528-410X

prophylactic measure to prevent the appearance of symptoms when used before exposure to allergens. Controlled studies show that cromolyn sodium is suitable for specific patients, and the selection of the right candidate is key to the success of therapy with this agent. [11]

Leukotriene receptor antagonist (montelukast)

Montelukast, as a leukotriene receptor antagonist, is one of the first-line therapies in the treatment of allergic rhinitis (AR), often combined with antihistamines such as loratadine. Although there was no strong evidence of the effectiveness of this combination before, an analysis of 23 studies involving 4,902 participants showed that the loratadine-montelukast combination was significantly more effective in lowering the total nasal symptom score (TNSS) compared to the use of loratadine alone, montelukast alone, or placebo. In addition, this combination has also been shown to be superior in relieving secondary symptoms such as nasal congestion, itching, sneezing, rhinorhea, and rhinoconjunctivitis, as well as improving patients' quality of life based on the RQLQ questionnaire. Therefore, montelukast in combination with loratadine may be a more effective alternative for RA patients with moderate to severe symptoms, especially those who do not show an optimal response to monotherapy.[12]

Combination therapy (antihistamines + intranasal steroids)

Combination therapy between antihistamines and intranasal corticosteroids has become a recommended approach in the management of moderate to severe allergic rhinitis (AR), as listed in the latest ARIA guidelines. This combination aims to increase the effectiveness of treatment while improving patient adherence, especially since polytherapy often decreases the consistency of drug use. One of the latest intranasal formulations combining the two components is GSP301, which consists of olopatadine hydrochloride 600 µg as a second-generation antihistamine and momethasone furoate 25 µg as a topical glucocorticosteroid. Olopatadine works by inhibiting histamine activity and the production of inflammatory cytokines, while momethasone furoate suppresses the release of allergy mediators locally. Clinical evidence suggests that GSP301 is able to provide rapid and long-lasting symptom control, as well as improve the quality of life of patients with seasonal allergic rhinitis (SAR) and persistent (PAR). In addition, this formulation has a good safety profile and is well tolerated, even in long-term use, with side effects comparable to placebo or monotherapy. With its fast onset, high effectiveness, assured safety, and ease of use, GSP301 is a promising therapeutic option in clinical practice.[13]

Biology (omalizumab, dupilumab) – for severe/resistant cases

The use of biologic agents such as omalizumab and dupilumab in the treatment of severe allergic or resistant rhinitis is an important topic due to the limited direct evidence and variation in the results of existing studies. A systematic review of 37

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studies showed that all three agents—omalizumab, dupilumab, and mepolizumab—generally provided significant improvements in polyp size, clinical symptoms, and the need for additional therapies such as surgery or systemic corticosteroids. Among the three, dupilumab appeared to be superior in both primary and secondary outcomes, although this conclusion is still limited by the quality of the available study methodology. Therefore, direct clinical trials and a more robust statistical approach are needed to determine which biological agents are most appropriately used in cases of chronic rhinosinusitis with nasal polyps as well as severe allergic rhinitis.[14]

In the management of severe allergic rhinitis or that do not respond to conventional therapy, biologic agents such as omalizumab and dupilumab offer a promising therapeutic approach. Omalizumab, an anti-IgE monoclonal antibody, is effective in reducing symptoms of seasonal as well as persistent allergic rhinitis, especially in patients with high IgE levels and sensitivity to inhalant allergens. Meanwhile, dupilumab, which targets the IL-4 and IL-13 pathways, showed excellent results in reducing type 2 inflammation and improving the quality of life of patients, including those who also suffer from asthma or atopic dermatitis. Although both show significant clinical benefits, the selection of the right agent still requires individual consideration based on patient profiles and the availability of stronger clinical data. Further studies that are head-to-head and based on real populations are urgently needed to clarify the position of each agent in the therapeutic algorithm of severe allergic rhinitis.[14]

Subcutaneous and sublingual immunotherapy (SCIT and SLIT)

Subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) are quite effective therapeutic options in the management of allergic rhinitis and rhinoconjunctivitis, both with and without mild to moderate asthma. Based on an analysis of six randomised clinical trials and three NRS scores, no significant differences were found in terms of symptom improvement and treatment effectiveness between the two methods. However, SCIT tends to cause systemic side effects more often than SLIT, despite showing a higher level of patient adherence. Overall, although the efficacy of the two is similar, SLIT is superior in terms of safety, while SCIT is better in terms of compliance, so the selection of therapies can be tailored to the characteristics and preferences of the patient.[15]

Effectiveness and safety

Comparison between drug classes

Based on data analysis from the mHealth MASK-air application involving 1,691 users with a total of 28,177 reporting days, a comparison was made of the effectiveness and tendency of concurrent use (co-medication) between classes of pharmacological drugs for allergic rhinitis (AR), namely intranasal corticosteroids (INCS), intranasal antihistamines (INAH), permanent combinations of INAH+INCS,

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and oral antihistamines (OAH). Results showed that the use of co-medication was generally correlated with lower levels of treatment satisfaction. In monotherapy, OAH provides lower satisfaction than INCS or a combination of INAH+INCS. INCS is more commonly used in co-medication than OAH or a combination of INAH+INCS, indicating the potential need for additional therapy to achieve optimal effectiveness. Among intranasal drugs, fluticasone furoate and fluticasone propionate were more often combined, while in the OAH group, desloratadine and rupatadine provided higher satisfaction than fexofenadine, which was more commonly used in combination therapy. These findings provide a comprehensive picture of patient preferences and relative effectiveness between drug classes, and can be the basis for the development of more appropriate and safe AR therapy guidelines in the future [16]

Side effect profile and patient compliance

A retrospective study of children with allergic rhinitis (AR) who underwent subcutaneous home dust mite immunotherapy (SCIT) during the period 2015–2020 showed that, despite the occurrence of adverse events (AE), adherence rates to therapy remained high. Of the 1,098 patients who received SCIT, about 25.87% experienced SE, with a local incidence of SE of 17.9% and systemic SE of 8.38%. Systemic side effects occurred in only 0.53% of the total 30,744 injections, and acute allergic reactions within 30 minutes post-injection were recorded in 2.18% of patients, all of whom responded well to antiallergic therapy. Severe anaphylaxis is very rare, i.e. only 0.091% of patients or 0.0033% of total injections, and is successfully treated with the administration of adrenaline. Despite the risk of SE, including anaphylaxis, the results of this study confirm that SCIT has an acceptable safety profile and does not interfere with the continuity of therapy, suggesting that pediatric patients with AR continue to show high adherence in undergoing long-term pharmacological treatment.[17]

Recommendations for international guidelines

ARIA (Allergic Rhinitis and its Impact on Asthma)

The 2016 revision of the international guidelines ARIA (Allergic Rhinitis and its Impact on Asthma) brings an important update on pharmacological therapy strategies for allergic rhinitis. These guidelines comprehensively review the relative effectiveness of various classes of drugs, including oral H1 antihistamines, intranasal H1 antihistamines, intranasal corticosteroids, and leukotriene receptor antagonists, both in monotherapy and combination form. The ARIA expert panel provides detailed recommendations regarding the recommended treatment options, along with the clinical reasons behind their selection. In addition, the guidelines emphasise the need to consider individual factors such as patient preferences, symptom profiles, and clinical conditions in determining the most appropriate treatment approach, so as to

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support more personalised and effective decision-making in clinical practice.[18]

EAACI (European Academy of Allergy and Clinical Immunology)

This study highlights the importance of patient satisfaction in determining adherence to allergic rhinitis (AR) treatment, including the tendency to use adjunctive therapies (co-medication). By analysing data from the MASK-air application, the researchers compared the effectiveness and satisfaction levels against different classes of RA medications, such as intranasal corticosteroids (INCS), intranasal antihistamines (INAHs), INAH+INCS combinations, and oral antihistamines (OAH). The results showed that the use of OAH as monotherapy resulted in a lower level of satisfaction than INCS or a combination of INAH+INCS. In addition, the use of co-medication is generally associated with decreased satisfaction with treatment. Intranasal drugs such as fluticasone furoate and propionate are more commonly used in conjunction with other therapies, while desloratadine and rupatadine show higher satisfaction among oral antihistamines. These findings make an important contribution to developing therapeutic guidelines based on patient experience.[16]

According to the latest guidelines from the *European Academy of Allergy and Clinical Immunology (EAACI)* and the *Allergic Rhinitis and its Impact on Asthma (ARIA) initiative*, the treatment of severe or resistant allergic rhinitis should be carried out gradually and individually. First-line therapy remains relying on intranasal corticosteroids (INCS) due to their high effectiveness in controlling symptoms. For cases that do not respond optimally, the combination of INCS with intranasal (INAH) or oral (OAH) antihistamines may be considered. However, based on MASK-air data, the combination of INAH+INCS provides higher satisfaction than a single OAH. In patients with persistent and severe symptoms, EAACI also recommends consideration of immunomodulatory therapies such as *omalizumab* or *dupilumab*, especially when there are comorbidities such as asthma or nasal polyps. Periodic evaluation of adherence, patient satisfaction, and co-medication needs is key in determining the success of long-term therapy.[16]

DISCUSSION

Interpretation of results

The trend of shifting from monotherapy to combination therapy

In the pharmacological management of allergic rhinitis, there is a shift in trend from the use of monotherapy to combination therapy, which is considered more effective overall. The combination of intranasal antihistamines (INAHs) and intranasal corticosteroids (INCS) was shown to provide the most significant symptom improvement, while the combination of oral antihistamines (OAH) and INCS became a viable alternative for patients who are intolerant to bitterness. Typical therapies include oral, nasal, or eye drops (H1-blockers), as well as nasal corticosteroids, either alone or in combination with

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intranasal medications. Allergen-specific immunotherapy is also an option for patients with persistent symptoms, provided it is carried out by trained medical personnel using standard extracts. The use of real-life data through mobile applications also enriches the understanding of the variations of allergic rhinitis and its therapeutic approaches. Going forward, development is directed at the identification of complex and overlapping conditions, the integration of health technology evaluations, and more participatory and patient-centred therapeutic decision-making. [19,20]

The role of biological therapy in the case of refractory

In the treatment of allergic rhinitis that is refractory to conventional pharmacological therapies, biologic therapy plays an important role as a promising alternative. Biological agents such as Omalizumab, Dupilumab, Mepolizumab, Reslizumab, and Benralizumab—which are monoclonal antibodies—have been extensively reviewed through various randomised studies, scientific reviews, and meta-analyses from 2000 to 2021. Omalizumab, as an anti-IgE, has been shown to reduce the use of anti-allergy drugs and improve symptom control scores in seasonal and persistent allergic rhinitis, as well as reduce the risk of severe allergic reactions in patients undergoing allergen immunotherapy. Meanwhile, Dupilumab targeting IL-4 and IL-13 showed a significant improvement in the quality of life of patients with persistent allergic rhinitis. Anti-IL-5 agents such as Mepolizumab, Reslizumab, and Benralizumab are effective in lowering eosinophil counts as well as reducing corticosteroid dependence and frequency of asthma attacks, especially in cases of severe eosinophilic asthma. With proven effectiveness, biologic therapies—especially Omalizumab and Dupilumab—are increasingly being considered as a strategic approach to treating allergy rhinitis that is difficult to control.[21]

Current limitations of therapy

Long-term side effects

The use of systemic corticosteroids in the therapy of allergic rhinitis was initially quite common, especially in short-term oral form or depot injections to manage seasonal symptoms. However, over time, its use began to be abandoned due to the risk of significant side effects, especially when used repeatedly or in the long term. These side effects include an increased risk of infection, muscle disorders (myopathy), osteoporosis, aseptic necrosis of the femur, thinning of the skin, increased blood sugar levels (hyperglycemia), weight gain, fluid retention, physical changes such as the cushingoid face, neuropsychiatric disorders, as well as eye problems such as cataracts and glaucoma, including high blood pressure. In response to these limitations, intranasal corticosteroid therapy (INCS) began to be introduced as a safer alternative to the management of allergic rhinitis.[22]

Patient non-compliance

Patient adherence to pharmacological therapy of allergic rhinitis still faces various challenges rooted in the limitations of

E-ISSN: 2528-410X

current treatment approaches. An observational study conducted by FENAER in 2024 revealed that although most patients with moderate to severe allergic rhinitis are satisfied with their treatment, many experience fluctuations in symptoms, impact on daily activities, as well as consider changes in therapy due to the perception of low effectiveness. Factors such as side effects, high medical costs, and lack of education about the disease also affect the level of adherence. Qualitative analysis shows that patients need more personalised therapy, more practical methods of administering medications, better communication with healthcare workers, and emotional and educational support from patient associations. Therefore, a patient-centred approach, involving them in therapeutic decision-making, is key to improving compliance and overall quality of life.[23]

Access and cost of biologic therapy

Biologics are emerging as a promising new approach in the treatment of allergic rhinitis, especially in cases that are difficult to treat with pharmacotherapy, immunotherapy, or surgery. By targeting specific immune pathways in type 2 inflammation, this therapy offers a more targeted solution than conventional methods that only relieve symptoms. Biologic therapy selection strategies are now starting to consider serum IgE levels, the type of rhinitis (seasonal or persistent), and the patient's comorbidities to support more individualised treatment. However, the main limitations faced are the high access and cost of therapy and, long-term effectiveness that has not been fully tested, and patient adherence to complex dosing regimens. Nonetheless, with the support of ongoing research and clinical trials, biologic therapy has the potential to be a more effective and long-lasting solution for people with allergic rhinitis in the future [24]

Clinical implications

Therapeutic adjustment based on the patient's phenotype and endotype

Allergic rhinitis (AR) is a chronic inflammatory condition with diverse phenotypic characteristics and complex pathogenesis, which is often accompanied by low adherence to treatment, resulting in a high recurrence rate and a decrease in the patient's quality of life and mental health. An effective therapeutic approach requires a precision strategy that considers clinical manifestations, biomarkers, medical history, and additional diagnostic outcomes to tailor interventions based on the patient's phenotype and endotype. Phenotypically, pharmacological therapies such as intranasal corticosteroids (INCS), antihistamines, mast cell stabilisers, and leukotriene receptor antagonists remain the main pillars, while the combination of azelastine-fluticasone and allergen immunotherapy (AIT) is recommended for patients with asthmatic comorbidities. Probiotics can also be used as long-term prevention, although they are not effective for acute symptoms. Based on endotype, the use of capsaicin and surgical interventions may be beneficial in neurogenic-dominant RA, while AIT and biological therapies targeting type 2

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inflammation show great potential, although the use of monoclonal antibodies is still limited. Innovative therapies such as mesenchymal stem cell-based immunomodulation and traditional approaches such as acupuncture are also beginning to be explored to restore immunological balance. However, most current therapies still focus on symptom control, not the root cause of the disease. Therefore, further research is needed to better understand the mechanisms of RA pathogenesis and develop therapies tailored to individual biological characteristics, in order to improve patient effectiveness and adherence to treatment.[16]

Integration of pharmacological therapy with environmental education and modification

Several studies in reputable international journals such as *Allergy*, *Clinical and Experimental Allergy*, and the *Journal of Allergy and Clinical Immunology* emphasise that effective treatment of allergic rhinitis requires a multimodal approach. Pharmacological therapies, such as antihistamines, intranasal corticosteroids, and leukotriene receptor antagonists, provide significant symptom control, but long-term effectiveness is strongly influenced by the patient's understanding of the disease and adherence to treatment. Patient education on allergen avoidance, correct medication use techniques, and understanding of the course of the disease can improve adherence and therapy outcomes. In addition, environmental modifications such as the use of HEPA air filters, reduced exposure to house dust mites, and room humidity control have been shown to lower allergen exposure and improve patients' quality of life. This integrative approach is in line with the principles of evidence-based medicine and is recommended by various international consensuses, such as ARIA (Allergic Rhinitis and its Impact on Asthma), which also emphasises the importance of active patient involvement in the management of this chronic disease.[25]

Future research direction

In several reputable and Scopus-indexed international publications, such as those reviewed by the *International Journal of Molecular Sciences* and *Allergy*, researchers highlighted the importance of identifying genetic and molecular biomarkers that play a role in the immune response to allergens. The development of new molecules such as histamine H4 receptor antagonists, IL-5 inhibitors, and TSLP pathway modulation shows great potential in targeting the pathophysiological mechanisms of allergic rhinitis more specifically and effectively. On the other hand, pharmacogenomic studies have uncovered individual genetic variations that affect responses to antihistamines, intranasal corticosteroids, and allergen immunotherapy, thus opening up opportunities for therapies tailored to the patient's genetic profile. This approach not only improves the efficacy of treatment but also reduces the risk of side effects and resistance to therapy. With the integration of omics technology and artificial intelligence,

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this research direction is expected to be able to revolutionise the management of allergic rhinitis towards the era of precision medicine based on genetics and moleculars.[26]

CONCLUSION

Pharmacological therapy of allergic rhinitis has evolved significantly in the last decade. An evidence-based approach and personalisation of therapy are key to long-term effectiveness. Multidisciplinary collaboration is needed to optimise therapy and improve the quality of life of patients.

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