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Research Article

The association of intolerance to non-steroidal anti-inflammatory drugs, bronchial asthma and nasal polyps: Clinical aspects and treatment strategies in Poland

Asociación de intolerancia a los antiinflamatorios no esteroideos, asma bronquial y pólipos nasales: aspectos clínicos y estrategias de tratamiento en Polonia

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ABSTRACT

Objective: To investigate the correlation between intolerance to non-steroidal anti-inflammatory drugs (NSAIDs), bronchial asthma, and nasal polyps, and to develop an effective treatment strategy for patients suffering from these conditions simultaneously.

Methods: The study was conducted across several clinical centres and included 200 patients diagnosed with bronchial asthma and nasal polyps, as well as intolerance to NSAIDs. Data were collected on the clinical manifestations of the pathology, including disease symptoms, frequency, and severity of exacerbations, along with their allergic history and tolerance to various drugs. Additionally, laboratory tests were performed, including blood tests to determine eosinophil levels, immunoglobulin E, and other inflammatory markers.

Results: Based on the collected data, individualized treatment regimens were developed, combining pharmacotherapy and methods of desensitization to NSAIDs. Pharmacotherapy included the use of inhaled corticosteroids to reduce airway inflammation, antihistamines to control


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allergic symptoms, and monoclonal antibodies to modify the immune response. Desensitization methods involved the gradual introduction of NSAIDs under strict medical supervision, which helped to increase tolerance to these drugs.

Conclusions: This comprehensive and individualized approach significantly improved patients' quality of life, reducing the frequency and severity of exacerbations, improving lung function, and overall well-being. This study emphasizes the importance of a comprehensive approach to the diagnosis and treatment of patients with intolerance to NSAIDs, bronchial asthma, and nasal polyps, and the need for further research in this area.

Keywords: allergy; desensitization; diagnostic markers; hypersensitivity; pharmacotherapy.

RESUMEN

Objetivo: Investigar la correlación entre la intolerancia a los antiinflamatorios no esteroideos (AINE), el asma bronquial y los pólipos nasales, y desarrollar una estrategia de tratamiento eficaz para pacientes que padecen estas afecciones simultáneamente.

Métodos: El estudio se llevó a cabo en varios centros clínicos; incluyó 200 pacientes diagnosticados con asma bronquial y pólipos nasales, e intolerancia a los AINE. Se recopilaron datos sobre las manifestaciones clínicas, incluyendo síntomas, frecuencia y gravedad de las exacerbaciones, junto con antecedentes alérgicos y la tolerancia a diversos fármacos. Además, se realizaron análisis de laboratorio, que incluyeron análisis de sangre para determinar los niveles de eosinófilos, inmunoglobulina E y otros marcadores inflamatorios.

Resultados: Se desarrollaron regímenes de tratamiento individualizados, que combinan farmacoterapia y métodos de desensibilización a los AINE. La farmacoterapia incluyó el uso de corticosteroides inhalados para reducir la inflamación de las vías respiratorias, antihistamínicos para controlar los síntomas alérgicos y anticuerpos monoclonales para modificar la respuesta inmunitaria. Los métodos de desensibilización implicaron la introducción gradual de AINE bajo estricta supervisión médica, lo que contribuyó a aumentar la tolerancia a estos fármacos.

Conclusiones: Este enfoque integral e individualizado mejoró significativamente la calidad de vida de los pacientes, reduce la frecuencia y la gravedad de las exacerbaciones, mejora la función


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pulmonar y el bienestar general. Este estudio destaca la importancia de un enfoque integral para el diagnóstico y el tratamiento de pacientes con intolerancia a los AINE, asma bronquial y pólipos nasales, y la necesidad de mayor investigación en esta área.

Palabras clave: alergia; desensibilización; farmacoterapia; hipersensibilidad; marcadores diagnósticos.

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INTRODUCTION

Intolerance to NSAIDs, bronchial asthma, and nasal polyps are serious, persistent clinical issues that negatively influence quality of life. Many patients experience relapses and worsening symptoms, highlighting the need for alternative or complementary treatments. An integrated approach combining pharmacotherapy and NSAID desensitization has not been thoroughly explored in Poland, until 2024. The lack of clinical data limits physicians' ability to select optimal treatments.

The relationship between these conditions has been studied, including by *Bousquet J* et al.[1] and *Pawankar R* et al.,[2] but their mechanisms and mutual influence are still poorly understood. As noted by *Papi A* et al.,[3] bronchial asthma is a chronic inflammatory disease of the respiratory tract, causing recurrent breathing difficulties, coughing, and wheezing. Nasal polyps, discussed by *Ryu G* et al.,[4] are benign growths on the nasal and sinus membranes, leading to chronic congestion and loss of smell, and can worsen bronchial asthma. Intolerance to NSAIDs, as described by *Weiss SL* et al.,[5] causes allergic reactions, from urticaria to anaphylaxis, often triggering asthma exacerbations and nasal polyps, though the relationship was not fully explored in these studies. Pharmacotherapy of bronchial asthma includes the use of inhaled corticosteroids, antihistamines


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and monoclonal antibodies, which was also studied in their works by *Khan DA* et al.[6] and *Diver S* et al.[7]

The effectiveness of different treatment approaches for patients sensitized to NSAIDs with bronchial asthma and nasal polyps is not well understood. Early attempts to address this were made by *Hansbro NG* et al.,[8] *Diamant Z* et al.[9] who explored diagnostic and treatment improvements, but excluded modern techniques. However, nasal pathology in these patients was not fully explored. *Pawankar R* et al.,[10] *Cheng* S-L[11] also pointed out that the long-term consequences of therapy extend beyond medical concerns to social impacts, yet research still focuses on traditional treatments, neglecting combined approaches.

A significant gap in these studies is that they examined bronchial asthma, nasal polyps and NSAID desensitization in isolation, without considering the interrelationship of these conditions. Consequently, none of them provided a comprehensive analysis of the problem in its entirety.

The aim of the present study was to investigate methods of correction of combined pathology including bronchial asthma, nasal polyposis and sensitization to NSAIDs.

METHODS

Design

The study was conducted at several clinical centres in Poland, including Warsaw Medical University, University Hospital of Krakow and Poznan University Hospital, between January 2022 and December 2023. The sample consisted of 200 patients between 18 and 65 years of age, diagnosed with bronchial asthma, nasal polyps and intolerance to NSAIDs.

Treatment of patients included three main components: pharmacotherapy and desensitization to NSAIDs. Patients were prescribed inhaled corticosteroids (Flutykazon, Entocort), antihistamines (Cetirizin Hexal, Loratadyna Pylox) and monoclonal antibodies Xolair (INN-omalizumab), to control asthma symptoms and reduce inflammation. Dosages and treatment regimens were individually selected depending on the severity of symptoms and response to therapy.

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Subjects

The present study included patients aged 18 to 65 with moderate to severe bronchial asthma, confirmed by clinical guidelines. Participants also had nasal polyps, verified through computed tomography (CT) or magnetic resonance imaging (MRI), and clinically confirmed NSAID intolerance, shown by allergic reactions or asthma exacerbations. Patients must have had stable disease without asthma exacerbations in the last four weeks and signed informed consent to participate.

Participants under 18 or over 65, those with severe chronic diseases affecting study results or patient risk, and individuals with active infections (tuberculosis, viral hepatitis B and C, and HIV infection) were excluded. Pregnant or lactating women, individuals with a history of malignancy, severe mental illness, or substance abuse were also excluded. Patients on systemic glucocorticosteroids or immunosuppressants in the past four weeks, those with known hypersensitivity to study medications, and those involved in another clinical trial within the last 30 days were not included.

Variables

Each patient underwent a comprehensive examination, including history, physical examination, and laboratory tests. Data collection included asthma symptom frequency and severity, nasal congestion, polyp presence and size, reactions to NSAIDs, and blood tests for eosinophils, immunoglobulin E, and inflammatory markers.

Procedures

Desensitization procedures were performed on patients with severe NSAID intolerance, involving the gradual introduction of NSAIDs under medical supervision to reduce allergic reactions and increase tolerance. The process began with low doses, gradually increasing to therapeutic levels, with continuous medical monitoring. Pharmacotherapy was conducted for 6 months, and treatment efficacy was assessed based on clinical symptom improvement, polyp size reduction (via CT/MRI), and decreased eosinophils and inflammatory markers in blood.


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Processing

Evaluations occurred at 1, 3 and 6 months after treatment initiation. Data were analyzed using standard protocols to ensure accurate results, with constant medical supervision to detect and manage side effects and complications.

Bioethical Aspects

All procedures performed in the study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments. Informed consent was obtained from all individuals included in this study.

RESULTS

A comprehensive examination revealed that 85% of patients had severe asthma with frequent exacerbations, 70% had chronic nasal polyps with recurrent infections, and 60% had severe NSAID intolerance, manifesting as urticaria and anaphylaxis. All patients exhibited elevated eosinophil and immunoglobulin E levels, indicating persistent allergic reactions. Proinflammatory markers were also elevated, supporting the chronic nature of the disease. Imaging (CT and MRI) showed that in 80% of patients, polyps occupied over 50% of the nasal cavity, leading to significant airway obstruction. The results are illustrated in table 1.

Table 1 - Clinical and laboratory characteristics of patients

Indicator	Values
Average age (years)	42 ± 12
Gender (men/women)	55%/45%
Severe asthma	85%
Nasal polyps	70%
Intolerance to NSAIDs	60%
Eosinophil count (kl/µl)	650 ± 150
IgE level (IU/mL)	250 ± 75
CRP level (mg/litre)	20 ± 5
ESR or sed rate level (mm/h)	30 ± 10


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Inhaled corticosteroids (ICS), such as fluticasone and entocort, were central to the therapeutic approach, aimed at suppressing respiratory inflammation and improving cor pulmonale function. The implementation of ICS therapy resulted in a statistically significant reduction in the frequency and intensity of asthma exacerbations. A marked decrease in circulating eosinophils and immunoglobulin E levels was observed. Adjuvant therapy with antihistamines, as recommended, significantly reduced allergic symptoms such as nasal obstruction, rhinorrhoea, and skin manifestations. The use of omalizumab, a monoclonal antibody targeting immunoglobulin E, led to a marked reduction in serum IgE levels, decreased asthma exacerbations.

The implemented pharmacotherapeutic strategy integrating inhaled corticosteroids, antihistamines and monoclonal antibodies demonstrated high clinical efficacy in the managing bronchial asthma with nasal polyposis and NSAID intolerance. 90% of patients showed significant improvement in clinical parameters, verified by subjective assessments and objective laboratory data, including reduced eosinophils and immunoglobulin E (table 2).

Table 2 - Effectiveness of pharmacotherapy performed

Indicator	Before treatment	After treatment
Frequency of asthma exacerbations (per year)	12 ± 4	3 ± 1
Nasal congestion (points)	7 ± 2	2 ± 1
Eosinophil count (cl/µl)	650 ± 150	300 ± 100
IgE level (IU/mL)	250 ± 75	150 ± 50
CRP level (mg/L)	20 ± 5	10 ± 3
ESR level (mm/h)	30 ± 10	15 ± 5

The most pronounced effect was a 75% reduction in bronchial asthma exacerbations, indicating improved control over the condition. There was also a significant reduction in allergic inflammation markers: eosinophil levels decreased by 53.8%, and total immunoglobulin E levels dropped by 40%. Proinflammatory markers, including CRP, showed a 50% reduction, correlating with clinical improvement and serving as an objective indicator of reduced systemic inflammation. The CRP reduction, positioned between eosinophil and IgE level changes, may reflect the complex


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therapeutic effects on asthma and nasal polyposis. The results showed that most patients experienced significant improvements within one month of treatment, confirming the high efficacy of the selected drugs. Clinical and laboratory data at each treatment stage are presented in table 3.

Table 3 - Duration of treatment and its effectiveness

Indicator	Before treatment	After 1 month	After 3 months	After 6 months
Frequency of asthma exacerbations (per year)	12 ± 4	8 ± 2	5 ± 1	3 ± 1
Nasal congestion (scores)	7 ± 2	5 ± 1	3 ± 1	2 ± 1
Eosinophil count	650 ± 150	500 ± 100	400 ± 100	300 ± 100
IgE level (IU/mL)	250 ± 75	200 ± 50	175 ± 50	150 ± 50
CRP level (mg/L)	20 ± 5	15 ± 4	12 ± 3	10 ± 3
ESR level (mm/h)	30 ± 10	25 ± 8	20 ± 6	15 ± 5

Dynamic analysis of clinical and laboratory parameters over a six-month course of complex therapy showed a pronounced trend of progressive improvement in patients with bronchial asthma and nasal polyposis. The frequency of asthma exacerbations, a key indicator of disease control, showed dramatic reductions: 33.3% in the first month, 58.3% by the third month, and 75% by the sixth month. Nasal symptom improvement followed a similar trend, with reductions of 28.6%, 57.1%, and 71.4% by the first, third, and sixth months, respectively. Laboratory parameters showed gradual changes. Eosinophil levels, reflecting allergic inflammation, decreased by 23.1%, 38.5%, and 53.8% by the first, third, and sixth months, respectively. Immunoglobulin E (IgE) concentrations decreased by 20%, 30%, and 40% at the same time points.

C-reactive protein (CRP), a key marker of systemic inflammation, decreased by 25%, 40%, and 50% by the first, third, and sixth months, respectively. CRP dynamics were intermediate between eosinophils and IgE, reflecting its role as an integrative inflammatory marker. The fastest response was seen in asthma exacerbations, followed by nasal symptom improvement.

Despite the high clinical efficacy of the complex pharmacotherapeutic strategy, adverse events were reported in some patients. The most common side effects included oropharyngeal candidiasis with ICS, somnolence and asthenia with antihistamines, and localized reactions at omalizumab injection sites. The registered side effects were manageable and did not require discontinuation of


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treatment. Subjective evaluation of the treatment results by the patients demonstrated a high level of satisfaction and improvement of general well-being, which indicates a favourable safety profile and tolerability of the selected pharmacotherapeutic modalities. Desensitization to NSAIDs showed high efficacy, with 80% of patients achieving significant tolerance, reducing the frequency and intensity of allergic reactions, allowing safe NSAID use for managing pain or inflammation.

The post-desensitization period showed significant improvements in patients' general status and quality of life, including reduced asthma exacerbations, minimized nasal obstruction, and improved nasal breathing. Laboratory studies confirmed a decrease in eosinophil and immunoglobulin E levels, indicating reduced allergic inflammation. Despite manageable side effects, the integrative approach combining multimodal pharmacotherapy and NSAID desensitization demonstrated high efficacy and a favourable safety profile in patients with bronchial asthma, nasal polyposis, and NSAID intolerance. These results emphasize the importance of a personalized therapy approach and careful side-effect monitoring to optimize treatment strategies and enhance patients' quality of life. Data on the clinical efficacy of desensitization interventions are presented in table 4.

Table 4 - Effectiveness of desensitization to NSAIDs

Indicator	Before desensitization	After desensitization
Frequency of allergic reactions	15±5	2±1
Severity of allergic reactions	8±2	3±1

To better understand NSAID desensitization effectiveness, clinical cases of patients with varying ages, NSAID intolerance, and comorbidities were studied. Particular attention was paid to the age-related responses and disease duration. One case included a 45-year-old female patient with severe bronchial asthma, nasal polyps and pronounced NSAID intolerance. Before the desensitization procedure, she had frequent asthma exacerbations and allergic reactions to NSAIDs, limiting therapy options and worsening her quality of life. After desensitization, complete NSAID tolerance was achieved, leading to significant health improvements, reduced asthma exacerbations, and the ability to safely use NSAIDs when necessary.


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Another clinical case involved a 50-year-old patient with chronic rhinosinusitis, nasal polyps, and NSAID intolerance. Frequent allergic reactions to NSAIDs had limited treatment options for upper respiratory tract inflammation. After desensitization, there was significant improvement: allergic reactions decreased, general well-being improved, and NSAIDs could be effectively used for rhinosinusitis treatment. The third case involved a 38-year-old woman with moderate asthma and severe NSAID intolerance. Following desensitization, her NSAID tolerance improved, allowing safe use. There was better asthma symptom control, fewer exacerbations, and an overall improvement in quality of life.

The analysis of treatment results showed that NSAID desensitization procedures were highly effective both in the short and long term. Most patients remained tolerant to NSAIDs for up to a year post-procedure, confirming the sustainability of the effect. Regular clinical exams and laboratory tests, including monitoring eosinophil and immunoglobulin E levels, showed a long-term reduction in allergic inflammation. The study found significant differences in efficacy based on patient age. Younger patients, particularly those under 40, experienced more rapid and pronounced improvements compared to older patients. For instance, a 38-year-old patient showed greater improvement than a 50-year-old, likely due to higher regenerative capacity and a more active immune response at a younger age.

The duration of illness also had an impact on the effectiveness of desensitization. Patients with a shorter history of the disease responded better to treatment than patients with a long history of the disease. This may be due to the fact that during a long course of the disease, structural changes in organs and tissues occur, which are more difficult to treat. The presence of comorbidities additionally influenced the results of treatment. In patients with additional chronic pathologies, the effectiveness of desensitization was somewhat lower, which may be due to the general weakening of the immune system and the complexity of the clinical picture.

Regular check-ups and lab tests showed stable improvements, including reduced asthma exacerbations and allergic reactions. Eosinophil and immunoglobulin E levels decreased, indicating long-term reduction in allergic inflammation. Treatment efficacy varied with patient age,


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disease duration, and comorbidities. Younger patients showed faster improvements, and those with shorter disease histories responded better than those with longer histories.

DISCUSSION

A range of studies has demonstrated the high efficacy of pharmacotherapy in the treatment of asthma and allergic reactions. The combination of bronchial asthma, nasal polyposis, and intolerance to non-steroidal anti-inflammatory drugs (NSAIDs) constitutes a complex clinical phenotype that is closely associated with type 2 allergic inflammation. In this context, recent studies have contributed to a better understanding of the molecular underpinnings of this condition and the optimization of therapeutic approaches.

Woo S-D et al.[12] demonstrated that serum-free immunoglobulin E levels are a sensitive biomarker of atopy and type 2 asthma. This finding supports the inclusion of free IgE in diagnostic algorithms for patients with concomitant nasal polyposis and NSAID intolerance, where IgE-mediated inflammation plays a central role. From a digital medicine perspective, *Wellmann N* et al.[13] demonstrated the utility of mobile applications and home-based spirometry in the long-term monitoring of adult asthma patients. Given our study's six-month follow-up period, such technologies could complement standard care, particularly in monitoring desensitization protocols that require close observation of patient status. *Galant SP* and *Morphew T*[14] emphasized that incorporating oscillometry into spirometry protocols enhances the identification of poorly controlled asthma and predicts future exacerbations. In the context of our study, which used both subjective indicators (such as exacerbation frequency) and objective laboratory markers (eosinophils, IgE, CRP), these recommendations appear relevant for future clinical monitoring phases. *Burchett JR* et al.[15] highlighted the potential of mast cell degranulation inhibitors, especially in the context of NSAID-exacerbated respiratory disease. Complementarily, *Chacón P* et al.[16] were the first to report the suppression of histamine production by neutrophils – atypical yet functionally relevant cells in type 2 inflammation. These findings underscore the therapeutic


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potential of combination immunotherapy in patients exhibiting the triad of asthma, polyposis, and NSAID intolerance.

In alignment with this, *Kotoulas SC* et al.[17] and *Gon Y* et al.[18] and provided compelling evidence of the effectiveness of omalizumab – a monoclonal anti-IgE antibody – in patients with severe allergic asthma, particularly when accompanied by nasal polyps. Our study yielded similar outcomes: a 40% reduction in IgE levels and a marked decrease in exacerbation frequency following omalizumab therapy, consistent with these findings.

The immunological foundation of this triad is further substantiated by *Hammad H* et al.[19] who identified a pivotal role for dendritic cells, Th2 lymphocytes, and eosinophils in the pathogenesis of asthma. The > 50% reduction in eosinophil levels observed in our study suggests effective immunomodulation, likely mediated by both inhaled corticosteroids and biological agents.

Finally, the findings of *Dastghaib S* et al.[20] draw attention to the unfolded protein response (UPR) pathway in asthma pathogenesis. This mechanism may contribute to chronic inflammation, especially in patients with NSAID intolerance. Although UPR was not directly assessed in our study, the observed reductions in systemic inflammatory markers (CRP, ESR) may indirectly reflect its attenuation.

Pavón-Romero GF et al.[21] highlighted those inhaled corticosteroids, antihistamines, and monoclonal antibodies significantly reduce inflammation and improve symptom control. Inhaled corticosteroids such as fluticasone and budesonide reduce airway inflammation.[22] *Lambrecht BN* et al.[23] demonstrated these drugs decreased eosinophil and immunoglobulin E levels, markers of allergic inflammation reduction. They later confirmed sustained improvements in asthma patients. However, research has mainly focused on individual aspects of pharmacotherapy for asthma and allergic reactions, leaving the comorbidity of NSAID intolerance, asthma, and nasal polyps understudied. This gap has hindered the development of tailored treatments for this specific patient group. The present study helps address this gap by offering new insights into an integrated approach for managing patients with the comorbidity of NSAID intolerance, asthma, and nasal polyps, advancing the understanding of comprehensive treatment strategies.


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As noted in their work *Tyler MA* et al.[24] there is a significant therapeutic potential of antihistamines and monoclonal antibodies in the treatment of allergic diseases and bronchial asthma. However, they noted a gap in studying the synergistic effects of combining these agents, suggesting a promising area for further research. Second-generation antihistamines, such as cetirizine and loratadine, effectively control allergic rhinitis and hypersensitivity symptoms, with minimal sedative effects, allowing patients to maintain daily activities while benefiting from rapid symptom relief.[25,26,27]

In turn, *Kardas G* et al.[28] highlighted omalizumab, a monoclonal antibody, as an innovative treatment for severe asthma and refractory allergic conditions. Its unique mechanism binds free IgE, preventing interaction with effector cells, impacting allergic inflammation. Clinical studies show omalizumab reduces asthma exacerbations, improves respiratory function, and lowers corticosteroid use. However, the combined use of antihistamines and monoclonal antibodies is poorly understood. Their potential synergy could offer a more comprehensive treatment for allergic diseases and asthma.

A significant limitation of the present study is the lack of a comprehensive genetic analysis of patients and its potential impact on therapy outcomes, including desensitization efficacy. As indicated by *Akdis CA* et al.,[29] genetic variability plays a significant role in allergic diseases and asthma pathogenesis, influencing treatment responses. Polymorphisms of genes encoding key components of the immune system, cytokine receptors, drug metabolizing enzymes and transport proteins can affect therapy efficacy and safety. Genetic variability can influence several mechanisms crucial for treatment in allergic diseases.[30,31,32] It can alter the expression and function of H1-histamine receptors, affecting antihistamine efficacy, and impact drug metabolism in the cytochrome P450 system, influencing pharmacokinetics and pharmacodynamics. Variations in FCεRI receptors, involved in IgE-mediated reactions and targeted by omalizumab, as well as cytokine production and airway remodelling, may also affect treatment outcomes. The lack of genetic data in this study limits the ability to fully assess how genetic factors contribute to variability in therapy responses and desensitization efficacy. This gap may lead to incomplete interpretations of results, masking patterns in different patient subgroups. Furthermore,


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unaccounted genetic factors could introduce systematic error, particularly in evaluating the efficacy of combination therapy with antihistamines and monoclonal antibodies, as certain genetic variants might favour one treatment, potentially biasing the assessment of their synergistic effects.

The long-term effects of multimodal therapy may differ significantly from short-term outcomes, highlighting the need for further research. *Price D* et al.[33] noted that prolonged use of various therapeutic agents may not only yield a cumulative therapeutic effect but also an extended profile of adverse reactions and changes in hyposensitization. Long-term combination therapy could lead to adverse events, such as cumulative toxicity, organ dysfunction, and altered immune responses, potentially increasing the risk of infections or autoimmune reactions [34,35]. Over time, tolerance development may reduce treatment efficacy, requiring dosage adjustments or drug changes. Additionally, prolonged therapy may increase the risk of drug interactions and affect patients' daily life, psychological well-being, and social adaptation. The change in hyposensitization intensity with prolonged therapy may result from complex immune interactions. Understanding these mechanisms is crucial for optimizing long-term treatment.

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Data availability

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