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Allergic reactions to medicines: Mechanisms of development, clinical manifestations and prevention strategies

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Abstract

Introduction: Allergic reactions to medications present a significant public health challenge, necessitating deeper insights into their mechanisms and effective prevention strategies.

Aim: The study aimed to identify the mechanisms of development, clinical manifestations, and effective strategies for preventing allergic reactions to medications, considering individual patient characteristics.

Material and methods: It analysed the pathophysiological mechanisms of the immune response, focusing on the interaction of cellular and humoral components, such as T-lymphocytes, B-lymphocytes, mastocytes, and inflammatory mediators. The impact of key risk factors, including genetic predisposition, age, gender, and comorbidities, on the likelihood of allergic reactions was also examined. The analysis evaluated the frequency and severity of allergic reactions among patients in Europe and North America, where β-lactam antibiotics and nonsteroidal anti-inflammatory drugs were the most common triggers, accounting for up to 10% of cases.

Results and discussion: Existing preventive methods, including pharmacogenetic testing, desensitisation, and the selection of alternative medications, were reviewed. These methods demonstrated a reduction in allergic reaction risk by up to 85-95%. Personalised patient management algorithms were developed, incorporating biomarkers, pharmacogenetic technologies, and advanced diagnostic tools to enhance risk identification and minimise severe systemic manifestations.

Conclusions: The findings provided a basis for refining the diagnosis, prevention, and treatment of drug-induced allergic reactions in clinical practice. The proposed personalised strategies offer effective management of high-risk patients, improving the safety of drug therapy. The study addressed gaps in understanding the mechanisms of hypersensitivity and formulated recommendations to advance clinical practices in allergy management.

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1. INTRODUCTION

Allergic reactions to medicines represented a significant public health issue due to their prevalence, heightened frequency among vulnerable populations, and severe outcomes, such as anaphylaxis, toxic epidermal necrolysis, and Stevens-Johnson syndrome.[1] This syndrome is a very serious skin disease that manifests itself through inflammation and detachment of the skin and mucous membranes. Stevens-Johnson syndrome is often caused by a reaction to a medication or infection, which can lead to painful blisters, erosions, and ulcers on the skin and in the mouth, eyes, and genitals. The disease can cause serious complications, including infections, organ failure, and even death, and therefore requires immediate medical intervention. Urticaria is a skin reaction characterized by the appearance of red or pale-pink hives, accompanied by itching. The rash can be localized or widespread and often occurs as a result of an allergic reaction to medications, food, insect bites, or other external triggers. Urticaria is typically temporary and resolves after the triggering factor is removed, but in some cases, it can become chronic.

The increasing use of antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and other medications highlights the need to address allergic reactions. Despite extensive research, the mechanisms, risk factors, and preventive strategies remain insufficiently understood. Allergic reactions involve the activation of T lymphocytes, mast cells, basophils, and the release of inflammatory mediators like histamine, leukotrienes, and cytokines. Genetic factors, including polymorphisms in drug metabolism and immune response, play a crucial role in these reactions.[2]

The literature review highlighted key aspects and identified areas requiring further development. For instance, Jiang et al.[3] demonstrated the efficacy of Fenton reactions for antibiotic removal from aquatic environments but did not adequately address the environmental impact of residual oxidation products or the long-term sustainability of these technologies. Fenton reactions refer to a chemical process that uses hydrogen peroxide (H_2O_2) and iron salts (typically ferrous iron, Fe^{2+}) to produce hydroxyl radicals (OH). These highly reactive radicals can break down a wide range of organic pollutants, making Fenton reactions useful in environmental applications, such as the removal of contaminants from water. The process is often used for wastewater treatment, including the degradation of antibiotics and other harmful substances in aquatic environments.

Recent studies focus on rare allergic reactions to vaccines, especially polyethylene glycol. While diagnostic algorithms aim to reduce risks, gaps remain in understanding long-term effects and preventive measures for high-risk groups, as discussed by Sampath et al.,[4] Malamed SF.[5] Efforts to improve anaphylaxis management include innovations like nasal and oral epinephrine, aiming to enhance treatment timeliness, though economic barriers and long-term effectiveness remain challenges, as noted by Lieberman et al.,[6] Cox et al.[7] Biologics show promise in complementing traditional methods like oral immunotherapy for managing food allergies, but their long-term safety and economic feasibility remain underexplored, hindering practical application, according to Fiocchi et al.[8] Omics technologies show potential in refining clinical practices, but their widespread adoption faces barriers related to long-term integration and adaptability to diverse populations, as examined by Ogulur et al.,[9] Gohal et al.[10]

2. AIM

The purpose of the study was to elucidate the mechanisms of allergic reactions to medicines, analyse associated risk factors, and develop recommendations to improve diagnostic, preventive, and therapeutic approaches, accounting for individual patient characteristics. To achieve this goal, the following tasks were addressed:

(1) Analyse the literature to identify key mechanisms of the immunological response underlying drug-induced allergic reactions, with particular attention to genetic factors and cross-reactivity.
(2) Summarise data on clinical manifestations of various allergic reaction types, including anaphylaxis, to develop algorithms for early diagnosis and treatment.
(3) Evaluate existing methods for preventing allergic reactions to medicines and formulate recommendations for their enhancement, incorporating individual risk factors.

3. MATERIAL AND METHODS

The study analyzed publications from 2018 to 2025, focusing on peer-reviewed works written in English that directly addressed critical aspects of drug-induced allergic reactions, including their mechanisms, clinical features, and prevention strategies. Studies that relied solely on non-human models, lacked accessibility to full texts, or were unrelated to the scope of drug hypersensitivity were excluded. Emphasis was placed on materials that covered the mechanisms of reaction development, clinical manifestations, and modern preventive methods.

The review process included the analysis of sources from scientific journals, monographs, and leading electronic databases such as PubMed, Scopus, and Web of Science. The search strategy was carefully designed to identify relevant literature using targeted keywords, including drug allergy, immune hypersensitivity, adverse drug reactions, pharmacogenetics in allergy, anaphylaxis management, biomarkers in allergic diseases, and food and drug cross-reactivity. Boolean operators were employed to refine the search, ensuring specificity and relevance with queries like 'drug allergy AND immune hypersensitivity' and 'biomarkers AND allergic diseases NOT food allergy.'

The initial search identified 142 publications, which were narrowed down to 30 studies following a detailed screening process. These sources provided essential insights

into the mechanisms and management of allergic reactions to medicinal products. The study used systematic review methods, qualitative analysis, and statistical data processing to explore allergic reactions. The systematic review gathered and evaluated scientific sources on mechanisms, clinical manifestations, and prevention strategies, highlighting critical knowledge gaps.

Qualitative analysis focused on immunological mechanisms, particularly the four hypersensitivity types, inflammatory mediators like histamine, leukotrienes, and cytokines, and genetic and environmental factors influencing allergic reactions. Statistical analysis assessed the frequency, prevalence, and severity of allergic reactions across age and gender groups, considering comorbidities and polypharmacy. Clinical data analysis revealed patterns in allergic reaction development, forming the basis for improving preventive strategies, diagnostic algorithms, and therapeutic interventions. The interpretation of results involved comparing the findings with existing theoretical frameworks and clinical guidelines on drug-induced allergic reactions. Statistical indicators, such as reaction frequency, prevalence, and severity, were thoroughly analysed to identify key trends. Special attention was given to correlations between clinical manifestations, reaction mechanisms, and individual risk factors. The results were synthesised to formulate conclusions that could enhance preventive measures and therapeutic approaches.

The analysis identified the mechanisms of allergic reactions, their clinical manifestations, and associated risk factors, enabling the development of effective prevention strategies. These findings provided a robust scientific foundation for refining diagnostic and therapeutic approaches, aligning with the study's objectives.

4. RESULTS

Prior studies have explored the connection between allergic reactions and immune system dysfunction, highlighting heightened sensitivity to normally harmless antigens. This study examined the mechanisms of allergic reactions, revealing that immune dysfunction leads to increased sensitivity. The interaction of cellular and humoral immune components, including T-lymphocytes, B-lymphocytes, dendritic cells, macrophages, mastocytes, and basophils, was analyzed, with humoral components consisting of antibodies and cytokines that modulate the immune response. Hypersensitivity mechanisms were categorised into four main types. Immediate-type reactions immunoglobulin E-dependent (IgE-dependent) arose from the formation of IgE antibodies, which bound to the surface of mastocytes and basophils. Upon subsequent exposure to the antigen, these cells released inflammatory mediators like histamine, triggering rapid clinical symptoms. Cytotoxic reactions involved cellular damage through the activation of the complement system by immunoglobulin G (IgG) or immunoglobulin M (IgM) antibodies. Immunocomplex reactions occurred due to the deposition of immune complexes in tissues, leading to localised inflammation. Delayed-type reactions, mediated by T lymphocytes, caused chronic inflammation or tissue injury.

IgG and IgM are the main classes of antibodies that perform important functions in the immune system, in particular in the context of immune responses. IgG is the most abundant class of antibodies in blood and interstitial fluids and plays a key role in secondary immune responses. They are able to bind to antigens, activating the complement system, which leads to cell lysis or cleansing the body of pathogens. IgG also interact with phagocytic cells, facilitating the absorption and destruction of microorganisms. In the context of allergic reactions, both classes of antibodies can contribute to the development of inflammation.[11]

Inflammatory mediators like histamine, leukotrienes, and prostaglandins play key roles in allergic reactions, causing vasodilation, increased permeability, and bronchospasm. Cytokines such as IL-4 and IL-5 regulate eosinophil activity, contributing to later allergy phases. Genetic factors, including polymorphisms in the major histocompatibility complex (MHC), affect antigen recognition and drug metabolism, influencing hypersensitivity reactions and toxic metabolite accumulation. Genetic predisposition can affect the rate of drug metabolism, which is important for personalized treatment. Different variations in the genes that control drug metabolism can lead to the accumulation of toxic metabolites, which increases the risk of side effects or toxicity.[12]

Risk factors, including age, gender, and comorbidities, further modulated the likelihood of allergic reactions. Comorbidities such as bronchial asthma and atopic dermatitis elevated the risk of allergic reactions. Immunosuppressive therapies in patients with autoimmune diseases or cancer altered normal immune responses, increasing hypersensitivity risks.[13,14] Bronchial asthma and atopic dermatitis are diseases associated with impaired immune responses to external stimuli and are often accompanied by hypersensitivity to allergens. In the case of bronchial asthma, the mechanisms of an allergic reaction include the activation of T lymphocytes, in particular Th2 cells, which produce interleukins such as IL-4, IL-5, and IL-13. These molecules stimulate eosinophils and other cells of the immune system, leading to inflammation in the airways, breathing restriction, and increased sensitivity to allergens such as pollen, dust mites, or mold. Atopic dermatitis, in turn, is a skin disease that is also characterized by impaired skin barrier function and chronic inflammation. It occurs due to genetic predisposition and exposure to external allergens or irritants.

Activation of T cells leads to cytokine synthesis, regulating the immune response. B-lymphocytes produce antibodies, such as IgE, which activate mastocytes and basophils in immediate-type reactions, causing rapid clinical manifestations like edema, urticaria, or bronchospasm. Delayed-type reactions involve macrophages and cytotoxic T lymphocytes, inducing tissue damage and chronic inflammation. Clinical manifestations range from drug rashes to toxic epidermal necrolysis.[15]

Table 1. Frequency, prevalence and severity of allergic reactions to different groups of drugs.[16]

Group of drugs	Response rate, %	Severe reactions, %	Prevalence in patients with allergies, %
β-lactam antibiotics	10	2.0	45
Nonsteroidal anti-inflammatory drugs (NSAIDs)	8	1.5	25
Sulfonamides	5	1.2	15
Antiepileptic drugs	6	2.5	10
Chemotherapeutic drugs	3	0.8	5

Table 2. Effectiveness of existing methods of preventing allergic reactions to drugs.[19–21]

Method of prevention	Efficiency (%)	Main advantages	Limitations
Anamnesis is taken	60–70	Easy to implement, low cost	Dependence on subjective patient data
Skin tests	75–85	Accuracy for individual drug groups	Impossibility of application for all medicines
Desensitisation	80–90	Suitable for high-risk patients	The need for specialised conditions
Pharmacogenetic testing	85–95	Individualisation of therapy	High cost, limited availability
Selection of alternative drugs	70–80	Avoidance of allergenic drugs	Dependence on the availability of alternatives

The frequency, prevalence, and severity of allergic reactions were evaluated through statistical data collection from clinical trials and retrospective analyses of medical records. Table 1 provides a detailed breakdown of the distribution of allergic reactions by drug type and clinical severity.

The data in Table 1 indicated that the most frequent allergic reactions occurred with β-lactam antibiotics, particularly penicillins and cephalosporins, causing both mild and severe manifestations. NSAID and sulfonamides were also identified as common allergens, especially in patients with comorbid conditions. Severe reactions, including anaphylaxis and toxic epidermal necrolysis, were most commonly associated with antiepileptic drugs and β-lactam antibiotics. Based on statistical analysis, methods were developed to identify high-risk patients, including detailed medical histories, hereditary assessments, sensitization testing, and pharmacogenetic testing.[17] When necessary, alternative medications or desensitization protocols were used.[18]

Multicentre trial results were analysed using descriptive statistics and comparative methods to identify the most effective preventive approaches for specific patient and drug groups. The results, presented in Table 2, compared the effectiveness of various methods based on key indicators, such as reduction in reaction frequency, severity, and improved safety.

Table 2 showed that pharmacogenetic testing was the most effective method for preventing allergic reactions, although high costs limited its adoption. Desensitization proved effective for sensitized patients, while anamnesis remained essential but dependent on the accuracy of collected information. The analysis emphasized integrating pharmacogenetics, sensitivity testing, and alternative drug selection to reduce allergic complications.[22–24]

Biomarker utilisation was another promising advancement. Research indicated that levels of cytokines (e.g., IL-4, IL-5) and IgE could serve as indicators for early detection of drug sensitisation. These biomarkers are important indicators for the early detection of sensitization, as their levels increase when the immune response to an allergen is activated. For example, elevated IgE levels are typically associated with allergic reactions, including immediate reactions such as anaphylaxis. Interleukins, such as IL-4 and IL-5, regulate the activation of eosinophils, which are important cells in the inflammatory processes that occur in allergies.

Pharmacogenetic testing has been recognised as a critical strategy for diagnosing allergic reactions, enabling the consideration of individual genetic characteristics of patients. This method facilitates the identification of allergy risks associated with specific medications before initiating therapy, enhancing treatment safety. Omics technologies are a set of modern scientific methods that allow studying and analyzing large amounts of biological information at the molecular level. The main omics technologies include genomics (study of genetic material), transcriptomics (RNA analysis), proteomics (study of proteins), and metabolomics (study of metabolites). These technologies allow us to study all elements of the biological system that interact and affect the functioning of the body.

The developed strategies for improving diagnostics, prevention, and treatment included integrating advanced technologies, creating management algorithms for high-risk patients, and promoting personalised approaches. The combination of these measures minimised allergic reaction risks, improved pharmacotherapy safety, and established a foundation for further advancements in clinical practice.

5. DISCUSSION

The results obtained provided a detailed analysis of the mechanisms of allergic reactions, including the activation of cellular and humoral components of the immune system, as well as the identification of key risk factors such as genetic predisposition, age, gender, and comorbidities. The high incidence of allergic reactions to β-lactam antibiotics and NSAID, reaching up to 10%, highlighted the necessity

of implementing personalised diagnostic and therapeutic approaches. The evaluation of prevention methods, particularly pharmacogenetic testing, demonstrated its effectiveness in reducing allergic reaction frequency by 85%–95%, supporting its integration into clinical practice.

The study by Pérez-Garza et al.[12] explored the mechanisms of allergic reactions, classifying hypersensitivity into four types and identifying common triggers like β-lactam antibiotics, neuromuscular blockers, and specific NSAIDs. Their work highlighted the clinical significance of reactions such as urticaria, angioedema, and anaphylaxis, emphasizing the need for accurate diagnosis and timely intervention. However, they overlooked critical genetic factors like HLA-B polymorphisms, which are essential for predicting drug reactions.

In their research, Insani et al.[13] delved into allergic reactions associated with polyethylene glycol (PEG), documenting five confirmed cases, including life-threatening anaphylaxis. Their study underscored the diagnostic potential of skin and intradermal tests, albeit with associated risks of triggering anaphylactic episodes. The authors proposed a targeted diagnostic algorithm, advocating for specialised diagnostic protocols in cases of suspected PEG allergies. This focus on PEG aligns with the current study's emphasis on diagnostic accuracy for managing hypersensitivity reactions.

The study by Accarino et al.[14] highlighted the prevalence of cutaneous adverse drug reactions (CADR), affecting up to 10% of hospitalized patients and 1%–3% on polypharmacy. Their research identified antibiotics, NSAIDs, and antiepileptics as primary causes, which aligns with the current study confirming the high prevalence of skin-related drug reactions. The work by Thong et al.[19] along with Chow et al.[16] demonstrated the effectiveness of traditional Chinese medicine (TCM) in managing allergic reactions, including food allergies and eczema. TCM formulations like FAHF-2 suppressed T cell, basophil, and mast cell activation, reducing IgE levels and pro-inflammatory cytokine production in mouse models.

The work by Sitek et al.[17], Karunarathna et al.[18] highlighted the importance of personalized medicine in managing allergic diseases, emphasizing genetic, phenotypic, and patient-specific factors. Their studies showed that molecular diagnostics can identify IgE targeting specific allergens and differentiate cross-reactive molecules. The application of omics technologies, such as proteomics and epigenomics, helps predict patient responses, identify biomarkers, and improve allergenic immunotherapy efficacy.

The analysis of scientific literature reaffirmed the importance of a multifactorial perspective in studying allergic reactions, incorporating genetic, environmental, and immunological factors. Research has largely concentrated on the role of inflammatory mediators, specific antibodies (IgE and IgG), and cellular mechanisms in allergic reaction development. At the same time, diverse approaches have been proposed for advancing diagnostics and therapy, including omics technologies, bioinformatics, and traditional Chinese medicine.

6. CONCLUSIONS

(1) The study highlighted the role of cellular components and inflammatory mediators like histamine and interleukins (IL-4, IL-5) in drug allergies, with genetic factors, particularly HLA-B gene polymorphisms, significantly influencing hypersensitivity likelihood.
(2) β-lactam antibiotics, nonsteroidal anti-inflammatory drugs, and antiepileptics were identified as high-risk drugs for severe allergic reactions. Patients with chronic conditions, children, and the elderly were more likely to experience severe outcomes.
(3) Pharmacogenetic testing tools were developed to more accurately identify individuals at risk of hypersensitivity, offering precise evaluations and improving treatment safety.
(4) The study suggests enhancing healthcare professionals' expertise in advanced diagnostic technologies and integrating personalized treatment protocols, including desensitization and alternative drug options.
(5) Future studies should explore integrating omics technologies (proteomics, epigenomics), investigate new biomarkers and molecular pathways, and examine the role of the microbiota in allergy development and prevention.
(6) Limitations of this study include possible incompleteness of data due to restrictions on access to certain publications, in particular those that were not available in full text. The exclusion of studies based only on non-human models or not relevant to the topic of drug hypersensitivity may also limit the diversity of sources.

Conflict of interest

Author declares no competing interest.

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