

Available online on 15.02.2022 at <http://jddtonline.info>

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the CC BY-NC 4.0 which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited



Open Access Full Text Article



Review Article

A Comprehensive Literature Review of Allergic Conjunctivitis

Nugraha Wahyu Cahyana

Department of Ophthalmology, Faculty of Medicine, Jember University, Jember, East Java, Indonesia

Article Info:



Article History:

Received 16 December 2021
Reviewed 14 January 2022
Accepted 19 January 2022
Published 15 February 2022

Cite this article as:

Cahyana NW, A Comprehensive Literature Review of Allergic Conjunctivitis, Journal of Drug Delivery and Therapeutics. 2022; 12(1-s):PageNo.

DOI: <http://dx.doi.org/10.22270/jddt.v12i1-s.5300>

Abstract

Allergic disease is a complex disease caused by a combination of genetic and environmental factors. Allergic diseases are on the rise, affecting about 30% to 40% of the world's population. In addition to a decrease in quality of life, this disease can affect the social and economic. This study aims to determine the concept of allergic conjunctivitis and its current management. Results: Allergic conjunctivitis is an inflammatory response of the conjunctiva to allergens such as pollen, environmental antigens (eg dust), and animal dander. Conclusion: Allergic diseases can be managed strategically, both non-pharmacologically and pharmacologically. Pharmacological use is usually preferred when non-pharmacological methods prove ineffective or insufficient in reducing allergy symptoms. Topical therapy consists of combination drugs such as antihistamines and vasoconstrictors, or antihistamines with mast cell stabilizing properties. The first are vasoconstrictors that target eye redness and antihistamines that target allergy symptoms.

Keywords: Allergic Conjunctivitis, Concept, Drugs

*Address for Correspondence:

Nugraha Wahyu Cahyana, Department of Ophthalmology, Faculty of Medicine, Jember University, Jember, East Java, Indonesia.

ORCID ID: <https://orcid.org/0000-0002-8919-6411>

Introduction

Allergic disease is a complex disease caused by a combination of genetic and environmental factors. Allergic diseases are on the rise, affecting about 30% to 40% of the world's population. In addition to a decrease in quality of life, this disease can affect the social and economic.¹

The allergic response is a hypersensitivity reaction mediated by the adaptive immune system. The presence of a trigger, such as an allergen or antigen, induces a humoral immunological response, which in turn triggers a complex immunological reaction. This dysregulation in immune function increases plasma levels of immunoglobulin E (IgE). The release of IgE is followed by binding to the allergen or antigen, which further stimulates mast cells to degranulate and release several pro-inflammatory substances including histamine, chemokines and various cytokines.²

There are many different factors that come into play when looking for the cause of an allergy. Environmental influences that occur in pregnancy and early childhood can alter an individual's physiological, immune, structural and behavioral development and thereby alter response patterns that influence susceptibility to future disease.³ Genetics also plays an important role in a person's susceptibility to allergic diseases. The most common allergic conditions worldwide include atopic dermatitis, rhinitis, asthma, rhinosinusitis, allergic conjunctivitis and most recently allergic esophagitis.^{3,4}

Allergic conjunctivitis is basically a condition that affects young adults, with the average age of onset being 20 years and these symptoms decreasing with age.⁵

1. Atopic Characteristics

Atopic refers to an increased sensitivity of IgE to a particular antigen, which in turn, results in a hypersensitive response upon exposure to the specific allergen in question.⁶ "Atopic features" is a term that refers to the development of various atopic diseases that may develop during childhood.

2. Atopic Pathophysiology

There is ample evidence to suggest that T-lymphocytes play a major role in allergic disease. The T-helper cell type 1 (Th1)/T-helper type 2 (Th2) paradigm has been studied extensively and appears to be a major pathological pathway in allergic disease. There is an association between the Th1 and Th2 subsets of T lymphocytes. Th1 and Th2 subsets tend to differentiate from CD4⁺-naïve T lymphocytes. This means that whenever a response is raised towards a Th1 or Th2 subset occurs, the others are reduced.⁷ When there is a decrease in Th1 production, there is a decrease in the levels of interferon gamma (IFN- γ), interleukin (IL)-2 and tumor necrosis factor (TNF)-beta. This in turn leads to increased levels of Th2 effects, due to decreased production of IgG, which inhibits Th2 formation.^{7,8}

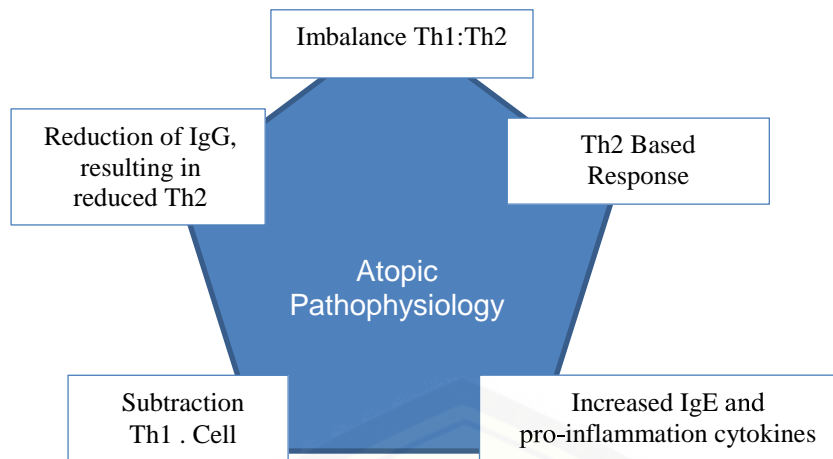


Figure 1: Imbalance of Th1 and Th2 that causes atopic disease

3. The role of histamine in allergies

Histamine is an endogenous substance synthesized from histidine. It has the ability to cause autacoid effects in peripheral tissues and also acts as a neurotransmitter in the central nervous system (CNS).⁹ The role of histamine in the inflammatory process remains significant in understanding its pathophysiology. Histamine release in peripheral tissue areas is mediated by mast cell degranulation. This degranulation can be triggered in a number of ways. In allergic disease, the interaction between IgE antibodies (immunoglobulin E) and the appropriate IgE antigens (i.e. formation of antigen-antibody complexes) leading to allergic reactions (local histamine release) or anaphylaxis (systemic histamine release), appears to be the main trigger.⁹

There are currently four identified histaminergic receptor subtypes (i.e. H1 to H4 receptors). The H1-receptor is the main active subtype in mediating acute allergic reactions. There are different effects that may be induced by H1-receptor stimulation. Some of these effects cause allergic conditions, including allergic rhinitis and conjunctivitis, urticaria, pruritus and angioneurotic edema.⁹

Stimulation of these receptors is also responsible for vasodilation and increased vascular (capillary) permeability that accompanies allergic reactions and inflammatory erythema and edema, including potentially fatal glottic edema. Understanding histamine regulation helps the type of treatment to be initiated in various allergic reactions. For example, histamine is released systemically in anaphylaxis but the use of antihistamines alone is not effective in treating anaphylaxis.

4. Genetic Predisposition

Allergies tend to be familial, with patients suffering from allergies tending to have a higher risk of having children with some form of atopic.² There is ample evidence to suggest that T lymphocytes play an important role in allergic disease. Several studies have looked at the role of genetics in allergic diseases. Some studies have mitochondrial RNA (miRNA) as the main focus of these studies. Previous studies have shown that certain types of miRNA increase the sensitivity of T cells to peptide antigens. Evidence suggests that inhibition of miR-181a expression in immature T cells significantly decreases sensitivity to antigens and enhances impaired T-cell selection. T-cell apoptosis is critical in regulating the length and strength of T-cell responses. MiR-21 has also been studied extensively, exhibiting significant upregulation during T-cell activation and plays a role in the suppression of apoptosis in activated T-cells. T-cell regulation as the development of polarized TH

cells is central to the pathogenesis of allergic inflammation because allergic inflammation is dominated by the TH2 response.¹⁰

5. Allergen Exposure

Allergen exposure in individuals with atopic disease increases the risk occurrence of a hypersensitivity reaction, regardless of the degree of exposure to the antigen. Evidence showing that immune sensitization is independent of the level of allergen exposure lends credibility to the belief that the presence of atopic disease is hereditary.¹¹

6. Infection and endotoxin exposure

The hygiene hypothesis is applied to most atopic diseases. This predicts that the prevalence of atopic disease decreases when a child is exposed to more infectious agents. It is thought that exposure to animals, viruses, bacteria, and various endotoxins makes children less likely to develop atopic diseases. The hygiene hypothesis arises from the understanding that bacterial, viral and endotoxin factors trigger the immune response of Th1 lymphocytes. Th1 lymphocytes increase the production of IgG antibodies. Th1 (via IgG) indirectly suppresses Th2 activity that mediates the release of various cytokines including IgE. Th2 cytokines are common culprits in the development of allergic disease.^{2,12,13}

7. Intestinal Flora

The presence of microbes in the walls of the intestinal tract helps regulate the immune response. Exposure to microbial flora in the gastrointestinal tract early in life allows changes in the balance of Th1:Th2 cytokines, favoring Th1 cell responses. Shifts in microbial balance initiate altered immune responses.² Later evidence suggests that early neuronal high-dose antibiotic exposure can alter the composition of the gut flora, skewing an immune response with elevated Th2 levels. High Th2 leads to increased IgE production and therefore the possibility of developing atopic disease.¹⁴

Method

From a systematic look out through a decided approach, we have collected 387 articles from the Google Scholar. After being filtered, 179 articles were excluded because of duplicate research; 165 articles were irrelevant title or abstract, not in full-text format, and not in English; 21 articles were irrelevant content. Only 22 articles fulfilled the requirements of this study.

Results

Allergic diseases can be managed strategically both non-pharmacologically and pharmacologically.¹⁵ Pharmacological use is usually preferred when non-pharmacological methods prove ineffective or insufficient in reducing allergy symptoms. Different treatment procedures (systemic, intranasal, topical, etc.) are used depending on the symptoms and type of allergic disease.^{15,16}

Topical therapy consists of combination drugs such as antihistamines and vasoconstrictors, or antihistamines with mast cell stabilizing properties. The first are vasoconstrictors that target eye redness and antihistamines that target allergy symptoms. Examples are the tetrazoline/antazoline combination; however, it can cause increased redness for several days after use.⁵ The latter have a dual mechanism of action; they block histamine receptors and they also stabilize mast cells and inhibit their degranulation which in turn limits the release of histamine, tryptase and prostaglandin D2. They also have an effect on leukocyte activity. These drugs are dosed twice daily and as a prophylactic they require two weeks of therapy to achieve maximum effect.

Discussion

Rhinitis is inflammation of the nasal mucosa. According to the Australasian Society of Clinical Immunology and Allergy,¹⁷ there are various causes of rhinitis which include: allergies (fever), increased sensitivity to irritants such as smoke, temperature changes or excessive use of decongestant nasal sprays.¹⁷ The most common antigens for allergic rhinitis are inhaled allergens, the most common being dust mites, animal dander, and pollen.¹⁸

Allergic Rhinitis (AR) affects about 20% of the world's population and is considered as the most common chronic disease.¹⁹ AR is a type 1 allergic disease that reduces the quality of life depending on its severity.²⁰ Exposure to nasal allergens stimulates an IgE-mediated type 1 hypersensitivity reaction, resulting in a symptomatic reaction to the allergen. Early typical symptoms of allergic rhinitis are rhinorrhea, nasal congestion and sneezing.^{19,21} AR can also be associated with various conditions such as bronchial asthma, allergic conjunctivitis, rhinosinusitis and others.¹⁹

Sinusitis is defined as inflammation of the paranasal sinus mucosa. Sinusitis has been replaced by the more appropriate term 'rhinosinusitis'.²² The term rhinosinusitis is preferred over sinusitis because sinusitis, in most cases, is almost always accompanied by inflammation of the adjacent nasal mucosa. The classification of rhinosinusitis is usually based on whether rhinosinusitis is acute (ARS) or chronic rhinosinusitis (CRS). Many scientists agree that the duration of CRS is more than 12 weeks whereas ARS still has different duration classifications from different scientists but is usually less than 12 weeks.²³

Atopic dermatitis (AD) is one of the most common chronic inflammatory disorders of the skin with a strong association with genetic predisposing factors. It affects about 20% of children and 1%-3% of adults in industrialized countries.²⁴ There is a clearly identifiable hyper-proliferative skin disorder in AD that is associated with a damaged skin barrier and a mixed TH1/TH2 inflammatory response. This exposes the skin and makes it susceptible to moderate to severe pruritic skin infections.¹⁰

Eosinophilic esophagitis is an allergic condition that has emerged recently and has been reported on all continents except Africa.¹⁰ Inflammation of the esophagus that is observed with abnormal eosinophils in allergic reactions is the main characteristic of this disease. Potential allergens include cross-reacting molecules, which are common between pollen

antigens or latex food allergens. The emergence and prevalence of this disease is a global concern and requires further investigation.^{1,10,20}

Allergic conjunctivitis is an inflammatory response of the conjunctiva to allergens such as pollen, environmental antigens (eg dust), and animal dander.¹⁶ Hyperemic conjunctivitis is a common type of conjunctivitis; most patients show symptoms of itchy eyes, lacrimation, hyperemia, eye discharge, etc. Severe symptoms cause swollen eyelids. A number of conditions can present with conjunctivitis (pink eye), but it is best to try and differentiate allergic conjunctivitis from other eye conditions.

Asthma is one of the most common chronic inflammatory diseases affecting both children and adults. The inflammatory process causes hyper-responsiveness of the bronchial tree, with reversed obstruction of airflow. Inflammation of the bronchial tree can cause airway constriction through smooth muscle contraction, mucus hyper-secretion, bronchial hyper response, and additional narrowing of the airway due to mucosal edema and sloughing of epithelial cells.¹⁰ Allergic asthma is observed to be the most common type of asthma, mainly caused by inhaled allergens, which trigger an immune system response.¹⁰ The application of therapy should be carried out after the classification of asthma severity is accurate. It assists in reviewing condition management when periodic assessments for asthma control have been established. Diagnosing asthma is based on two methods: identification of the characteristic pattern of respiratory symptoms and restriction of expiratory airflow; this is different for each patient.²⁵

Conclusion

Allergic diseases can be managed strategically both non-pharmacologically and pharmacologically. Pharmacological use is usually preferred when non-pharmacological methods prove ineffective or insufficient in reducing allergy symptoms. Topical therapy consists of combination drugs such as antihistamines and vasoconstrictors, or antihistamines with mast cell stabilizing properties. The first are vasoconstrictors that target eye redness and antihistamines that target allergy symptoms.

Acknowledgement

The author is grateful for Dean of Medical Faculty University of Jember, Mr. Supangat, MD, M.Kes, Ph. D., Sp. BA for his constructive with feedback on my manuscript.

Conflict of Interest

The authors have no conflict of interest.

References

1. Tamari M, Shota Tanaka, Hirota T. Genome-wide association studies of allergic diseases. *Allergology International*, 2013; 62(1):pp.21-28. <https://doi.org/10.2332/allergolint.13-RAI-0539>
2. Van der Poel L, Warner J. Pediatric allergy in review. *Pediatrics and Child Health*. 2012; 22(7):259-263. <https://doi.org/10.1016/j.paed.2012.02.002>
3. Prescott S. (2013). Early-life environmental determinants of allergic diseases and the wider pandemic of inflammatory noncommunicable diseases. *J Allergy Clin Immunol*. 2013 Jan; 131(1):23-30. <https://doi.org/10.1016/j.jaci.2012.11.019>
4. Akdis M, Akdis C. (2013). Mechanisms of allergen-specific immunotherapy: multiple suppressor factors at work in immune tolerance to allergens. *J Allergy Clin Immunol*. 2014 Mar; 133(3):621-31 <https://doi.org/10.1016/j.jaci.2013.12.1088>
5. Vally M, Irhuma MOE. Allergic conjunctivitis. *South African Family Practice*, 2017; 59(5). <https://doi.org/10.4102/safp.v59i5.4744>

6. Bieber T. Atopic dermatitis. *Ann Dermatol*. 2010; 22(2):125-137. <https://doi.org/10.5021/ad.2010.22.2.125>
7. Sinigaglia F, D'Ambrosio D, Rogge L. Type I interferons and the Th1/Th2 paradigm. *Developmental and Comparative Immunology*. 1999; 23(7-9):657-663. [https://doi.org/10.1016/S0145-305X\(99\)00039-7](https://doi.org/10.1016/S0145-305X(99)00039-7)
8. Alvarez Zallo N, Aguinaga-Ontoso I, Alvarez-Alvarez I, Guillén-Grima F, Azcona San Julian C. The influence of gender and atopy in the relationship between obesity and asthma in childhood. *Allergologia et Immunopathologia*. 2017; 45(3):227-233. <https://doi.org/10.1016/j.aller.2016.09.005>
9. Brunton L, Chabner B, Knollman B. (Editors). *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. Twelfth Edition. New York: McGraw-Hill Medical Publishing Division. 2011.
10. Lu T, Rothenberg M. (2013). Diagnostic, functional, and therapeutic roles of microRNA in allergic diseases. *J Allergy Clin Immunol*. 2013 Jul; 132(1):3-13 <https://doi.org/10.1016/j.jaci.2013.04.039>
11. Tang R, Chang J, Chen H. Can probiotics be used to treat allergic diseases? *Journal of the Chinese Medical Association*. 2015; 79(3):154-157. <https://doi.org/10.1016/j.jcma.2014.08.015>
12. Marko M, Pawliczak R. The role of microbiota in allergy development. *Allergologia Polska - Polish Journal of Allergology*. 2017; 13. <https://doi.org/10.1016/j.alergo.2017.03.002>
13. Strachan D. Hay fever, hygiene, and household size. *BMJ*. 1999; 299(6710): 1259-1260. <https://doi.org/10.1136/bmj.299.6710.1259>
14. Brown E, Arrieta M, Finlay B. A fresh look at the hygiene hypothesis: How intestinal microbial exposure drives immune effector responses in atopic disease. *Seminars in Immunology*. 2013; 25(5):379-397. <https://doi.org/10.1016/j.smim.2013.09.003>
15. Trubo R. Seasonal ocular allergy: new options for a recurring problem. *Cornea*. 2015 Mar; 31-3.
16. Bielory BP, O'Brien T, Bielory L. Management of seasonal allergic conjunctivitis: a guide to therapy. *Acta Ophthalmologica*. 2012; 90:399-407. <https://doi.org/10.1111/j.1755-3768.2011.02272.x>
17. Australasian Society of Clinical Immunology and Allergy. Sinusitis and allergies. *Balgowlah*, 2015; 1-3.
18. Brenner GM, Stevens CW. *Pharmacology*. Fourth Edition. China: Elsevier Saunders. 2013.
19. Matsushita K, Kato Y, Akasaki S, Yoshimoto T. Proallergic cytokines and group 2 innate lymphoid cells in allergic nasal diseases. 2017
20. Okubo K, Kurono Y, Ichimura K, et al. Japanese Guidelines for Allergic Rhinitis 2017. <https://doi.org/10.1016/j.alit.2016.11.001>
21. Shah A. (2014). Allergic rhinitis, chronic rhinosinusitis and nasal polyposis in Asia Pacific: impact on quality of life and sleep. *Asia Pacific Allergy* 2014; 4(3): 131-133 <https://doi.org/10.5415/apallergy.2014.4.3.131>
22. Schubert M. Allergic fungal sinusitis: pathophysiology, diagnosis and management. *Medical Mycology*, 2009; 47(s1):S324-S330. <https://doi.org/10.1080/13693780802314809>
23. Rosenfeld R, Piccharillo J, Chandrasekhar S, et al. Clinical Practice Guideline (Update): Adult Sinusitis. *Otolaryngology-Head and Neck Surgery*, 2015; 152(2_suppl):S1-S39. <https://doi.org/10.1177/0194599815572097>
24. Bae J, Choi Y, Park C, Chung K, Lee K. Efficacy of allergen-specific immunotherapy for atopic dermatitis: A systematic review and meta-analysis of randomized controlled trials. 2017
25. Carr W, Schaeffer J, Donnenfeld E. Treating allergic conjunctivitis: A once-daily medication that provides 24-hour symptom relief. *Allergy and Rhinology (Providence, R.I.)*, 2016; 7(2):107-114. <https://doi.org/10.2500/ar.2016.7.0158>