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Review Article

Ocular allergy

Khathutshelo Percy Mashige

University of KwaZulu-Natal, Discipline of Optometry, Private Bag X54001, Durban, 4000, South Africa

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ABSTRACT

Aim: To systematically review relevant literature investigating the classification and nomenclature, epidemiology and pathophysiological mechanisms, as well as diagnosis and treatment of ocular allergy.
Method: The Medline, PubMed, Elsevier Science Direct, and Google Scholar databases were used to search for evidence-based literature on ocular allergy.
Main outcome measures: Classification and nomenclature, epidemiology and pathophysiological mechanisms, diagnosis and management of ocular allergy.
Results: The search retrieved 5200 number of studies of which 6 met the criteria.
Conclusions: While numerous studies regarding pharmacological and immunological research have identified new treatment options, there is a dearth of clinical studies to discover the biomarkers and immune therapeutic management to control sensitisation and effector phases of this condition. Given the complexity of this condition due to the multifactorial nature of the possible aetiologies, rigorous well-designed scientific studies are needed to determine the exact classification, prevalence and underlying immune pathological processes of ocular allergy.

1. Introduction

Ocular allergies encompass a group of hypersensitivity disorders to normally harmless substances, known as allergens and can be observed as the only dominant presentation of an allergic sensitisation, or are associated with rhinitis, asthma, atopic dermatitis or food allergy (Leonardi et al., 2012). The most common clinical presentations of ocular allergy are conjunctival hyperaemia (redness) and chemosis (swelling), itching and tearing, and vision loss in severe cases (Chowdhury, 2013; Leonardi, De Dominicis, & Motterle, 2007). Management of this condition is based on minimising contact of the causal allergen with the conjunctiva using a series of protective measures, with medication assisting in controlling the symptoms produced by the allergic inflammatory process (Chowdhury, 2013; La Rosa et al., 2013).

There is currently no universal standard nomenclature and classification, making an estimation of ocular allergy prevalence challenging. In addition, as most ocular allergic diseases are comorbidities of rhinitis, available prevalence data encompasses both ocular and nasal symptoms, making it impossible to separate ocular allergy and allergic rhinitis (La Rosa et al., 2013). Moreover, controversy continues to surround the exact pathophysiological mechanisms involved in ocular allergic diseases. The purpose of this paper is therefore

E-mail address: mashigek@ukzn.ac.za.
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to systematically review scientific and published research studies on the classification and nomenclature, epidemiology and pathophysiological mechanisms, diagnosis and management of ocular allergy.

2. Method and scope of review

The initial search term was 'ocular allergy' by the Information Specialist (IS). An article was considered for review if it met the inclusion criteria of reporting on the classification, nomenclature, epidemiology, pathophysiology, clinical presentation, or an approach to diagnosis and management of ocular allergy. Articles published between 1994 and 2015 years in English, and indexed in the following electronic databases were searched: Medline, PubMed, Elsevier Science Direct, and Google Scholar. The standard process for a systematic literature review was adopted:

1. Titles were reviewed and those which were not relevant were rejected.
2. Abstracts of publications that were not rejected were obtained.
3. Two individuals reviewed the abstracts independently and rejected further papers that were not eligible. A third individual adjudicated if there were any differences.
4. Full text of the abstracts selected was obtained.
5. Further papers were rejected if, on closer inspection, were not relevant or did not provide sufficient detail.
6. Tables for data extraction were prepared.
7. Two people extracted data and compared entries.

The full copies of articles identified by the search, and considered to meet the inclusion criteria based on their title, abstract and subject descriptors, were obtained for the data synthesis. Articles identified through reference lists and bibliographic searches were also considered for data collection based on their title. Two reviewers independently selected articles against the inclusion criteria. Discrepancies in reviewer selections were resolved at a meeting of the reviewers prior the selected articles being retrieved.

2.1. *Critical appraisal*

Identified studies were assessed independently for quality and validity by two reviewers using the corresponding checklist from the Critical Appraisal Skills Programme (CASP) tools (Critical Appraisal Skills Programme, 2014) before being included in the review. Any disagreements that arose between the reviewers were resolved through discussion and with the assistance of a third person where required.

The initial search yielded a total of 5200 records, of which the Information Specialist (IS) removed 360 duplicates and pre-screened 4840 records. Thereafter 3870 records which were not relevant to the scope of the review were removed. The reviewers screened the remaining 970 records and discarded a further 800 records as not meeting the inclusion criteria. A total of 170 full text reports were obtained for further assessment, of which 6 articles met the inclusion criteria and 164 articles were excluded, with reasons, as they were not relevant to the objectives of the review. The flow chart and check list of the CASP tool used are shown in Appendices 1A and 2 respectively. The 6 studies included in the synthesis covered all aspects with respect to the classification and nomenclature, epidemiology, pathophysiological mechanisms, diagnosis and treatment of ocular allergy. A summary of the selected studies is shown in Appendix 1B.

3. Classification and nomenclature

According to the traditional classification of ocular allergy, the six forms are: seasonal (SAC) and perennial allergic conjunctivitis (PAC), vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC), contact dermatoconjunctivitis (CDC), and giant papillary conjunctivitis (GPC) (Leonardi et al., 2007). This traditional classification is based on clinical presentation (Table 1) or on pathophysiology, according to the different hypersensitivity mechanisms introduced by Gell and Coombs. Their classification divides allergies into four pathophysiological types, namely anaphylaxis (type I), antibody-mediated cytotoxic reactions (type II), immune complex-mediated reactions (type III), and delayed type hypersensitivity (type IV) (Sánchez et al., 2011). However, many hypersensitivity reactions cannot be explained in this context and its use is therefore no longer recommended (Sánchez et al., 2011). Despite these limitations, the Gell and Coombs's classification is still valid in a few well-defined circumstances.

Efforts have recently been made to further clarify the classification and nomenclature of ocular allergy. If different aspects of the condition are considered, such as its clinical presentation and duration or the immunopathogenesis, the criteria for ocular allergy may change (Leonardi et al., 2007). For example, ocular allergies can be classified as 'intermittent' or 'persistent', and 'mild', 'moderate' or 'severe' depending on their evolution and severity. Similarly, symptoms can be considered as 'acute' or 'chronic' and 'recurrent' according to onset and duration, or as 'follicular' and 'papillary conjunctivitis', 'cicatrising' and 'noncicatrising', emphasising the predominant clinical presentations (Leonardi et al., 2007).

In 2001, the European Academy of Allergy and Clinical Immunology (EAACI) and the Nomenclature Review Committee of the World Allergy Committee (WAO) jointly introduced a revised nomenclature that distinguishes between allergic and nonallergic hypersensitivity reactions, with allergic diseases being further divided into IgE- and non-IgE hypersensitivities (Johansson et al., 2001, 2004). The advantage of this new classification was that it gave a more schematic immunopathological approach, with IgE-mediated ocular allergy being divided into intermittent and persistent forms, the latter being classified as VKC and AKC. However, a serious limitation of this classification is contact dermatoconjunctivitis (CDC), which is a 'non-IgE-mediated form of localized contact dermatitis, but immunologically different from VKC or AKC' (Leonardi et al., 2007). In addition, 'contact lens-related GPC should be considered as non-IgE mediated, mechanically related to the lens micro-trauma, which, however, shares some immunopathological aspects with VKC' (Leonardi et al., 2007), which can lead to more confusion. The above-mentioned limitations prompted the international