

Study Protocol

A Study of Clinical Profile and Management of Allergic Conjunctivitis in Rural Tertiary Care Centre

Abstract

Background: Among the allergic diseases witnessed over the last few decades, ocular allergy is one of the most common conditions. Many factors like pets, dust, pollen, grain exposure, air pollution play a role in allergies. Ocular allergy impairs the daily routine activities, and if left undertreated, it may progress to atopic keratoconjunctivitis, resulting in vision impairment. This study aimed to observe an association of dry eye in allergic conjunctivitis and management of allergic conjunctivitis cases reporting in tertiary health care Centre.

Material and Method: This will be a cross sectional observational research conducted at AVBRH, Wardha. Baseline data of 85 enrolled patients will be collected after obtaining their informed written consent and all procedures will be explained to patients. Patients included in study will undergo Comprehensive ophthalmic examination, slit lamp examination, fundoscopy, tear break up time and Schirmer's test with topical anaesthesia. Follow-up of all patients will be done at 1, 3, 6, and 8 weeks. Data on medical history, allergies, and lifestyle factors will be collected using a pretested standard questionnaire.

Expected results: Estimation of correlation between dry eye in allergic conjunctivitis and efficacy of different standard drugs in the treatment of allergic conjunctivitis.

Keywords: Allergic, conjunctivitis, Antihistamines, Mast cell stabilizers, Corticosteroids, Dry eye, Schirmer's test.

Introduction

In the last few decades allergic diseases have increased extensively. Ocular allergy is one of the most common ocular condition found in clinical practice.^{1,2} It is one of the most common clinical condition which is often under-diagnosed and under treated. Specific cause of allergic conjunctivitis cannot be pinpointed as it is multifactorial. It is considered that allergic diseases are caused due to numerous factors like pets, dust, pollen grain exposure, air pollution, genetic variation, and frequent exposure to allergens in early childhood^[1]. Ocular allergy causes unpleasant signs and symptoms and impair their everyday activities. If undertreated severe type of allergic conjunctivitis, such as atopic keratoconjunctivitis, could finally lead to visual loss if undertreated. The recent advances in understanding the inflammatory cell mediators and immunologic events related to ocular allergy has led to development of newer diagnostic and therapeutic means for it. There can be a wide range of immunological responses due to allergens, resulting in conjunctiva and cornea inflammation.^[2] In the Gell and Coombs classification system, different reactions are recognized based on the immunologic hypersensitivity reaction³. Allergic conjunctivitis is commonly referred to as the major type I hypersensitivity reaction affecting the conjunctiva and is sub-classified further into perennial allergic conjunctivitis and seasonal allergic conjunctivitis. The most severe types of allergic conjunctivitis, such as giant papillary conjunctivitis, limbal and tarsal vernal keratoconjunctivitis, and atopic keratoconjunctivitis, are very rare forms of allergic conjunctivitis.

Allergic conjunctivitis is normally diagnosed by a detailed history and close clinical

evaluation (see Clinical). The presence of an antigen activates the allergic cascade, and thus the main behavioural modification for all forms of allergic conjunctivitis is avoidance of the offending antigen. Since the conjunctiva is a nasal mucosa-like mucosal surface, the pathogenesis of allergic conjunctivitis may involve the same allergens that cause allergic rhinitis. Symptoms of acute allergic conjunctivitis, such as itching, redness, burning sensation, and watering from eyes, may be caused by common airborne antigens, including dust, mould, pollen, grass, and weeds.[2] The timing of symptoms is the main distinction between seasonal allergic conjunctivitis and perennial allergic conjunctivitis, as the names implies. Typically, individuals with seasonal allergic conjunctivitis have symptoms of acute allergic conjunctivitis for a defined period for specific allergen, i.e., in spring, tree pollen is the predominant airborne allergen; in summer, grass pollen is the predominant allergen; or in fall, weed pollen is the predominant allergen. Due to the reduced airborne transmission of these allergens in cooler climates or winter months, people with seasonal allergic conjunctivitis are symptom-free in this period.³ During the pollen season, seasonal allergic conjunctivitis may manifest itself through tear film instability and symptoms of eye discomfort. One study showed that allergic inflammation did not cause permanent tear film instability outside the pollen season. In comparison, people with perennial allergic conjunctivitis may have year-round symptoms, so perennial allergic conjunctivitis may not be caused by seasonal allergens alone, although it may play a part. The symptoms of perennial allergic conjunctivitis may be triggered by other common household allergens, such as pollen mites, cockroach dust, cigarette smoke, airborne allergens, moulds, and pet dander.

Perennial allergic conjunctivitis and seasonal allergic conjunctivitis are the most common types of ocular allergies. The presence of specific IgE antibodies is known in almost all perennial and seasonal allergic conjunctivitis cases.[3]

Vernal keratoconjunctivitis is also called as spring catarrh, is a chronic inflammation of the conjunctiva, present bilaterally onset is at a very young age. Patient comes with complaints of itching associated with ropy discharge. patient presents with history of allergies personal and/or in the family. Atopic conditions, such as eczema, seasonal allergic rhinitis, or asthma, present in more than 90% of patients with vernal keratoconjunctivitis. It is a type I hypersensitivity reaction mediated by IgE and mast cells. In more severe cases conjunctival scarring and Corneal complications are frequently seen in patients with vernal keratoconjunctivitis.

Atopic keratoconjunctivitis is an inflammatory condition of eye. It is also a type I hypersensitivity disorder like vernal keratoconjunctivitis. Atopic keratoconjunctivitis has many similarities with vernal keratoconjunctivitis though they have are different causes, signs and symptoms. Atopic keratoconjunctivitis is mostly associated with atopic dermatitis.

Giant papillary conjunctivitis presents with "giant" tarsal papillae as the primary finding, which are greater than 0.3 mm in diameter. These are typically seen in this in this condition. The development of giant papillary conjunctivitis is an immune-mediated reaction due to presence of antigen in predisposed individuals. The pathogenesis of giant papillary conjunctivitis is due to combination of type-I hypersensitivity reaction and type IV hypersensitivity reaction.³ It is an inflammatory disorder of an immune-mediated type seen in the superior tarsal conjunctiva.

The severity and nature of allergic conjunctivitis in terms of chronicity has been defined as per the guidelines given by GOKHALE N[4].

MILD – symptomatic (redness and itching) patient with congestion and fine velvety papillae but no corneal involvement

MODERATE – corneal involvement in the form of fine punctuate erosions, Horner- Trantas dots and focal limbal inflammation and thickening of <6 clock hours

SEVERE – large active cobblestone papillae, coarse erosions or keratitis, macro erosions, and severe limbal inflammation >6 clock hours

Intermittent disease – inflammation free intervals of >2-3 months during which the patient is off medications

Chronic VKC – inflammation free intervals of <1 month during which the patient is off medication

Upto 40% of population is affected by allergic conjunctivitis, seasonal allergic conjunctivitis or perennial allergic conjunctivitis attributes to majority of cases. The prevalence of allergic conjunctivitis is reportedly increasing now a days[5]. Diagnosis and management of allergic conjunctivitis is difficult due to symptomatic resemblance with other ocular diseases and frequent co-morbidity of allergic conjunctivitis in other conditions. Due to mere negligence of the patients, allergic conjunctivitis is undertreated very often.

In India prevalence of allergic conjunctivitis is 12.22%. Occurrence of allergic conjunctivitis is more common in males (13.44%) than in females (10.71%). The most prevalent cause of allergic conjunctivitis is pollen or dust. Perennial co-morbidities are more common. Allergic rhinitis, hay fever, dermatitis and asthma are the reported co-morbidities in allergic conjunctivitis[6,7].

It has been reported that Increased papillary formation of the upper tarsal conjunctiva is seen in patients complained of itching sensation and those with decreased break up time, which is suggestive of an overlap syndrome in allergic conjunctivitis with dry eye disease[8]. Chronic allergic conjunctivitis contributes to activation of the immune system, causing damage to the ocular surface and in particular, loss of goblet cells.[7] Some types of non-inflammatory allergic conjunctivitis are similar to dry eye, have extreme symptoms and often change in tear breakup time. It is difficult to differentiate between dry eye disease and allergic conjunctivitis in such conditions.[8,9] Tear secretions are essential substances that help maintain an intact tear film.10 It has been noted that with increase in age there is decrease in tear secretion and tear break up time, especially in women11. It has been postulated that a decrease in androgen and estrogen hormones is associated with dysfunction of the lacrimal and meibomian glands. So there is age-dependent decrease of tear secretion due to a decrease in functions of these glands, particularly in women after 40 years of age which is due mainly to hormonal variation.

Dry eye and allergic conjunctivitis are increasingly prevalent in recent days. The causes of allergic conjunctivitis are multifactorial. Clinical diagnosis can be made largely on the basis of symptoms and biomicroscopic signs.[10,11] Recent advances in understanding the mechanisms and pathogenesis involved in dry eye and allergic conjunctivitis have enabled new treatments to treat these ocular surface disorders.

Many standard medications, including topical antihistamines, mast cell stabilizers in combination with antihistamines, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids and tear substitutes, are useful to treat allergic conjunctivitis.[12] Surgical intervention is required in severe cases of Vernal Keratoconjunctivitis or Atopic Keratoconjunctivitis.

Aim and Objectives

Aim: A clinical study and management of allergic conjunctivitis in tertiary health care centre.

Objectives:

- 1) To observe an association of dry eye in allergic conjunctivitis.
- 2) To study the response of different drug therapies in treatment of allergic conjunctivitis.
- 3) Compare the response of different drug therapies in allergic conjunctivitis.

Material and Methods

Setting: The thesis will be performed at the Department of Ophthalmology in the rural hospital of Acharya Vinoba Bhave (AVBRH), a tertiary care teaching hospital located in the Wardha District rural area. The research will be performed after approval by the Ethical Committee of the Institute (applied for).

Patients: We will prospectively enroll all consecutive patients regardless of age, gender or ethnicity at AVBRH, Sawangi. Informed consent in written form will be obtained from all participants.

Study design: This is a Cross-sectional observational study.

Inclusion criteria: All patients, regardless of age, gender or ethnicity diagnosed with allergic conjunctivitis, are taken into consideration. Patients with a history of seasonal or systemic allergies are also included. The patient at Ophthalmology Out Patient Department at AVBRH, Sawangi who have given written consent will be included in this study.

Exclusion criteria: Patients with other forms of conjunctivitis are excluded. Patients with post refractive surgeries, conjunctival degenerative disorders are excluded. Patients with clinically suspected autoimmune disease (Sjogren's syndrome, rheumatoid arthritis, polyarteritis nodosa) are excluded. Patients with clinically diagnosed vitamin A deficiency are also excluded. Women during pregnancy and after 40 years of age, there is decrease in androgen and estrogen hormones associated with dysfunction of the lacrimal glands and the meibomian glands leads to decrease of tear secretion due to decrease in functions of these glands. So Women at pregnancy and menopausal stage and are also excluded. Patients on topical or systemic medication causing dry eye disease or other secondary causes of dry eye are also excluded. Post radiation or chemical injuries to the eye and patients not willing for study will be excluded from the study.

Methods:

The research will adhere to the principles of the Helsinki Declaration and will be accepted by the DMIMS (DU) Institutional Ethical Committee (IEC). All the patients will be made fully aware of the details of the procedure. The patients fulfilling the inclusion criteria will be sequentially recruited for the study. Clinical history will be taken and Complete ophthalmic examination, including best corrected visual acuity, slit-lamp examination, IOP measurement (applanation tonometer) and fundoscopy (slit lamp biomicroscopy with 90D lens) will be performed on all patients considering the inclusion-exclusion criteria and patients will be followed up at 1, 3, 6 and 8 weeks. Clinical history will be taken and detailed ophthalmic examination including best corrected visual acuity, slit lamp examination, IOP measurement (applanation tonometer) and fundoscopy (slit lamp biomicroscopy with 90D lens) will be conducted on all patients, taking into account the inclusion - exclusion criterion and patients will be followed up at 1, 3, 6 and 8 weeks. All patients will be asked for previous medical history and lifestyle (e.g., smoking, drinking alcohol, sunlight exposure, eating habits, physical activity) using a standard questionnaire administered in the study. General examination will be done, vitals and higher function status will be noted. This is a cross sectional observational study on consecutive patients from eye OPD assigned to undergo slit lamp examination, fundoscopy, tear film break up time, Schirmer's test with topical anaesthesia. Study will be done for a period of two years at AVBRH hospital. Institutional Ethical Committee permission will be taken. Also, the

informed consent will be obtained from each patient. BP will be measured at a non-dominant arm using an automated device. All these tests are done and patient will be diagnosed and treated accordingly.

Table 1. OCULAR EXAMINATION :-

Findings on admission		
EYE	RE	LE
Vision		
Head Posture		
Forehead		
Eyebrows		
Lid		
Lid margin		
Lid proper		
Conjunctiva		
Palpebral		
Bulbar		
Tarsal		
Cornea		
Size		
Shape		
Surface		
Transparency		

Sensation		
Anterior Chamber		
Depth		
Contents		
Iris		

Colour		
Pattern		
Pupil		
Lens		
Ocular Movements		

Subjective Refraction		
Slit Lamp Exam. Conjunctiva Cornea Anterior chamber Iris Lens		
Funduscopy		

INVESTIGATION:

- **TEAR BREAK UP TIME**

Table 2. SCHIRMER'S TEST WITH TOPICAL ANAESTHESIA

DRUGS	MILD AC	MODERATE AC	SEVERE AC
Antihistaminics			
Mastcell stabilizers +Antihistaminics			
Corticosteroids			
Tear substitute			

Sample size:

Using sample size formula with desired error of margin

$$n = \frac{Z^2 \alpha/2 * P * (1-P)}{d^2}$$

Where

$Z_{\alpha/2}$ is the level of significance at 5 % ie: 95 % confidence interval =1.96

P=Prevalence of allergic conjunctivitis=12.22%=0.1222 (Reference: Rita Sharma et al)

D=Desired error of margin=7%=0.07 $n = 1.962 \times 0.1222 \times (1-0.1222) / 0.072$
=84.05

=85 patients needed in the study

Statistical analysis:

It will be done using Student's unpaired t and Chi square tests, and values will be considered significant when $p < 0.005$.

Expected Results:

The study aims to correlate dry eye in allergic conjunctivitis and to know management of allergic conjunctivitis and efficacy of different standard drugs used for allergic conjunctivitis in patients.

Discussion:

Allergic conjunctivitis is sufficiently bothersome due to its signs and symptoms, that the patients experience increased absenteeism in working hours, decreased work productivity, reduced quality of life and limitation of daily activities. Few of the related studies were reported [13-18]. Very few studies have been conducted in this region on the clinical study and management of allergic conjunctivitis. Therefore, we intend to study the clinical correlation of allergic conjunctivitis with dry eye and management of allergic conjunctivitis and efficacy of different standard drugs in patients attending eye department at AVBRH.

Conclusion:

In conclusion, we will come to know the co-relation of dry eye in allergic conjunctivitis. We also compare the efficacy of different drugs used in allergic conjunctivitis and drugs with better prognosis can be identified. Considering this, further studies should be done in larger group to validate the clinical co-relation of dry eye in allergic conjunctivitis, and efficacy of different drugs in allergic conjunctivitis.

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UNDER PEER REVIEW