

Original research article

An Observational Study of Dry Eye in Allergic Conjunctivitis**Dr. Pranay Kumar¹, Dr. Rajiv Kumar Singh²**¹Senior Resident, Department of Ophthalmology, SKMCH, Muzaffarpur, Bihar²Associate Prof. & HOD, Department of Ophthalmology, SKMCH, Muzaffarpur, Bihar**Corresponding Author: Dr. Rajiv Kumar Singh****Abstract**

Background: Allergic conjunctivitis and dry eye disease are major ocular surface disorders affecting millions of people interfering with their quality of life. These diseases can occur simultaneously or independently of each other. The symptoms are non-specific of any type of ocular disease.

Methods: This Study was carried out in SKMCH, Muzaffarpur. Study duration of Fifteen months. on the subjects who attended the outpatient department of Ophthalmology. This was an observational study of 100 cases of allergic conjunctival disease after informed consent which satisfied the inclusion and exclusion criteria. Based on novel scoring system (NSS), the severity of allergic conjunctival disease was graded as mild, moderate and severe.

Conclusion: We conclude that for the effective management of allergic conjunctivitis, we should always consider treatment of dry eye as well.

Keywords: allergic conjunctivitis, dry eye, itching, dry eye grading.

Introduction

Allergic conjunctival disease and dry eye disease are major ocular surface disorders affecting millions of people. The chronic discomfort interferes with the quality of life of the patients for a long period of time.¹ The most common symptoms presented are red eye, itching and burning of the eyes. This group of symptoms is nonspecific for any class of ocular surface disease or diagnosis. Dry eye and ocular allergy can occur simultaneously or independently of each other. Due to the overlap of signs and symptoms, it can be confusing to diagnose and treat patients without inducing further complications. Toda et al has reported that 12 out of 80 patients with dry eye complained of an itchy feeling. Patients with decreased tear break up time had increased papillary formation of the upper tarsal conjunctiva and an increased serum antigen specific IgE. This report suggested an overlap syndrome in allergic conjunctivitis and dry eye disease. Patients who suffer from ocular allergy are significantly more likely to experience signs and symptoms of dry eye disease. Studies of the tear film in allergic conjunctival disease demonstrate a shared pathology between dry eye and ocular allergy namely inflammation of the cornea and the conjunctival surface. Atopic keratoconjunctivitis and vernal keratoconjunctivitis are severe manifestations of ocular allergy. Research shows that an allergy related alteration in quality and quantity of aqueous tear production can translate into altered lipid and mucin components of tear film as well. The resulting imbalanced tear film produces inadequate barrier protection resulting in ocular inflammation. Patients complain of persistent symptoms and very often consider that their original disease has not been treated properly. This leads to an increase or prolonged use of topical treatment that becomes inappropriate or even

toxic. This study attempts to highlight the probable association of ocular surface inflammation, in this case, allergic conjunctival disease with dry eye.

Objectives

To observe an association of dry eye disease in allergic conjunctivitis patients, To correlate presence and severity of dry eye disease with severity of allergic conjunctivitis.

Review of Literature

Allergic conjunctivitis and dry eye diseases are highly variable ocular surface disorders. Ocular allergies are over diagnosed, whereas dry eye disease is underdiagnosed.⁷ There are segments of patients who concomitantly suffer from allergic conjunctivitis and dry eye syndrome. In a study conducted by Hom et al, out of 194 patients who complained of itchiness, 57.7% (112/194) had clinically significant dryness.³ Thereby in many cases it will be difficult to differentiate pure dry eye versus dry eye with allergic component as there is a wide overlap between the two diseases symptomatically. There are significant comorbidities, associated diseases, and behavioural and environmental factors that may contribute to the severity of dry eye. Reduction in the modifiable risk factors of dry eye is essential to reduce its prevalence.⁶ Dry eye syndrome has significant economic implications, including costs associated with increased health care utilization, missed work and quality-of-life. The middle aqueous layer is secreted by the main and accessory lacrimal glands. It consists of electrolytes, water and proteins. The main lacrimal gland is divided into 2 anatomical parts, the orbital and palpebral portions, by the levator aponeurosis. The glands of Krause, which constitute two thirds of the accessory glands, are located in the lateral part of the upper fornix. A number of Krause glands are also present in the lower fornix. The glands of Wolfring are variably located along the proximal margin of each tarsus. The main lacrimal gland is richly innervated by parasympathetic nerves containing the neurotransmitters acetylcholine and VIP. The sympathetic innervation is less dense than the parasympathetic and contains norepinephrine and NPY as neurotransmitters. The accessory lacrimal glands are densely innervated, but the majority of the nerves are unidentified. Some of this innervation consists of nerves containing VIP, substance P, and calcitonin gene-related peptide (CGRP). Corneal innervation is predominantly sensory, but it also has a sympathetic and parasympathetic nerve supply. The aqueous layer of tears consists of electrolytes, water, protein and a variety of other solutes secreted by the main and accessory lacrimal glands. In conjunctival inflammation and in response to histamine, the blood vessels of the conjunctiva can leak plasma like fluid into the aqueous layer of the tears. Electrolytes and small molecules in the aqueous layer regulate the osmotic flow of fluids between the corneal epithelial cells and the tear film. They also buffer tear pH, and serve as an enzyme cofactor in controlling membrane permeability. Tear mucins are secreted principally by the conjunctival goblet cells and the stratified squamous cells of the conjunctiva and corneal epithelium. Tear mucins are also secreted minimally by lacrimal glands of Henle and Manz. Goblet-cell mucin production is 2-3 μ l/day, which contrasts with the 2-3 ml/day of aqueous tear production. Both conjunctival and tear mucins are negatively charged, high molecular weight glycoproteins. Tear dysfunction may result when tear mucins are deficient in number such as in avitaminosis A and conjunctival destruction. Dry eye is recognized as a disturbance of the Lacrimal Functional Unit (LFU) which is an integrated system comprising of the lacrimal glands, ocular surface (cornea, conjunctiva and meibomian glands, lids) and the sensory and motor nerves that connect them.⁹ Disease or damage to any component of the lacrimal functional unit (LFU) can destabilize the tear film and lead to ocular surface disease that expresses itself as dry eye. The risk factors for dry eye are multifactorial. Among the various diseases affecting the ocular surface, dry eye is the most common condition.⁹ In standard outpatient clinics, it has been reported that 15–30% of new patients are affected by dry eye.¹³

Although a decrease in tear production is a common condition in many types of dry eye, the severity of ocular surface lesions varies greatly from disease to disease.¹⁴ The prevalence of dry eyes varies from 10.8% to 57.1%, thereby showing wide disparity. Much of this disparity stems from the fact that there is no standardisation of the types of patients selected for the study like dry eye questionnaires, objective tests and dry eye diagnostic criteria. It is due to a failure of lacrimal tear secretion. In any form of dry eye due to lacrimal acinar destruction or dysfunction, dryness results from reduced volume of tears. This in turn causes tear hyperosmolarity, as water evaporates from the ocular surface at normal rates, from already reduced volume of tears. Tear film hyperosmolarity causes hyperosmolarity of the ocular surface epithelial cells and stimulates a cascade of inflammatory events involving MAP kinases and NF κ B signalling pathways and the generation of inflammatory cytokines (interleukin (IL)-1 α ; -1 β ; tumor necrosis factor (TNF)- α) and matrix metalloproteinases (MMP-9). Sjogren syndrome is an exocrinopathy in which the lacrimal and salivary glands are targeted by an autoimmune process, other organs are also affected. The lacrimal and salivary glands are infiltrated by activated T-cells, which cause acinar and ductular cell death and hyposalivation of the tears or saliva. Inflammatory activation within the glands leads to the expression of autoantigens at the surface of epithelial cells (eg, fodrin, Ro and La) and the retention of tissue-specific CD4 and CD8 T-cells.^{33,34} Hyposalivation is amplified by a potentially reversible neurosecretory block, due to the effects of locally released inflammatory cytokines or due to the presence of circulating antibodies (eg, anti-M3 antibody) directed against muscarinic receptors within the glands. Allergic conjunctival disease (ACD) is defined as “a conjunctival inflammatory disease associated with a type I allergy accompanied by some subjective and objective symptoms.” Conjunctivitis associated with type I allergic reactions is considered allergic conjunctival disease. AKC represents a severe chronic ocular allergy primarily in adult population. Cytokines derived from Th1 and Th2 cell types and inflammatory cells such as mast cells and eosinophils are the major mediators of inflammatory response. Atopic keratoconjunctivitis usually presents in adults, who have other systemic signs of atopy. Most commonly, there is a hypersensitivity to allergens associated with asthma, rhinitis, dermatitis or food allergies. Allergic conjunctivitis and dry eye are major ocular surface disorders affecting millions of people. Although neither of them are sight threatening diseases, the chronic discomfort interferes with the quality of life of the patients for a long period of time.

Material and methods

This is an observational study of patients reporting to the ophthalmology out-patient department, at SKMCH, Muzaffarpur, Bihar. Study duration of Fifteen months. on the subjects who attended the outpatient department of Ophthalmology. This was an observational study of 100 cases of allergic conjunctival disease after informed consent which satisfied the inclusion and exclusion criteria. Based on novel scoring system (NSS), the severity of allergic conjunctival disease was graded as mild, moderate and severe, Allergic conjunctivitis (seasonal or perennial): bilateral, conjunctival injection, chemosis, watery discharge, mild mucous discharge. Atopic conjunctivitis: bilateral eczematoid blepharitis, eyelid thickening, scarring, lash loss, papillary hypertrophy of superior and inferior tarsal conjunctiva, conjunctival scarring, watery or mucoid discharge, boggy oedema, corneal neovascularisation, ulcers and scarring, punctate epithelial keratitis, keratoconus, subcapsular cataract. Vernal conjunctivitis: bilateral, giant papillary hypertrophy of superior tarsal conjunctiva, bulbar conjunctival injection, conjunctival scarring, watery and mucoid discharge, The 100-point-grade group (100 points for each observation) includes active giant papillae, gelatinous infiltrates of the limbus, exfoliative epithelial keratopathy, shield ulcer and papillary proliferation at lower palpebral conjunctiva.

The 10-point-grade group (10 points for each observation) includes blepharitis, papillary proliferation with velvety appearance, Horner Trantas spots, edema of bulbal conjunctiva, and superficial punctate keratopathy.

Inclusion criteria

All patients diagnosed with allergic conjunctivitis of any age, History of allergic conjunctivitis, seasonal or frequently relapsing, Patients with history of systemic allergies.

Exclusion criteria

Contact lens wearers, post refractive surgeries, conjunctival infective/degenerative disorders, On medications, topical and systemic causing dry eye disease and other secondary causes of dry eye.

Results

This was a hospital based, case series study of 100 patients of allergic conjunctivitis with informed consent which satisfied the inclusion and exclusion criteria. For analysis of data the subjects were divided into allergic conjunctivitis, atopicconjunctivitis and vernal conjunctivitis. Based on severity they were further sub divided into mild, moderate and severe. Dry eye grading was done for each individual and divided into grades 0, 1, 2, 3 and 4. Occupation for each individual was grouped as indoors or outdoors. Other parameters taken into consideration for assessing dry eye were the SPEED questionnaire, Tear break up time, Schirmer's test and Tear meniscus height. Categorical data was represented in the form of frequency and percentage. Quantitative data was represented using mean \pm standard deviation. Statistical analysis was done using the chi square test.

Age profile of patients

Age(years)	
Mean	29.01
Std. Deviation	14.47
Minimum	5.00
Maximum	60.00

Patients ranged in age from 5 to 60 years. The mean age was 29.01 \pm 14.47 years.

Age distribution of patients

Age in Yrs	No of Cases	Percent
≤ 10	9	9.0
11-20	26	26.0
21-30	20	20.0
31-40	21	21.0
41-50	15	15.0
51-60	9	9.0
Total	100	100.0

The number of patients < 10 years were 9, between 11-20 years were 26, 21-30 years were 20, 31-40 years were 21, 41- 50 years were 15, 51-60 years were 9.

Distribution of allergic conjunctival disease in the study group

Type of allergicconjunctivitis	No of Cases	Percent
Allergic conjunctivitis	58	58.0
Atopic conjunctivitis	31	31.0
Vernal conjunctivitis	11	11.0
Total	100	100.0

The total number of patients diagnosed to have allergic conjunctivitis were 58, atopic conjunctivitis were 31 and vernal conjunctivitis were 11

Distribution based on the novel scoring system (severity grading for allergicconjunctival disease)

Allergic conjunctivitis grading	No of Cases	Percent
Mild	22	22.0
Moderate	46	46.0
Severe	32	32.0
Total	100	100.0

The total number of patients based on severity of allergy according to novel scoring, included in our study having mild disease were 22, moderate were 46 and severe were 32 patients.

The number of patients with an indoor occupation having no dry eye were 5, mild dry eye were 11, moderate were 22, severe were 11 and 4 had very severe symptoms of dry eye. Patients with an outdoor occupation with no dry eye were 2, mild were 10, moderate were 16, severe dry eye were 15 and very severe were 4. There was no significant association between occupation and dry eye. In 58 patients of allergic conjunctivitis, 37 and 36 had Schirmer test >10 mm, 20 and 21 had 6-10 mm and 1 had <5mm in right and left eyes respectively. Among 31 patients of atopic conjunctivitis, 17 had Schirmer test >10 mm, 13 had 6-10 mm and 1 had <5 mm in both the eyes. In 11 patients of vernal conjunctivitis, 7 had Schirmer test > 10 mm and 4 had 6-10 mm in both the eyes. This association was not statistically significant. 17 and 16 patients of allergic conjunctivitis, 12 of atopic and 6 of vernal conjunctivitis have TMH <1mm in right and left eyes respectively. 41 and 42 patients of allergic conjunctivitis, 19 of atopic and 5 of vernal conjunctivitis have TMH >1mm in right and left eyes respectively.

Discussion

Allergic conjunctivitis and dry eye diseases are highly variable ocular surface disorders. The unpredictability of each disorder lies in its pathogenesis, as the clinical manifestations can be dramatically modified by external stimuli. Few studies have highlighted the overlap between these two ocular surface disorders. In studies conducted by Hom MM et al³ out of 194 patients with itchiness 57.7% (112/194) had clinically significant dry eye, thereby highlighting that there are a segment of patients who concomitantly suffer from allergic conjunctivitis and dry eye. In our study we have tried to observe if there is significant association of dry eye in patients presenting with allergic conjunctivitis in the study group. The effects of conjunctivitis on the ocular surface and tear balance have been discussed in many reports. Increased inflammatory cytokines are associated with goblet cell loss and tear volume insufficiency.

There are many instances in the literature connecting tear film dysfunction with AC. One study theorizes that tear film dysfunction is a possible complication of the ocular allergic disease. Our study concurs with previous reports that AC is the initial condition and predisposes to DES. Studies support the observation that AC establishes an environment that generates a dry ocular surface. Our study includes a wide range of patients by age. This gives a broader view of the clinical profile of patients of all age group affected by allergic conjunctivitis. We have also included patients from all types of Allergic conjunctival disease i.e, AC, AKC and VKC which more commonly affects different age group viz. all age, childhood to middle age and childhood respectively. Thus, covering a wider range of age would fetch us an overall view of all types of allergic conjunctival disease. the total number of patients with no signs and symptoms of dry eye were 7%, mild were 21%, moderate were 38%, severe were 26% and 8% had very severe dry eye. Thus prevalence of dry eye is 93%. This is high compared to other studies. In the study by Anuradha et al, prevalence of dry eye was 66%. 34% had no dry eye, 38% had mild dry eye, 24% had moderate dry eye, 4% had severe dry eye and none had very severe dry eye based on the dry eye grading severity scheme. In the study by Akil et al, the prevalence of dry eye in the AC group was 24% (6 of 25 patients). On the other hand, in the study done by Chen et al, the prevalence of dry eye was found to be 97.5% (78 of 80 patients). Dry eye evaluation in allergic conjunctivitis has been done by different dry eye diagnostic criteria and different cut-off values have been employed for objective dry eye tests. This has led to vast disparity in dry eye prevalence in various studies. Hence dry eye might have been underdiagnosed in various studies. Research shows that an allergy related alteration in quality and quantity of aqueous tear production can translate into altered lipid and mucin components of tear film as well. The resulting imbalanced tear film produces inadequate barrier protection resulting in ocular surface inflammation.⁹This further exaggerates the dry eye and thus leading to an increased prevalence of dry eye. Among 93 who had dry eye, 17 belonged to mild, 44 to moderate, 32 to severe allergic conjunctivitis. This association was statistically significant ($P < 0.004$). Thus, dry eye is common in mild, moderate and severe allergic conjunctivitis. Patients with mild allergic conjunctival disease with no dry eye were 5, mild were 7, moderate were 9, severe was 1 and none had very severe dry eye. In moderate allergic conjunctival disease, 2 had no dry eye, 11 had mild, 18 had moderate, 14 had severe and 1 had very severe dry eye. In severe allergic conjunctival disease, all had some form of dry eye. 3 had mild, 11 had moderate, 11 had severe and 7 had very severe dry eye. There was a positive correlation observed between severity of allergic conjunctival disease and dry eye severity showing a strong statistically significant association. Study by Akil et al, also revealed a statistically significant TBUT of < 10 sec in 40% of patients with allergic conjunctivitis. In a study by Chen et al, there was a statistically significant ($p < 0.001$) reduction in TBUT in children with allergic conjunctivitis i.e, TBUT was ≥ 10 seconds in two eyes (2.50%) in the case group and in 58 eyes (72.50%) in the control group. Anuradha et al in their study found that TMH was normal in 36 out of 66 patients who had dry eye with allergic conjunctivitis. TMH had no statistical correlation with dry eye associated with allergic conjunctivitis. In the study by Akil et al, TMH was abnormal in 36% of the AC group and it was significantly lower compared to the control group.

Conclusion

There is a significant association of Dry eye with Allergic conjunctival disease, There is a significant correlation of severity of Dry eye with severity of Allergic conjunctivitis Thus we recommend recognition and early institutionalization of treatment for Dry eye in patients with Allergic conjunctivitis.

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Received: 20-01-2022.

Revised:30-01-2022.

Accepted:10-02-2022