A RANDOMIZED PROSPECTIVE OPEN LABEL COMPARATIVE STUDY OF OLOPATADINE WITH SODIUM CROMOGLYCATE IN ALLERGIC CONJUNCTIVITIS

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CERTIFICATE

This is to certify that this dissertation entitled,**A RANDOMIZED PROSPECTIVE OPEN LABEL COMPARATIVE STUDY OF OLOPATADINE WITH SODIUM CROMOGLYCATE IN ALLERGIC CONJUNCTIVITIS**submitted by **Dr.Sanu Sain**, in partial fulfillment for the award of the degree of M.D.(Pharmacology) by The Tamilnadu Dr.M.G.R.Medical University, Chennai is a bonafide record of the research work done by her, under the guidance of**Dr.K.Baskaran,M.D.,**Professor and Head,Department ofPharmacology,Chengalpattu Medical College during the academic year 2014-17 in the Department of Pharmacology,Chengalpattu Medical College ,Chengalpattu- 603 001.

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DECLARATION

I solemnly declare that the dissertation entitled **"A RANDOMIZED PROSPECTIVE OPEN LABEL COMPARATIVE STUDY OF OLOPATADINE WITH SODIUM CROMOGLYCATE IN ALLERGIC CONJUNCTIVITIS"** is done by me at Chengalpattu Medical College and hospital,Chengalpattu during the period of 2015-2016 under the guidance and supervision of **Dr.K.Baskaran, M.D.,** Professor and Head, Department of Pharmacology,Chengalpattu Medical College. This dissertation is submitted to The Tamilnadu Dr.M.G.R.Medical University, Chennai towards the partial fulfilment of the requirements for the award of **M.D. DEGREE IN PHARMACOLOGY.**

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ABSTRACT

Title : A Randomized Prospective Open Label Comparative Study Of Olopatadine With Sodium Cromoglycate In Allergic Conjunctivitis

Background:

Allergic conjunctivitis is the second most common cause of ocular morbidity in India and it accounts about20% of cases attending ophthalmology clinics. Ocular itching and nasal symptoms adversely affect the quality of life of patients.

Aim

To compare the efficacy and tolerability of 0.2% olopatadine hydrochloride once daily with 2% sodium cromoglycate four times daily in allergic conjunctivitis

Materials and Method

After obtaining written informed consent, 120 patients who satisfy the eligibility criteria were enrolled into the study. Participants were randomly allocated into 2 groups; one receiving olopatadine hydrochloride 0.2% ophthalmic solution OD and the other sodium cromoglycate 2% ophthalmic solution QID for 4 weeks. Patient's ocular signs and symptoms assessment were done by a 4-point scale at the end of 2^{nd}, 3^{rd} and 4^{th} week. Adverse events, if any will be noted during the study and patients will be followed up to two weeks.

Results :

Change from baseline itching score were 2.5 in olopatadine group compared to 2.2 in sodium cromoglycate group(P value-0.006) during 4th week. Change from baseline redness score were 2.36 in olopatadine group compared to sodium cromoglycate group is 1.96(P value0.002) during 4th week. Both treatments show reduction of signs and symptoms scores(p value<0.001). No treatment related adverse effects noted during study.

Conclusion :

Both 0.2%olopatadine and 2% sodium cromoglycate are effective in treating allergic conjunctivitis. 0.2%olopatadine once daily shows better reduction of itching and redness score during 4th week than 2% sodium cromoglycate. Both drugs are safe and well tolerated.

Key Words: Olopatadine, Sodium Cromoglycate. Allergic Conjunctivitis.

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Introduction

INTRODUCTION

Allergic diseases are the fifth leading diseases among chronic diseases in the world. It affects about 40% percentage of entire population(1).There is a worldwide increase in Allergic diseases over the last ten years (2).The prevalence of allergic diseases among school children is gradually increasing and varies from 0.3% to 20.5%. A single cause for allergic disease cannot be pointed out and we should consider a contribution of many factors like genetics, air pollution in urban areas, pets and early childhood exposure for this increase(2) .

Ocular allergy is one of the most common type of allergy .Ocular allergy accounts for 15%-20% of population all over. It is common among school going children and adolescent age group. It is usually associated with other allergic diseases. They are having great impact on our day to day activities(3).

The term allergic conjunctivitis includes seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), vernal kerato conjunctivitis (VKC), and atopic kerato conjuntivitis (AKC).However the clinical and pathophysiological features of AKC and VKC are quite different from SAC and PAC, in spite of common allergy markers. The use of contact lenses or ocular prosthesis are associated with giant papillary conjunctivitis (GPC) which is often included in the group of ocular allergy, however they should not be considered as real allergic diseases(4).

The most common form of ocular allergy is SAC, which represents about 90% of cases (3). The most prevalent allergens for SAC are grass, tree, weed pollen and outdoor molds. Although the signs and symptoms of SAC usually mild, it can hinder school performance, everyday activities, like reading, sleeping etc which results in overall reduction in the quality of life(2). Allergic conjunctivitis is a type I hypersensitivity reaction mediated by IgE.The pathophysiology of allergic conjunctivitis starts with an intial antigen sensitization,followed by mast cell activation, release of histamine, tryptase,synthesis of prostaglandins and leukotreines.In the later phase, there is activation of eosinophils ,basophils, T cells,macrophages and neutrophils leading to a chronic stage of the disease(1).

The treatment and management goals of allergic conjunctivitis are to minimize the inflammatory cascade associated with allergic response in the early stages of the pathological mechanism. It is noted that activation of histamine receptors on immune and non immune cells are associated with allergen-induced inflammation of the conjunctiva and its associated ocular allergic manifestations, including itching, edema, hyperemia and tearing(5).The treatment of allergic conjunctivitis depends on severity and chronicity(4). Non specific treatment measures like cold compression, artificial tears and avoidance of allergens is helpful to alleviate symptoms. The medications which are available for the treatment of allergic conjunctivitis belongs to different classes.

Table 1.1 : Medications for Allergic Conjunctivitis[4]

Types of Medications	Examples
H_1 Receptor Antagonist	Levocabastine Emedastine, Bepostatine, Alcaftadine
Mast Cell Stabilizers	Commonly Sodium Lodoxamide Pemirolast Nedocromil Sodium
Antihistamines With Mast Cell-Stabilizing Property.	Ketotifen Fumarate, Azelastine Olopatadine.
Topical NSAIDS	Ketorolac
Vasoconstrictors,	Naphazoline Pheniramine
Topical Steroids	Prednisolone, Hydrocortisone Loteprednol, Fluorometholone,
Oral Antihistamines,	Fexofenadine Loratadine Cetirizine

Olopatadine is a H_1 selective antagonist with a mast cell stabilizing property, along with suppressing action on TNF α, IL-6 and IL-8 release. It is a well tolerated drug which gives rapid and long duration of relief from signs and symptoms of allergic conjunctivitis.[6]

Sodium cromoglycate is a mast cell stabilizer. Studies shows that sodium cromoglycate selectively and rapidly phosphorylate proteins in mast cell membrane which is responsible for stopping the secretion and mast cell re-stabilization after degranulation(7) .

Recently Olopatadine hydrochloride 0.2% ophthalmic solution is approved to be given as single daily dosage for allergic conjunctivitis. Few studies were done in allergic conjunctivitis comparing efficacy and tolerability of 0.1% olapatadine and sodium cromoglycate 2% in India. In Tamil Nadu, not much studies have been done on allergic conjunctivitis.In this study we are going to compare the efficacy and tolerability of olopatadine 0.2% ophthalmic solution administered OD with sodium cromoglycate 2% ophthalmic solution administered QID in allergic conjunctivitis patients of Chengalpattu government hospital for 6 weeks duration.

Review of literature

REVIEW OF LITERATURE

Ocular allergy is considered to be a Cinderella in allergic diseases. In clinical practice allergic conjunctivitis is most common cause of red eye. About 10% of ophthalmological clinical consultation around the world is for ocular allergy(8).It is showing a great increase in incidence of ocular allergy during last decades. This increase in incidence of ocular allergic conditions are mainly accountable to climatic change, increased pollution, pollen loads and patient's increased sensitivity for immunological response to these environmental changes. The mast cells are present in large amount in conjunctiva, which makes it a best and preferred area for immediate hypersensitivity reactions. Severity of Allergic conjunctivitis ranges from mild form to severe form(9).

History

Various milestones in history of allergic conjunctivitis and immunology helps in better understanding of immunological process and treatment of allergy(10).It was in 1819 London physician John Bostock describes his own case of summer catarrah in his publication " *a case of periodical affection of the eyes and chest"*(11).For the first time conjunctival provocation test was reported in the work by Charles Blackley entitled "*Experimental Researches On The Causes And Nature Of Catarrhus Aestivus"* published on 1873(10) .The description of allergic disease as a type I hypersensitivity was done by Coombs "and Gell in 1970(10).Later the mast cell preference in ocular tissue

was shown in studies of Mathea Allansmith(10). The relevance of role of eyes in the study of autoimmune disorders was defined by Author Silverstein in his work *"ocular immunology on the birth of the new discipline"*in1991(10).

Definition

The term ocular allergy include a group of conditions like seasonal allergic conjunctivitis(SAC), perennial allergic conjunctivitis(PAC), vernal keratoconjuntivitis(VKC),atopic kerato conjunctivitis(AKC) and giant papillary conjunctivitis(GPC)(12). Among these SAC and PAC are most common and self limiting without any ocular surface damage(9).SAC and PAC are having some differences from VKC and AKC even though all are having common allergic markers.VKC and AKC affect cornea resulting in corneal ulcers and scaring which may even lead to vision loss.(12) Giant papillary conjunctivitis is not a real allergic disease .But they are included in ocular allergy (12).

Classification of Ocular Allergy

I. Based on Onset of Disease

Acute Form

1. Seasonal Allergic Conjunctivitis
2. Perennial Allergic Conjunctivitis

Chronic form

1. Vernal Keratoconjunctivitis
2. Atopic Kerato Conjunctivitis
3. Giant Papillary Conjunctivitis
4. Contact Dermo conjunctivitis

II. Based on signs and symptoms (13)

1. Mild
2. Moderate
3. Severe

III. Based on duration of episodes activity (14)

Allergic Conjunctivitis classified into

1. Quiescent
2. Intermittent
3. Persistent

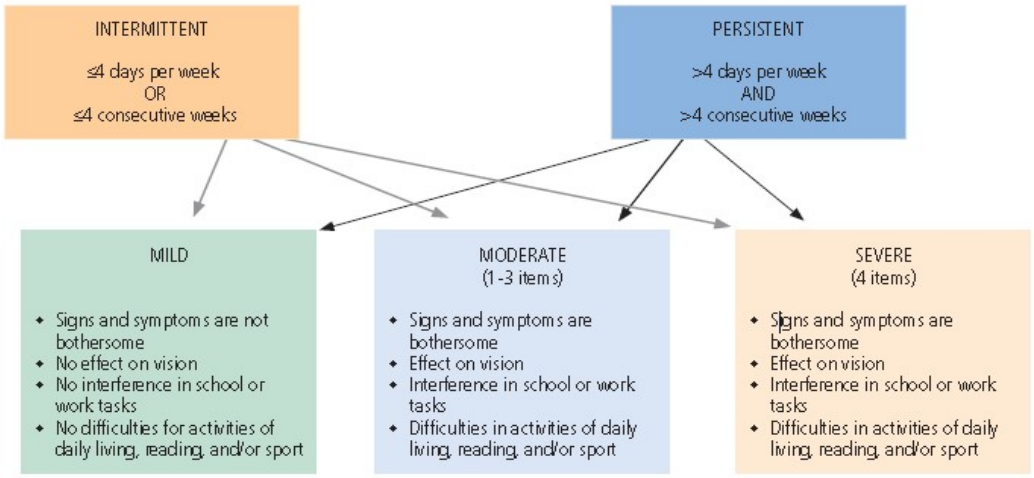


Fig. 2.1 : Classification of allergic conjunctivitis.(15)

Table 2.1 : Clinical and Immunopathological Classification of Ocular Allergy(9)

TYPE OF ALLERGIC CONJUNCTIVITIS	IgE Mediated	IgEand Non -IgE Mediated	Non –IgE Mediated
Intermittent	**SAC**		
Persistent	**PAC**	**VKC**	**GPC**
Chronic		**AKC**	**CDC**

Etiology

The factors affecting ocular allergy are genetics, air pollution, urban areas, pets and early childhood exposure.(12) .The main cause of SAC is air-born pollens from grasses,trees,rag weeds etc.SAC clinically presents more during spring and summer and less during winter season. Perennial allergic conjunctivitis can occur any time throughout the year, usually with allergens like animal dander, molds and dust mites.(16)

Immunopathogenesis

Allergic conjunctivitis is a IgE mediated type 1 hypersensitivity reaction. (16) The pathophysiology of allergic conjunctivitis have two stages When a person comes in contact with allergen for the first time there is an

activation of immune response predominantly Th2 immune response and production of IgE antibodies. This is sensitization phase reaction.

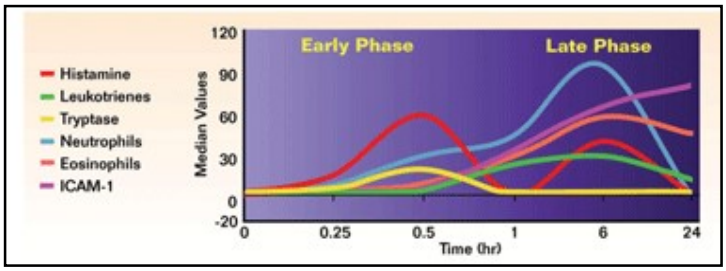


Fig:2.2 Time Course of Selected Inflammatory Mediators.(17)

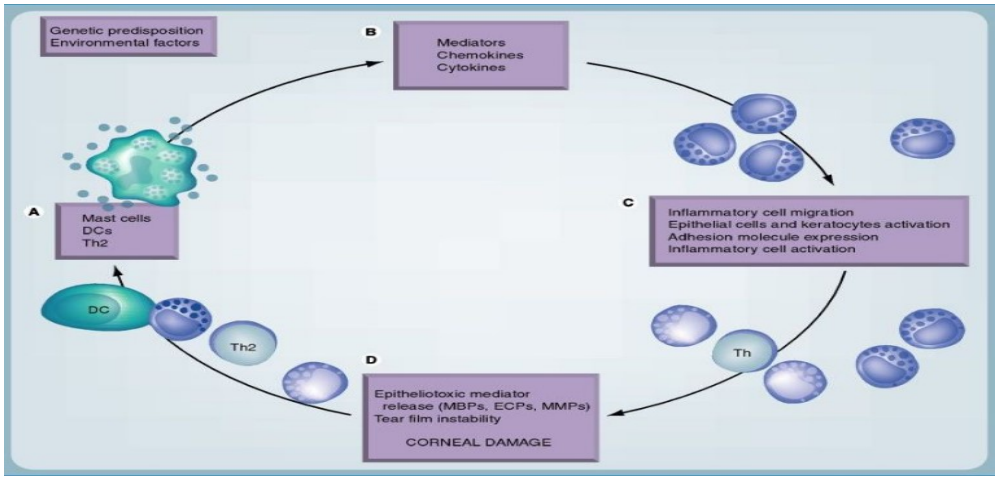


Fig: 2.3 Etiopathogenesis Of Corneal Epithelial damage.(18)

In effecter phase reaction an already sensitized person comes in contact with allergen for the second time, there is an activation of effecter mechanism leading to degranulation of mast cells, releasing the contents into the surrounding area. This early response lasts for 20-30 minutes .(12) The released histamine will initiate a cascade of reactions. The release of many chemical mediators will cause vasodilatation, raised capillary permeability and increased mucous production .The chemical mediators like histamine, tryptase,

kinnogenase, esinophil chemotactic factor of anaphylaxis (ECF-A) will be released. About 6-72 hours after exposure to allergens, late phase of response begin. This phase of reaction will involve eosinophils, basophils, T cells, macrophages and neutrophils infiltrating into the conjunctiva. The chemical mediators released during late phase period are leukotriene B_4, leukatreine C_4, leukotreine D_4, prostaglandins, platelet activation factor.

The histamine released during mast cell degranulation is mainly responsible for symptoms of allergic conjunctivitis like itching, redness etc .Recently in a mouse model leukotriene B4 was recognized to be a mediator of itching(19). Like mast cells basophils also play an important role in allergic inflammation. Esinophil will secrete cytokines and cytotoxic proteins which will cause structural damage and fibrosis.T cells play an important role in severe and chronic allergic eye conditions(20).Tryptase are involved in inflammatory cell infiltration of conjunctiva and extra cellular matrix degradation. The presence of tryptase in tears is regarded as biomarker for IgE mediated allergic eye conditions(21).

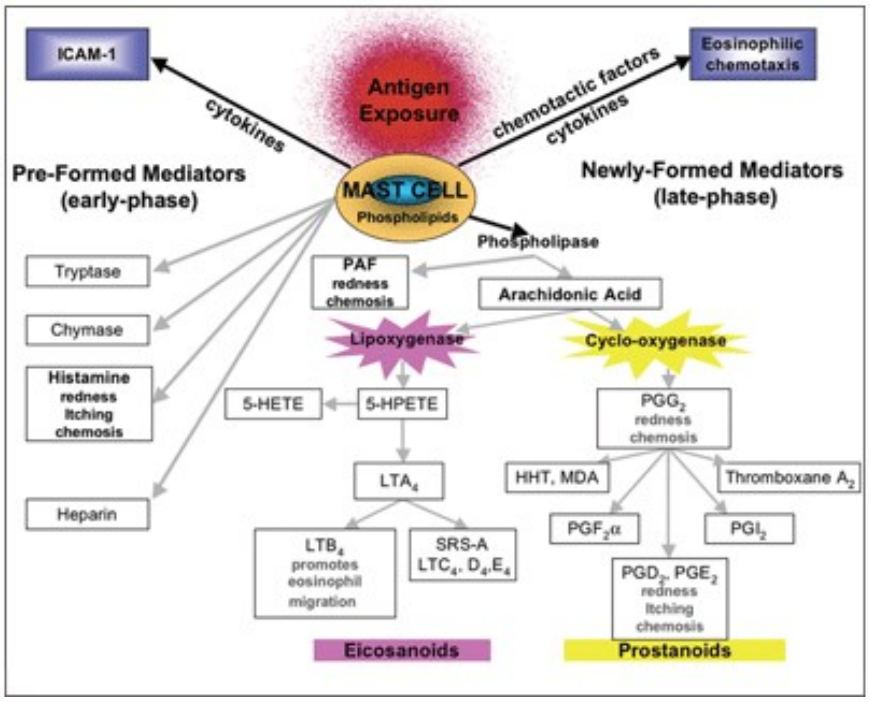


Fig:2.4 Inflammatory Cascade In Allergic Conjunctivitis (17)

In VKC and AKC there is type I and T cell mediated type IV hypersensitivity reaction. Alterations in MMP and tissue inhibitors of MMP responsible for excessive extracellular matrix deposition and papillae formation in VKC. In chronic ocular allergy fibroblast will induce pro-inflammatory mediators like chemokines and adhesion molecules which are responsible for corneal lesion(19)

Clinical Features

The symptoms and signs of acute form of allergic conjunctivitis are

Symptoms

1. Itching
2. Watering
3. Foreign body sensation

4. Photophobia
5. Discharge
6. Blurring of vision
7.Discomfort

Signs

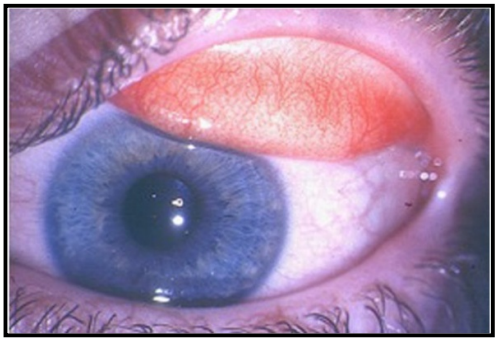
1. Redness
2. Chemosis
3. Eyelid edema

Types of Allergic Conjunctivitis

Seasonal and Perennial allergic Conjunctivitis

SAC and PAC are two forms of allergic conjunctivitis disease affecting both eyes. They presents with itching, redness, watering blurring of vision, photophobia, gritty sensation of eyes. They have self limiting character. Symptoms and signs of SAC depend on types of exposed allergens.The incidence of SAC s more during August to September which is mainly related of outdoor molds. It is mainly related to tree pollens during spring season. It has got association with allergic rhinitis and bronchial asthma.

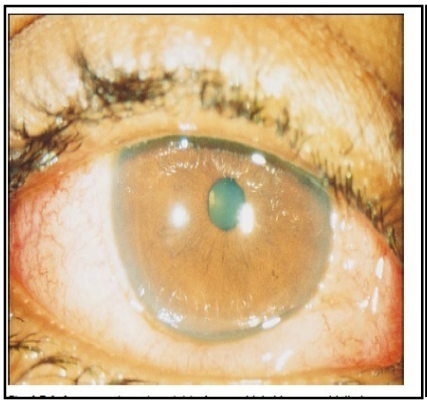
Eyes in Allergic Conjunctivitis

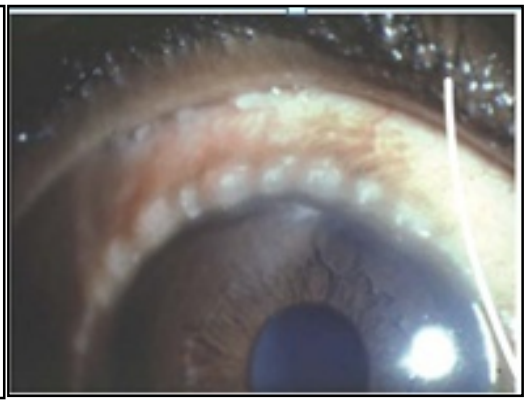


Perennial conjunctivitis (PAC) is another form of AC usually induced by exposure to dust mites,fungi, animal epithelial or occupational allergy(22). PAC patients have symptoms all throughout the year. It has no age or sex prediliction.PAC are common in patients with allergic rhinitis and other allergic diseases .The swabs from conjunctiva of these patients shows more eosinophil count. Co-morbidities like dry eyes are seen in PAC patients because of prolonged disease duration.

Atopic Keratoconjunctivitis (AKC)

It is a form of allergic conjunctivitis with chronic course which is common among males. Majority of AKC patients have concomitant associationwith eczema or bronchial asthma .The AKC patients usually present as allergic shiners. The clinical symptoms of AKC are intense itching, burning, photophobia, tearing, blurring of vision and discharge of eyes of both sides. Periorbital eczema, lid edema, conjunctival chemosis are the other common clinical signs of AKC. Papillary hypertrophy is seen with both upper and lower tarsal conjunctival hyperplasia and the limbal nodules may be present with or without Horner-Trantas dots. Horner-Trantas dots are collection of degenerated cellular debris and eosinophils. In severe condition of AKC ,the scaring and cicatrizing of conjunctivain severe forms of AKC results in formation of symblepharon , sub epithelial tissue fibrosis,and fornices shortening (23).

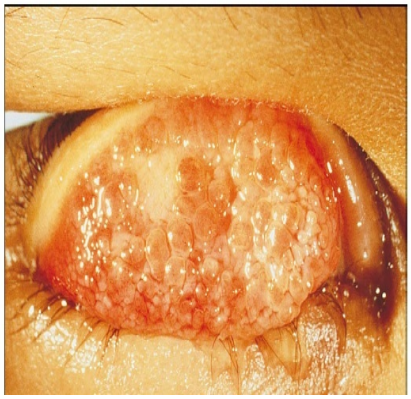


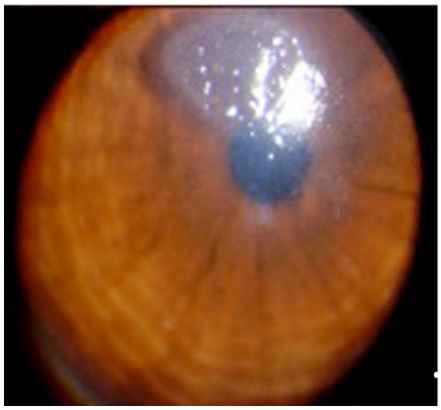


Atopic conjunctivitis. **Vernal Catarrah**

Histological examination of the conjunctival epitheliumof an AKC patient gives a picture of mast cells,lymphocytes and eosinophils mixture.The T -cell is considered as a major triggering primer in both chronic AKC and VKC (23). As AKC are seen in immune compromised atopic patients, there is a chance for secondary infection which should be ruled out and treated early.(10)

Vernal keratoconjunctivitis (VKC)





Vernal Conjunctivitis **Vernal conjunctivitis: corneal plaque**

Vernal conjunctivitis is a disease of both eyes with inflammation of conjunctiva. It is common during the spring and summer season (4).In VKC the children and adults having a history of seasonal allergy, bronchial asthma or eczema are commonly affected. VKC show a higher incidence in warm and temperate regions with chance of infection twice greater in boys compared to girls .VKC is commonly seen around the age of 11to 13 years. The disease in children are mild and self-limited where as in adults, it is a severe disease with indefinite recurrence. The most common symptom is intense pruritis along with other symptoms likephotophobia, burning, watering, ptosis and thick, ropy, yellowish mucoid discharge(4).

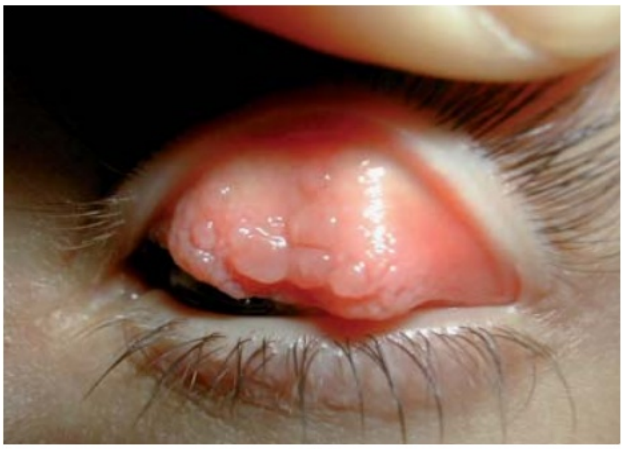
The three varieties of the vernal conjunctivitis are palpebral, limbal and mixed type(24).In palpebral type of VKC the main sign is the cobblestone pattern of papillae on the superior tarsal conjunctiva.First there is a papillary hypertrophy after that there is hyperplasia and proliferation of substantia propria to form giant papillae. The pressure by cornea flattens the tops of the giant papillae leading to a patterned impression that resembles cobblestones. The presence of tiny group of vessels at the center of the papillae helps us to differentiate these follicles from those seen in trachoma patients.

Chronic Atopic Conjunctivitis showing Cobblestone Papillae

A broad, thickened, gelatinous opacification of the superior limbus that can override the cornea is seen in the limbal variety of VKC. In limbal form of VKC, the tiny vessels appear around the sides of the elevations of follicles. Microscopically examination shows an infiltration of lymphocytes, macrophages, basophils, plasma cells and many eosinophils in tissues. An important feature in limbal variety of VKC is the presence of Horner-Trantas dots. It is a white, chalk-like dot, filled with eosinophils and epithelial debris which is located at the limbus. We can see that 50% of VKC cases have corneal involvement.It include superficial pannus and a punctate epithelial keratitis. Small, gray patches of necrotizing epithelium may involve the upper one third to two thirds of the cornea – in severe cases, the cornea appears to be dusted with flour. Under fluorescent staining, vernal “shield ulcer” is seen as an oval, shallow,non vascularized, indolent ulcer on the superior surface of cornea. The ulcer edges are composed of shaggy, dead epithelial cells,with superficial stromal infiltrates.After healing of ulcer, a mild corneal opacity will persist at the level of Bowman’s layer of cornea.

Giant Papillary Conjunctivitis

Giant papillary conjunctivitis (GPC) is a syndrome of inflammation of the upper palpebral conjunctiva seen in people with contact lens or ocular prostheses or protruding ocular sutures for a longer period of time(25,26).It is related to contact lens users and frequently seen in soft lens users than in rigid lens users (26).The soft lens wearers will develop symptoms in 8 months and hard lens wearers take 8 years for the same to develop.The symptoms of GPC appear before the signs of superior tarsal involvement. Conditions that favor the development of GPC in lens users include increased lens deposits, increased wearing time and extended number of years the lenses have been worn, larger diameter lenses and soft lenses



Giant papillary conjunctivitis

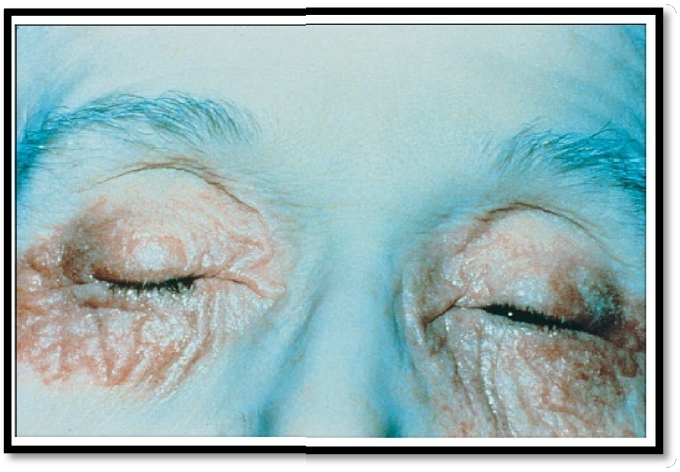
GPC patients mainly complains of mild itching on removal of contact lenses and which is associated with increased mucus on the lenses and in the nasal canthus on getting up in the morning.Other complains of patients are increased lens awareness, blurring of vision after removing contact

lens,excessive lens movement leading to contact lens intolerance. Signs of GPC include a generalized thickening and hyperemia of the superior pretarsal conjunctiva during the early stage and small papillae become elevated.

The conjunctiva becomes opaque as a result of cellular infiltration.Both macro papillae (0.3–1.0 mm) and giant papillae (1.0–2.0 mm) can be formed(4).Trantas dots and gelatinous nodules are formed near the limbus(27). The histology of GPC shows irregular thickening of the conjunctival epithelium over the papillae, with epithelial downgrowth into the stroma.The epithelium and stroma show infiltration of lymphocytes, basophils, polymorphonuclear neutrophil leukocytes, plasma cells eosinophils and macrophages along with proliferation of fibroblast. The number of eosinophils and basophils infiltrating conjunctiva is lower compared to that of vernal conjunctivitis.GPC arise due to multiple factors. Patients always have environmental antigens adhere to the mucus and proteins that normally forms a coat on the surface of all types of contact lenses(28).These antigens, which persist as deposits on the contact lenses, are forced to come into contact with the superior tarsal conjunctiva while blinking. Mechanical trauma remains as an important factor in the process of GPC pathogenesis and it develops in patients who have ocular prostheses and exposed suture ends. This repeated exposure to antigen combined with the trauma from contact lens wear to the upper tarsal conjunctiva result in triggering of a type IV basophil hypersensitivity reaction in conjunctiva.This is similar to cutaneous basophil

hypersensitivity reaction. Along with this reaction a type I IgE mediated immediate hypersensitivity reaction also occurs.

ContactDermatoConjunctivitis



Contact allergy of the eyelids and conjunctiva are common among patients in ophthalmology department. It is a delayed type of cell-mediated (type IV) hypersensitivity reaction in which Previous sensitization can have occur a little as 5 days or as long as years before. The most common stimuli are eye drops, cosmetics, cloths, jewelry, plastics, animal or vegetable products, and industrial chemicals.12 The ocular drugs which are commonly associated with this reaction include gentamicin, idoxuridine, neomycin, atropine, thimerosal, and penicillin.13 Other preservatives can also produce similar allergic reactions.

The reaction begins with intense itching and papillary conjunctivitis greatly affecting inferior palpebral conjunctiva. A mucoid or mucopurulent discharge is seen along with it. The adjacent skin of the lower eye lids and

lateral canthi show typical eczematous dermatitis involvement. Chronic use of the allergen lead to keratinization of eye lid leading to punctal edema and stenosis. The cornea may show punctate epithelial keratitis and erosions on examination. Conjunctival scrapings show monocytes, polymorphonuclear neutrophil leukocytes, mucus and eosinophils.

Diagnosis of Allergic Conjunctivitis

The diagnosis of AC can be made from family history, personal history, history of atopy, clinical signs and symptoms, results of additional appropriate tests (21). Patients may have clinical history of AC during any age. Rhinitis often accompany AC in 66% of adults population (20) about 97% among children group (29), asthma (in 16% of adults (30) and 56% of children (29), and with atopic dermatitis in 25%-42% of adults (31) and 33% in children (29)). AC has conjunctival itching as its main symptom(32), watering and a stinging sensation. Photophobia and Blurring of vision can occur in severe cases. Blurring of vision is because of change in composition and the tear film stability. It is present in more than 78% of patients and measured with the help of interferometry (33).

The signs in AC pateints are examined using slit lamp biomicroscopy. When this is not possible, a light source along with fluorescein staining can be used. The defects in ocular epithelial cells is visualized using this technique. Mild to moderate redness and moderate conjunctival edema can be observed. The eyelids are mostly edematous, and the palpebral conjunctiva will have a

pale pink in colour. In some AC patients, areas of mild papillary hypertrophy are seen in upper palpebral conjunctiva. Aqueous or mucoid type of discharge is seen. The cornea remains often unaffected (34).AC is confirmed by skin tests with suspected allergens or serum specific IgE to various whole allergens or their purified forms (21).The main disadvantage is that these skin tests or specific IgE tests are that the results not often conclusive.24% of AC patients are seemed to be sensitized to variety of allergens(35).Some AC patients show negative skin test even when there is no association with allergic rhinitis(36).

Other methods which help in diagnosing AC are

Tear fluid analysis

The levels of free specific IgE, total IgE, cytokines,and markers of inflammation like eosinophil cationic proteins can be measured in tear fluid.

Conjunctival cyto diagnosis

It is used in research purposes, but is not valuable in routine clinical practice(37).

Responses to medication

By observing response to drugs like topical antihistamines or mast cell stabilizers diagnosis of AC can be made(38).

By performing a conjunctival challenge test.

The conjunctival challenge test can be used to confirm the reactivity of allergen in the AC patient's conjunctiva showing positive skin test results. The challenge test is very useful in

- AC patients with negative skin tests.
- Determining serum specific IgE level.
- Assessing the local and specific responseof the conjunctiva in patients with history suggestive of AC.
- In making diagnosis of patients who are sensitized to multiple allergens and in cases of occupational allergy (39).

COMORBIDITIES

The co morbidities like dry eye disease and blepharitis should be ruled out.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of allergic conjunctivitis are:

- Infectious conjunctivitis
- Toxic conjunctivitis
- Ocular rosacea
- Keratitis
- Episcleritis/scleritis
- Angle closure glaucoma
- Phlectenular Conjunctivitis

COMPLICATIONS(12)

For allergic conjunctivitis complications are usually rare. The complications arise due to the presence of secondary infections. This may include

a) Corneal scar
b) Loss of vision
c) Bacterial infections
d) Sinusitis
e) Recurrence

2.2 Scoring of signs and symptoms of allergic conjunctivitis(6,13,42)

Sign Symptom	Sign Symptom Scoring of sign symptom of allergic conjunctivitis			
	Score			
	0-absent	1- mild	2-moderate	3- severe
Redness	Absent	Slightly dilated bloodvessels, pink in colour	More apparent vessel dilatation,vessel colour is more intense,involves most of vessel bed	Numerous and obvious dilated blood vessels, colour deep red
Itching	Absent	Occasional itching,without tendency toscratch or rub the eyes	Frequentitching with tendency toscratch or rub the eyes	Continuous itching, frequently rubbingthe eyes
watering	Absent	Occasional, No complaints of discomfort.	Frequent, patient felt as discomfort	Persistentand frequently accompanied by swabbing of the eye
Chemosis	Absent	slight edema detectable only by slit lamp	diffuse edema visible in normal room light	Ballooning of overall bulbar conjunctiva.
Lid edema	absent	Slight swelling on palprebal conjunctiva.	Diffuse swelling on palprebal conjunctiva.	Bullous swelling on palprebal conjunctiva.
Photophobia	Absent.	Occasionally photophobic	Continuously photophobic	Eye responds with blepharospasm on exposure to light
Foreign Body Sensation	absent	Occasionally feeling sandy	Frequent gritty sensation	Continuous gritty sensation

2.3 Differential Diagnosis of Ocular Allergy.(40,41)

	SAC	PAC	VKC	AKC	GPC	CDC
Personal/ family history of atopy	Common	Common	constant	Possible	Possible	Possible
Age	Children/adult	Children/adult	children	Adult	Adult/adolescent	Adult
Gender	No pre-dilection	Nopre-deliction	Male	Male	No pre-dilection	No pre-dilection
Season	Spring	perennial	Perennial/spring	perennial	spring	No
Corneal involvement	No	no	yes	yes	no	No
Vision	Minimal	minimal	mild	severe	minimal	Minimal
Papillary hypertrophy	No	no	7-8mm limbal involved	<1mm	>1mm	No
Per ocular skin involvement	Edema	edema	edema	dermatitis	edema	Dermatitis
Exposure to topical drugs	No	No	No	No	No	Yes
Contact lens wearers	No	No	No	No	yes	No
IgE level	Elevated	elevated	variable	Grossly elevated	variable	Variable
Esinophil cells	Frequent	Very frequent	characteristic	characteristic	Not frequent	Not frequent
Globlet cells	Increased	increased	increased	decreased	variable	Variable
Skin test	Positive	positive	Non specific	positive	variable	Variable
Other atopic disease	Rhinitis, asthma	Rhinitis, asthma	variable	Rhinitis Asthma Dermatitis	variable	Variable
Response to anti allergic drugs	Characteristic	Characteristic	low	low	variable	No
Response to corticosteroids	constant	constant	constant	constant	constant	Constant

TREATMENT

Pharmacological properties of decongestants

DRUG GROUP	AGENTS	MECHANISM OF ACTION	SIDE EFFECTS	COMMENTS
Topical ocular decongestants	Naphazoline Tetrahydrozoline Phenylephrine Ephedrine Brimonidine	α_1 adrenergic agonists	Rebound hyperemia, conjunctivitis medicamentosa, follicular reaction, contraindicated in narrow angle glaucoma	Only for redness or in conjunction with first generation antihistamine preparations; Action last for 2 - 4 h only

Drugs like Tetrahydrozoline for AC patients came to market as early from 1950s(43).Naphazoline an α_1 agonist was introduced for treatment of ocular allergy in 1970.It is a vasoconstrictor acting on $\alpha_1$adrenergic receptor which continues to produce immediate vasoconstriction. This helps in decongestion of reddened eyes. When they are used alone it only reduces redness but as combination with anti histamines it reduces both itching and redness .(1,43).When topical α_1 adrenergic agonists are used in AC patients for long period, it causes down regulation of α_1 adrenergic receptors producing tachyphylaxis and rebound redness on discontinuation of drugs(44). These drugs are contraindicated in narrow angle glaucoma and angle closure glaucoma patients (1).Brimonidine , a α_2 agonist drug in low-dose and concentration is being tried in many studies of AC patients .It is in final stage of FDA approval for the treatment of ocular redness (1).

Antihistamines

Pharmacological properties of antihistamines

DRUG GROUP	AGENTS	MECHANISM OF ACTION	SIDE EFFECTS	COMMENTS
Topical antihistamines	AntazolinePheniramine,LevocabastineEmedastine	Competitive inhibition of histamine receptors	Sedation, irritation, dry eye	This group is taken over by dual actingdrugs

Systemicantihistaminic drugs have little efficacy in allergicconjunctivitis .It cause drying of the ocular surface, so it should be used only in patients having concurrent rhinitis or sinusitis (45). Histamine receptors are primary targets in treatment of ocular allergy since histamine signaling is the main reason for signs and symptoms(46). H_1 , H_2 ,H_3 and H_4 are the four histamine receptors involved in ocular allergy(1). H_1 and H_2 receptors take part in pruritus, redness, and cytokine release, proliferation of fibroblast, adhesion molecule expression, vascular permeability and production of procollagens (1,47–49). H_4 receptor is mainly involved in cytokine and chemokine release, chemotaxis and adhesion molecule expression (48).

Topical antihistaminic drugs competitively and reversibly inhibit histamine receptors in conjunctiva (46,49). The symptomatic relief of drugs like antazoline and pheniramine are immediate and temporary. So it requires frequent dosing. First-generation antihistamines are lipid soluble and pass

through blood brain barrier, causing central side effects such as sedation (50). The topical combination of antihistamine--decongestant are available as OTC drugs owing to its good safety and experience profile among patients. The immediate relief shown in the pateints by these group of drugs are the main reason for their great acceptance (49,51) even though there is a mismatch in time of action between anti histamines and decongestants. Newer-generation topical antihistamines are more potent inhibitors of histamine stimulated cytokine synthesis in intact conjunctival epithelial cells (49). The second-generation antihistamine levocabastine was the first drug to be used in isolation and had a longer duration of action than the first-generation agents.

Levocabastine was also the first antihistamine shown to have multiple mechanisms of action in reducing the early phase immune response and the late-phase response by reducing eosinophil activation and infiltration(49,52).

Emedastine is second-generation anti-histamine that has a similar duration of action to levocabastine, but its superiority in prevention and treatment of allergic conjunctivitisis shown in one of the prospective clinical trial (53). The second generation topical antihistamines having 4 h of duration of action are given as four times daily dosing. Emedastine is approved for use in patients more than 3 years of age Emedastine shown to inhibit histamine evoked increased vascular permeability (49).

Systemic Antihistamines

Systemic antihistamine drugs are used only in restricted manner in treatment of ocular allergies. In many studies it is seen that ocular symptoms are more reduced effectively by topical antihistamines (54–56). Systemic antihistamines can increase dryness of eyes by decreasing tear production (57). The main issues with this group of drugs are sedation and cardio toxicity side effects even though they are less common (46). Systemic antihistamines are added to treatment when AC patients have other symptoms like rhinitis or generalized itching (46). Newer antihistamines like bilastine show no sedating effect. They are very successful in treating rhino conjunctivitis (58).

Mast cell stabilizers

Pharmacological properties of mast cell stabilizers.

DRUG GROUP	AGENTS	MECHANISM OF ACTION	SIDE EFFECTS	COMMENTS
Topical mast cellstabilizers	Nedocromil sodiumPemirolastLodoxamide	Inhibition of mast celldegranulation andrelease of histamine	Burning sensation Headache.	Commonly very weak activity;Lodoxamide perhaps most effective in VKC.

Drugs like cromolyn (sodium cromoglycate), nedocromil sodium, pemirolast and lodoxamide belongs to this group. Cromolyn is the oldest drug in this group The mast cell stabilizers prevent degranulation of mast cells and prevent release of histamine and other mediators.It reduces the effects of both

histamine and the influx of monocytes, eosinophils and neutrophils. But these ant allergic effects have been difficult to demonstrate in the eye clinically(59,60). Nedocromil sodium inhibits influx of chloride ion in mast cells, epithelial cells and neurons. Drugs like Pemirolast show inhibition of eosinophil chemotaxis along with mast cell degranulation (60,61).But in human conjunctival mast cells, cromolyn sodium failed to show inhibition of histamine release and it was only marginally effective at very high concentrations (61).While drug lodoxamide was much more potent than cromolyn which block eosinophil chemotaxis (61).Lodoxamide appears to be most efficacious for treating epitheliopathy and shield ulcers seen with VKC(1,62). The pemirolast shows considerable clinical efficacy in SAC (1)

Corticosteroids

Pharmacological properties of corticosteroids.

DRUG GROUP	AGENTS	MECHANISM OF ACTION	SIDE EFFECTS	COMMENTS
Topical corticosteroids	ClobetasonebutyrateDexamethasone,Fluoromethalone,Hydrocortisone,Prednisolone,Rimexalone,Triamcinolone,Loteprendol	Inhibition ofphospholipase Aresulting in inhibitionofPG andLeukotri	Increased intraocularpressure, cataract formation, delayed wound healing, headac	Should be used only for pulse therapyin chronic forms of

		ene synthesis.	he, pharyngitis, rhinitis	allergy (VKC,AKC, etc.)

Glucocorticoids are effective therapy for various forms of allergic disease, ranging from allergic rhinitis to asthma, and including ocular allergy. Specifically, topical corticosteroids are highly effective in treating severe or chronic ocular allergy (63,64).This is because the corticosteroid acts on many steps of the allergic cascade, working on both molecular and cellular targets. The main mechanism of action of corticosteroid is inhibition of prostaglandin and leukotriene synthesis by arachidonic acid through blockage of phospholipase A (46).Corticosteroids works by inhibit proliferation and recruitment of mast cells (1,46,65–67). Steroids decrease the eosinophil production and induce apoptosis and phagocytic destruction of eosinophil (1,65–67). The other effects of steroids include reducing the availability of histamine, both by increasing cellular stores and decreasing the expression of histamine receptors (67).

Side effects

- Immunosuppression
- Superinfection
- Cataract Formation
- Corneal Hazing
- Delayed Wound Healing,
- Ptosis (Steroid Myopathy).

- Increased Intraocular Pressure (IOP) (68).
- Growth Suppression (1,69).

When SAC is refractory to all other treatment, topical corticosteroids can be considered for short-term treatment with vigilant monitoring (46,63). Medications such butyrate, have been used. Side effects like increased IOP and cataract formation limit their use(46,64)

Loteprednol Etabonate0.2 %(LE)

It is a 'soft steroid,' developed in view of reducing risks associated with raised IOP and cataract formation (64). It is an ester corticosteroid with a 17 b-chloromethyl ester at the carbon-20 position instead of a ketone, a substitution that allows the drug to undergo predictable hydrolysis (70,71). In two randomized, double-masked placebo-controlled studies it is found that LE has similar safety profile with placebo(70,71).From a retrospective review of 159 patients examined safety in patients using LE daily for more than 12 months and found no adverse effects related to its long-term use(72).

Ocular Therapeutic has developed technology for encapsulating ophthalmic drug preparations within a hydro gel to deliver sustained therapeutic levels of various drugs via punctual plugs (73). One example is OTX-DP, it is a dexamethasone depot preparation which is tested and is showing promising effect (74–76)on chronic allergic conjunctivitis treatment using CAC models. Other routes of drug administration are being explored even though topical corticosteroids are the most frequently used route for

severe ocular allergy. The use of supratarsal injection of corticosteroids in severe VKCcases has shown improvement (74–76). A retrospective, noncomparative study of 35 childhood patients with refractory allergic keratoconjunctivitis suggested that supratarsal injection of triamcinolone acetonide was effective and safe, with only one patient experiencing elevated IOP (77). Prospective studies are needed in this respect. Intranasal corticosteroids (INSs), widely used in the treatment of allergic rhinitis, have also been examined with respect to treating ocular symptoms(78). The exact mechanism of reducing ocular symptoms is not known. Three possible mechanisms are one by inhibiting mast cells proliferation and recruitment (1,46,65–67).Second by decreasing the eosinophil production and third by inducing their apoptosis and phagocytic destruction (1,46,65–67). Numerous other effects like reducing the availability of histamine, both by increasing cellular stores and decreasing the expression of histamine receptors(67) in severe VKC (78).

The INSs directly enter the eye via the nasolacrimal duct, decreased inflammation of the nasolacrimal duct improving drainage of allergens, or decreased nasal inflammation normalizes the excess reflex neural activity that occurs during allergic reactions (79). From many studies it is seen that INS reduce the level of substance P in tear fluid ,suggesting that substance P may have a significant role in naso-ocular interactions in allergic rhino conjunctivitis (80). The drugs like mometasone furoate, fluticasone furoate, fluticasone propionate and budesonide (81–83) are promising ones for the

treatment of AC. The meta-analysis of 10 randomized, placebo-controlled trials show that mometasone furoate nasal spray are effective at relieving ocular allergy symptoms in allergic rhinitis patients(84).The published data for INSs use in patients with rhinitis do not show an increased incidence of ocular hypertension, glaucoma or cataracts (83). In a study the effects of topical olopatadine and mometasone nasal spray in allergic subjects were assessed using the CAC and nasal allergen challenge (NAC) models of allergy. It is seen that the olopatadine provide effective management of both ocular allergy and nasal symptom(54).

Topical NSAIDs

Pharmacological properties of topical NSAIDS

DRUG GROUP	AGENTS	MECHANISM OF ACTION	SIDE EFFECTS	COMMENTS
Topical non-steroidal anti-inflammatory agents	KetorolacFlurbiprofenIndomethacinDiclofenac	Inhibition ofCOX-1 and COX-2 resulting in PG inhibition	Burning sensation, itching, corneal melt	Used for postoperativeinflammation; notmuch effective in PAC and SAC

Topical NSAIDs inhibit cyclooxygenase enzymes (COX-1 and COX-2) resulting in inhibition of inflammatory mediators such as prostaglandins and leukotrienes(85). They reduce pain, irritation and redness, and are used in treatment for post-operative inflammation. Many drugs have been tested for the treatment of ocular allergy, including ketorolac, flurbiprofen indomethacin and diclofenac. But they are generally ineffective or inferior to topical antihistamine therapy (1,86,87). Topical NSAIDs have side effects like burning and stinging, so these drugs have less patient compliance. Although for inflammation they are to be preferred corticosteroids whenever possible but topical NSAIDs are associated with the dangerous adverse effect of corneal melting, usually when there is a previous history ocular surface disease (1,88,89)

Immunomodulatory therapy

Pharmacological properties of immunomodulators.

DRUG GROUP	AGENTS	MECHANISM OF ACTION	SIDE EFFECTS	COMMENTS
Topical immuno-modulatory therapy	Cyclosporine A	Inhibition of T-cellactivation	Irritation, burningsens ation	Approved for use in dry eye;

Immunomodulatory drugs alter normal immune pathways and give a steroid-sparing alternative for allergic conjunctivitis. Different drugs in this group are cyclosporine A, tacrolimus, mycophenolate mofetil, leflunomide, rapamycin (sirolimus), copaxone, laquinimod and infliximab (90). Many of them have shown limited success because of their low water solubility and lipophilic properties leading to poor corneal penetration (50). Both cyclosporine and tacrolimus have shown promise results in treating severe and chronic inflammatory forms of ocular allergy. Cyclosporine A works by inhibiting T-cell activation and infiltration of eosinophil into the conjunctiva and they get involved with both late-phase and delayed-type allergic reactions (1,50,91).

The side effect like intense stinging with Cyclosporine A limit patient tolerance (92). Tacrolimus inhibits T-cell activation with a potent immunosuppressive effect, which is about 100 times stronger than that of cyclosporine (93). One common adverse effect is mild irritation of eye

(94).Ointment formulations of tacrolimus shown to be effective as a steroid-sparing agent in both 0.1 and 0.03%concentrations (91,95).

DUAL-ACTING AGENTS

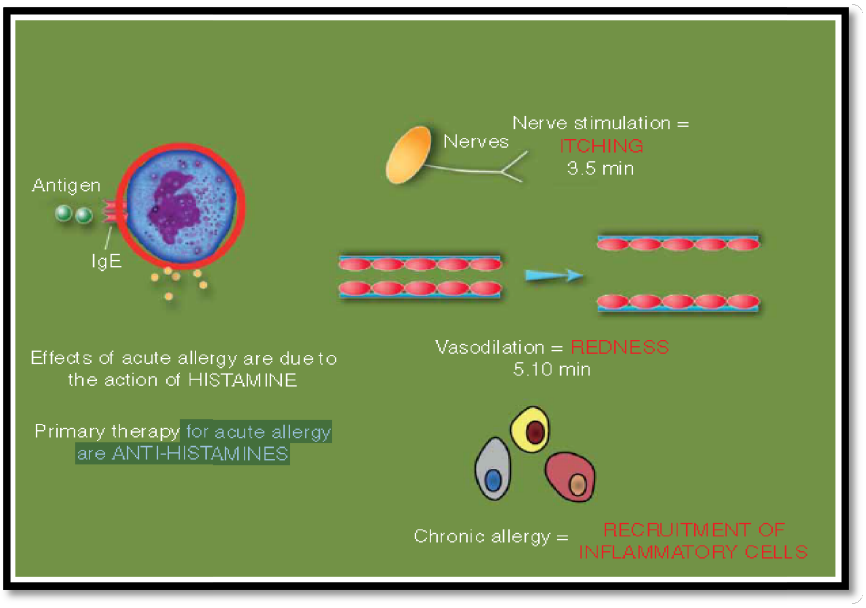


Fig.2.5 :Mechanism of itching

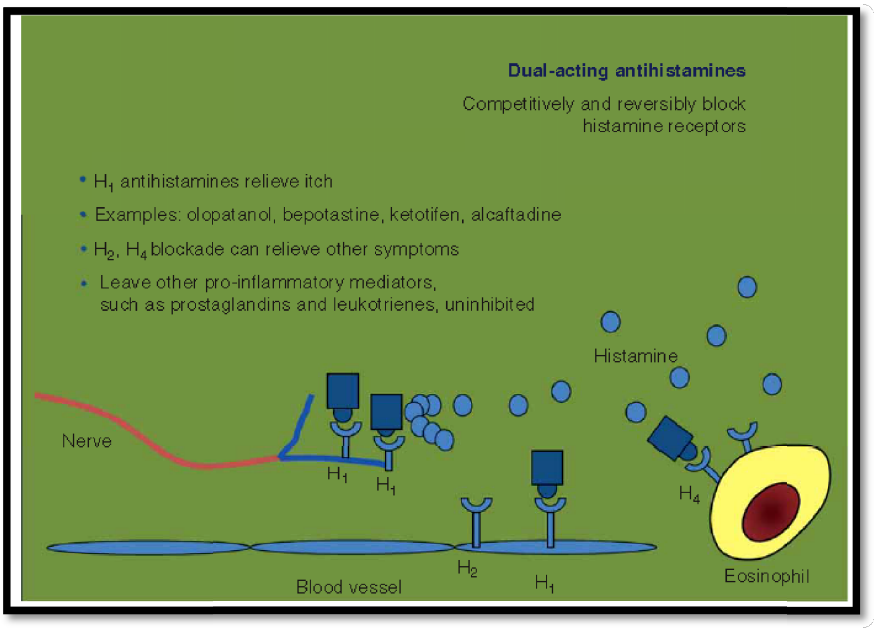


Fig.2.6 : Action of dual acting agents

Pharmacological properties of dual acting agents.

DRUG GROUP	AGENTS	MECHANISM OF ACTION	SIDE EFFECTS	COMMENTS
Topical dual-actingagents	KetotifenAzelastineEpinastineBepostatineOlopatadineAlcaftadine	Blockage ofH1 receptors andinhibits mast celldegranulation andhistamine release	Headache, hyperemia,burning sensation, bittertaste, dry eye	Most are used by twice daily dosing;Olopatadine and alcaftadine approved for once-daily dosingAlcaftadine shown to besuperior for ocular itching by many parameters

Olopatadine and ketotifen are two drugs which are commonly used for different types of ocular allergy. Olopatadine0.1% is the first topical anti-allergic drug, which was approved for twice-daily dosing (50). Ketotifen is used in many OTC anti-allergy drops. Azelastine has an extra mechanism of action of platelet-activating factor inhibition and intercellular adhesion molecule 1 expression, which are the main reasons for its efficacy in PAC (96). Epinastine blocks both H_1 and H_2 receptors competitively, which reduce eyelid edema (97). Epinastine have any CNS side effects as it does not cross the blood--brain barrier, compared to ketotifen, it has no effect on working memory in children (98).

Another difference from topical antihistamines is its drop comfort for example, it is found from patients response that olopatadine and epinastine are more comfortable than azelastine, and epinastine is more comfortable than ketotifen (49).In a study of 66 patients treated with bepotastine versus placebo it is shown that bepotastine produce statistically significant decrease in non ocular-associated symptoms, including nasal congestion, rhinorrhea,ear palate pruritus and nasal pruritus (99). All drugs in this group reduce ocular itching for up to 8 h, allowing twice-daily dosing, and recently olopatadine 0.2% is approved for once-daily dosing. Alcaftadine possess a different pharmacological action with activity against H_1, H_2 and H_4 receptors(100), also reducing conjunctival eosinophil infiltration and the late-phase immune re c dr

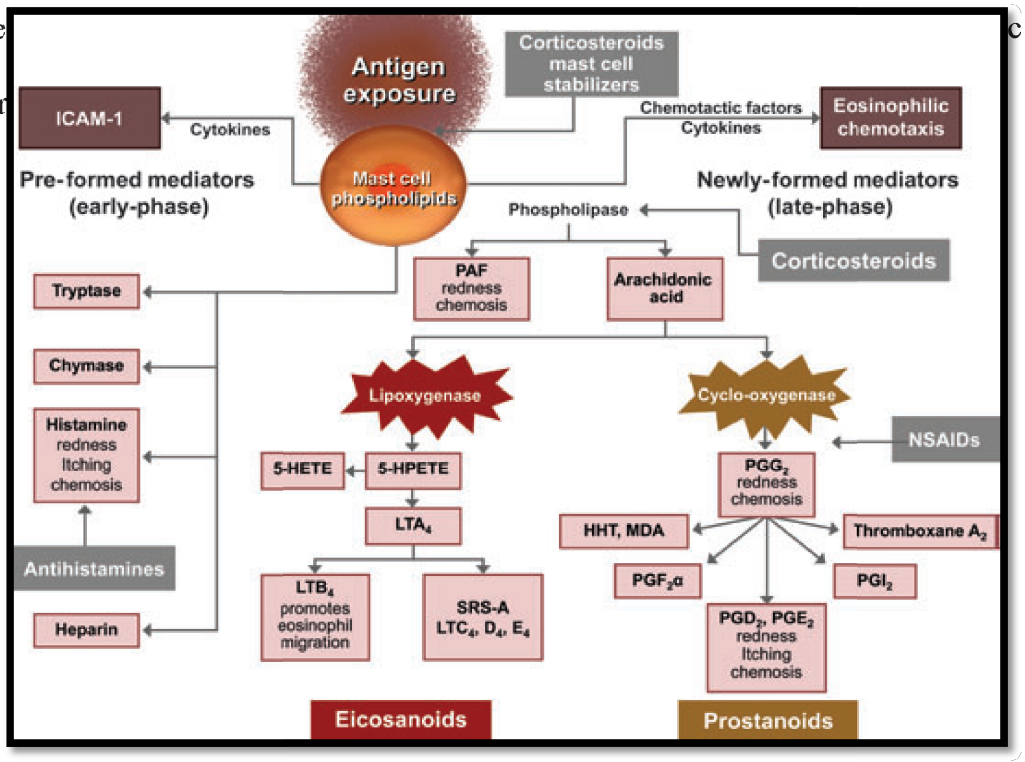


Fig.2.7 Allergic Conjunctivitis Responses Phases and Treatment (102)

Aims and objectives

AIM

To compare the efficacy and tolerability of olopatadine hydrochloride 0.2% ophthalmic solution once daily with sodium cromoglycate 2% ophthalmic solution four times daily in patients with allergic conjunctivitis

Primary Objective

To study efficacy of olopatadine hydrochloride 0.2% ophthalmic solution once daily with sodium cromoglycate 2% ophthalmic solution four times daily in allergic conjunctivitis

Secondary Objective

To study tolerability of olopatadine hydrochloride 0.2%ophthalmic solution once daily with sodium cromoglycate 2% ophthalmic solution four times daily in allergic conjunctivitis .

Methodology

METHODOLOGY

Study design:

Randomized prospective, open labeled comparative study.

Study population:

Patients attending ophthalmology outpatient department of Chengalpattu medical college satisfying the eligibility criteria will be included in the study.

Study centre:

Chengalpattu Medical College Hospital

Department of Pharmacology, in collaboration with Department of Ophthalmology Chengalpattu Medical College

Period of study:

March 2015 – February 2016

Duration of study

6 weeks

4 weeks study and 2 weeks follow up per patients

Sample size:

120 patients

Group A-olopatadine-60 patients

Group B-Sodium Chromoglycate-60 patients

Eligibility Criteria:

Inclusion criteria:

- All patients age > 4 years with clinically diagnosed allergic conjunctivitis.
- Willing to give written informed consent
- Willing to do follow up visits.

Exclusion criteria:

- Patients age < 4 yrs.
- **Patient having active ocular infections, serious ocular pathological conditions**
- Patients havingocular surface disorders like pterygium, dry eyes blepharitis, history of ocular surgery within 3 months.
- Patients who have known hypersensitivity to the study drugs including benzalkonium chloride which is used as preservative in ophthalmic solution
- If the patient has used the study medications 1 week before the start of the study
- Patients who are unwilling to discontinue contact lens during study period
- Pregnant and lactating women.

- ❖ Patient taking oral immuno-suppressive agents like steroids, topical medications, artificial tear drops, steroid eye drops.

Study Procedure

The study was conducted after obtaining the approval from Institutional Ethics Committee. Written informed consent was obrained from all study participant of age more than 18 years in a prescribed format in regional language after explainng about study purpose and study procedures.For the patients less than the age of 18 years ,their parents were explained about the study purpose and procedures and a written informed consent was obtained from them. If the participant was illiterate, left thumb impression was sought. This was done in the presence of an impartial witness.

Screening

After getting informed consent, the demographic details of 145 patients were obtained and recorded. After taking complete medical history, clinical examination, slit lamp examination of eyes were done by an ophthalmologist. After screening145 patients, 120 patients who satisfy the inclusion and exclusion criteria were enrolled in the study during 1st visit.

Randomization

The enrolled patients were randomized by simple randomization(odd/even number) method into group A or group B.

Treatment Plan

Group A-olopatadine hydrochloride 0.2% ophthalmic solution 1 drop on affected eye OD for 4 weeks

Group B-sodium cromoglycate 2% ophthalmic solution1drop on affected eye QID for 4 weeks

Follow Up Visits.

After baseline (visit 1) history taking ,clinical examination, slit lamp examination of eyes of the patients in each group, group A and group B were given medications for 2 week. To assure compliance, the patients were asked to mark the time when they are instilling medication and record on his or her own impression on relief of symptoms during each day in a dairy (provided during visit 1).The patients were also asked to return back the empty bottles of medications and diary during follow up visits. Follow up visits were made at 2^{nd}week, 3^{rd}week and 4^{th} week Adverse effects were noted during each visit and in case of any serious adverse effect patient were asked to report immediately to the hospital or investigator. After 4^{th}week medications were stopped and they were asked to come on 6^{th} week for post treatment follow up.

Visit 1 – Screening and enrolment

- Informed consent obtained
- Demographic details obtained
- Randomization done
- Medical history obtained

- Vital signs recorded
- General & systemic examination done
- Examination of eyes done by ophthalmologist
- Slit lamp examination done by ophthalmologist
- Study medications given for 2 weeks
- Parents asked to return empty drug bottles and dairy during subsequent visits

Visit 2 (2nd week)

- Empty drug bottles and dairy received and compliance checked .
- Vital signs recorded
- General & systemic examination done
- Examination of eyes done by ophthalmologist.
- Slit lamp examination done by ophthalmologist.
- Adverse events if any noted.
- Study medications given for 1 week.
- Subjects asked to return empty drug bottles and dairy during subsequent visits.

Visit 3(3rd week)

- Empty drug bottles and dairy received and compliance checked
- Vital signs recorded
- General & systemic examination done
- Examination of eyes done by ophthalmologist.

- Slit lamp examination done by ophthalmologist.
- Adverse events if any noted.
- Study medications given for 1 week.
- Subjects asked to return empty drug bottles and dairy during subsequent visits.

Visit 4(4th week)

- Empty drug bottles and dairy received and compliance checked.
- Vital signs recorded
- General & systemic examination done
- Examination of eyes done was by ophthalmologist.
- Slit lamp examination done by ophthalmologist.
- Adverse events if any monitored
- Study medications were stopped
- Subjects asked to return after 2 weeks**.**

Visit 5 (6th week) Post Treatment Follow Up Visit

- General & systemic examination done
- Examination of eyes done by ophthalmologist.
- Slit lamp examination done by ophthalmologist.
- Adverse events if any noted.

Assessment of Patients

The assessment of patients is done by history taking ,clinical examination and slit examination by ophthalmologist. The ocular signs such as conjunctival congestion, chemosis, lid edema were assessed .the signs are graded depending upon the severity (grade0-absent, grade1-mild, grade 2-moderate, grade 3 severe).The ocular symptoms like itching, discomfort, stinging, photophobia and watering foreign body sensation were assessed by interviewing the patients and graded according to severity as grade 0-absent, grade1-mild, grade 2-moderate, grade 3 severe were assessed by interviewing the patients(3).

Assessment of Efficacy, Safety and Tolerability.

The change in mean scores from baseline for signs and symptoms during 2^{nd} week and 4^{th} week were compared between two groups. Treatment related adverse events, compliance of patients are were compared between the two groups.

STATISTICAL ANALYSIS

The obtained data is analyzed statistically using SPSS 20 software . Descriptive data were analyzed by Chi square test.

The reduction of signs and symptoms scores during each visit from baseline scores during (visit1) within the groups were analyzed using wilcoxon signed rank test. Comparison between the groups A and group B in reduction of symptoms and signs scores were analyzed using Mann Whitney U test.

P value ≤ 0.05 considered to be statistically significant. The collected data is computed into various tables and figures

Results

RESULTS

This study was conducted to compare the efficacy and tolerability of olopatadine to sodium cromoglycate in allergic conjunctivitis patients.

For the purpose of study 145pateints were screened, of which 25 were excluded from the study. Among 25 patients excluded, 10 patients not willing to give consent,11 patients not willing to stop other medications,3 were lactating mothers, one patient was not willing to stop using contact lens.

120 patients were included in the study, Of 120 patients 60 each was randomly allotted to group A and group B. Out of 120 patients,117 patients completed study. There was 1 drop out in group A and 2 drop outs in group B. These three drop outs were lost during follow up.

STUDY FLOW CHART

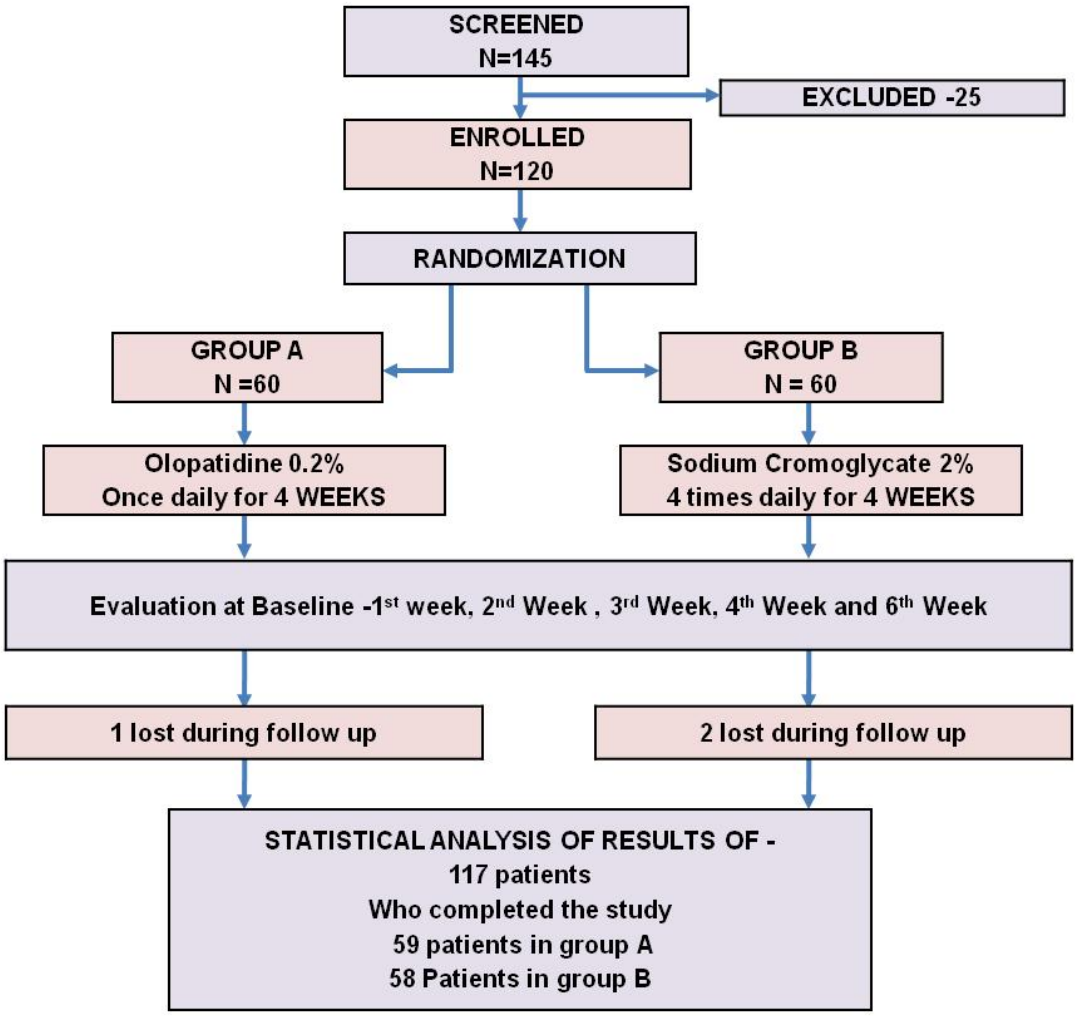


Fig : 5.1 Flow chart

Table5.1 : Number Of Patients Completed And Number Of Dropouts

Groups	Total no:of patients	Number ofpatients completed the study	No: of drop outs
Group A	**60**	59	1
Group B	**60**	58	2
Total	**120**	**117**	**3**

Table 1 shows total number of patients who completed the study and total number of drop outs from the study in both group A and group B.

Table 5.2: Age Distribution

Age	Group A	Group B	Chi SquareTest
<15	36	35	$X^2 = 0.006$ P=0.9
>15	23	23	
Total	59	58	

Table 5.2 shows no statistically significant difference between group A and group B regarding age less than 15 years and more than 15 years.

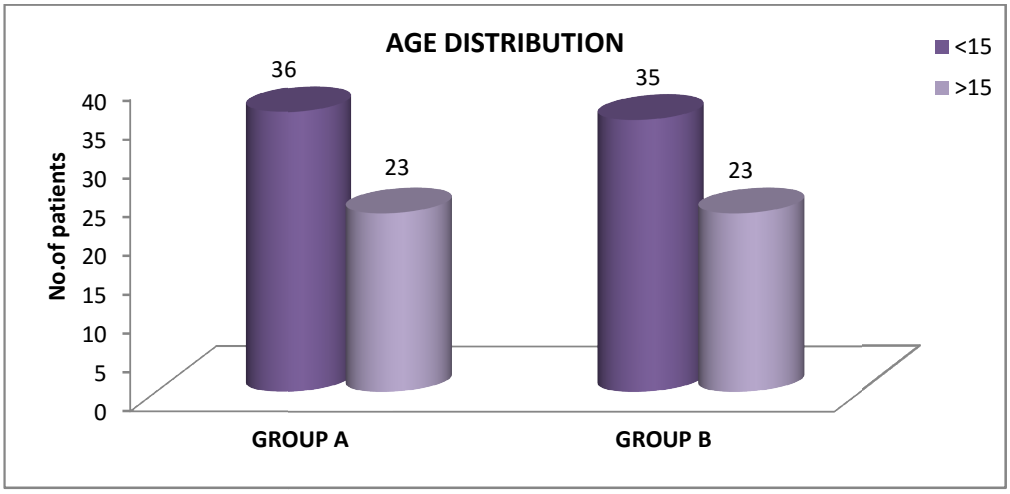


Fig.5.2Age distribution

Figure 5.2shows age distribution 15years >age and age >15 years among group A and group B.

Table 5.3: Mean Age Distribution

Groups	No. of patients	Mean age (in years)	Sd	Statistical Analysis
GROUP A	**59**	**16.03**	**11.791**	**P=0.858**
GROUP B	**58**	**16.43**	**12.153**	

Table5.3: shows the mean age for group A is 16.03 years and 16.43 years in group B. Pvalue is >0.05, means that there is no significant difference in mean ages between the groups.

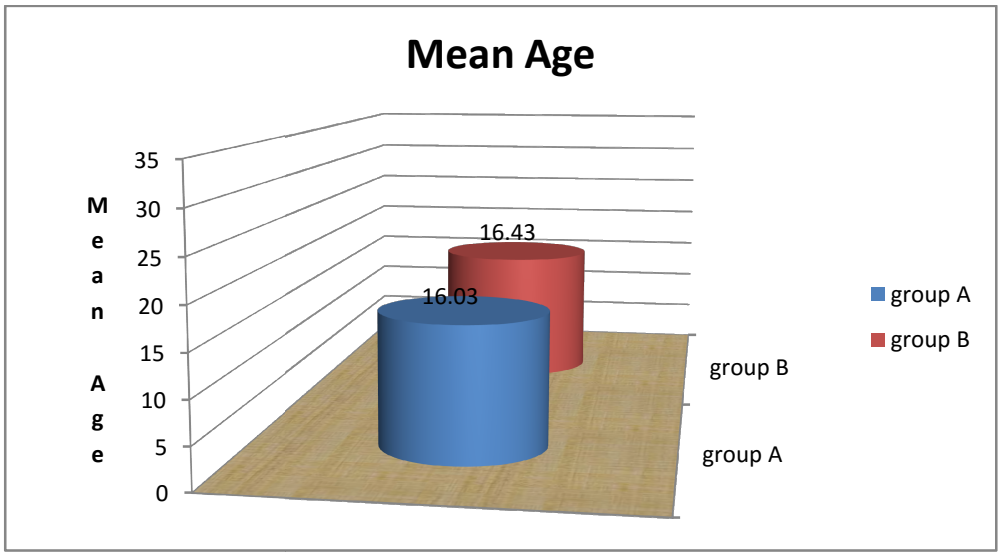


Fig.5.3 Mean Age Distribution

Fig.5.3shows the mean age distribution in group A and group B.

Table5.4: Sex Distribution

Sex distribution	Groups				
	Group A		Group B		PearsonChisquare test P Value
	n	%	n	%	
Male	37	63	37	64	X^2=0.015 P=0.9
Female	22	37	21	36	
Total no. Of patients	59		58		

Table 5.4 shows sex distribution in groupA and group B. About 63% and 64% are males in group A and group B respectively. The females accounts for 37% and 36% in group A and group B respectively. Statistically there is no difference in sex distribution between the group.

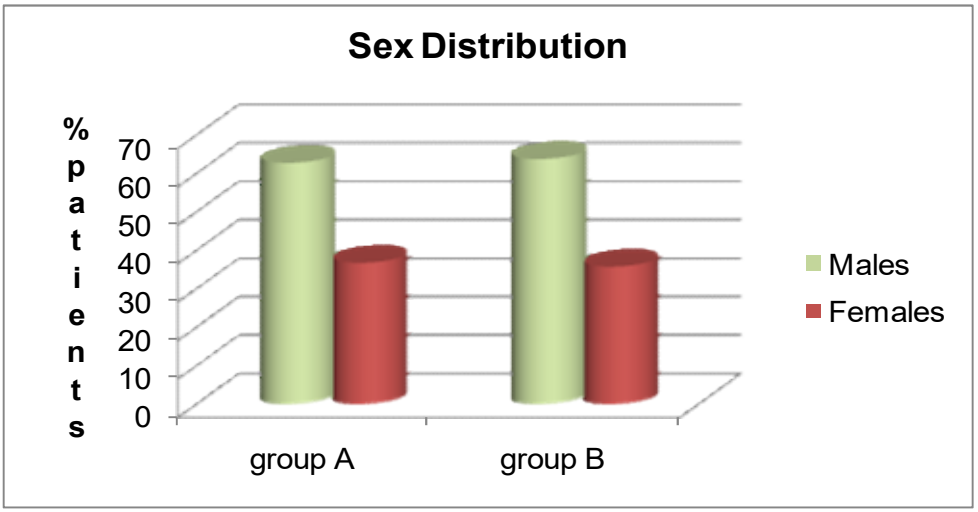


Fig.5.4: Sex Distribution

Fig.5.4: a graphical representation showing sex distribution among group A and group B.

Table 5.5:Itching Scores

	Group A	Group B	MannWhitney U test
Itching	**Mean Score+SD**	**Mean Score+SD**	**PValue**
Baseline	2.6±0.494	2.45± 0.534	0.127
visit 2(2nd week)	1.02+0.676	1.15± 0.708	0.232
visit 3(3rd week)	0.2 ± 0.403	0.57± 0.5325	0.01**
visit4(4th week)	0.1 ± 0.237	0.25± 0.473	0.04*
Wilcoxon Signed Rank pvalue.	0.01**	0.01**	

*significant at P≤0.05, ** highly significant at P≤0.01,*** very high significant at P≤0.001

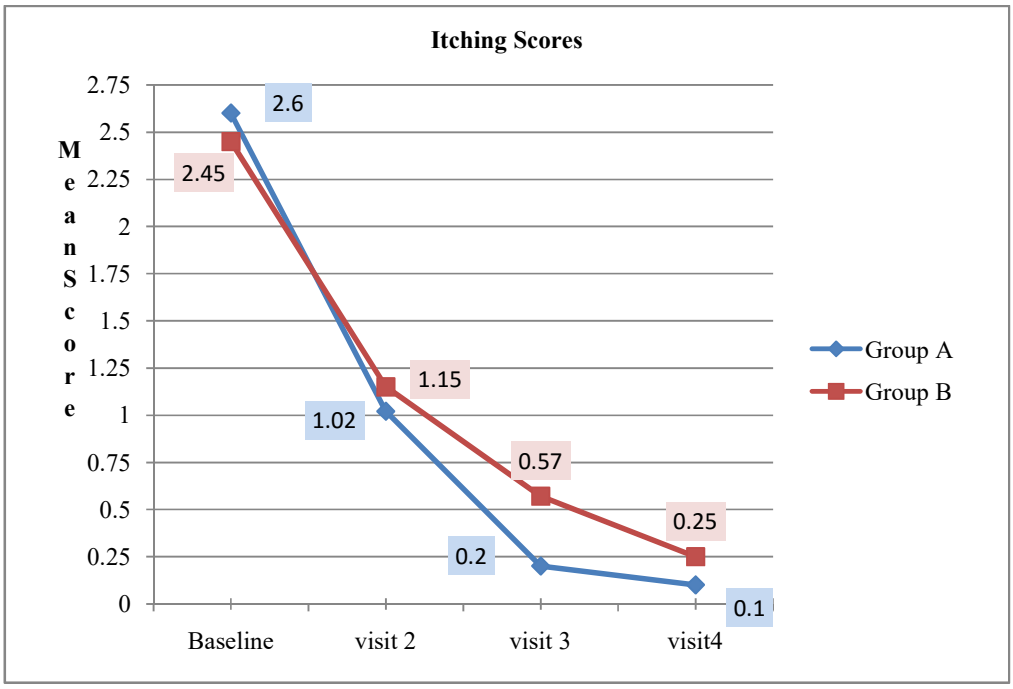


Fig.5.5 : Itching Scores

Visit 1-Baseline, visit 2- 2nd week, visit 3-3rd week, visit 4-4th week.

Fig.5.5 shows graphical representation of itching scores during each visit.

Table 5.5 shows mean itching scores with standard deviation at baseline(visit 1), 2ndweek(visit 2), visit 3(week 3) and visit 4(4th week).There is reduction in itching score from baseline(visit 1) at visit 2,visit3, visit 4. Wilcoxon singed rank test is used to compare the reduction in itching score between baseline visit and 2ndweek(1-2), 3rd week(1-3), 4th week(1-4), there is statistically significant [p vale<0.01] difference in both group A and group B. Mann Whitney U test is used to compare group A and group B at visit 1,visit2,visit 3,visit 4.There is no difference in itching score between the groups at baseline visit[p value >0.05].There is statistically significant difference in itching score at visit 3 and visit 4.[p value<0.05]

Table5.6: Mean Reduction In Itching Score At 2nd week and 4th week

	Mean change at 2nd week			Mean change at 4th week		
	group A	**group B**	**P value**	**group A**	**group B**	**P value**
Itching Score	1.58	1.4	0.248	2.5	2.2	0.006**

Table 5.6 shows comparison between mean change in itching score at 2nd week and 4th week.

There is no difference in mean change in itching score at 2nd week in both group A and Group B statistically [p value>0.05]. There is statistically significant difference between the group A and group B during 4th week [P value<0.05] in reduction of itching.

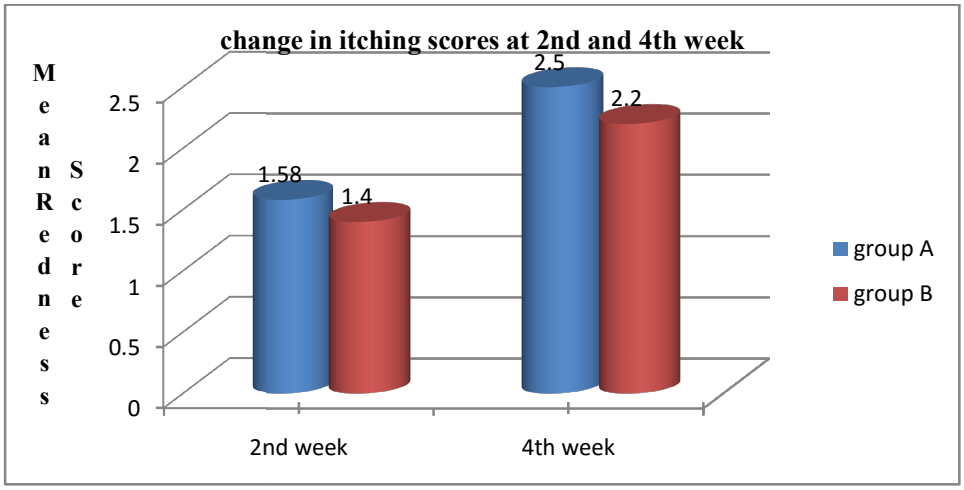


Fig. 5.6 Change In Itching Score at 2ndweek and 4th week

Fig.5.6 : a graphical representation of mean change in itching score at 2nd week and 4th week. Mean change is more in group A during 2nd and 4th week.

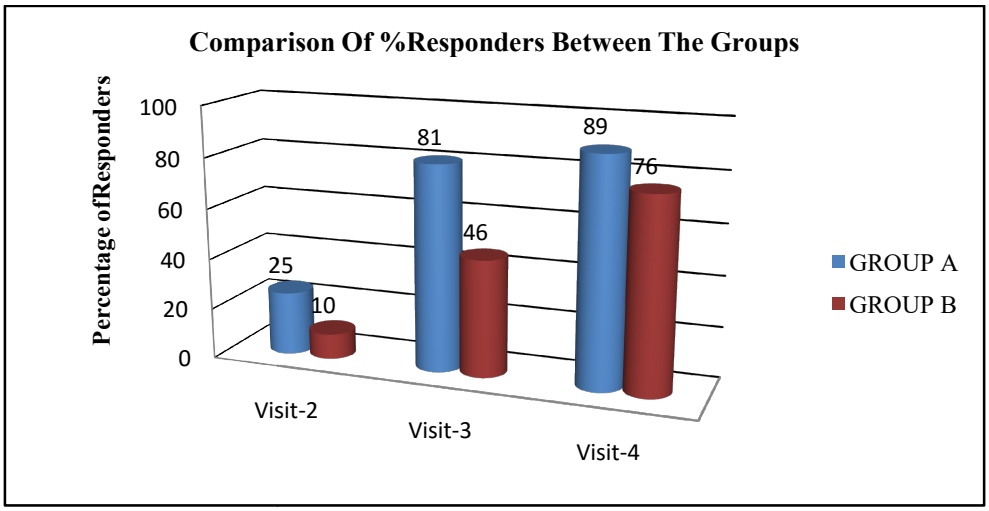


Fig.5.7%Responders in ItchingScores

Fig.5.7shows graphical representation of%Responders to treatment for itching.

The patient whose score is 0 is considered as responders. In group A 25% patients score become zero by 2nd week, 81% attained zero by 3rd week and 89% get cured by 4th week. In group B it was about 10%, 46% and 76% during 2nd week, 3rd week and 4th week respectively.

Table5.7:Redness Score

	Group A	Group B	Mann whitney U test
Redness	**MEAN SCORE± SD**	**MEAN SCORE± SD**	**pValue**
Baseline	**2.51 ± 0.504**	**2.4 ± 0.560**	**0.367**
visit 2	**1.23 ± 0.722**	**1.25 ± 0.531**	**0.857**
visit 3	**0.42 ± 0.532**	**0.65 ±0.503**	**0.037***
visit4	**0.15 ± 0.363**	**0.43 ± 0.479**	**0.001*****
Wilcoxon Signed Rank test pvalue	**P< 0.001*****	**P< 0.001*****	

*significant at P≤0.05,** highly significant at P≤0.01,*** very high significant at P≤0.001

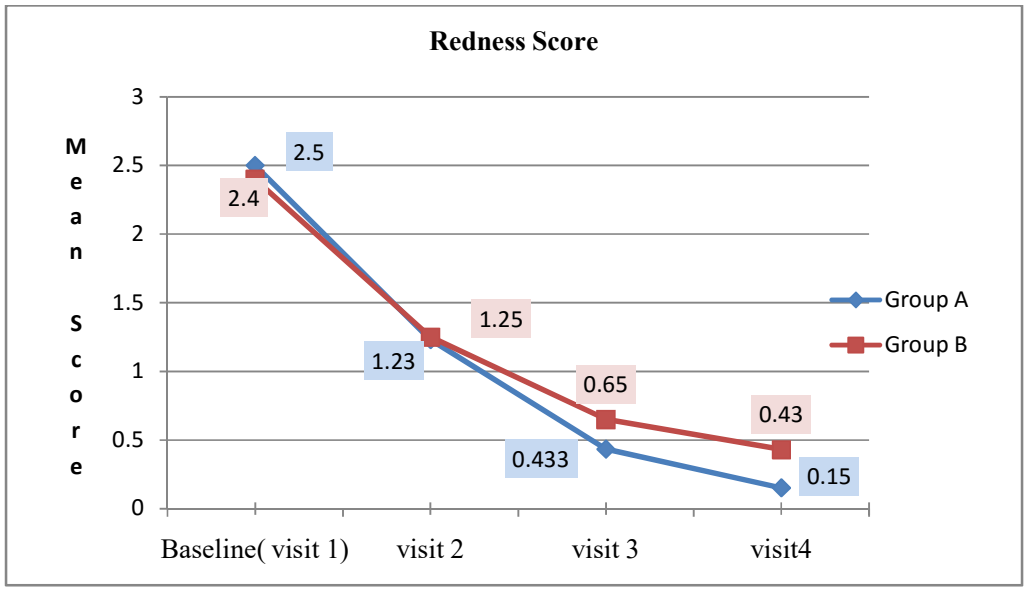


Fig.5.8Redness Score

Visit 1-Baseline, Visit 2- 2nd week, Visit 3-3rd week,Visit4-4th week.

Table 5.7 shows mean redness score at visit-1, visit-2,visit 3,visit 4. There is no statistically significant difference between the groups at visit 1(baseline) [p value>0.05]. Comparison within the

Group is done by Wilcoxon Signed Rank text and between the groups done by mann whitney U test. There is significant difference in reduction of redness scores between the groups during 3rd visit and 4th visit.[P value< 0.05].Both the treatment is effective in reducing redness score from baseline score [P value<0.001,very highly significant.].

Fig.5.8:a graphical representation showing mean redness score at visit 1,visit 2,visit 3,visit 4. There is decrease in mean redness score from visit 1 to visit 4 .In group A, the mean redness score reduced from 2.51 to 0.15.In group B, the mean redness score reduced from 2.4 to 0.43. In both group the reduction in redness score from visit 1 to visit 4 is statistically significant (by wilcoxon test).When we compare the reduction in redness score between groups. There is a statistically significant difference in the reduction of redness score in group A compared to group B during visit 3 and visit 4.

Table 5.8 : Mean reduction in redness score in 2nd week and 4th week

	Mean change at 2nd week			**Mean change at 4th week**		
	group A	**group B**	**P value**	**group A**	**group B**	**P value**
Redness Score	1.26	1.15	0.350	2.36	1.96	0.002

*significant at P≤0.05,** highly significant at P≤0.01,*** very high significant at P≤0.001

Table 5.8 shows comparison, mean change in redness score during 2nd week and 4th week between the groups. There is a significant difference between the groups during 4th week.

[P value<0.01].Reduction is more in group A compared to group B which is statistically significant during 4th week.

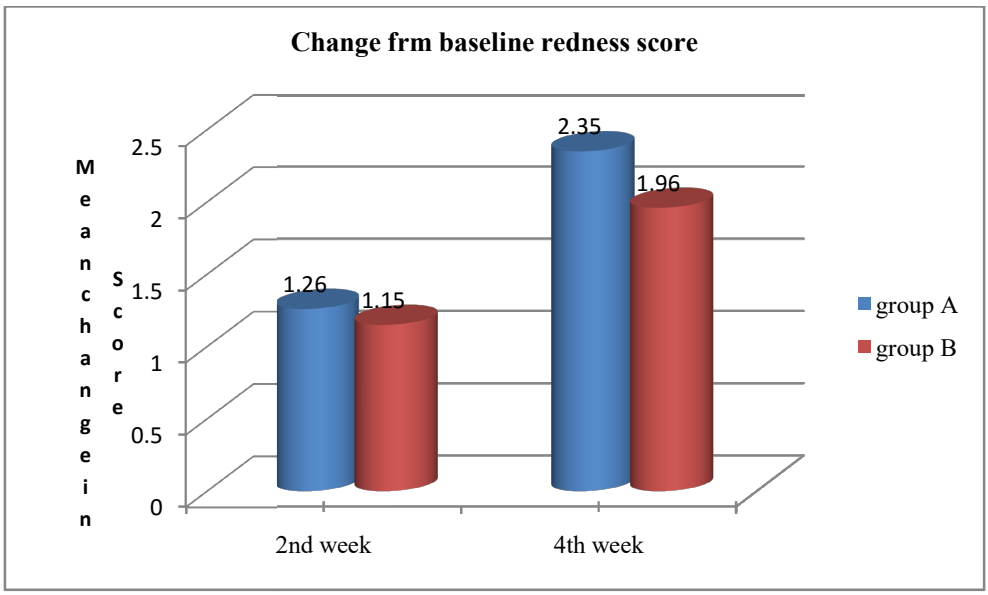


Fig.5.9:Change in rednessscore at 2nd week and 4thweek

Fig.5.9 shows graphical representation showing mean change in redness score from baseline during 2nd week and 4th week.

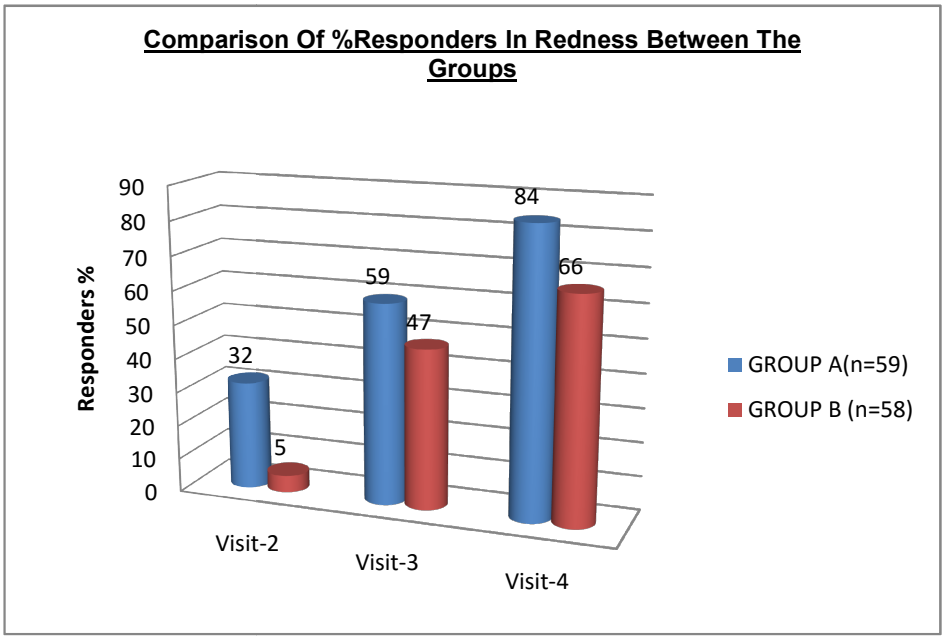


Fig.5.10%Responders in redness scores

Fig:5.10shows graphical representation of%Responders to treatment for redness.

The patient whose score is 0 is considered as responders. In group A 32% patients redness score become zero by 2nd week, 59% attained zero by 3rd week and 84% cured at 4th week. In group B it was about 5%, 47% and 66% during 2nd week, 3rd week and 4th week respectively.

Table5.9 :Chemosis Score

Chemosis	Group A	GroupB	MannWhitneyUtest
visits	Mean Score± SD	MeanScore±SD	P value
Basline	0.85±0.685	0.70±0.618	0.238
visit 2	0.24± 0,426	0.30± 0.462	0.411
visit 3	0.1± 0.302	0.12± 0.342	0.571
visit 4	0.00± 0.000	0.03± 0.181	0.156
Wilcoxon signed rank test	P< 0.001***	P<0.001***	

*significant at P≤0.05,** highly significant at P≤0.01,*** very high significant at P≤0.001

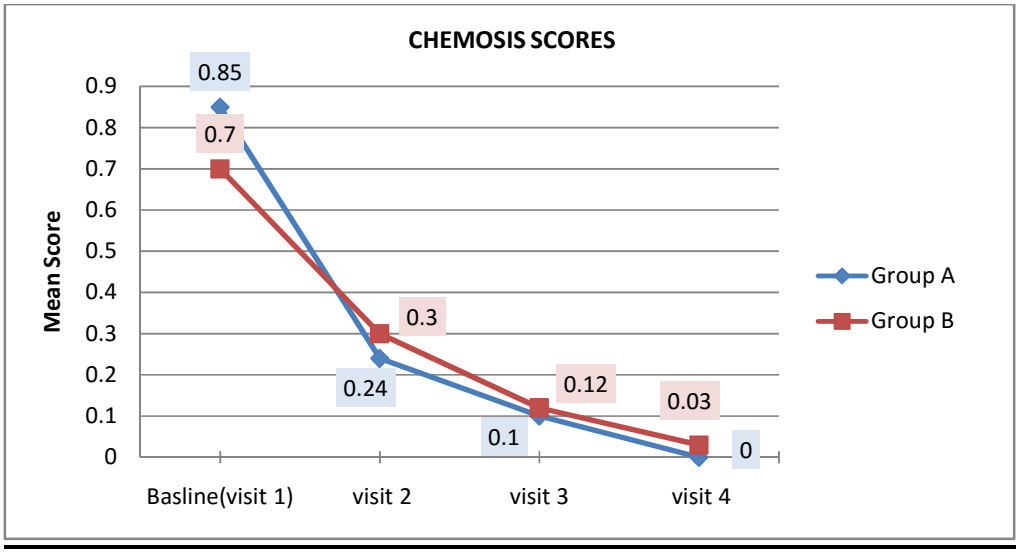


Fig.5.11Chemosis Scores

Visit 1-Baseline ,Visit 2- 2nd week, Visit 3-3rd week,Visit4-4th week

Fig:5.11 shows a graphical representation of mean scores of chemosis at each visit. Table 5.9 shows mean scores with standard deviation of chemosis at each visit. The mean scores reduce from 0.85 at baseline visit to 0.00 during 4th visit in group A and in group B the mean score reduce from0.7 to0.03 at visit 4.

The reduction of chemosis in both group A and group B is statistically significantP value<0.001 by Wilcoxon signed rank test.

When the group A is compared with group B there is no significant difference statistically in reduction in chemosis score at visit 2(2nd weeek) ,visit 3(3rdth week) and visit 4(4th week).[P value > 0.05].

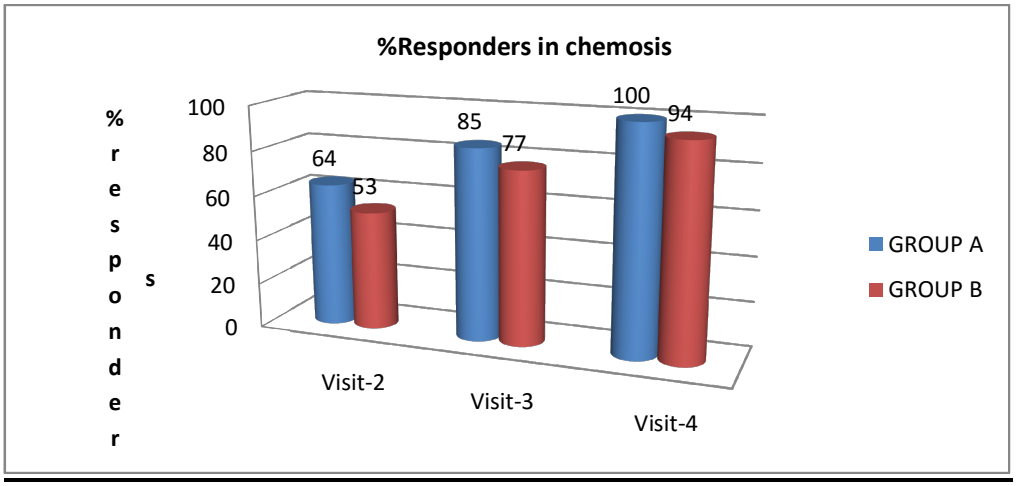


Fig.5.12: **%Responders in chemosis scores**

Fig 5.12 shows a graphical representation of % responders in group A and group B for chemosis score.

The patients whose scores are 0 at visit 2, visit 3,visit 4 are considered as responders. During 2nd week about 64 % patients in group A achieved score0.100% patients in group A attained score 0 at 4th week . In group B about 53%, 77% and 94% become responders at week 2,week 3 and week 4 respectively.

Table5.10: Lid Edema Scores

Lid Edema	Group A	Group B	Mann Whitney U test
	Mean Score± SD	Mean Score± SD	P VALUE
Baseline (visit 1)	0.69 ± 0.65	0.61 ± 0.62	0.603
visit 2	0.25 ±0.439	0.28±0.459	0.681
visit 3	0.1 ± 0.305	0.12 ± 0.329	0.77
visit 4	0.02 ± 0.13	0.08 ± 0.283	0.095
Wilcoxon Test	P < 0.001	P<0.001	

*significant at P≤0.05,** highly significant at P≤0.01,*** very high significant at P≤0.001

Visit 1-Baseline ,Visit 2- 2nd week, Visit 3-3rd week,Visit4 4th week

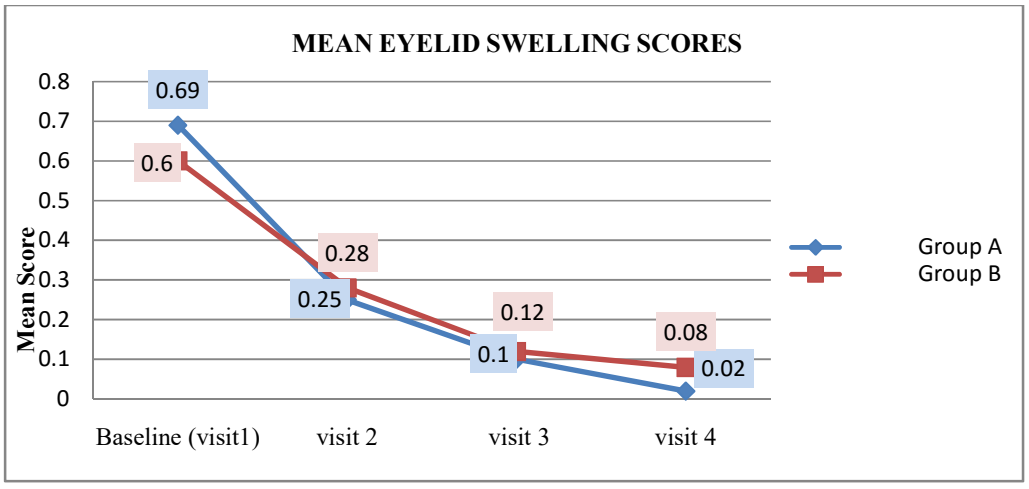


Fig.5.13Lid Edema Scores

Fig.5.13 shows a graphical representation of mean scores of lid edema during each visit.

Table 5.10 shows mean lid edema scores with standard deviation .There is reduction in mean lid edema scores from visit 1 at visit 2,visit3, visit 4.Both in group A and Group B the treatments are effective in reducing eyelid swelling score and is statistically significant.(Wilcoxon signed rank test P<0.001) in group A and group B respectively)

When we compare the mean lid edema scores between group A and group B There is no statistically significant difference between the treatment in groups by Mann Whitney U Test.(the p value>0.05 during all visits.)

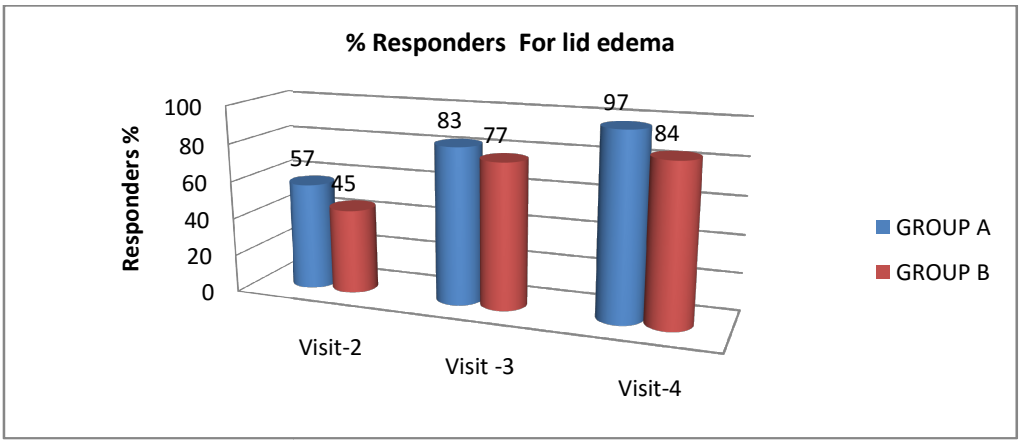


Fig5.14 %Responders in Lid Edema Scores

Fig.5.14 a graphical representation of % responders in group A and group B for lid edema scores. During visit 2,visit 3, visit 4 the patient whose score is 0 are taken as responders.In group A there is 57%, 83%,and 97% responders during 2nd week ,3rd week and 4th week respectively. In group B there is 45%, 77% and 84% responders during 2nd week, 3rd week and 4th week respectively

Table 5.11 Tearing Scores

	Group A	Group B	Mann Whitney U Test
Tearing	Mean Score±SD	Mean Score+SD	P value
visit 1(Baseline)	1.33 ±0.617	1.34±0.515	0.769
visit 2	0.29±0.457	0.31±0.467	0.991
visit 3	0.12±0.305	0.05±0.223	0.188
visit 4	0.02±130	0.03±0.184	0.56
Wilcoxon signed rank test	P < 0.001*	P<0.001*	

*significant at P≤0.05,** highly significant at P≤0.01,*** very high significant at P≤0.001

Visit 1-Baseline ,Visit 2- 2nd week, Visit 3-3rd week, Visit4-4th week

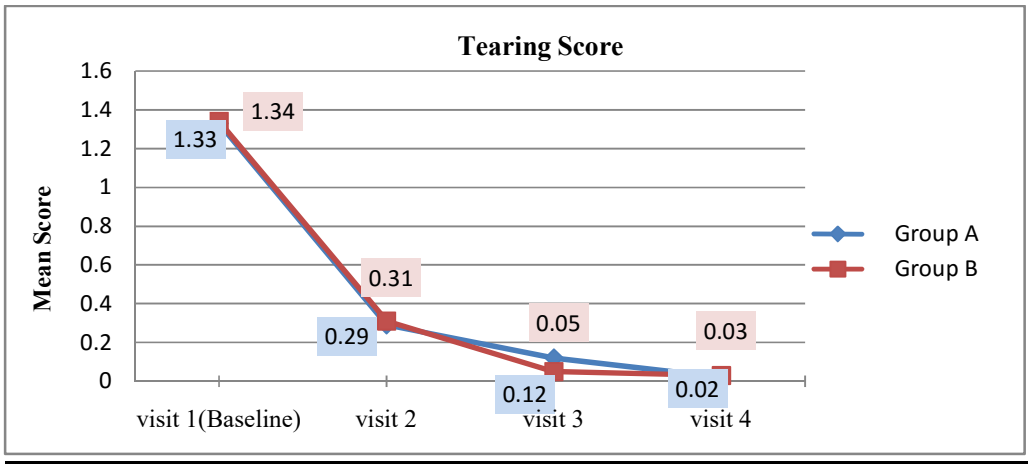


Fig.5.15Tearing Scores

Table 5.11 shows mean tearing scores with standard deviation during each visit is given in the table .There is a reduction in mean tearing scores from visit 1 at visit 2, visit 3,visit 4.

Both in group A and Group B the treatments are effective in reducing symptom tearing which is statistically highly significant. (Wilcoxon signed rank test $p< 0.001$ in both group A and group B).When we compare mean tearing scores between group A and group B There is no statistical significant difference in tearing score between the groups by Mann Whitney U Test.(the p value>0.05 during all visits).

Fig.5.15 shows a graphical representation of mean tearing scores during each visit.

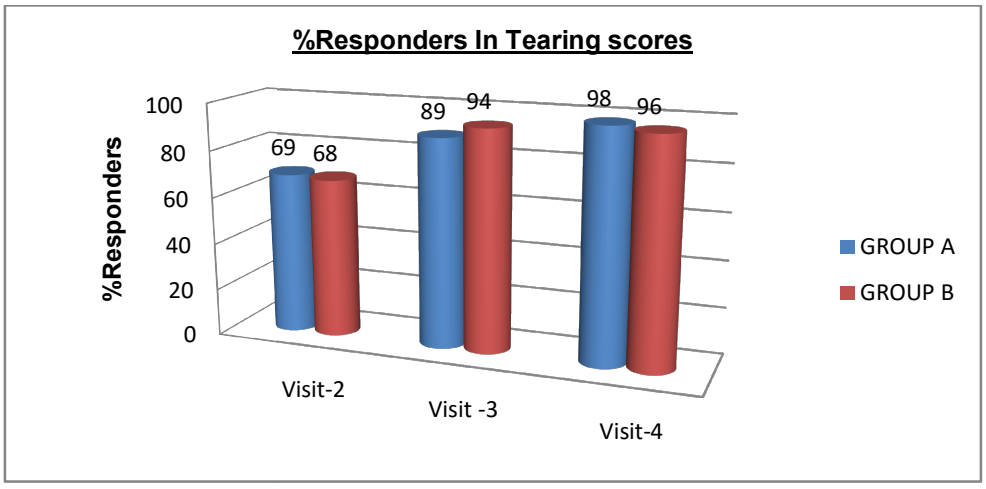


Fig.5.16 %Responders in tearing scores

Fig.5.16 a graphical representation of % responders in group A and group B for symptom tearing. During visit 2, visit 3,visit 4 the patient whose score is 0 are taken as responders. In group A there is 69%,89% and 98% responders for symptom tearing during 2nd week ,3rd week and 4th week respectively. In group B there is responders for symptom tearing 68%, 94% and 98%during 2nd week, 3rd week and 4th week respectively.

Table 5.12 Discomfort Scores

Discomfort	Group A	Group B	Mann Whitney U test
	Mean Score ± SD	Mean Score ± SD	Pvalue
Visit 1(Baseline)	1.67 ± 0.876	1.60±0.527	0.886
visit 2	0.62± 0.738	0.65±0.633	0.574
visit 3	0.283±0.454	0.30±0.497	0.954
visit 4	0.07±0.252	0.08±0.278	0.780
Wilcoxon signed rank test	P<0.001***	P<0.001***	

*significant at P≤0.05,** highly significant at P≤0.01,*** very high significant at P≤0.001

Visit 1-Baseline , Visit 2- 2nd week, Visit 3-3rd week, Visit4 -4th week

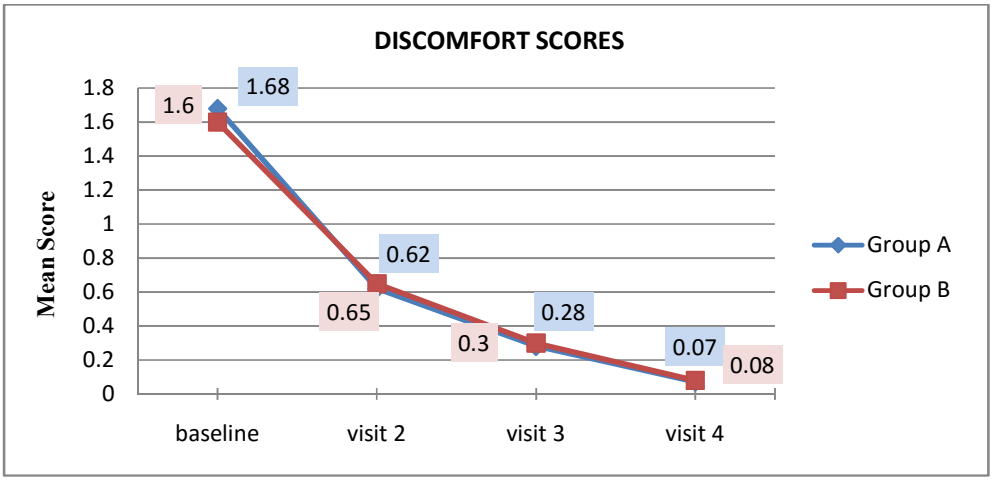


Fig.5.17 Discomfort Scores

Table5.12 shows mean discomfort scores with standard deviation during each visits.

There is a reduction in mean discomfort scores from visit 1 at visit 2, visit 3,visit 4.

In group A and Group B the treatments are effective in reducing discomfort scores is statistically significant.(Wilcoxon signed rank test P<0.001) in both group A and group B

When we compare the reduction in discomfort scores between group A and group B during each visit, there is no statistically significant difference in reduction of discomfort score between the groups [using Mann Whitney U Test, p value > 0.05 during visit 2, visit 3 and visit 4].

Fig.5.17 shows a graphical representation of mean discomfort scores during each visit.

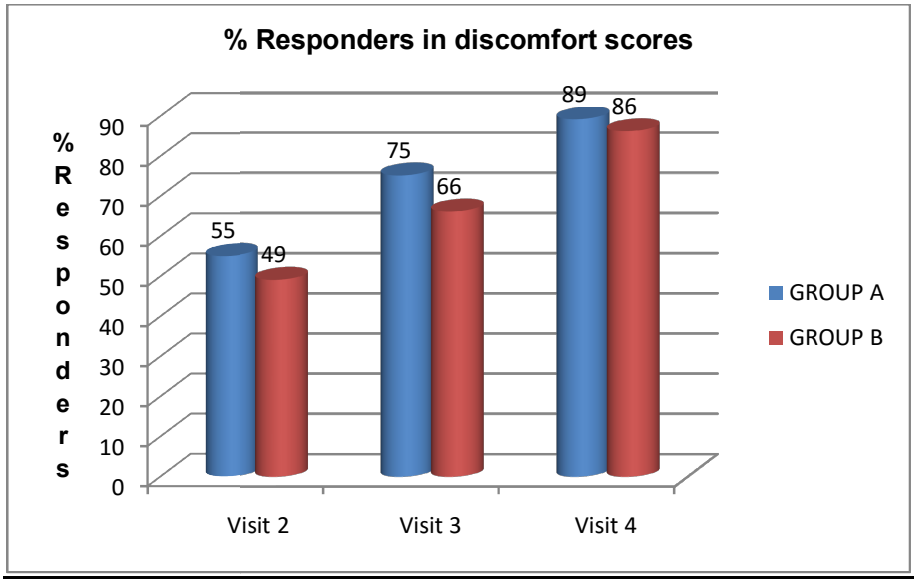


Fig.5.18 %Responders in discomfort scores

Fig.5.18 shows a graphical representation of % responders in group A and group B for discomfort symptom .During visit 2,visit 3,visit 4 the patient

whose score is 0 are taken as responders. In group A there is 55%, 75%and89% responders for symptom discomfort during 2nd week, 3rd week and 4th week respectively. In group B there is 49%, 66% and 86% responders for symptom discomfort during 2nd week, 3rd week and 4th week respectively

Table 5.13: Photophobia Scores

Photophobia	Mean Score±SD	Mean Score± SD.	Mann Whitney U testP value
visit 1(Baseline)	0.46 ±0.502	0.32±0.467	0.135
visit 2	0.08±0.183	0.06 ± 0.256	0.834
visit 3	0.00+ 0.000	0.02 ±0.131	0.317
visit 4	0.00±0.000	0.00± 0.000	1.000
Wilcoxon Rank Sum Test	P< 0.0001*	P < 0.0001*	

*significant at P≤0.05,** highly significant at P≤0.01,*** very high significant at P≤0.001

Visit 1-Baseline, Visit 2- 2nd week, Visit 3-3rd week, Visit4 -4th week.

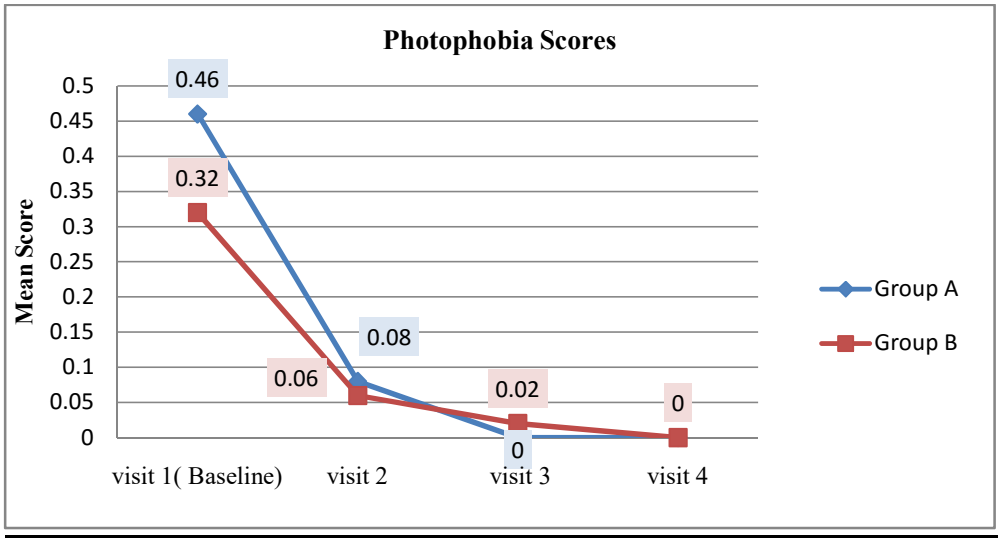


Fig.5.19 Photophobia Scores

Table 5.13 shows mean photophobia scores with standard deviation during each visitFig 19 shows a graphical representation of mean photophobia scores during each visit.There is a reduction in mean photophobia scores from visit 1at visit 2,visit 3,visit 4.Both in group A and group B, the reduction of photophobia score is statistically significant.(P< 0.001) . So both treatments are effective in reducing photophobia.

When we compare the reduction in photophobia scores between group A and group B during each visit, there is no statistically significant difference between the groups in reduction of discomfort score [p value > 0.05 during visit 2, visit 3, visit 4.]

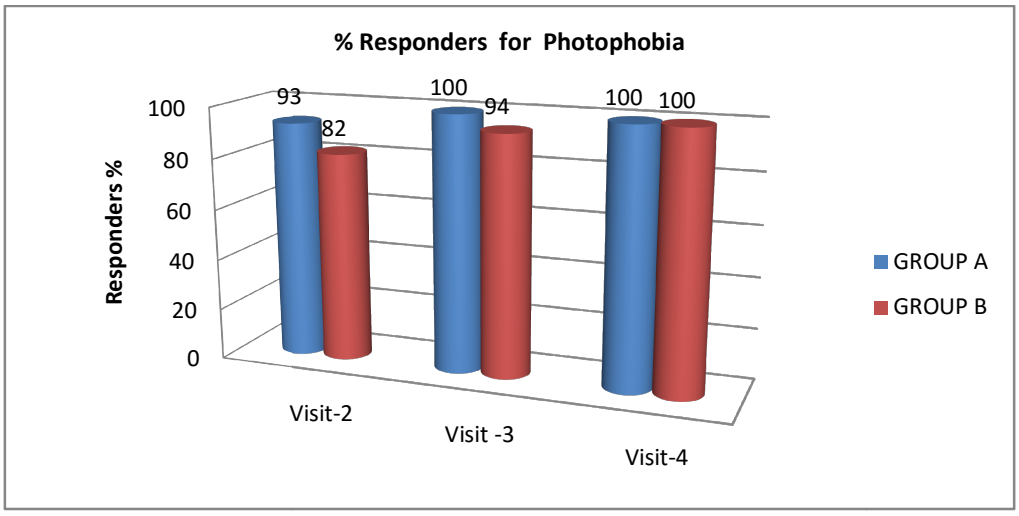


Fig.5.20%Responders in Photophobia Scores

Fig.5.20 shows a graphical representation of % responders in group A and group B for symptom photophobia .During visit 2,visit 3,visit 4 the patient whose score is 0 are taken as responders.In group A there is 93%responders during 2nd week, and 100% responders during 3rd week for symptom photophobia.

In group B there is 82% responders during 2nd week, 94% responders during 3rd week and 100% responders during 4th week for symptom photophobia.

Table 5.14: Foreign Body Sensation Scores

Foreign Body	Group A	Group B	Mann Whitney U test
	Mean Score± SD	Mean Score ±SD	P value
Visit 1(Baseline)	2.28 ± 0.457	2.12 ± 0.564	0.079
Visit 2	0.52 ± 0.598	0.40 ± 0.459	0.262
Visit 3	0.07 ±0.254	0.02 ±0.131	0.730
Visit 4	0.00±0.000	0.03±0.033	0.156
Wilcoxon signed rank test	P<0.001***	P<0.001***	

*significant at P≤0.05, ** highly significant at P≤0.01,*** very high significant at P≤0.001

Visit 1-Baseline, Visit 2- 2nd week, Visit 3-3rd week, Visit4 -4th week

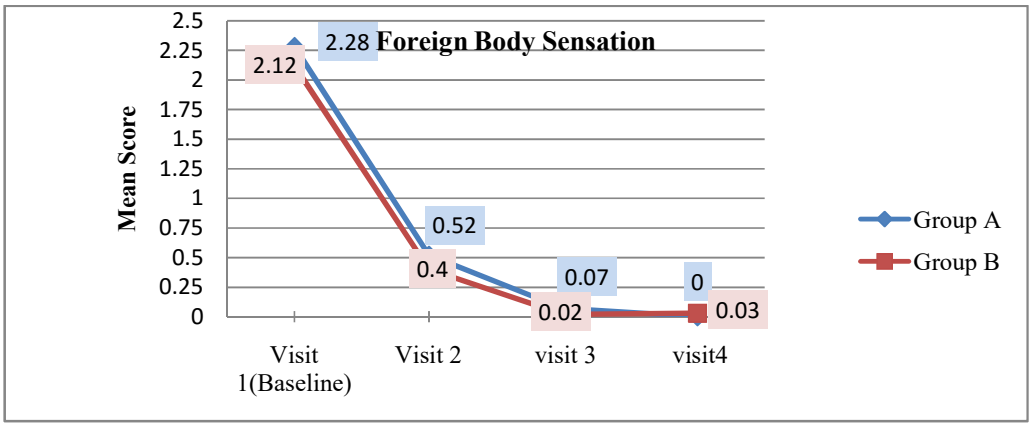


Fig.5.21Foreign Body Sensation Scores

Table 5.14 shows mean foreign body sensation scores with standard deviation during each visit

Fig.5.21 shows a graphical representation of mean foreign body sensation scores during each visit. There is a reduction in mean foreign body sensation scores from visit 1at visit 2, visit 3, visit 4.Both in group A and group B, the reduction of foreign body sensation score is statistically significant.(P< 0.001). So both treatments are effective in reducing foreign body sensation.

When we compare the reduction in foreign body sensation between group A and group B during each visit, there is no statistically significant difference between the groups in reduction of foreign body sensation [p value > 0.05 during visit 2, visit 3, visit 4.]

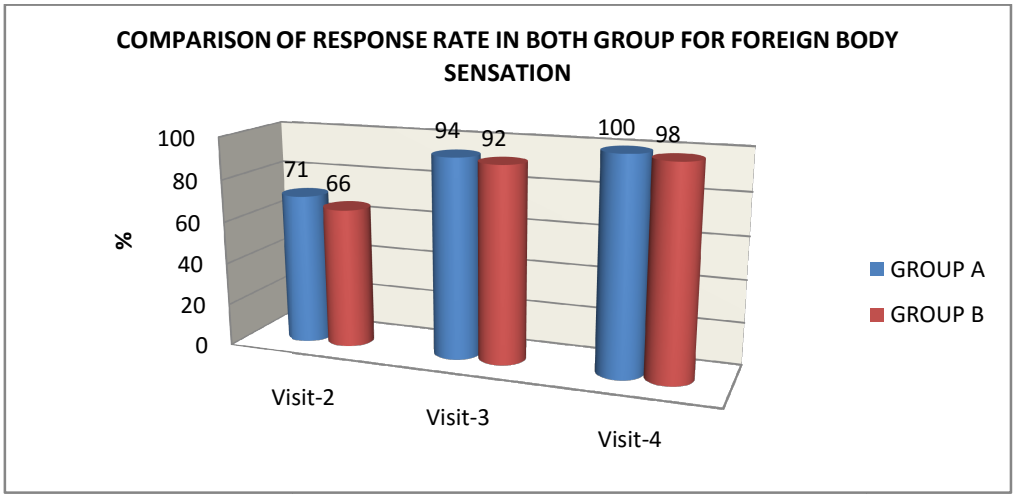


Fig.5.22%Responders in Foreign Body Sensation Scores

Fig.5.22 shows a graphical representation of % responders in group A and group B for symptom for foreign body sensation .During visit 2,visit 3,visit 4 the patient whose score is 0 are taken as responders.

In group A there is 71% responders during 2nd week,94 % responders during 3rd week and 100% responders for symptom foreign body sensation.

In group B there is 66 % responders during 2nd week, 92% responders during 3rd week and 98% responders during 4th week for symptom foreign body sensation.

Table 5.15: Stinging Scores

Stinging	Mean Score± SD	Mean Score± SD	Mann Whitney U test (Pvalue)
Visit 1(Baseline)	2.27 ±0.485	2.1 ±0.667	0.358
Visit 2	0.15 ±0.363	0.217 ±0.627	0.451
Visit 3	0.07 ±0.254	0.133±0.438	0.225
Visit 4	0.02 ±0.13	0.05±0.329	0.172
Wilcoxon signed rank test	P<0.001*	P<0.001*	

*significant at P≤0.05,** highly significant at P≤0.01,*** very high significant at P≤0.001

Visit 1-Baseline, Visit 2- 2nd week, Visit 3-3rd week, Visit4 -4th week.

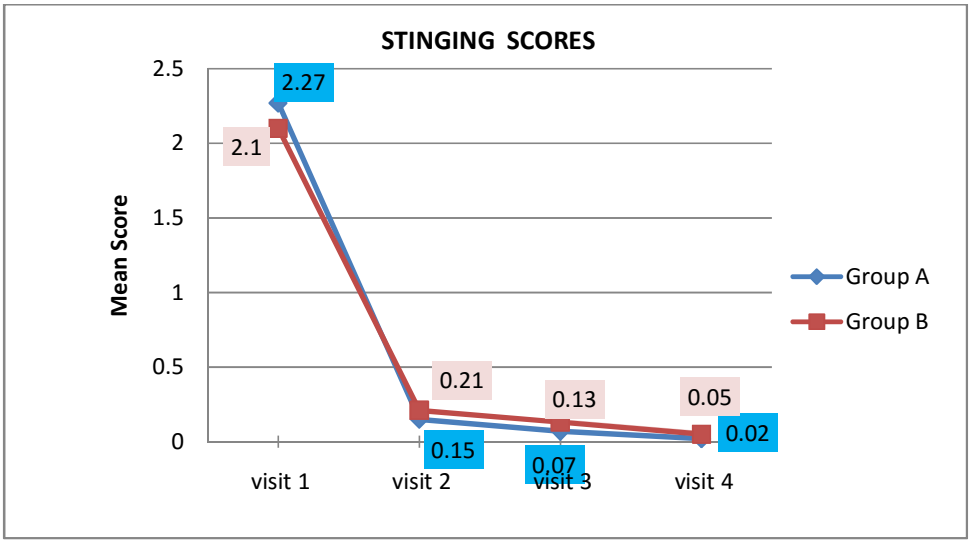


Fig.5.23: Stinging Scores

Table 5.15 shows mean stinging scores with standard deviation during each visitFig.5.23 shows a graphical representation of mean stinging scores during each visit. There is a reduction in mean stinging scores from visit 1at visit 2, visit 3,visit 4.Both in group A and group B, the reduction of stinging

score is statistically significant.(P< 0.001) . So both treatments are effective in reducing symptom stinging. When we compare the reduction in stinging between group A and group B during each visit, there is no statistically significant difference between the groups in reduction of stinging [p value > 0.05 during visit 2, visit 3.

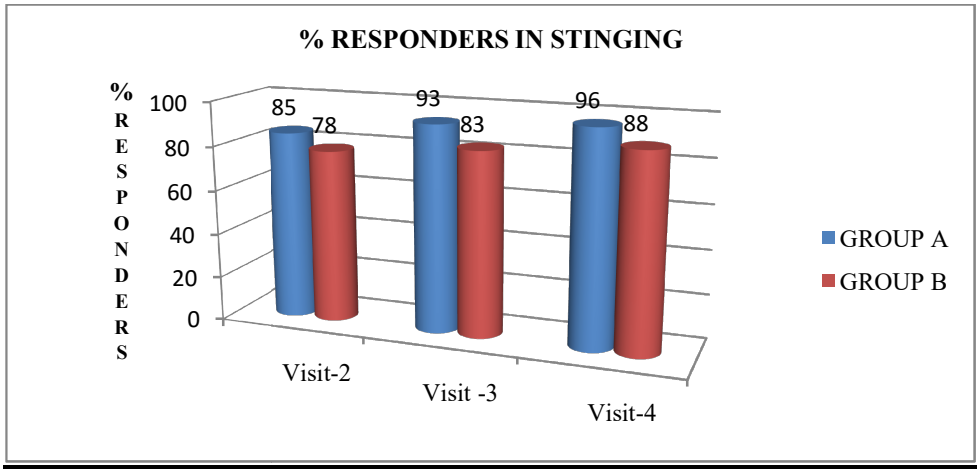


Fig.5.24:%Responders in Stinging Score

Fig.5.24shows a graphical representation of % responders in group A and group B for symptom for stinging sensation .During visit 2,visit 3,visit 4 the patient whose score is 0 are taken as responders.

In group A there is 85%responders during 2nd week, 93% responders during 3rd week and 96% responders for symptom stinging sensation.

In group B there is 73% responders during 2nd week, 83% responders during 3rd week and 88% responders during 4th week for symptom stinging sensation.

Table 5.16:Mean Change in Signs and Symptoms at 2nd week and 4th week.

	Mean change from baseline in 2 nd week			Mean change from baseline in 4th week		Mannwhitney U test
	Group A	Group B	P value	Group A	Group B	P value
Redness	1.26	1.15	0.350	2.36	1.96	0.002**
Itching	1.58	1.40	0.248	2.55	2.22	0.006**
Chemosis	0.62	0.4	0.06	0.85	0.67	0.152
EyeLid Edema	0.43	0.33	0.318	0.67	0.53	0.262
watering	1.01	1.033	0.668	1.28	1.3	0.889
photophobia	0.37	0.23	0.113	0.45	0.32	0.135
discomfort	1.05	0.95	0.291	1.6	1.51	0.790
Foreignbody Sensation	1.75	1.72	0.683	2.28	2.08	0.087
Stinging	2.05	1.87	0.058	2.18	2.02	0.138

*significant at P≤0.05,** highly significant at P≤0.01,*** very high significant at P≤0.001

Table 5.16 show change from baseline score during visit 2 (2nd week) and visit 4(4th week)

Table 5.17 : Adverse Events

Groups	Adverse events		Total	Chi square test
	Present	Absent		
Group A	5	54	59	X^2 =1.905
Group B	9	49	58	P=0.138

Table 5.17 show the adverse events in group A and Group B. In group A, 2 patients had sinusitis and 3 patients had fever. In group B, 5 patients had sinusitis and 4 patients had fever. In both groups there is no treatment related adverse events. There is no significant difference between the group A and group B statistically on adverse effect occurrence [P value>0.05].

Table 5.18:Safety Parameters Observed

Parameters Observed	Group A	Group B
IOP Changes	Nil	Nil
Visual Acuity Changes	Nil	Nil
Fundoscopy changes	Nil	Nil
Stinging	Nil	Nil
Blurring of Vision	Nil	Nil
Headache	Nil	Nil

Table 5.18 shows the safety parameters measured during all visits.

Discussion

DISCUSSION

To choose the best drug in allergic conjunctivitis with understanding of underlying mechanisms implicated in triggering the allergy is very important. Olopatadine with a wide action spectrum has shown to be very effective in allergic conjunctivitis(103). In this study the patients with allergic conjunctivitis in ophthalmic OPD were randomized into group A and group B. In group A patients were given olopatadine0.2% once daily for 4 weeks and in group B sodium cromoglycate 2% four times daily. The efficacy and tolerability of the drug olopatadine were compared to that of drug sodium cromoglycate. The results of the study are discussed here.

From 120 patients who were randomized to group A and group B 117 patients completed the study. Three patients were lost in follow up.59 patients in group A and 58 patients in group B completed the study. In group A there were 36 patients in age group less than 15 years and 23 patients of age more than 15 years. In goup B there were 35 patients of age less than 15 years and 23 patients of age more than 15years. There is no difference between groups in age distribution during baseline visit.

The mean age for group A is 16.03 years and in group B I s16.43 years. There is no significant difference in mean ages between the groups. There is 63% males in group A and 64% males in group B . The females accounts for 37% and 36% in group A and group B respectively. Statistically there is no difference in sex distribution between the group.

In this study the mean itching score in group A and group B during baseline visit are 2.6 and 2.45 respectively. The itching scores in both groups are comparable during baseline visit [p value>0.05]. There is no significant difference in reduction of itching between the groups (3)during 2^{nd} week .During 4^{th} week(3) the reduction of itching scores in group A was more compared to group B which is statistically significant. When mean reduction from baseline in itching score was compared between group A and group B there is significant reduction in group A during 4^{th} week. [P value<0.05] .The percentage of responders are more in group A compared to group B during all visits. Both treatment are effective in treating itching [p value<0.01, p value<0.01].

The mean redness score during baseline is 2.5 in group A and 2.4 in group B. There is no significant difference between the groups in mean baseline score during visit1 [P value > 0.05].The redness score reduced from 2.5 to0.15 during 4^{th} week in group A[pvalue<0.001]. In group B the redness score reduced from 2.4 to 0.433 during 4^{th} week[pvalue<0.001].Both treatment A and treatment B is effective in reducing redness When we compare the reduction in redness score, it is more in group A during 2^{nd} week but the difference is not significant[P value>0.05]. During 4^{th} week the reduction in redness score in group A is significant compared to group B*[P value <0.01]. When we compare the change from baseline redness score during 2^{nd} week and 4^{th} week there is significant difference during 4^{th} week [P value >0.05] similar to other studies.(3)The percentage responders in redness are higher in group A

during 2nd week,3rd week, and 4th week compared to group B similar to other studies.(3)

The mean chemosis score in group A during first visit is 0.85 and in group B is 0.7. In group A 0.85 reduced to 0.00 during visit 4 and in group B 0.7 reduced to 0.03 during visit 4There is no significant difference between the groups during visit-1[p value>0.05].Both in group A and Group B, treatments are effective in reducing chemosis score from baseline score[P value <0.001].The reduction in mean chemosis scores are more in group A compared to group B .This difference is not statistically significant. The percentage responders in chemosis score are higher in group A during 2nd week, 3rd week, and 4th week compared to group B.

The mean lid edema scores during baseline is 0.68 in group A and 0.61in group B. There is no difference in mean score during (baseline) visit1 [P value > 0.05].The lid edema scores reduced from 0.68to0.02 and 0.61 to0.08 during visit 4 in group A and group B respectively. Both treatment A and treatment B is effective in reducing lid edema scores [P value<0.001,Pvalue<0.001]. There is no significant difference in reduction of lid edema scores between group A and group B [P value>0.05]. The percentage responders in lid edema scores are higher in group A during 2nd week, 3rd week, and 4th week compared to group B

The mean tearing scores during baseline is 1.33 in group A and 1.34in group B. There is no difference in mean score during (baseline) visit 1[P value

> 0.05].The tearing scores reduced from 1.33 to0.02 in group A and from 1.34 to0.03 in group B during visit 4. Both treatment A and treatment B are effective in reducing tearing scores [P value<0.001, P value<0.001].There is no significant difference in reduction of tearing scores between group A and group B [P value>0.05]. The percentage responders tearing scores are higher in group A during 2^{nd} and 4^{th} week compared to group B.

The mean discomfort score in group A during visit1 is 1.68 and in group B is1.60.There is no statistical difference between the groups during visit- 1[p value>0.05].Both in group A and Group B, treatments are effective in reducing discomfort score from baseline score [P value <0.001].In group A 1.68 is reduced to 007.during visit 4 and in group B 1.60 is reduced to 0.08 during visit 4. The difference in reduction of discomfort scores between group A and group B are not statistically significant [P value>0.05]. The percentage responders in discomfort scores are higher in group A during 2^{nd} week, 3^{rd} week, and 4^{th} week compared to group B.

The mean photophobia scores in group A during visit-1 is 0.46 and in group B is 0.32.There is no statistical difference between the groups during visit- 1[p value>0.05].Both in group A and Group B, treatments are effective in reducing photophobia symptom. [P value <0.001]. The difference in reduction of photophobia score between group A and group B are not statistically significant. [p value>0.05]. The percentage responders in photophobia scores are higher in group A during 2^{nd} week,3^{rd} week, and 4^{th} week compared to group B.

The mean foreign body sensation scores in group A during visit-1 is 2.28 and in group B is 2.12.There is no significant difference between the groups during visit- 1[p value>0.05].Both in group A and Group B, treatments are effective in reducing foreign body sensation [Pvalue <0.001].In group A 2.28 reduced to 0.00 during visit 4 and in group B 2.12 reduced to 0.03 during visit 4.The reduction in mean foreign body sensation scores are more in group A compared to group B .this difference in reduction is not significant. The percentage responders in foreign body sensation scores are higher in group A during 2^{nd} week, 3^{rd} week and 4^{th} week compared to groupB.

The mean stinging scores during baseline is 2.27 in group A and 2.12 in group B. There is no difference in mean score during (baseline) visit1 [P value > 0.05].The stinging scores reduced from 2.27 to0.02 in group A and from 2.1 to 0.05 in group B during visit 4..The mean stinging scores reduced in both groups. Both treatment A and treatment B is effective in reducing stinging scores [P value<0.001, P value<0.001]. But there is no difference in reduction of stinging scores between the groups [Pvalue>0.05].The percentage responders stinging scores are higher in group A during 2^{nd} , 3^{rd} and 4^{th} week compared to group B.

The adverse events occurred in 14 participants out of 117 participants,5 in group A and 9 in group B. There is no significant difference between the groups[P value >0.05].The adverse events noted were fever and rhinitis. There is no treatment related adverse events in both groups during 2^{nd} visit, 3^{rd} visit,

4th visit and 5th visit (6th week).There is no serious adverse events observed during the study.

During follow up visit at 6th week safety parameters like IOP changes, visual acuity changes, fundoscopic changes were examined. Patients in both groups give no history of stinging, blurring of vision, headache during the visit. No changes in safety parameters are noted in both groups.

The compliance of patients are more in group A compared to group B on the basis of empty bottles count , patient's diary record and interview with patient during visit2,visit 3 and visit 4.

Summary

SUMMARY

This study is an open labeled randomized comparative study of olopatadine 0.2% once daily dose with 2% sodium cromoglycate four times daily.

After following inclusion and exclusion criteria 120 patients were randomized into 2 groups group A and group B .Group A received olopatadine 0.2% once daily dose and group B received 2% sodium cromoglycate four times daily for four weeks. During the study 3 patients were lost to follow up.117 patients completed the study.

This study show that both olopatadine 0.2% single dose and 2% sodium cromoglycate four times daily are equally effective in providing relief from signs and symptoms of allergic conjunctivitis during 2^{nd} week. Compared to 2% sodium cromoglycate, 0.2% olopatadine single dose produce better reduction of itching and redness of eye during 4^{th} week. Number of responders were more in olopatadine group .There were no treatment related adverse effects in both groups.

Both drugs were equally safe and tolerable. Patient compliance was more with 0.2% olopatadine single dose when compared to 2% sodium cromoglycate four times daily

Conclusion

CONCLUSION

From this study we can conclude that

Both olopatadine 0.2% 1 drop once daily and sodium cromoglycate 2% 1 drop four times daily are effective in reducing symptoms and signs of allergic conjunctivitis during 2^{nd} and 4^{th} week.

Olopatadine 0.2% once daily is found to be more effective than sodium cromoglycate 2% four times daily in reducing redness and itching scores during 4^{th} week.

Treatment with Olopatadine 0.2% once daily has more patient compliance than sodium cromoglycate2% four times daily.

Both olopatadine 0.2% once daily and sodium cromoglycate 2% four times daily show good patient tolerability and safety profile.

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Annexures

LIST OF ABBREVIATIONS

AC	–	Allergic Conjunctivitis
AKC	–	Atopic Keratoconjunctivitis
CAC	–	Conjunctival Allergen Challenge
CDC	–	Contact Dermato Conjunctivitis
Cox-1	–	Cyclo-Oxygenase -1
Cox-2	–	Cyclo-Oxygenase-2
DC	–	Dendritic Cells
GPC	–	Giant Papillary Conjunctivitis
h	–	Hour
H_1 H_2 H_3H_4	–	Histamine Receptors(1,2,3,4).
HETE	–	Hydroxyeicosatetraenoic acid
HHT	–	Heptadecatrienoic.
HPETE	–	Hydroperoxyeicosatetraenoic acid
ICAM-1	–	Intercellular adhesion molecule-1
IgE	–	Immunoglobulin E
INS	–	Intra Nasal Steroids
IOP	–	Intraocular Pressure
LE	–	Lotrendol Etabonate
LT	–	Leukotriene
MCP	–	Monocyte chemoattractant protein
MDA	–	Malonyldialdehyde,
MMP	–	Matrix Metalloproteinase

NAC – Nasal Allergy Challenge

NSAID – Non Steroidal Anti-inflammatory Drugs

OPD – Out Patient Department

OTC – Over The Counter

PAC – Perennial Allergic Conjunctivitis

PAF – Plateletactivating

PG – Prostaglandins

SRS-A – Slow-reacting substance of anaphylaxis

SAC – Seasonal Allergic Conjunctivitis

TH-2 – T helper cels 2

VKC – Vernal kerato Conjunctivitis

INSTITUTIONAL ETHICS COMMITTEE

CHENGALPATTU MEDICAL COLLEGE , CHENGALPATTU

APPROVAL OF ETHICAL COMMITTEE

To

Dr. Sanu Sain,
1st Year PG student (Pharmacologoy),
Chengalpattu Medical College,
Chengalpattu

Dear Dr.

The Institutional Ethical Committee of Chengalpattu Medical College reviewed and discussed your application to conduct the clinical / dissertation work entitled

A RANDOMISED PROSPECTIVE OPEN LABEL COMPARATIVE STUDY OF OLOPATADINE WITH SODIUM CROMOGLYCATE IN ALLERGIC CONJUNCTIVITIS

ON 19.02.2015

The following documents reviewed

1. Trial protocol, dated _____version no
2. Patient information sheet and informed consent form in English and / or vernacular language.
3. Investigators Brochure, dated _____version
4. Principal Investigators current CV
5. Investigators undertaking

The following members of the Ethics committee were present at the meeting held on

Date 19.02.2015 Time 11.00 am Place Chengalpattu Medical College

Approved _____ Chairman Ethics Committee

_____ Member secretary of Ethics Committee.

19/2/15

Name of each member with designation:-

Clinical Members

1. Dr.K.Srinivasagalu MD.,
   Prof & HOD of Medicine, CHMC

2. Dr.C.Srinivasan MS.,
   Prof & HOD of Surgery, CHMC

Biological Scientist

3. Dr.K.Baskaran MD.,
   Asso Prof of Pharmacology, CHMC

Non Clinical Member

4. Dr.P.Parasakthi MD
   Prof & HOD of Forensic Medicine,CHMC

5. Member from Nongovernmental
   Voluntary Organisation : Mr.P.Durairaj

6. Philosopher : Mr.K.S.Ramprasad

7. Lawyer : Lr. I. M. Karimala Basha

8. Layperson : Mr.Dilli

We approve the clinical trial to be conducted in its presented form

The Institutional Ethics Committee expects to be informed about the progress of the study and any SAE occurring in the course of the study, any changes in protocol and patient information / informed consent and asks to provide copy of final report.

Yours sincerely

19/2/15

Member secretary, Ethics Committee

INFORMED CONSENT FORM

(This is only a guideline –Relevant changes to be made as per the study requirements)

Title of the study: **"A RANDOMIZED PROSPECTIVE OPEN LABEL COMPARATIVE STUDY OF OLAPATADINE WITH SODIUM CROMOGLYCATE IN ALLERGIC CONJUNCTIVITIS"**

Name of the patient :_____

Name of the Investigator : Dr SANU SAIN

Name of the Institution : Chengalpattu Medical College Hospital

Documentation of the informed consent.

I _____have read the information in this form (or it has been read to me).I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in '**"A RANDOMIZED PROSPECTIVE OPEN LABEL COMPARATIVE STUDY OF OLAPATADINE WITH SODIUM CROMOGLYCATE IN ALLERGIC CONJUNCTIVITIS"**

1. I have read and understand this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.
5. I have been informed the investigator of all the treatments I am taking or have taken in the past_____including any native (alternative) treatment.
6. I have been advised about the risks associated with my participation in this study.
7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.
8. I have not participated in any research study within the past_____.
9. I have not donated blood within the past_____- Add if the study involves extensive blood sampling.
10. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.
11. I am also aware that the investigator may treatment my participated in the study at any time for any reason, without my consent.
12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt.Agencies, and IEC. I understand that they are publicly presented.
13. I have understood that my identity will be kept confidential if my data are publicly presented.
14. I have had my questions answered to my satisfaction.
15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the Investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

For adult participants:

Name and signature/thumb impression of the participant (or legal representative if participant incompetent)

Name_____signature_____Date_____

Name and signature of impartial witness (require for illiterate patients)

Address and contact number of the impartial witness:

Name_____signature_____Date_____

Name and signature of the investigator or his representative obtaining consent:

Name_____signature_____Date_____

For children being enrolled in research:

Whether child's assent was asked: Yes/No

(If the answer to be above question is Yes,write the following phrase:

You agree with the manner in which assent was asked for from your child and given by your child. You agree to have your child take part in this study.

(If answer to be above question No, give reason:_____

Although your child did not or could not give his or her assent, you agree to your child's participation in this study.

Name and signature of/thump impression of the participant's parent(s) (or legal representatives)

Name_____signature_____Date_____

Name_____signature_____Date_____

Name and signature of impartial witness (require for parents of participant child illiterate):

Address and contact number of the impartial witness: _____

_____

Name and signature of the investigator or his representative obtaining consent:

Name_____signature_____Date_____

NOTE:-

For observational studies in nature or those in which only patient's tissue, body fluids are collected for any kind of analysis the following elements in the patient information leaflet will need be included – background of the study the purpose for which the sample will be used: confidentially of data are right to refuse to give specimens should be included.

Points 6, 7,8,9,10,11 of consent document may be excluded in such cases.

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு:

செங்கல்பட்டு அரசு பொது மருத்துவமனையில் கண் சிகிச்சை நலப்பிரிவில் ஒவ்வாமை விழி வெண்படல அழற்சி நோய்க்கு வழங்கப்படும் ஒலப்பாட்டிடின் ஹைடிரோ குளோரைடு, சோடியம் குளோரைடு, சோடியம் குரோமோ கிளைக்கேடு ஆகிய மருந்துகளின் பயன்பாடு மற்றும் பாதுகாப்பு குறித்தான ஒப்பீட்டு ஆய்வு.

பெயர் : தேதி :

வயது : ஆராய்ச்சி சேர்க்கை எண்:

பாலினம் :

- ❖ எனக்கு அளிக்கப்பட்ட தகவல் படிவத்தில் உள்ள விஷயங்களைப் படித்தும் கேட்டும் புரிந்து கொண்டேன்.
- ❖ இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் நான் பங்கு பெறுகிறேன்.
- ❖ ஆய்வில் தொடர்ந்து பங்குபெற விருப்பம் இல்லையென்றால் விலகிக் கொள்ளலாம் என்று அறிந்து கொண்டேன்.
- ❖ ஆய்வின் முடிவினை சொந்த அடையாளங்களை வெளியிடாமல் மருத்துவ ஆராய்ச்சிக்காக பயன்படுத்திக் கொள்ள சம்மதிக்கிறேன்.

குழந்தைகளுக்கான ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு:

செங்கல்பட்டு அரசு பொது மருத்துவமனையில் கண் சிகிச்சை நலப்பிரிவில் ஒவ்வாமை விழி வெண்படல அழற்சி நோய்க்கு வழங்கப்படும் ஒலப்பாட்டிடின் ஹைடிரோ குளோரைடு, சோடியம் குளோரைடு, சோடியம் குரோமோ கிளைக்கேடு ஆகிய மருந்துகளின் பயன்பாடு மற்றும் பாதுகாப்பு குறித்தான ஒப்பீட்டு ஆய்வு.

பெயர் : தேதி :

வயது : ஆராய்ச்சி சேர்க்கை எண்:

பாலினம் :

- ❖ எனக்கு அளிக்கப்பட்ட தகவல் படிவத்தில் உள்ள விஷயங்களைப் படித்தும் கேட்டும் புரிந்து கொண்டேன்.
- ❖ இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் நான் பங்கு பெறுகிறேன்.
- ❖ ஆய்வில் தொடர்ந்து பங்குபெற விருப்பம் இல்லையென்றால் விலகிக் கொள்ளலாம் என்று அறிந்து கொண்டேன்.
- ❖ ஆய்வின் முடிவினை சொந்த அடையாளங்களை வெளியிடாமல் மருத்துவ ஆராய்ச்சிக்காக பயன்படுத்திக் கொள்ள சம்மதிக்கிறேன்.
- ❖ நான் என்னுடைய சுயநினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என் குழந்தையை சேர்த்துக் கொள்ள சம்மதிக்கிறேன்.

பெற்றோர் கையொப்பம்

Information to participants

Principal Investigator :- Dr. SANU SAIN,

MD Pharmacology Postgraduate

Chengalpattu medical College

Chengalpattu.

Name of the participant:_____

Title : **"A RANDOMISED PROSPECTIVE OPEN LABEL COMPARATIVE STUDY OF OLAPATADINE WITH SODIUM CROMOGLYCATE IN ALLERGIC CONJUNCTIVITIS"**

This study is conducted in our institution, Chengalpattu medical College, Chengalpattu.

You are invited to take part in this study. The information in this document is meant to help you to decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

You are being asked to participate in this study conducted in the department of ophthalmology and department of pharmacology, Chengalpattu Medical College.

Purpose of research :

To compare efficacy and tolerability of olapatadine 0.2 % ophthalmic solution once daily with sodium cromoglycate 2% ophthalmic solution four times daily in patients with allergic conjunctivitis.

The study is conducted with permission from the Institutional ethical committee.

Study design : Randomized prospective, open labelled comparative study.

STUDY PROCEDURE

The study involves dividing allergic conjunctivitis patients to two groups, after initial baseline assessment, one group will receive olopatadine 0.2% ophthalmic solution once daily for six weeks, other group will receive sodium cromoglycate 2% ophthalmic solution four times daily for six weeks.

Reassessment of patient will be done at 2nd week, 3rd week, 4th week and patients will be followed up to 2weeks after study.

You will be asked to review at regular intervals. At each visit ophthalmologist will examine your eyes.

In addition, if you notice any physical or mental change, you must contact the persons listed at the end of the document.

You may have to come to hospital for examination and investigations apart from your scheduled visits if require

You must not participate if you are pregnant, breast feeding a child or suffering from any serious ocular disease, active ocular infection, dry eyes, underwent an ocular surgery in past three months, allergic to study medications, known allergic to benzalkonium chloride, not willing to discontinue contact lens, taking oral immuno-suppressants, topical steroids, artificial tear drops.

Benefits of the study :

The results of the research may provide benefits to the society in terms of increase in patient's compliance to once daily dosage of olopatadine among allergic conjunctivitis patients compared to four times daily dosage of sodium cromoglycate.

தகவல் படிவம்

செங்கல்பட்டு அரசு பொது மருத்துவமனையில் கண் சிகிச்சைப் பிரிவில் ஒவ்வாதை விழி வெண்படல அழற்சி நோய்க்கு வழங்கப்படும் ஒலப்பாட்டிடின் ஹைட்ரோ குளோரைடு, சோடியம் குரோமோ கிளைக்கேடு ஆகிய மருந்துகளின் பயன்பாடு மற்றும் பாதுகாப்பு குறித்தான ஒப்பீட்டு ஆய்வு மேற்கொள்ளப்படுகிறது.

- இந்த ஆய்வு அனுபவம் வாய்ந்த மருத்துவர்களின் உதவியோடு நடத்தப்படுகிறது.
- இம்மருந்துகள் அனுதினம் பயன்பாட்டில் உள்ள மருந்துகளே இம்மருந்துகளினால் மிகப்பெரிய அளவில் பக்க விளைவுகள் ஏற்பட வாய்ப்பு இல்லை.
- ஆராய்ச்சியின் போது ஒரு பிரிவினருக்கு ஒலப்பாட்டிடின் ஹைடிரோ குளோரைடும், மற்றொரு பிரிவினருக்கு சோடியம் குரோமோ கிளைக்கேடும் வழங்கப்படும். இப்பிரிவில் ஏதேனும் ஒன்றில் ஆராய்ச்சியில் பங்கு பெறுபவர்கள் சேர்க்கப்படுவார்கள்.
- நோயாளிகளுக்கு இம்மருந்துகளின் மூலம் ஏற்படும் முன்னேற்றம் இரண்டு வாரங்களுக்கு ஒருமுறை கண் மருத்துவரால் பரிசோதித்து அறிப்படும்.
- நோயின் தன்மைகளை வெளியிடும் போது தங்களது பெயரையோ அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறேன்.
- இந்த ஆராய்ச்சியில் பங்கேற்பது உங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.
- இந்த சிறப்பு பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

குழந்தைகளுக்கான தகவல் படிவம்

செங்கல்பட்டு அரசு பொது மருத்துவமனையில் கண் சிகிச்சைப் பிரிவில் ஒவ்வாதை விழி வெண்படல அழற்சி நோய்க்கு வழங்கப்படும் ஓலப்பாட்டிடின் ஹைட்ரோ குளோரைடு, சோடியம் குரோமோ கிளைக்கேடு ஆகிய மருந்துகளின் பயன்பாடு மற்றும் பாதுகாப்பு குறித்தான ஒப்பீட்டு ஆய்வு மேற்கொள்ளப்படுகிறது.

- இந்த ஆய்வு அனுபவம் வாய்ந்த மருத்துவர்களின் உதவியோடு நடத்தப்படுகிறது.
- இம்மருந்துகள் அனுதினம் பயன்பாட்டில் உள்ள மருந்துகளே இம்மருந்துகளினால் மிகப்பெரிய அளவில் பக்க விளைவுகள் ஏற்பட வாய்ப்பு இல்லை.
- ஆராய்ச்சியின் போது ஒரு பிரிவினருக்கு ஓலப்பாட்டிடின் ஹைடிரோ குளோரைடும், மற்றொரு பிரிவினருக்கு சோடியம் குரோமோ கிளைக்கேடும் வழங்கப்படும். இப்பிரிவில் ஏதேனும் ஒன்றில் ஆராய்ச்சியில் பங்கு பெறுபவர்கள் சேர்க்கப்படுவார்கள்.
- நோயாளிகளுக்கு இம்மருந்துகளின் மூலம் ஏற்படும் முன்னேற்றம் இரண்டு வாரங்களுக்கு ஒருமுறை கண் மருத்துவரால் பரிசோதித்து அறிப்படும்.
- இந்த சிறப்பு பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.
- இந்த ஆராய்ச்சியில் உங்கள் குழந்தைகளும் பங்கேற்க நாங்கள் விரும்புகிறோம் அதற்கு தங்களின் ஒப்புதலைப் பெற விரும்புகிறோம்.
- நோயின் தன்மைகளை வெளியிடும் போது தங்களது குழந்தையின் பெயரையோ அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறேன்.
- இந்த ஆராய்ச்சியில் உங்கள் குழந்தைகள் பங்கேற்பது உங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் உங்கள் குழந்தைகளை இந்த ஆராய்ச்சியிலிருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

STUDY PROFORMA

DATE : Op no:

NAME :

AGE :

SEX :

ADDRESS :

OCCUPATION :

PHONE NUMBER :

PRESENTING COMPLAINTS :

HISTORY OF PRESENTING COMPLAINTS:

DURATION OF ILLNESS :

TREATMENT HISTORY :

DIAGNOSIS :

RELEAVENT PAST HISTORY: H/O BRONCHIAL ASTHMA : YES / NO

H/O DRUG ALLERGY: YES / NO

FAMILY HISTORY: YES /NO

HISTORY OF USE OF CONTACT LENS

GENERAL EXAMINATION :

VITALS :

PULSE RATE :

BLOOD PRESSURE :

RESPIRATORY RATE :

SYSTEMIC EXAMINATION :

CASE EXAMINATION :

LENS :

Name the medication given for the patient :

Olopatadine 0.2% OD OR Sodium cromoglycate 2% qid

SLIT LAMP EXAMINATION :

Table I

Efficacy Assessment

	Discomfort Score 0-3	**Stinging** Score 0-3	**Photophobia** Score 0-3	**Foreign body** Score 0-3	**Watering** Score 0-3	**Eyelid Swelling** Score0-3	**Chemosis** Score 0-3	**Redness** Score 0-3	**Itching** Score 0-3
Visit 1									
2nd wk									
3rd wk									
4th wk									

Table II

Tolerability Assessment

	VISIT-1 BASELINE	**2ND WEEK**	**3rd WEEK**	**4TH WEEK**
IOP				
VISUAL ACUITY				
FUNDUS EXAMINATION				
SLIT LAMP EXAMINATION				
OTHERS				

Follow up: During 6th week

MASTER CHART

sl no:	Age	sex	ITCHING (0)	ITCHING(2)	Change From Baseline	change from BL (4-0)	ITCHING (3)	Itching(4)	redness(0)	redness(2)	change from baseline	redness(3)	redness(4)	Change from baseline	chemosis(0)	chemosis(2)	change 2nd week	chemosis(3)	chemosis(4)	Change from baseline	eye lid edema(0)eye lid edema(2)		change from baseline	eye lid edema(3)	eyelid edema(4)	change from baseline	watering(0)	watering(2)	change from baseline	watering(3)	watering(4)	Change from baseline	fb sensation(0)	FB Sensation(2)	Change from baseline	fb(3)	fb(4)	change from baseline	discomfort(0)	discomfort(2)	change from baseline	discomfort(3)	change at 3week	discomfort(4)	Change from baseline	photophobia(0)photophobia (2)		Change from baseline	photophobia(3)	photophobia(4)	Change from baseline	stinging(0)stinging(2)		Change from baseline	stinging(3)	stinging (4)	Change from baseline
1	4	M	3	1	2	3	0	0	2	0	2	0	0	2	1	0	1	0	0	1	1	0	1	0	0	1	1	0	1	0	0	1	0	0	2	2	1	1	1	1	0	2	0	0	2	0	0	2	2	0	2	0	0	2
2	6	F	3	1	2	3	0	0	3	1	2	0	0	3	1	0	1	0	0	1	1	0	1	0	0	1	2	1	1	1	0	2	2	0	2	0	0	2	1	0	1	0	1	0	0	1	0	0	1	2	0	2	0	0	2
3	26	M	3	1	2	3	0	0	3	2	1	1	0	3	2	1	1	0	0	2	1	1	0	0	0	1	2	0	2	0	0	2	3	1	2	0	0	3	1	1	0	0	1	0	1	1	0	0	0	0	0	1	3	1	2	0	0	3
4	8	F	2	1	1	2	0	0	2	0	2	0	0	2	1	0	1	0	0	1	0	0	0	0	0	0	1	0	1	0	0	1	3	2	1	1	0	3	2	1	1	0	2	0	2	0	0	2	0	0	2	2	0	2	0	0	2
5	7	M	3	1	2	3	0	0	3	0	3	0	0	3	1	0	1	0	0	1	2	1	1	1	1	1	0	1	0	0	1	2	1	1	0	0	2	3	2	1	1	2	0	3	0	0	3	0	0	3	3	0	3	0	0	3
6	33	M	3	1	2	3	0	0	3	2	1	2	1	2	2	1	1	0	0	2	1	1	0	0	0	1	2	1	1	0	0	2	2	0	2	0	0	2	1	0	1	0	1	0	1	1	0	0	0	0	1	2	0	2	0	0	2
7	29	M	3	1	2	3	0	0	3	2	1	1	0	3	1	1	0	0	0	1	0	0	0	0	0	0	2	0	2	0	0	2	2	1	1	0	0	2	1	0	1	0	1	0	1	1	0	0	0	0	1	2	0	2	0	0	2
8	22	F	3	1	2	3	0	0	2	1	1	0	0	2	1	0	1	0	0	1	0	0	0	0	0	0	1	0	1	0	0	1	2	0	2	0	0	2	2	1	1	0	2	0	2	0	0	2	0	0	2	3	1	2	1	0	3
9	6	F	2	0	2	2	0	0	2	1	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	1	0	2	2	1	1	0	0	2	1	0	1	0	1	0	1	0	0	1	0	0	1	3	0	3	0	0	3
10	6	F	2	1	1	2	0	0	2	1	1	0	0	2	1	0	1	0	0	1	2	1	1	1	0	2	2	1	1	1	0	2	3	1	2	1	0	3	3	2	1	1	2	0	3	0	0	3	0	0	3	3	0	3	0	0	3
11	7	M	2	0	2	2	0	0	2	1	1	0	0	2	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	2	1	1	0	0	2	3	2	1	1	2	0	3	0	0	3	0	0	3	2	0	2	0	0	2
12	9	M	2	0	2	2	0	0	3	0	3	0	0	3	1	0	1	0	0	1	0	0	0	0	0	0	1	0	1	0	0	1	3	0	3	0	0	3	2	1	1	0	2	0	2	0	0	2	0	0	2	2	0	2	0	0	2
13	11	F	2	0	2	2	0	0	2	0	2	0	0	2	2	0	2	0	0	2	0	0	0	0	0	0	1	0	1	0	0	1	2	0	2	0	0	2	1	0	1	0	1	0	1	0	0	1	0	0	1	3	0	3	0	0	3
14	22	M	3	2	1	3	1	0	2	1	1	1	1	1	1	0	1	0	0	1	1	0	1	0	0	1	1	0	1	0	0	1	2	1	1	0	0	2	1	0	1	0	1	0	1	1	0	0	0	0	1	2	0	2	0	0	2
15	11	M	3	1	2	3	0	0	3	2	1	1	0	3	1	1	0	0	0	1	1	1	0	0	0	1	1	0	1	0	0	1	3	0	3	0	0	3	1	0	1	0	1	0	1	1	0	0	0	0	1	2	0	2	0	0	2
16	32	F	3	1	2	3	0	0	3	2	1	1	1	2	2	1	1	1	0	2	1	0	1	0	0	1	1	0	1	0	0	1	2	0	2	0	0	2	0	0	0	0	0	0	0	1	0	-1	0	0	0	2	1	1	0	0	2
17	12	F	3	2	1	3	1	0	3	0	3	0	0	3	1	0	1	0	0	1	0	0	0	0	0	0	2	1	1	1	1	1	3	2	1	1	0	3	0	0	0	0	0	0	0	1	0	-1	0	0	0	2	0	2	1	1	1
18	13	M	2	1	1	2	0	0	2	1	1	0	0	2	1	0	1	0	0	1	0	0	0	0	0	0	1	0	1	0	0	1	2	0	2	0	0	2	2	1	1	1	1	0	2	0	0	2	0	0	2	2	0	2	0	0	2
19	5	M	2	0	2	2	0	0	2	0	2	0	0	2	1	0	1	0	0	1	1	0	1	0	0	1	1	1	1	0	0	0	2	1	1	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0	3	1	2	0	0	3
20	5	F	2	0	2	2	0	0	3	1	2	0	0	3	0	0	0	0	0	0	1	1	0	1	0	1	0	0	0	0	0	0	2	1	1	0	0	2	2	1	1	1	1	1	0	0	0	1	0	0	1	3	0	3	0	0	3
21	8	F	2	1	1	2	0	0	2	0	2	0	0	2	0	0	0	0	0	0	1	0	1	0	0	1	0	0	0	0	0	0	2	0	2	0	0	2	1	1	0	0	1	0	1	0	0	1	0	0	1	2	0	2	0	0	2
22	4	M	3	2	1	2	1	1	3	1	2	0	0	3	1	0	1	1	0	1	0	0	0	0	0	0	1	0	1	0	0	1	3	0	3	0	0	3	3	2	1	1	2	1	2	1	0	1	0	0	2	2	0	2	0	0	2
23	6	F	3	2	1	2	1	1	3	1	2	0	0	3	2	1	1	1	0	2	1	1	0	1	0	1	2	0	2	0	0	2	2	1	1	0	0	2	1	0	1	0	1	0	1	1	1	0	0	0	1	3	0	3	0	0	3
24	55	M	3	1	2	3	0	0	3	2	1	1	0	3	1	1	0	0	0	1	0	0	0	0	0	0	1	0	1	0	0	1	2	0	2	0	0	2	1	0	1	0	1	0	1	1	0	0	0	0	1	1	1	0	0	0	1
25	17	M	2	0	2	2	0	0	2	0	2	0	0	2	1	0	1	0	0	1	0	0	0	0	0	0	1	1	0	1	0	1	2	0	2	0	0	2	2	0	2	0	2	0	2	0	0	2	0	0	2	2	0	2	0	0	2
26	24	F	2	1	1	2	0	0	2	1	1	1	0	2	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	1	3	1	2	0	0	3	3	2	1	1	2	0	3	0	0	3	0	0	3	2	0	2	1	0	2
27	6	M	3	1	2	3	0	0	2	1	1	0	0	2	1	0	1	0	0	1	1	0	1	0	0	1	0	0	0	0	0	0	3	0	3	0	0	3	2	2	0	1	1	0	2	1	0	1	0	0	2	2	1	1	0	0	2
28	7	M	3	0	3	3	0	0	3	1	2	1	0	3	2	0	2	0	0	2	1	1	0	0	0	1	2	1	1	0	0	2	2	1	1	0	0	2	1	0	1	0	1	0	1	1	0	0	0	0	1	2	1	1	0	0	2
29	22	F	2	1	1	2	0	0	2	0	2	0	0	2	1	0	1	0	0	1	0	0	0	0	0	0	1	0	1	0	0	1	2	0	2	0	0	2	2	1	1	1	1	1	1	0	0	1	0	0	1	2	0	2	0	0	2
30	15	F	2	1	1	2	0	0	2	0	2	0	0	2	1	0	1	0	0	1	0	0	0	0	0	0	1	0	1	0	0	1	3	1	2	0	0	3	1	0	1	0	1	0	1	0	0	1	0	0	1	2	0	2	1	0	2
31	14	F	3	1	2	3	0	0	2	1	1	1	0	2	1	0	1	0	0	1	1	1	0	0	0	1	1	0	1	0	0	1	3	0	3	0	0	3	1	0	1	0	1	0	1	1	0	0	0	0	1	3	0	3	0	0	3
32	44	M	3	1	2	3	1	1	2	1	1	0	0		1	0	1	0	0	1	1	0	1	0	0	1	1	0	1	0	0	1	2	0	2	0	0	2	2	1	1	0	2	0	2	1	0	1	0	0	2	3	0	3	0	0	3

sl no:	Age	sex	ITCHING (0)	ITCHING(2)	Change From Baseline	change from BL(4-0)	ITCHING (3)	Itching(4)	redness(0)	redness(2)	change from baseline	redness(3)	redness(4)	Change from baseline	chemosis(0)	chemosis(2)	change 2nd week	chemosis(3)	chemosis(4)	Change from baseline	eye lid edema(0)eye lid edema(2)		change from baseline	eye lid edema(3)	eyelid edema(4)	change from baseline	watering(0)	watering(2)	change from baseline	watering(3)	watering(4)	Change from baseline	fb sensation(0)	FB Sensation(2)	Change from baseline	fb(3)	fb(4)	change from baseline	discomfort(0)	discomfort(2)	change from baseline	discomfort(3)	change at 3week	discomfort(4)	Change from baseline	photophobia(0)photophobia (2)		Change from baseline	photophobia(3)	photophobia(4)	Change from baseline	stinging(0)stinging(2)		Change from baseline	stinging(3)	stinging (4)	Change from baseline
33	23	F	3	1	2	3	0	0	3	2	1	1	0	3	2	1	1	1	0	2	1	0	1	0	0	1	2	1	1	0	0	2	2	1	1	0	0	2	1	0	1	0	1	0	1	1	0	0	0	0	1	2	1	1	0	0	2
34	12	M	3	0	3	3	0	0	3	0	3	0	0	3	0	0	0	0	0	0	2	0	2	0	0	2	1	0	1	0	0	1	2	0	2	0	0	2	3	1	2	1	2	0	3	0	0	3	0	0	3	2	0	2	0	0	2
35	13	M	3	0	3	3	0	0	2	0	2	0	0	2	0	0	0	0	0	0	1	1	0	0	0	1	2	1	1	0	0	2	2	0	2	0	0	2	2	1	1	0	2	0	2	0	0	2	0	0	2	2	0	2	0	0	2
36	5	F	2	0	2	2	0	0	3	0	3	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	1	2	0	2	0	0	2	1	0	1	0	1	0	1	0	0	1	0	0	1	3	0	3	0	0	3
37	4	F	2	1	1	2	0	0	3	1	2	1	0	3	1	0	1	0	0	1	1	0	1	0	0	1	1	1	0	0	0	1	2	0	2	0	0	2	3	2	1	1	2	0	3	0	0	3	0	0	3	2	0	2	0	0	2
38	4	M	2	0	2	2	0	0	2	0	2	0	0	2	0	0	0	0	0	0	1	0	1	0	0	1	1	0	1	0	0	1	2	0	2	0	0	2	1	0	1	0	1	0	1	0	0	1	0	0	1	2	0	2	0	0	2
39	7	M	2	0	2	2	0	0	2	1	1	1	0	2	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	1	2	0	2	0	0	2	3	1	2	1	2	1	2	0	0	2	0	0	2	2	0	2	0	0	2
40	33	F	3	1	2	3	0	0	3	2	1	1	1	2	1	1	0	0	0	1	0	0	0	0	0	0	1	0	1	0	0	1	3	1	2	0	0	3	2	1	1	1	1	0	2	1	0	1	0	0	2	2	0	2	0	0	2
41	23	M	3	2	1	3	1	1	3	2	1	1	1	2	1	1	0	0	0	1	1	0	1	0	0	1	2	1	1	0	0	2	3	0	3	0	0	3	2	0	2	0	2	0	2	1	0	1	0	0	2	3	0	3	0	0	3
42	13	M	2	1	1	3	1	0	2	0	2	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	0	2	3	1	2	0	0	3	1	0	1	0	1	0	1	0	0	1	0	0	1	3	0	3	0	0	3
43	12	M	2	1	1	2	0	0	2	1	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	0	2	2	0	2	0	0	2	3	1	2	1	2	0	3	0	0	3	0	0	3	3	0	3	0	0	3
44	24	M	3	1	2	3	0	0	3	1	2	0	0	3	1	0	1	0	0	1	1	0	1	0	0	1	1	0	1	0	0	1	3	1	2	0	0	3	1	0	1	0	1	0	1	1	0	0	0	0	1	3	0	3	0	0	3
45	22	F	3	1	2	3	0	0	2	0	2	0	0	2	1	0	1	0	0	1	2	1	1	0	0	2	2	1	1	0	0	2	2	1	1	0	0	2	1	0	1	0	1	0	1	1	0	0	0	0	1	2	0	2	0	0	2
46	32	F	3	2	1	3	1	0	2	1	1	0	0	2	1	1	0	0	0	1	0	0	0	0	0	0	1	0	1	0	0	1	2	0	2	0	0	2	2	1	1	0	2	0	2	1	0	1	0	0	2	2	0	2	0	0	2
47	31	M	3	1	2	3	0	0	3	2	1	1	1	2	1	1	0	0	0	1	0	0	0	0	0	0	2	1	1	0	0	2	2	1	1	0	0	2	3	2	1	0	3	0	3	1	0	2	0	0	3	2	1	1	0	0	2
48	4	F	2	1	1	2	0	0	3	1	2	1	1	2	0	0	0	0	0	0	2	1	1	1	0	2	1	0	1	0	0	1	2	0	2	0	0	2	3	2	1	1	2	0	3	0	0	3	0	0	3	2	0	2	0	0	2
49	9	M	3	0	3	3	0	0	3	1	2	1	0	3	0	0	0	0	0	0	0	0	0	0	0	0	3	1	2	1	0	3	2	1	1	0	0	2	3	1	2	0	3	0	3	0	0	3	0	0	3	2	0	2	0	0	2
50	6	M	2	0	2	2	0	0	2	1	1	0	0	2	0	0	0	0	0	0	1	1	0	0	0	1	1	0	1	0	0	1	2	0	2	0	0	2	1	0	1	0	1	0	1	0	0	1	0	0	1	2	0	2	0	0	2
51	19	M	3	1	2	3	1	0	2	1	1	0	0	2	1	0	1	0	0	1	1	0	1	0	0	1	1	0	1	0	0	1	2	1	1	0	0	2	2	0	2	0	2	0	2	1	0	1	0	0	2	2	0	2	0	0	2
52	22	M	3	1	2	3	0	0	3	1	2	1	0	3	2	0	2	0	0	2	0	0	0	0	0	0	2	0	2	0	0	2	2	0	2	0	0	2	1	0	1	0	1	0	1	1	1	0	0	0	1	2	0	2	0	0	2
53	36	F	3	2	1	2	1	1	3	1	2	0	0	3	2	0	2	0	0	2	1	0	1	0	0	1	2	0	2	0	0	2	2	1	1	0	0	2	1	0	1	0	1	0	1	1	0	0	0	0	1	2	0	2	0	0	2
54	39	M	3	1	2	3	0	0	3	2	1	1	1	2	2	1	1	1	0	2	1	0	1	0	0	1	2	0	2	0	0	2	2	0	2	0	0	2	2	0	2	0	2	0	2	1	0	1	0	0	2	2	0	2	0	0	2
55	27	M	3	2	1	3	0	0	3	2	1	1	0	3	1	1	0	1	0	1	1	1	0	1	0	1	1	0	1	0	0	1	2	1	1	0	0	2	1	0	1	0	1	0	1	1	0	0	0	0	1	2	0	2	0	0	2
56	4	M	3	1	2	3	0	0	2	0	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	1	2	0	2	0	0	2	3	1	2	1	2	0	3	0	0	3	0	0	3	2	0	2	0	0	2
57	4	M	2	1	1	1	1	1	3	2	1	0	0	3	0	0	0	0	0	0	1	0	1	0	0	1	1	0	1	0	0	1	2	1	1	0	0	2	1	0	1	0	1	0	1	0	0	1	0	0	1	3	0	3	0	0	3
58	7	M	2	1	1	2	0	0	2	1	1	1	0	2	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	1	2	0	2	0	0	2	1	0	1	0	1	0	1	0	0	1	0	0	1	2	0	2	0	0	2
59	10	M	3	1	2	3	0	0	3	0	3	0	0	3	1	0	1	0	0	1	2	1	1	0	0	2	1	0	1	0	0	1	3	0	3	0	0	3	2	1	1	0	2	0	2	1	0	1	0	0	2	2	0	2	0	0	2

MASTER CHART - II

SL NO:	Age	Sex	itching(0)	itching(2)	change from baseline	itching(3)itching(4)	change at 3wk	itching (4)	change from baseline	redness(0)	redness(2)	change from baseline	redness(3)	change at3rd week	redness(4)	change from baseline	chemosis(0)	chemosis(2)	change from baseline	chemosis(3)	change at 3wk	chemosis(4)	change from baseline	eyelid swelling(0)	eye lid swelling(2)	change from baseline	eye lid swelling(3)	change at 3wk	eyelid swelling(4)	change from baseline	watering(0)	watering(2)	change from baseline	watering(3)	change at 3wk	watering(4)	change from baseline	discomfort(0) discomfort(2)	discomfort(2)	change from baseline	discomfort(3)	change at 3wk	discomfort(4)	change from baseline	fb (0)	fb(2)	change from baseline	fb(3)	change at3wk	fb(4)	change from baseline	photophobia(0)	photophobia(2)	change from baseline	photophobia(3)	change at 3wk	photophobia(4)	change from baseline	stinging(0)	stinging(2)	change from baseline	stinging (3)change at 3wk Stinging(4) change from baseline
1	4	F	2	0	2	0	2	0	2	3	2	1	1	2	0	3	1	0	1	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	1	1	0	2	0	2	2	1	1	1	1	0	2	1	0	1	0	1	0	1	2	1	1	11 1 1
2	5	M	3	2	1	1	2	0	3	2	2	0	1	1	1	1	1	1	0	1	0	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	0	0	0	0	0	0	0	2	0	2	02 0 2
3	6	F	2	1	1	1	1	0	2	3	1	2	1	2	0	3	1	0	1	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	0	2	0	2	0	2	2	2	0	1	1	1	1	1	0	1	0	1	0	1	3	1	2	03 0 3
4	5	M	3	2	1	1	2	0	3	2	1	1	0	2	0	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	1	1	0	2	1	1	1	0	1	0	1	0	1	0	0	0	0	0	0	0	3	0	3	03 0 3
5	11	M	2	2	0	1	1	0	2	2	2	0	1	1	0	2	1	1	0	0	1	0	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	0	2	0	2	0	2	2	1	1	0	2	0	2	0	0	0	0	0	0	0	3	0	3	03 0 3
6	13	M	3	1	2	1	2	0	3	3	1	2	1	2	0	3	1	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	0	2	0	2	0	2	2	1	1	0	2	0	2	1	1	0	0	1	0	1	3	0	3	03 0 3
7	6	F	3	2	1	1	2	0	3	3	1	2	1	2	0	3	1	1	0	0	1	0	1	1	0	1	0	1	0	1	2	0	2	0	2	0	2	1	0	1	0	1	0	1	1	0	1	0	1	0	1	0	0	0	0	0	0	0	2	0	2	02 0 2
8	4	F	3	1	2	0	3	0	3	2	2	0	1	1	1	1	1	1	0	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	0	0	0	0	0	0	0	2	0	2	02 0 2
9	33	M	3	1	2	1	2	1	2	2	1	1	0	2	0	2	1	0	1	0	1	0	1	1	1	0	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	1	1	0	2	0	2	1	0	1	0	1	0	1	2	0	2	02 0 2
10	23	F	3	1	2	0	3	0	3	2	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	2	0	2	1	0	1	0	1	0	1	1	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	1	01 0 1
11	11	M	2	1	1	0	2	0	2	3	2	1	2	1	1	2	2	1	1	0	2	0	2	1	1	0	1	0	0	1	2	1	1	0	2	0	2	1	0	1	0	1	0	1	2	1	1	0	2	0	2	1	1	0	0	1	0	1	1	0	1	01 0 1
12	21	F	2	0	2	0	2	0	2	3	1	2	0	3	0	3	1	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	0	2	0	2	0	2	2	0	2	0	2	0	2	0	0	0	0	0	0	0	1	0	1	01 0 1
13	14	M	2	1	1	1	1	0	2	3	1	2	0	3	0	3	2	1	1	1	1	0	2	2	1	1	0	2	0	2	1	0	1	0	1	0	1	2	1	1	1	1	0	2	2	1	1	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
14	4	M	2	1	1	1	1	0	2	2	2	0	1	1	0	2	1	1	0	0	1	0	1	1	1	0	0	1	0	1	2	1	1	1	1	0	2	1	1	0	0	1	0	1	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	1	1	02 0 2
15	5	M	3	1	2	0	3	0	3	2	1	1	1	1	0	2	2	1	1	0	2	0	2	1	0	1	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	3	1	2	0	3	0	3	1	0	1	0	1	0	1	1	0	1	01 0 1
16	6	M	2	2	0	1	1	0	2	2	1	1	1	1	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	2	0	2	2	1	1	1	1	1	1	2	1	1	0	2	0	2	0	0	0	0	0	0	0	3	2	1	12 0 3
17	9	M	2	1	1	1	1	0	2	3	2	1	2	1	1	2	2	1	1	1	1	1	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	1	1	0	2	0	2	0	0	0	0	0	0	0	3	1	2	03 0 3
18	12	M	2	1	1	0	2	0	2	3	2	1	1	2	1	2	2	1	1	1	1	1	1	2	1	1	0	2	0	2	2	1	1	0	2	0	2	2	1	1	0	2	0	2	2	1	1	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
19	11	M	2	1	1	1	1	1	1	1	1	0	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	1	1	1	1	1	1	2	1	1	0	2	0	2	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
20	43	F	2	0	2	0	2	0	2	2	1	1	0	2	0	2	0	0	0	0	0	0	0	1	0	1	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	3	0	3	0	3	0	3	1	1	0	1	0	0	1	2	0	2	02 0 2
21	12	F	2	0	2	1	1	0	2	2	1	1	0	2	0	2	0	0	0	0	0	0	0	1	1	0	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	0	2	0	2	0	2	1	0	1	0	1	0	1	2	0	2	02 0 2
22	4	F	3	2	1	0	3	0	3	3	1	2	0	3	0	3	1	1	0	1	0	0	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	1	1	0	2	0	2	3	0	3	0	3	0	3	0	0	0	0	0	0	0	1	0	1	01 0 1
23	7	M	3	2	1	2	1	2	1	3	1	2	0	3	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	1	1	0	2	0	2	2	1	1	0	2	0	2	0	0	0	0	0	0	0	2	1	1	11 0 2
24	8	F	3	1	2	0	3	0	3	3	2	1	1	2	1	2	1	0	1	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	1	1	0	0	1	0	1	2	1	1	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
25	7	M	2	2	0	1	1	0	2	2	1	1	1	1	1	1	0	0	0	0	0	0	0	1	1	0	0	1	0	1	1	0	1	0	1	0	1	3	2	1	2	1	0	3	2	1	1	0	2	0	2	0	0	0	0	0	0	0	3	1	2	12 1 2
26	9	F	2	2	0	0	2	0	2	2	1	1	1	1	1	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	1	1	0	2	0	2	1	1	0	0	1	0	1	3	0	3	0	3	0	3	1	0	1	0	1	0	1	3	1	2	03 0 3
27	11	M	2	1	1	0	2	0	2	2	1	1	1	1	0	2	0	0	0	0	0	0	0	1	0	1	0	1	0	1	1	1	0	0	1	0	1	1	1	0	1	0	0	1	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2

SL NO:	Age	Sex	itching(0)	itching(2)	change from baseline	itching(3)itching(4)	change at 3wk	itching (4)	change from baseline	redness(0)	redness(2)	change from baseline	redness(3)	change at3rd week	redness(4)	change from baseline	chemosis(0)	chemosis(2)	change from baseline	chemosis(3)	change at 3wk	chemosis(4)	change from baseline	eyelid swelling(0)	eye lid swelling(2)	change from baseline	eye lid swelling(3)	change at 3wk	eyelid swelling(4)	change from baseline	watering(0)	watering(2)	change from baseline	watering(3)	change at 3wk	watering(4)	change from baseline	discomfort(0) discomfort(2)	discomfort(2)	change from baseline	discomfort(3)	change at 3wk	discomfort(4)	change from baseline	fb (0)	fb(2)	change from baseline	fb(3)	change at3wk	fb(4)	change from baseline	photophobia(0)	photophobia(2)	change from baseline	photophobia(3)	change at 3wk	photophobia(4)	change from baseline	stinging(0)	stinging(2)	change from baseline	stinging (3)change at 3wk Stinging(4) change from baseline
28	32	M	3	1	2	0	3	0	3	2	1	1	1	1	1	1	0	0	0	0	0	0	0	1	1	0	0	1	0	1	1	0	1	0	1	0	1	1	1	0	1	0	0	1	3	0	3	0	3	0	3	1	0	1	0	1	0	1	2	0	2	02 0 2
29	33	M	3	2	1	1	2	1	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	0	2	0	2	0	2	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
30	42	M	3	2	1	1	2	1	2	3	1	2	1	2	0	3	1	1	0	1	0	0	1	2	1	1	1	1	1	1	2	1	1	0	2	0	2	2	0	2	0	2	0	2	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
31	23	F	3	2	1	1	2	1	2	3	2	1	1	2	1	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0	2	1	1	1	1	1	1	1	0	1	0	1	0	1	2	1	1	0	2	0	2	0	0	0	0	0	0	0	3	1	2	03 0 3
32	35	F	2	2	0	1	1	0	2	3	1	2	1	2	1	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	1	1	0	2	0	2	1	0	1	0	1	0	1	3	1	2	03 0 3
33	36	M	3	1	2	1	2	0	3	2	0	2	0	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	2	0	2	2	2	0	1	1	0	2	3	1	2	1	2	0	3	1	0	1	0	1	0	1	2	0	2	02 0 2
34	11	M	2	2	0	1	1	0	2	3	2	1	1	2	0	3	1	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	1	0	1	0	1	0	1	3	0	3	0	3	0	3	1	0	1	0	1	0	1	2	0	2	02 0 2
35	4	F	3	2	1	1	2	0	3	2	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
36	8	F	3	1	2	1	2	1	2	2	1	1	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	2	0	2	2	1	1	0	2	0	2	2	1	1	0	2	0	2	1	0	1	0	1	0	1	1	0	1	01 0 1
37	5	M	3	2	1	1	2	1	2	3	2	1	1	2	1	2	1	1	0	1	0	0	1	0	0	0	0	0	0	0	2	1	1	0	2	0	2	1	1	0	0	1	0	1	2	1	1	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
38	43	F	2	0	2	0	2	0	2	3	1	2	0	3	0	3	1	0	1	0	1	0	1	1	1	0	1	0	0	1	2	1	1	0	2	0	2	2	0	2	0	2	0	2	3	0	3	0	3	0	3	0	0	0	0	0	0	0	3	0	3	03 0 3
39	21	M	2	0	2	0	2	0	2	2	1	1	1	1	1	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	1	1	1	1	0	2	3	0	3	0	3	0	3	0	0	0	0	0	0	0	3	0	3	03 0 3
40	32	M	3	1	2	0	3	0	3	2	1	1	0	2	0	2	0	0	0	0	0	0	0	1	1	0	0	1	0	1	2	0	2	0	2	0	2	2	1	1	0	2	0	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0	3	1	2	12 0 3
41	6	F	2	1	1	0	2	0	2	2	2	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	0	2	0	2	0	2	0	0	0	0	0	0	0	3	0	3	03 0 3
42	5	F	3	2	1	1	2	1	2	2	2	0	0	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	2	0	2	1	0	1	0	1	0	1	2	0	2	0	2	0	2	1	0	1	0	1	0	1	3	1	2	12 1 2
43	22	M	3	2	1	1	2	1	2	3	2	1	0	3	0	3	1	1	0	1	0	0	1	2	1	1	1	1	1	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
44	23	M	2	0	2	0	2	0	2	3	1	2	1	2	1	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0	2	0	2	0	2	0	2	2	2	0	1	1	1	1	3	0	3	0	3	0	3	1	1	0	0	1	0	1	2	0	2	02 0 2
45	34	M	2	0	2	0	2	0	2	2	1	1	0	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	2	0	2	2	1	1	1	1	0	2	2	0	2	0	2	0	2	1	0	1	0	1	0	1	3	0	3	12 0 3
46	32	M	2	0	2	0	2	0	2	3	2	1	1	2	1	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	1	1	1	1	0	2	3	0	3	0	3	0	3	0	0	0	0	0	0	0	2	0	2	02 0 2
47	6	M	2	0	2	0	2	0	2	2	1	1	0	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	1	1	1	1	0	2	2	0	2	1	1	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
48	7	F	3	1	2	1	2	0	3	3	1	2	1	2	1	2	1	1	0	0	1	0	1	1	0	1	0	1	0	1	2	0	2	0	2	0	2	2	1	1	0	2	0	2	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
49	6	F	2	0	2	0	2	0	2	2	1	1	1	1	1	1	0	0	0	0	0	0	0	1	1	0	0	1	0	1	2	1	1	0	2	0	2	2	1	1	0	2	0	2	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
50	7	M	1	0	1	1	0	1	0	3	1	2	1	2	1	2	1	1	0	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	1	1	1	1	0	2	2	0	2	0	2	0	2	0	0	0	0	0	0	0	1	0	1	01 0 1
51	8	M	3	1	2	0	3	0	3	2	1	1	1	1	1	1	1	1	0	0	1	0	1	1	1	0	1	0	1	0	2	1	1	0	2	0	2	2	1	1	0	2	0	2	2	0	2	0	2	0	2	1	1	0	0	1	0	1	2	0	2	02 0 2
52	4	M	3	2	1	1	2	1	2	2	0	2	0	2	0	2	1	0	1	0	1	0	1	1	0	1	0	1	0	1	0	0	0	0	0	0	0	2	1	1	1	1	1	1	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
53	6	M	2	1	1	1	1	0	2	2	1	1	0	2	0	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	1	1	1	1	1	1	1	0	1	0	1	0	1	0	0	0	0	0	0	0	2	0	2	02 0 2
54	23	M	3	2	1	1	2	1	2	2	1	1	0	2	0	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	1	1	1	1	0	2	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
55	27	F	2	0	2	0	2	0	2	2	1	1	0	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	1	2	2	0	0	2	0	2	2	1	1	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
56	8	M	2	0	2	1	1	1	1	3	2	1	2	1	2	1	1	1	0	0	1	0	1	1	1	0	1	0	1	0	1	0	1	0	1	0	1	2	1	1	1	1	0	2	2	0	2	0	2	0	2	0	0	0	0	0	0	0	2	0	2	02 0 2
57	23	M	3	0	3	0	3	0	3	2	1	1	1	1	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	1	1	0	1	0	1	0	1	2	0	2	0	2	0	2	0	0	0	0	0	0	0	1	0	1	10 0 1
58	34	F	2	0	2	0	2	0	2	3	1	2	0	3	0	3	1	0	1	0	1	0	1	1	1	0	0	1	0	1	1	0	1	0	1	0	1	1	0	1	0	1	0	1	3	0	3	0	3	0	3	1	0	1	0	1	0	1	1	0	1	01 0 1